ISTITUTO NAZIONALE TUMORI "REGINA ELENA" • Roma
"REGINA ELENA" NATIONAL CANCER INSTITUTE • Rome

RELAZIONE SCIENTIFICA 2002

Scientific report

Codice Anagrafe Ricerca: L123003Z

IRE
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Presentazione

Francesco Cognetti
Direttore Scientifico

L'attività di ricerca Scientifica del 2002 è stata condotta in accordo con il programma di sviluppo della Direzione Scientifica approvato dal Comitato Tecnico Scientifico nel Settembre 2001.

Durante l'anno 2002 si è inoltre completato il programma di riassetto delle attività e dei servizi della Direzione Scientifica con relativo adeguamento delle risorse umane rese disponibili per l'attuazione del programma stesso.

Ciò ha consentito soprattutto di porre le basi per un più deciso impulso e regolare svolgimento soprattutto dalla ricerca clinica. Infatti l'istituzione del Centro di Biostatistica dell'Istituto ha consentito di censire le sperimentazioni cliniche in atto ed anche il numero dei pazienti reclutati nel corso dell'anno. Inoltre l'istituzione di un servizio per le attività didattiche e formative ha consentito di avviare un regolare programma interno di aggiornamento e di confronto sull'attività di ricerca dell'Istituto che ha anche ottenuto la concessione di un consistente numero di crediti ECM.

L'attività di ricerca clinica e sperimentale prodotta nel 2002 dai ricercatori dell'Istituto è stata maggiormente finalizzata ad una più stretta collaborazione fra i due settori della ricerca che ha trovato la sua applicazione nella ricerca traslazionale. Infatti mentre sono proseguite le ricerche sui filoni tradizionali dell'Istituto (post-genomica, chemioterapia sperimentale e nuovi approcci terapeutici preclinici, cancerogenesi virale, trattamenti integrati delle principali neoplasie etc.) è stata anche costituita ed avviata l'attività di ricerca nel settore della diagnostica molecolare ed in campo clinico particolare attenzione è stata dedicata alle problematiche relative alla qualità di vita del paziente con particolare riguardo ai pazienti a lunga sopravvivenza. Le pubblicazioni scientifiche prodotte in Istituto sono qualitativamente migliorate con un sensibile incremento dell'impact factor.

Nel corso dell'anno 2002 inoltre è stata fondata sotto l'egida del Ministero della Salute "Alleanza contro il Cancro", Associazione che riunisce i sette Istituti Nazionali Tumori Italiani. La missione principale di questa Associazione è la stretta collaborazione tra gli Istituti ed i loro ricercatori al fine di migliorare la qualità della ricerca oncologica del nostro Paese ed anche dei risultati ottenuti nei nostri pazienti nonché limitare al minimo la loro migrazione verso altri paesi o all'interno del nostro.

Sono stati identificati 16 progetti di ricerca comuni, quattro dei quali sono coordinati dall'Istituto Regina Elena. Questi progetti si riferiscono alle due aree di ricerca

sopra citate (classificazione molecolare dei tumori solidi e qualità di vita), ai tumori della tiroide ed, in collaborazione con il CRO d'Aviano, ad una biblioteca oncologica virtuale riservata a pazienti, familiari ed utenti "laici" (progetto Azalea).

Per quel che riguarda le collaborazioni in ambito internazionale è stato presentato dai ricercatori dell'Istituto, nell'ambito del VI programma Quadro Europeo un progetto integrato dal titolo: "Manipulating tumor suppression: a key to improve cancer treatment" di cui l'Istituto ha assunto il coordinamento.

Desidero ringraziare tutti i dirigenti della ricerca clinica e sperimentale, i Direttori dei Dipartimenti ed il personale tutto per l'ottimo lavoro svolto nel corso dell'anno 2002. Ringrazio inoltre le Dott.sse Ada Sacchi e Diana Giannarelli nonché tutto lo staff della Direzione Scientifica per il prezioso contributo al lavoro redazionale.

L'attività di ricerca illustrata in questo volume è stata possibile anche grazie ai contributi del Ministero della Salute, dell'Associazione Italiana per la ricerca sul Cancro (AIRC) e del Consiglio Nazionale delle Ricerche nonché di altri Enti o Aziende Private.

Francesco Cognetti
Direttore Scientifico

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Departments S.C. • S.S.D.

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- S.C. Laboratorio "B" Immunologia *(Pier Giorgio Natali)*
- S.C. Laboratorio "C" Oncogenesi Molecolare *(Ada Sacchi)*
- S.C. Laboratorio "D" Virologia *(Maria Luisa Marcante)*

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- S.C. Laboratorio "B" aggregato al Dipartimento di Oncologia Medica *(Gabriella Zupi)*
- S.C. Laboratorio "C" aggregato al Dipartimento di Prevenzione e Diagnostica *(Maria Luisa Marcante)*
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- Rapporti Internazionali
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Segretario:	Anna Maria D'Ambrosio

Publications

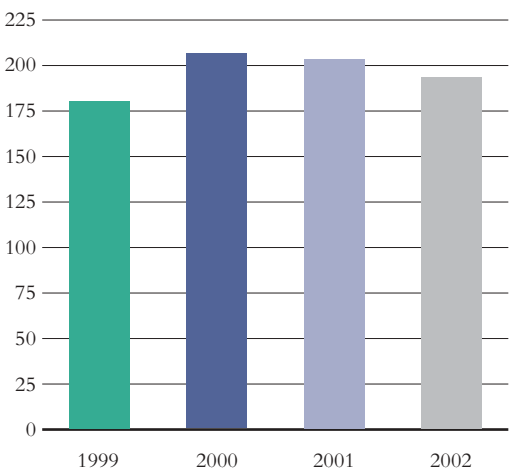
Departments	1999	2000	2001	2002
Central Facilities	15	17	25	21
Surgical Oncology	31	28	34	23
Medical Oncology	33	30	29	33
Prevention and Diagnosis	39	39	32	41
Neuroscience & Head - Neck Pathologies	5	8	4	5
Critical Area	5	7	15	2
Experimental Oncology	41	47	35	43
Therapeutic Programs Development	12	31	30	26
Total	**181**	**207**	**204**	**194**

Impact Factor ⋆

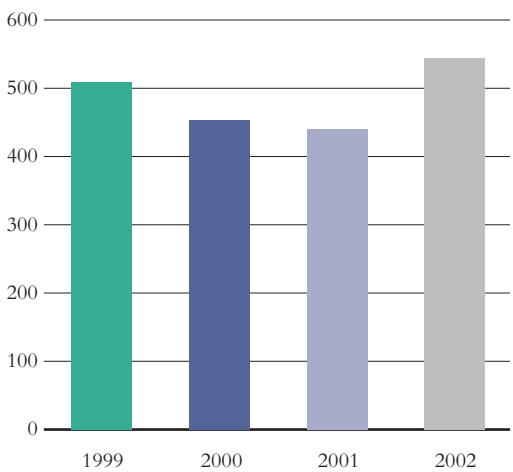
Departments	1999	2000	2001	2002
Central Facilities	68,77	36,14	62,62	49,30
Surgical Oncology	34,09	22,87	21,13	26,80
Medical Oncology	101,38	45,62	46,11	106,10
Prevention and Diagnosis	83,04	60,53	65,20	71,30
Neuroscience & Head - Neck Pathologies	11,77	9,49	2,83	13,00
Critical Area	4,20	6,95	0,00	2,50
Experimental Oncology	158,94	170,02	141,23	188,42
Therapeutic Programs Development	47,36	100,51	101,84	85,58
Total	**509,5**	**452,1**	**441,0**	**543,0**

⋆Normalized according to the Italian Ministry of Health's indications

Publications over the last 4 year



Impact Factor⋆ over the last 4 year



⋆Normalized according to the Italian Ministry of Health's indications

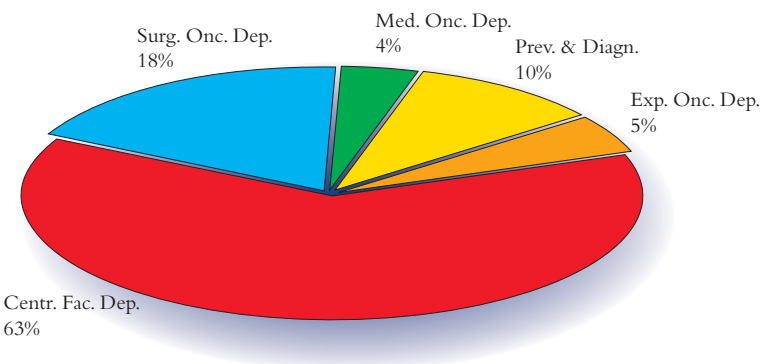
Credits (2002)

Departments	IRE	External	Total
Central Facilities	159	11	170
Surgical Oncology	44	19	63
Medical Oncology	10	33	43
Prevention and Diagnosis	26	0	26
Neuroscience & Head - Neck Pathologies	0	0	0
Critical Area	0	0	0
Experimental Oncology	12	0	12
Therapeutic Programs Development	0	0	0
Total	**251**	**63**	**314**

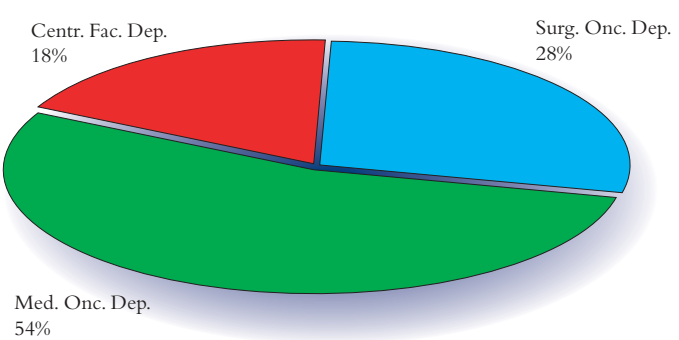
Credits (2002) - Extra Departmental

	Credits	Participants
Chief Medical Office	43	477
Scientific Direction of which:	32	201
Oncological Meetings at IRE	20	171
Experimental Oncology Seminars at CRS	12	30

IRE

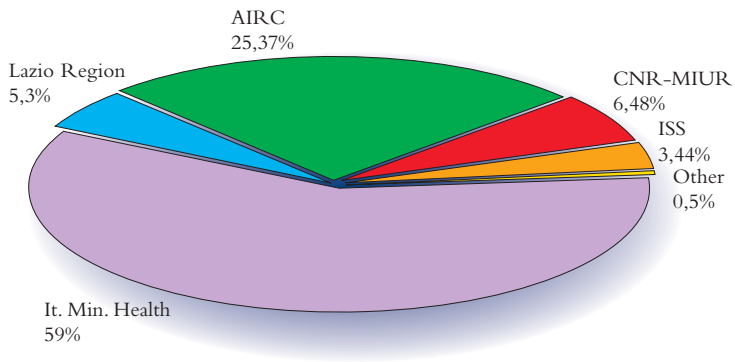


External



Institutional Grants

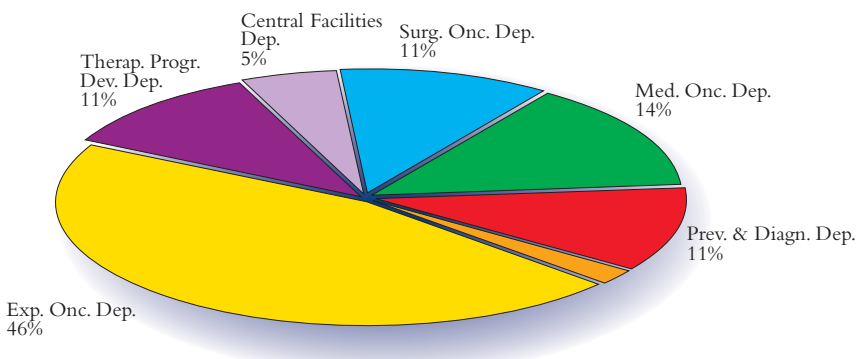
Institution	Project No.	Financial support
Italian Ministry of Health	18	€ 1.646.000,00
Lazio Region	1	€ 147.000,00
AIRC	16	€ 708.000,00
CNR-MIUR	7	€ 180.758,92
ISS	1	€ 96.000,00
Other	1	€ 12.911,42
Total year 2002	**44**	**€ 2.790.670,34**



Founded Projects

Departments	P.I.*	External Units P.I.*	Internal Units P.I.*	Total
Central Facilities	2	0	0	2
Surgical Oncology	5	2	0	5
Medical Oncology	4	4	2	6
Prevention and Diagnosis	1	3	4	5
Neuroscience & Head - Neck Pathologies	0	0	1	1
Critical Area	0	2	0	0
Experimental Oncology	16	5	4	20
Therapeutic Programs Development	4	0	1	5
Total year 2002	**32**	**16**	**12**	**44**

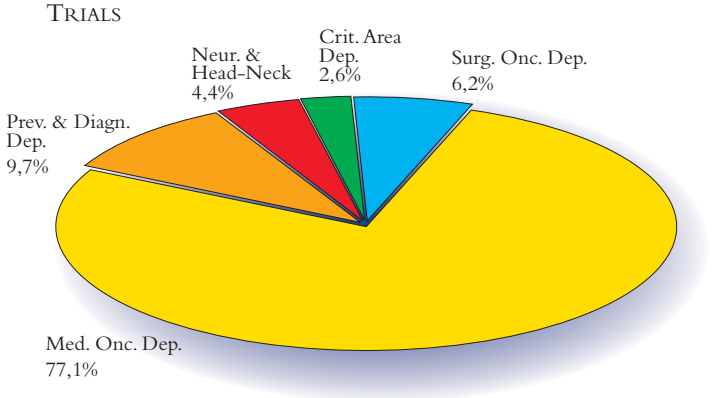
*Principal investigator



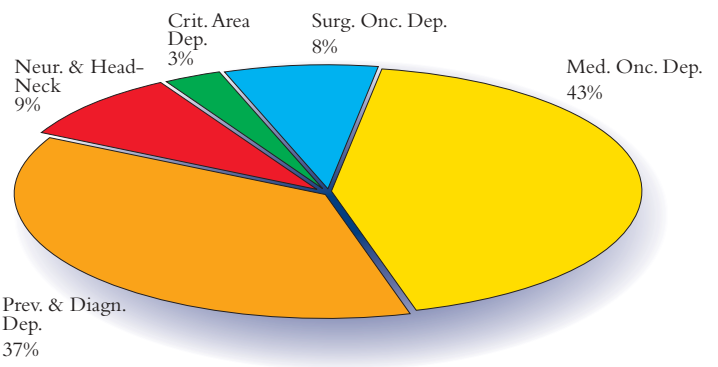
Active Clinical trials (2002)

Department	Trial No.	Patient No.
Surgical Oncology	7	79
Medical Oncology	87	413
Prevention and Diagnosis	11	360
Neuroscience & Head - Neck Pathologies	5	92
Critical Area	3	30
Total year 2002	**113**	**974**

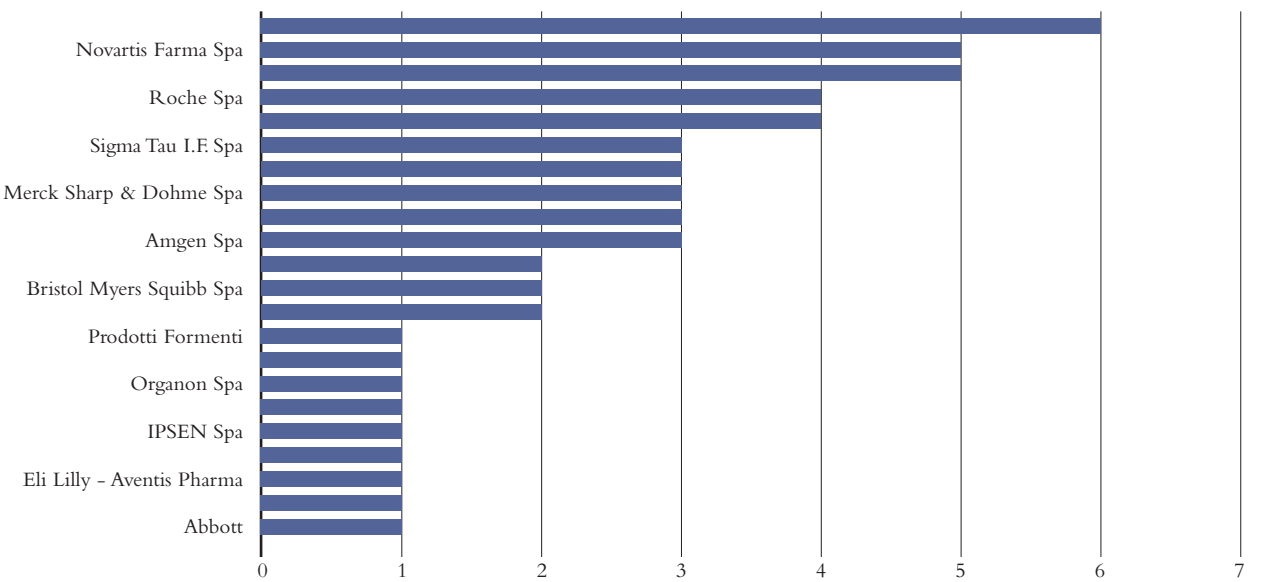
Trials



Patients



Number of supported clinical trials (2002)



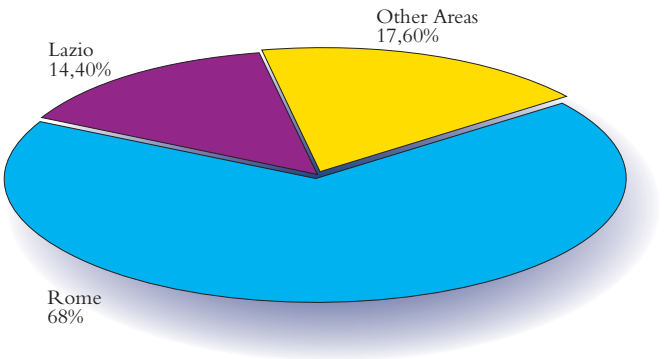
In patients

	1995	1996	1997	1998	1999	2000	2001	2002
Inpatient admissions	7220	7755	8627	8374	8083	6673	6721	8080
Inpatient Days	79022	75933	76092	73510	67728	55064	54832	65706
Alos	11	10	8,82	8,78	8,38	8,25	8,16	8,13
Surgical index %	52	55	52	53	51	50	51	51
Day Surgery Admissions						752	828	1079
Day Hospital Cycles						1674	2003	2084
Day Hospital Treatments						16634	16626	17865
Average n. of Treatments/Cycle						994	830	857
Total Admissions	**7220**	**7755**	**8627**	**8374**	**8083**	**9099**	**9552**	**11243**

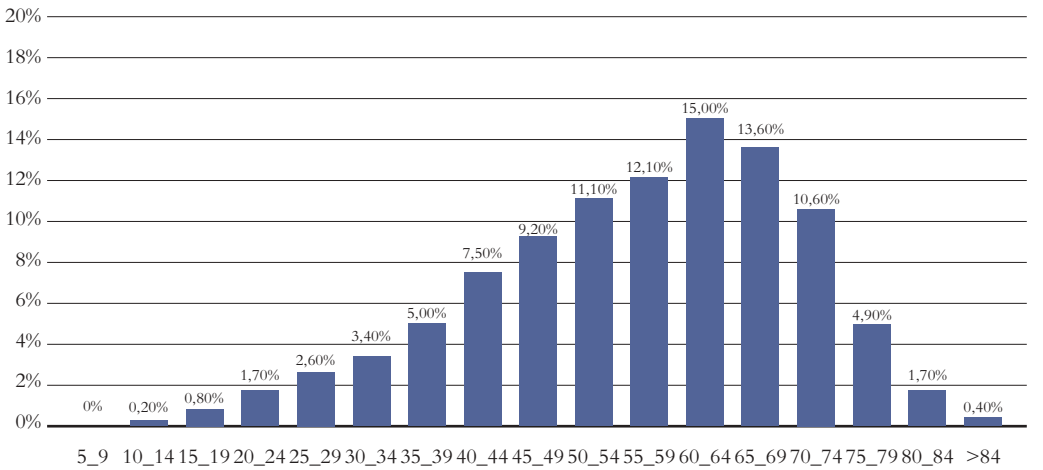
Case-mix by speciality (2002)

	Beds	Admissions	Days	ALOS	Surgical Index	Average Weight
General & Mammary Surgery	22	824	6474	7,86	92,48	1,328
Abdominal Surgery	37	787	12507	15,89	67,85	2,565
Chest Surgery	22	811	5849	7,21	69,05	2,089
Plastic Surgery	6	351	1669	4,75	94,87	1,025
Neurosurgery	14	335	4146	12,38	81,19	2,571
Gynecology	24	788	6685	8,48	83,25	1,188
Otorhinolaryngology	20	339	4474	13,2	76,7	2,082
Urology	25	735	6713	9,13	85,99	1,784
Anaesthesiology and Intensive Care	5	86	1730	20,12	53,49	4,176
Nuclear Medicine	4	313	1393	4,45	0	1,021
Medicine Oncology	52	2711	14066	5,19	2,36	1,03
Day Hospital		2084	17865	8,57		0,66
Day Surgery		1079	4462	4,135		0,79

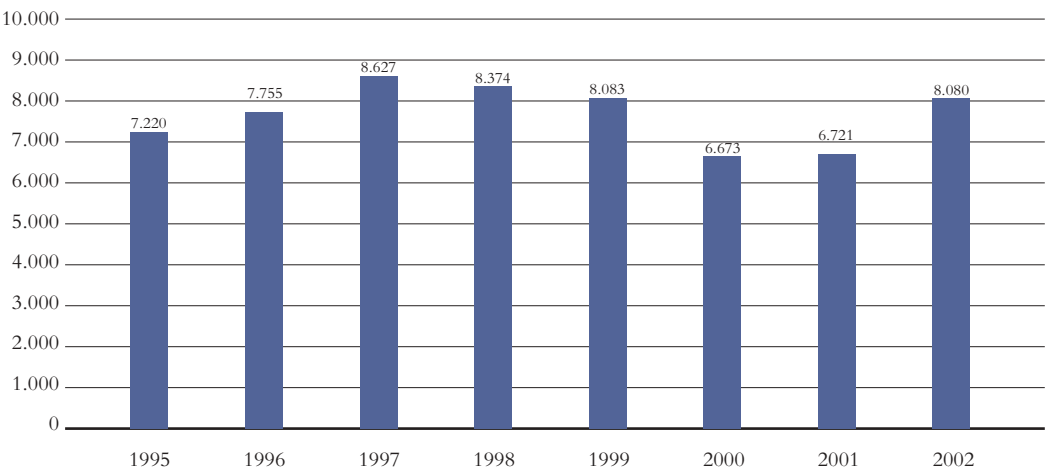
Inpatient Admissions by Geographical Area (2002)



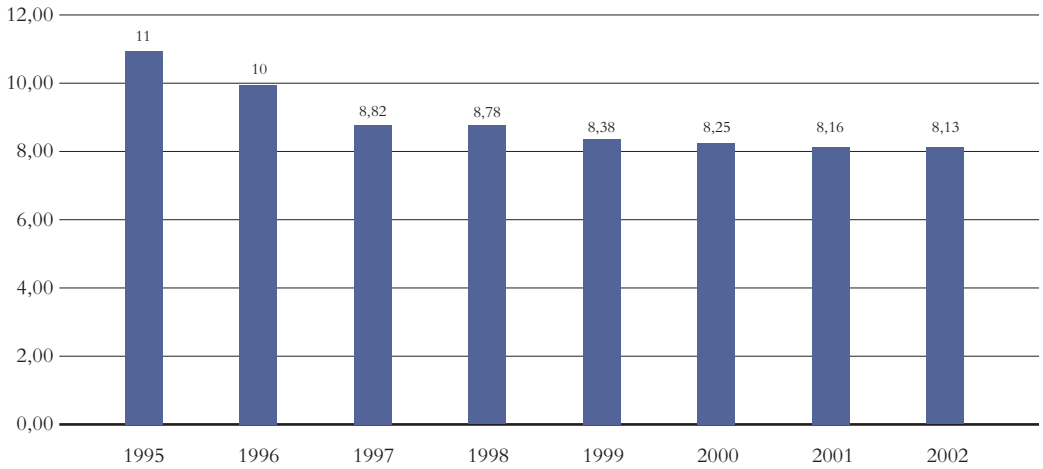
Inpatient Admissions by age (2002)



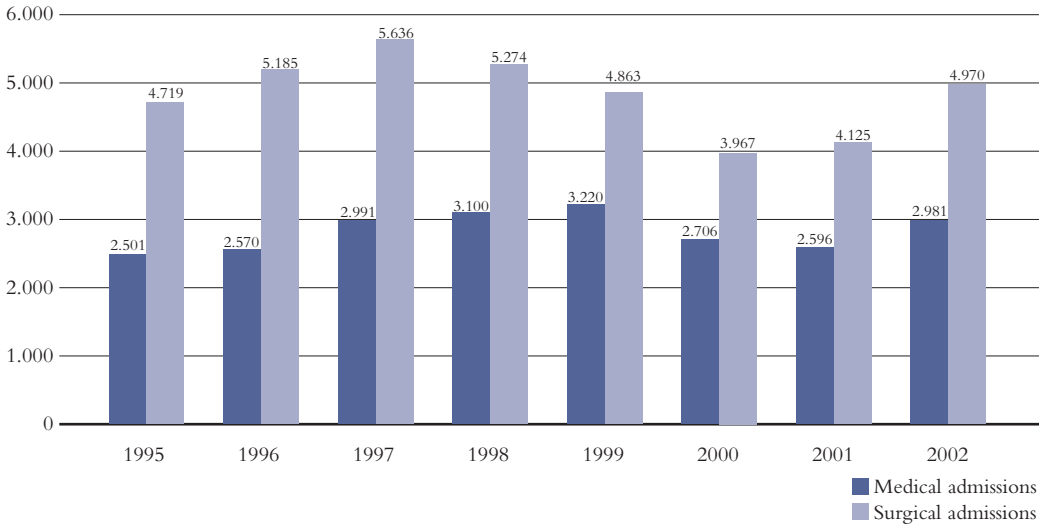
Inpatient Admissions



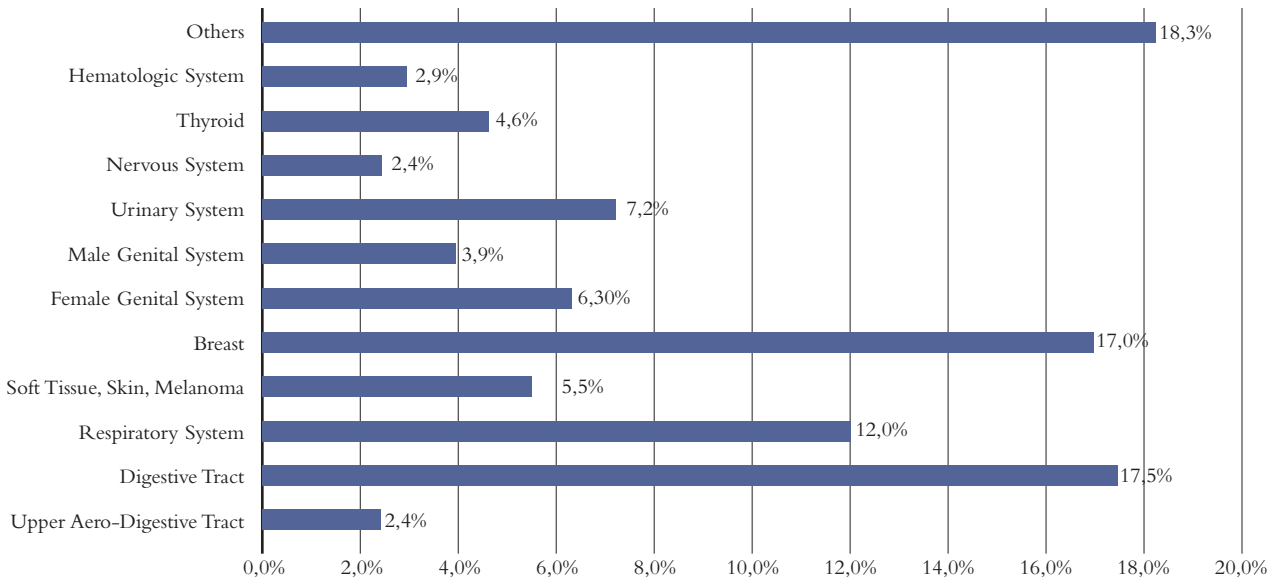
Average Length of Stay



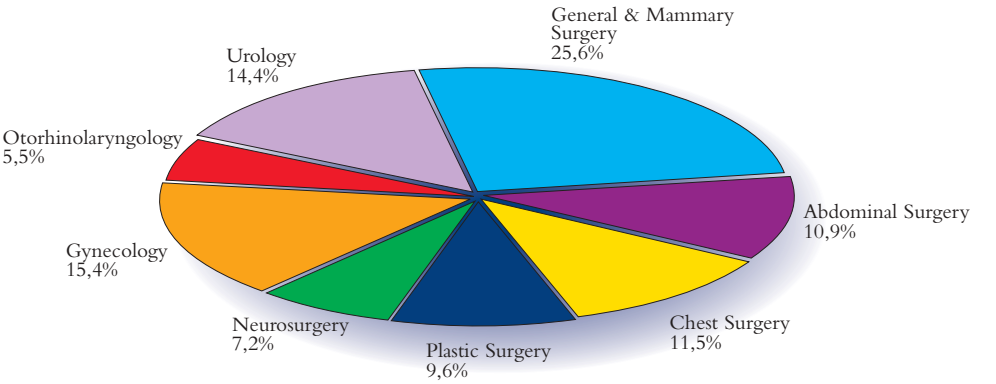
Hospital Admissions



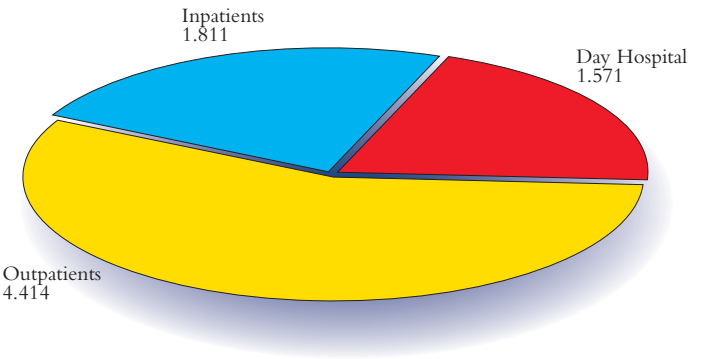
Neoplastic pathology (140-208) distribution by site (ICD9CM) of 7.867 (70% of the total No. of 2002 hospitalizations)



Surgical Interventions (2002)



Systemic Treatments (2002)



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(Impact Factor - I.F.: Institute for Scientific Information 2001)

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The prolyl isomerase Pin1 reveals a mechanism to control p53 functions after genotoxic insults.
Nature, 24, 419(6909), p.853-7, 2002 I.F. 27.955

Outcome after treatment of papillary thyroid microcarcinoma.

APPETECCHIA M., SCARCELLO G., PUCCI E., PROCACCINI A.

J. Exp. Clin. Cancer Res., 21(2), p.159-64, 2002

Patients with thyroid microcarcinoma (TMC) have favourable long-term prognoses. However, recurrences in the neck and distant metastases have been reported. The authors investigated independent factors associated with recurrence in an effort to define therapeutic guidelines. In this study they report the results of a retrospective review of patients followed at one Institution. 120 patients (96 females and 24 males; mean age 45.2 years) with a papillary thyroid microcarcinoma (PTC) < or =1 cm in greatest dimension were analyzed. All of them were followed for 5 to 15 years. 106 of them were managed aggressively (total thyroidectomy), the remainder treated with lobectomy alone. Radioiodine therapy was performed in 62/106 patients submitted to total thyroidectomy. Despite the different treatment and the presence of neck node metastases at the time of the diagnosis in 26 of the reported 120 patients (22%) and local invasion beyond the thyroid capsule in 20 (17%), only 1.7% of patients had neck nodal local recurrence. No patient died or developed distant metastases. In this preliminary study the authors conclude that the outcome of PMC is generally favourable, even in presence of lymph-node metastases and local invasion, independently of the primary treatment.

A long-standing cystic lymph-node metastasis from occult thyroid carcinoma.

APPETECCHIA M., MECULE A., SCIARRETTA F.

J. Exp. Clin. Cancer Res., 21(1), p.137-8, 2002

Here we report the case of a patient with a soft tissue mass of the neck. For more than 10 years it was thought to be a branchial cyst and was later diagnosed to be a cystic lymph node metastasis from an occult thyroid carcinoma.

A rare association between malignant mediastinal seminoma and other malignant neoplasms.

APPETECCHIA M., PUCCI E.

J. Endocrinol Invest, 25(4), p.373-6, 2002

Primary malignant mediastinal seminomas (PMMS) are rare tumors accounting for 1-6% of all mediastinal tumors. PMMS mostly affect young men, arising from primordial germ cells that abnormally migrate from the ectoderm of the yolk sac to the gonadal region. They are clinically and biologically distinct from primary testicular tumors and seem to have a worse prognosis. Due to the rarity of the disease, the choice of treatment is a matter of debate. Literature data do not show any association between this kind of tumor and malignant Schwannoma or thyroid carcinoma. In this report we describe the case of a patient affected by PMMS and 12 yr later by a malignant brachial plexus Schwannoma and papillary thyroid carcinoma (PTC). Since both mediastinal seminoma and Schwannoma were treated with surgery followed by local radiotherapy, we were not able to ascertain if either PTC or Schwannoma had been induced by radiotherapy or represented a casual neoplastic association.

Optimal adaptive control of treatment planning in radiation therapy.

ARCANGELI G., BENASSI M., NIEDDU L., PASSI C., PATRIZI G., RUSSO M.T.

European Journal of Operational Research 140, 399-412, 2002.

No abstract available.

Postoperative Adjuvant Chemoradiation in Completely Resected Locally Advanced Gastric Cancer.

ARCANGELI G., SARACINO B., ARCANGELI G., ANGELICI F., MARCHETTI P., TIRINDELLI DANESI D.

Int. J. Radiat. Oncol. Biol. Phys., 54(4), p.1069-1075, 2002

Background: The 5-year survival of patients with completely resected node-positive gastric cancer ranges from 15% to 25%. We explored the feasibility of a chemoradiation regime consisting of concomitant hyperfractionated radiotherapy and 5-fluorouracil protracted venous infusion (5-FU PVI).

Materials and methods: Forty patients received a total or partial gastrectomy operation and D2 nodal resection for Stage III gastric cancer; they were then irradiated by linac with 6-15-MV photons. The target included the gastric bed, the anastomosis, stumps, and regional nodes. A total dose of 55 Gy was given in 50 fractions using 1.1 Gy b.i.d. All patients received a concomitant 200 mg/m2/day 5-FU PVI. Patients were examined during the follow-up period as programmed. Toxicity was recorded according to RTOG criteria.

Results: After a median follow-up of 75.6 months (range: 22-136 months), 24 (60%) patients had died, and 16 (40%) were alive and free of disease. The 5-year actuarial incidence of relapse was 39%, 22%, and 2% for distant metastases, out-field peritoneal seeding, and in-field local regional recurrences, respectively. The 5-year actuarial cause-specific survival was 43%. Three patients survived more than 11 years. Acute > or = Grade 3 toxicity consisted of hematologic (22.5%) and gastrointestinal toxicity (nausea and vomiting 22.5%, diarrhea 2.8%, and abdominal pain 2.6%). No late toxicity was observed.

Conclusion: This regime of concomitant 5-FU PVI and hyperfractionated radiotherapy was well tolerated and resulted in successful locoregional control and satisfactory survival.

Accelerated hyperfractionated radiotherapy and concurrent protracted venous infusion chemotherapy in locally advanced head and neck cancer.

ARCANGELI G., SARACINO B., DANESI D.T., DE CAMPORA E., GIOVINAZZO G., COGNETTI F., CARLINI P., ARCANGELI S., MECOZZI A.

Am. J. Clin. Oncol., 25(5), p.431-7, 2002

Concurrent radiotherapy and chemotherapy result in a significant benefit with respect to induction chemotherapy followed by radiotherapy or radiotherapy alone, although with a significant increase of toxicity. To discover a more tolerated and effective chemoradiation regimen, the feasibility and efficacy of a hyperfractionated accelerated irradiation with concurrent protracted venous infusion chemotherapy was investigated. Sixty-five patients with advanced head and neck cancer underwent a definitive (53 patients) or a postoperative adjuvant (12 patients) chemoradiation treatment. Chemotherapy consisted of an intravenous protracted infusion of 5 and 200 mg/m /d cisplatin and 5-fluorouracil, respectively. Radiotherapy consisted of a split-course accelerated hyperfractionation of two 150-cGy (split twice a day) or three 100-cGy fractions per day (split three times a day) at more than 6-hour intervals, for 2 weeks followed, after a 1-week interruption, by 2-to-3-week treatment, with the same fractionation schedule, to a total dose of 60 Gy to 69 Gy. Confluent mucositis was tolerable and was the cause of treatment delay of more than 10 days in only 20% of patients. Grade 3 or greater systemic toxicity occurred only in 9 of 65 (14%) patients and was never the cause of drug dose reduction. Complete responses were observed in 69% of patients with gross diseases. At a median follow-up of 43.5 months, 45% of patients were alive and free of disease and 38% died of cancer. The 5-year actuarial local regional failure was 35%. The 5-year actuarial disease-specific survival was 50%. Preservation of larynx function was achieved in 47% of

living patients and in 74% of all patients, with advanced tumors of the laryngopharynx. The long-term results of this study suggest that this chemoradiation regimen has the potential of achieving a significant improvement over standard therapy while avoiding significant toxicity.

Preliminary in vivo experimental evidence on intratumoral morphine uptake. Possible clinical implications in cancer pain and opioid responsiveness.

ARCURI E., GINOBBI P., TIRELLI W., FROLDI R., CITRO G., SANTONI A.

Letter. J. Pain Symptom Manage., 24(1), p.1-3, 2002

No abstract available.

Induction therapy with idarubicin alone significantly influences event-free survival duration in patients with newly diagnosed hypergranular acute promyelocytic leukemia: final results of the GIMEMA randomized study LAP 0389 with 7 years of minimal follow-up.

AVVISATI G., PETTI M.C., LO-COCO F., VEGNA M.L., AMADORI S., BACCARANI M., CANTORE N., DI BONA E., ET AL.

Blood, 1,100(9), p.3141-6, 2002

Shortly before the all-trans retinoic acid (ATRA) era, the GIMEMA cooperative group initiated a randomized study comparing idarubicin (IDA) alone with IDA plus arabinosylcytosine (Ara-C) as induction treatment in patients with newly diagnosed hypergranular acute promyelocytic leukemia (APL). Of the 257 patients evaluable for induction treatment, 131 were randomized to receive IDA alone (arm A) and 126 to receive IDA + Ara-C (arm B). Treatment in arm A consisted of 10 mg/m(2) IDA daily for 6 consecutive days, whereas in arm B it consisted of 12 mg/m(2) IDA daily for 4 days combined with 200 mg/m(2) Ara-C daily in continuous infusion for 7 days. Once in complete remission (CR), patients received 3 consolidation courses of standard chemotherapy, and those still in CR at the end of the consolidation were randomized to receive or not receive 1 mg/kg 6-mercaptopurine daily and intramuscular injections of 0.25 mg/kg methotrexate weekly for 2 years. Overall, 100 (76.3%) patients in arm A and 84 (66.6%) patients in arm B achieved CR (P = NS). Event-free survival (EFS) rates were 35% and 23% for patients in arm A and arm B, respectively (P =.0352). Multivariate analysis revealed that EFS was favorably influenced by induction treatment with IDA alone (P =.0352) and unfavorably influenced by white blood cell (WBC) counts greater than 3000/microL (P =.0001) and increasing age (P =.0251). These results indicate that anthracycline monochemotherapy with IDA favorably influences the EFS of patients with newly diagnosed hypergranular APL.

HPV16 and HPV18 in genital tumors: Significantly different levels of viral integration and correlation to tumor invasiveness.

BADARACCO G., VENUTI A., SEDATI A., MARCANTE M.L.

J. Med. Virol., 67(4), p.574-82, 2002

The integration of the high-risk HPV16 and HPV18 types into the cell genome is considered an important step in malignant transformation. The relationship between the physical status of the virus and clinical/pathological parameters was studied by type-specific and multiplex PCR for E6, E2, and E1 sequences in 86 genital tumors from different sites, consisting of 69 invasive carcinomas (including 5 microinvasive carcinomas), 9 carcinomas in situ, 6 severe dysplasias, and 2 moderate dysplasias. Forty tumors contained HPV16 (46.6%), 7 HPV18 (8.1%), and 39 both viruses (45.3%). HPV16 DNA was found either as pure integrant (35.4%), or pure episome (36.7%), or a mixture of both (27.8%). Conversely, all 46 lesions containing HPV18 showed pure integrated forms. The physical status of both types was not related to the tumor site, the tumor/node/metastasis stage, or the histological differentiation grade of the invasive carcinomas. HPV16 integration was significantly associated with invasiveness. Interestingly, in double infections when HPV16 coexisted with HPV18, its genome was found more frequently in episomal form than in single infections where, conversely, it was mostly integrated (P < 0.0001), suggesting a sort of competition for cell integration sites. The complete HPV18 integration,

even in pre-neoplastic lesions, indicates a different behavior in genital transformation compared with HPV16 and may reflect a major aggressiveness of this viral type. In conclusion, virus typing in conjunction with the evaluation of the integration status may provide a better prognostic evaluation together with an improved diagnosis. Copyright 2002 Wiley-Liss, Inc.

Growth Inhibition of Cervix Carcinoma Cells in vivo by Endothelin A Receptor Blockade.

BAGNATO A., CIRILLI A., SALANI D., SIMEONE P., MULLER A., NICOTRA M.R., NATALI P.G., VENUTI A.

Cancer Res., 15, 62(22), p.6381-6384, 2002

In human papillomavirus (HPV)-positive cervical cancer cells, the endothelin A receptor (ET(A)R) mediates an endothelin-1-induced mitogenic effect, thus representing a relevant target for antitumor therapy. Here, we describe the complete inhibition of human cervix carcinoma growth by blocking the ET(A)R. In nude mice, the ET(A)R-selective antagonist atrasentan inhibits the growth and the neoangiogenesis of cervical carcinoma cell xenografts. Two cycles of treatment completely revert tumor growth. Atrasentan displays additive effects when administered in combination with the cytotoxic drug paclitaxel. These results demonstrate that by inhibiting cell proliferation and angiogenesis, this small molecule may help to control cervical cancer by either monotherapy or combination therapy.

Emerging role of endothelin-1 in tumor angiogenesis.

BAGNATO A., SPINELLA F.

Trends in Endocrinology Metabolism, 14(1), p.44-50, 2002

Tumor vessels express distinct molecular markers that are functionally relevant in the angiogenic process. Although tyrosine kinase receptor agonists are the major mediators of angiogenesis, several G-protein-coupled receptor agonists have also been shown to have a role. Among these, endothelin-1 (ET-1), by acting directly on endothelial cells via the ET(B) receptor, modulates different stages of neovascularization, including proliferation, migration, invasion, protease production and morphogenesis, and also stimulates neovascularization in vivo. ET-1 can also modulate tumor angiogenesis indirectly through the induction of vascular endothelial growth factor (VEGF). Engagement of the ET(A) receptor by ET-1 induces VEGF production by increasing levels of hypoxia-inducible factor 1alpha. Moreover, tumor cells themselves, predominantly expressing the ET(A) receptor, might form vessel-like channels within the tumors. The role of ET-1 and its signaling network in tumor angiogenesis suggests that new therapeutic strategies using specific ET(A)-receptor antagonists could improve antitumor treatment by inhibiting both neovascularization and tumor cell growth.

The HtrA1 serine protease is down-regulated during human melanoma progression and represses growth of metastatic melanoma cells.

BALDI A., DE LUCA A., MORINI M., BATTISTA T., FELSANI A., BALDI F., CATRICALÀ C., AMANTEA A., NOONAN D.M., ALBINI A., NATALI P.G., LOMBARDI D., PAGGI M.G.

Oncogene, 26;21(43), p.6684-8, 2002

Differential gene expression of cell lines derived from a malignant melanoma or its autologous lymph node metastasis using cDNA arrays indicated down-regulation of PRSS11, a gene encoding the serine protease HtrA1, a homolog of the Escherichia coli protease HtrA, in the metastatic line. Stable PRSS11 overexpression in the metastatic cell line strongly inhibited proliferation, chemoinvasion and Nm23-H1 protein expression in vitro, as well as cell growth in vivo in nu/nu mice. A polyclonal anti-HtrA1 serum demonstrated a significantly higher expression in primary melanomas when compared to unrelated metastatic lesions in a human melanoma tissue array, and down-modulation of HtrA1 expression in autologous lymph node melanoma metastases in seven out of 11 cases examined. These results suggest that down-regulation of PRSS11 and HtrA1 expression may represent an indicator of melanoma progression.

Expression of p21 in SV40 large T antigen positive human pleural mesothelioma: relationship with survival.

Baldi A., Groeger A.M., Esposito V., Cassandro R., Tonini G., Battista T., Di Marino M.P., Vincenzi B., Santini M., Angelini A., Rossiello R., Baldi F., Paggi M.G.

Thorax, 57(4), p.353-6, 2002

Background: Mesothelioma is the most commonly occurring primary pleural neoplasm. Several studies have documented an increase in the incidence of this malignancy during the last decades. Although the association between asbestos exposure and development of mesothelioma is generally accepted, the exact mechanism of carcinogenesis is unknown. Recently, Simian virus 40 large T antigen (SV40 Tag) expression has been detected in pleural mesothelioma. The ability of SV40 oncoproteins to inactivate p53 and retinoblastoma tumour suppressor proteins has been proposed as an important step in the pathogenesis of human mesothelioma.

Methods: To obtain a better understanding of the molecular mechanisms of the pathogenesis of mesothelioma, the expression of the cell cycle inhibitor p21(WAF1/CIP1) (p21), a downstream target of p53, was evaluated immunohistochemically in a group of 29 mesothelioma specimens already characterised for the presence of SV40 Tag sequences.

Results: Statistical analysis did not reveal any correlation between p21 expression and histopathological type of mesothelioma using the kappa(2) test ($p=0.577$). A significant positive relationship was found between p21 expression level and the patients' overall survival according to the Kaplan-Meier survival curves and using a log rank test (median difference in survival 7 months, 95% CI 4.8 to 9.9; $p<0.001$).

Conclusions: Determination of p21 expression bears a prognostic significance in patients affected with mesothelioma, further underlining the role of SV40 in the pathogenesis of malignant pleural mesothelioma.

Neoadjuvant chemotherapy and radical surgery versus exclusive radiotherapy in locally advanced squamous cell cervical cancer: results from the Italian multicenter randomized study.

Benedetti-Panici P., Greggi S., Colombo A., Amoroso M., Smaniotto D., Giannarelli D., Amunni G., Raspagliesi F., Zola P., Mangioni C., Landoni F.

J. Clin. Oncol., 1,20(1), p.179-88, 2002

Purpose: Neoadjuvant chemotherapy (NACT) and radical surgery (RS) have emerged as a possible alternative to conventional radiation therapy (RT) in locally advanced cervical carcinoma. In 1990, a phase III trial was undertaken to verify such a hypothesis in terms of survival and treatment-related morbidity.

Patients and methods: Patients with squamous cell, International Federation of Gynecology and Obstetrics stage IB2 to III cervical cancer were eligible for the study. They received cisplatin-based NACT followed by RS (type III to V radical hysterectomy plus systematic pelvic lymphadenectomy) (arm A) or external-beam RT (45 to 50 Gy) followed by brachyradiotherapy (20 to 30 Gy) (arm B).

Results: Of 441 patients randomly assigned to NACT+RS or RT, eligibility was confirmed in 210 and 199 patients, respectively. Treatment was administered according to protocol in 76% of arm A patients and 72% of arm B patients. Adjuvant treatment was delivered in 48 operated patients (29%). There was no evidence for any significant excess of severe morbidity in one of the two arms. The 5-year overall survival (OS) and progression-free survival (PFS) rates were 58.9% and 55.4% for arm A and 44.5% and 41.3% for arm B ($P = .007$ and $P = .02$), respectively. Subgroup survival analysis shows OS and PFS rates of 64.7% and 59.7% (stage IB2-IIB, NACT+RS), 46.4% and 46.7% (stage IB2-IIB, RT) ($P = .005$ and$P = .02$), 41.6% and 41.9% (stage III, NCAT+RS), 36.7% and 36.4% (stage III, RT) ($P = .36$ and $P = .29$), respectively. Treatment had a significant impact on OS and PFS.

Conclusion: Although significant only for the stage IB2 to IIB group, a survival benefit seems to be associated with the NACT+RS compared with conventional RT.

Osmotic resistance of high-density erythrocytes in transglutaminase 2-deficient mice.

Bernassola F., Boumis G., Corazzari M., Bertini G., Citro G., Knight R.A., Amiconi G., Melino G..

Biochem. Biophys. Res. Commun., 15,291(5), p.1123-7, 2002

Transglutaminase 2 (TGase 2) is a Ca(2+)-dependent enzyme responsible for the posttransttranslational modification of proteins by transamidation of specific polypeptide-bound glutamine residues. Elevating the intracellular concentration of Ca(2+)-ions in human erythrocytes leads to the formation of cytoskeletal and cytoplasmic protein polymers. The Ca(2+)-dependent TGase 2-dependent cross-linking activity has been proposed for its involvement in erythrocyte aging, by inducing irreversible modification of their cell shape and deformability. Accordingly, we found that high-density ("old") TGase 2(minus sign/minus sign) red blood cells (RBCs) were more resistant to osmotic stress-induced hemolysis than those from wild type mice. In addition, elevating the intracellular concentration of Ca(2+) by treatment of total RBCs with ionophore A23187 resulted in enhanced resistance of TGase 2-deficient erythrocytes compared to their normal counterpart. These findings indicate that TGase 2 may have a role in regulating structural flexibility of RBCs, possibly affecting their life span in physiopathological conditions, such as erythrocyte senescence, which are accompanied by increases in intracellular Ca(2+) concentration. (C)2002 Elsevier Science (USA).

Role of transglutaminase 2 in glucose tolerance: knockout mice studies and a putative mutation in a MODY patient.

Bernassola F., Federici M., Corazzari M., Terrinoni A., Hribal M.L., De Laurenzi V., Ranalli M., Massa O., Sesti G., McLean W.H., Citro G., Barbetti F., Melino G.

FASEB J., 16(11), p.1371-8, 2002

Transglutaminase 2 (TGase 2) is a Ca+2-dependent enzyme that catalyzes both intracellular and extracellular cross-linking reactions by transamidation of specific glutamine residues. TGase 2 is known to be involved in the membrane-mediated events required for glucose-stimulated insulin release from the pancreatic beta cells. Here we show that targeted disruption of TGase 2 impairs glucose-stimulated insulin secretion. TGase 2-/- mice show glucose intolerance after intraperitoneal glucose loading. TGase 2-/- mice manifest a tendency to develop hypoglycemia after administration of exogenous insulin as a consequence of enhanced insulin receptor substrate 2 (IRS-2) phosphorylation. We suggest that the increased peripheral sensitivity to insulin partially compensates for the defective secretion in this animal model. TGase 2-/- mouse phenotype resembles that of the maturity-onset diabetes of young (MODY) patients. In the course of screening for human TGase 2 gene in Italian subjects with the clinical features of MODY, we detected a missense mutation (N333S) in the active site of the enzyme. Collectively, these results identify TGase 2 as a potential candidate gene in type 2 diabetes.

Nutrient intake and ovarian cancer: an Italian case-control study.

Bidoli E., La Vecchi C., Montella M., Maso L.D., Conti E., Negri E., Scarabelli C., Carbone A., Decarli A., Franceschi S.

Cancer Causes Control, 13(3), p.255-61, 2002

Objective: The role of selected macronutrients, cholesterol, and fatty acids in the etiology of epithelial ovarian cancer was analyzed using data from a case-control study carried out in five Italian areas between January 1992 and December 1999.

Methods: Cases comprised 1,031 women with incident, histologically confirmed epithelial ovarian cancer, admitted to the major teaching and general hospitals of the study areas. Controls comprised 2,411 women admitted for acute, non-neoplastic conditions to the same network of hospitals. Information on dietary habits was elicited using a validated food-frequency questionnaire including 78 food groups and recipes. Odds ratios (OR) and their corresponding 95% confidence intervals (CI) were computed by subsequent quintiles of nutrient intake.

Results: Direct associations with ovarian cancer emerged for starch intake (OR = 1.4 in the highest vs the lowest quintile of intake; 95% CI 1.1-1.8), while inverse associations emerged for monounsaturated (OR=0.7; 95% CI 0.5-0.9), and polyunsaturated (OR = 0.7; 95% CI 0.5-0.9) fatty acids. Among fatty acids, oleic (OR = 0.7; 95% CI 0.5-0.9), linoleic (OR = 0.7; 95% CI 0.5-0.9), and linolenic (OR = 0.8; 95% CI 0.6-1.0) acids were inversely related to ovarian cancer. When, however, six macronutrients were included in the same model, only the

adverse effect of high starch intake remained significant. Results were consistent in separate strata of menopausal status, parity, and energy intake.

Conclusions: Starch was directly associated, and unsaturated fatty acids were inversely associated, with ovarian cancer risk.

Glutathione influences c-Myc-induced apoptosis in M14 human melanoma cells.

Biroccio A., Benassi B., Filomeni G., Amodei S., Marchini S., Chiorino G., Rotilio G., Zupi G., Ciriolo M.R..

J. Biol. Chem., 277, p.43763-43770, 2002

The objective of this article is to dissect the mechanisms by which the down-regulation of c-Myc induces programmed cell death in melanoma cells. In stable and doxycycline-inducible M14 melanoma cells, down-regulation of c-Myc induced apoptosis subsequent to a decrease in the intracellular reduced glutathione content and a concomitant accumulation of its oxidized form. This redox alteration was associated with a decrease of the enzyme activities of gamma-glutamyl-cysteine synthetase and NADPH-dependent GSSG reductase, as well as a consequent glutathione release in the extracellular medium. Cytochrome c was released into the cytosol at very early stages of apoptosis induction, long before detectable production of reactive oxygen species and activation of caspase-9 and -3. Macroarray analysis revealed that down-regulation of c-Myc produced striking changes in gene expression in the section related to metabolism, where the expression of gamma-glutamyl-cysteine synthetase and GSSG reductase was found to be significantly reduced. The addition of N-acetyl-l-cysteine or glutathione ethyl ester inhibited the apoptotic process, thus confirming the key role of glutathione in programmed cell death induced by c-Myc

Reconstitution of hTERT restores tumorigenicity in melanoma-derived c-Myc low-expressing clones.

Biroccio A., Amodei S., Benassi B., Scarsella M., Cianciulli A., Mottolese M., Del Bufalo D., Leonetti C., Zupi G.

Oncogene, 2, 21(19), p.3011-9, 2002

c-Myc is involved in the control of telomerase activity through its ability to induce the expression of the catalytic subunit of the enzyme, the human telomerase reverse transcriptase (hTERT). Our aim was to study whether telomerase plays a critical role in c-Myc-dependent tumorigenicity of melanoma cells. By using M14-derived clones, expressing low levels of c-Myc, we demonstrated that the down-regulation of c-Myc reduced cell proliferation rate, cloning efficiency and tumorigenicity and increased the apoptotic rate. Decreased tumorigenic potential correlated with reduced hTERT gene expression, telomerase activity and telomere shortening. Introduction of wild-type hTERT into these cells increased their proliferation rate and partially re-established their tumorigenic potential, at early passages, even though the apoptotic rate of the population remained unaltered. After several in vitro passages, hTERT-mediated cell proliferation made the tumorigenic potential of the c-Myc low-expressing clones comparable to that of the M14 parental line. Over-expression of the mutant biologically inactive hTERT did not drive cells to proliferate. In conclusion, our results demonstrate that the reconstitution of high levels of telomerase activity reverses the low tumorigenicity due to low c-Myc expression.

Olive oil, seed oils and other added fats in relation to ovarian cancer (Italy).

Bosetti C., Negri E., Franceschi S., Talamini R., Montella M., Conti E., Lagiou P., Parazzini F., La Vecchia C.

Cancer Causes Control, 13(5), p.465-70, 2002

Objective: This study investigates the potential role of olive oil and other added fats used for seasoning or cooking on ovarian carcinogenesis.

Methods: We analyzed data from a multicentre case-control study conducted between 1992 and 1999 in Italy, including a total of 1031 incident with a first diagnosis, histologically confirmed epithelial ovarian cancer cases and 2,411 hospital controls with acute, non-malignant and non-gynecological conditions. The subjects' usual diet was investigated through a validated food-frequency questionnaire, including specific questions aimed at assessing added fat intake patterns.

Results: After allowance for study centre, year at interview, age, education, parity, oral contraceptive use, and total energy intake, a reduced risk of ovarian cancer was observed for high intake of olive oil (odds ratio (OR) = 0.68, 95% confidence interval (CI) 0.50-0.93 for the highest quintile of intake, compared to the lowest one) and for a group of specific seed oils (i.e. sunflower, maize, peanut, and soya) (OR = 0.59, 95% CI 0.46-0.76). No significant associations were observed for mixed seed oils, butter, and margarine.

Conclusions: The present study suggests a favorable effect of olive oil and other vegetable oils on ovarian cancer in this Italian population.

Acquired cystic kidney disease following long-term peritoneal dialysis for congenital nephrotic syndrome.

Bosman C., Diomedi Camassei F., Del Nonno F., Corsi A., Boldrini R.

Scand. J. Urol. Nephrol., 36(1), p.83-6, 2002

We describe here the clinicopathological findings in a child with congenital nephrotic syndrome (CNS) non-responsive to medical therapy who developed acquired cystic kidney disease (ACKD) in both native kidneys after long-term peritoneal dialysis. This case indicates that CNS is a further pathologic condition related to the development of ACKD.

Cutaneous pleomorphic T-cell lymphoma coexisting with myelodysplastic syndrome transforming into acute myeloid leukemia: successful treatment with a fludarabine-containing regimen.

Breccia M., Petti M.C., D'Elia G.M., D'Andrea M., Carmosino I., Alimena G.

Eur. J. Haematol., 68(1), p.1-3, 2002

The coexistence of a primary myelodysplastic syndrome (MDS) and a T-cell cutaneous non-Hodgkin's lymphoma is an extremely rare event, which has so far only been reported in a single instance in the literature. We describe herein an additional case in which the lymphoid disease was combined with an MDS at the time of its evolution into acute myeloid leukemia (AML). Both diseases were successfully treated with a regimen containing fludarabine. We discuss possible pathogenetic mechanisms and suggest the use of nonalkylating drugs, such as fludarabine, for the treatment of this rare association of malignancies usually characterized by a very poor response to therapy.

Diabetes insipidus as first manifestation of acute myeloid leukaemia with EVI-1-positive, 3q21q26 syndrome and T cell-line antigen expression: what is the EVI-1 gene role?

Breccia M., Petti M.C., Ottaviani E., Mancini M., D'Elia G.M., Mecarocci S., Alimena G.

Br. J. Haematol., 118(2), p.438-41, 2002

Two cases of acute myeloid leukaemia (AML) with CD2 and CD7 expression associated with diabetes insipidus (DI) as the initial symptom are presented. Both patients had t(3;3)(q21;q26) associated with monosomy 7 and EVI-1 overexpression. No neurohypophysis infiltration was evident. One patient died during induction chemotherapy, the other did not respond to therapy and died with persistent DI. Our findings further support the existence of a distinct AML entity characterized by the presence of DI, abnormalities of chromosome 3q, dysmegakaryopoiesis and poor outcome, and provide evidence of EVI-1 gene involvement. The possible role of chromosome 3q26 abnormalities in determining this peculiar clinical-biological association is emphasized.

Sentinel lymphadenectomy in cutaneous melanoma.

Buonomo O., Felici A., Granai A.V., Piccirillo R., De Liguori Carino N., Guadagni F., Mariotti S., Orlandi A., Tipaldi G., et al.

Tumori, 88(3), p.S49-51, 2002

Aims and background: In the last ten years validation of the sentinel lymph node (SLN) concept has led to modification of the surgical approach for patients with intermediate-risk cutaneous melanoma.

Methods and study design: Forty-eight patients affected by cutaneous melanoma with a Breslow thickness between 0.65 and 4 mm were enrolled in the study. Approximately 2 mCi of radiotracer and 1 mL of vital blue dye were injected

in each patient around the site of the primary lesion. Lymphoscintigraphy was performed until the lymphatic basin and the respective SLN were localized. The whole surgical procedure consisted of enlargement of the surgical margins followed by localization and excision of the SLN(s) by using both radiotracer and vital dye. Whenever the SLN proved to be histologically positive for metastasis, complete regional lymphadenectomy was performed.

Results: Within 15 minutes of radiotracer administration the lymphatic basin was localized in all 4 patients by lymphoscintigraphy. Vital dye and radiotracer successfully allowed SLN localization and excision in 46 of 48 patients (97%); in one case the SLN was detected by radiotracer alone. The SLN proved to be metastatic in six (13%) of 46 evaluable patients; interestingly, in three of them the presence of metastatic cells was revealed only by immunohistochemistry. All patients with tumor-positive SLNs had primary lesions with a Breslow thickness = 2 mm.

Conclusions: Sentinel lymphadenectomy is able to identify lymph node involvement in patients with cutaneous melanoma with a Breslow thickness > 1 mm, thus avoiding the risks associated with radical regional lymphadenectomy. Lymphoscintigraphy proved to be an important tool to obtain correct preoperative localization of the drainage basin, especially for melanomas located on the face and trunk.

Day-surgical management of ductal carcinoma in situ (DCIS) of the breast using wide local excision with sentinel node biopsy.

BUONOMO O., GRANAI A.V., FELICI A., PICCIRILLO R., DE LIGUORI CARINO N., GUADAGNI F., POLZONI M., MARIOTTI S., CIPRIANI C., ET AL.

Tumori, 88(3), p.S48-9, 2002

No abstract available

Expression of transglutaminase 5 in normal and pathologic human epidermis.

CANDI E., ODDI S., PARADISI A., TERRINONI A., RANALLI M., TEOFOLI P., CITRO G., SCARPATO S., PUDDU P., MELINO G.

J. Invest. Dermatol., 119(3), p.670-7, 2002

To explore the expression and gain more information on the function of transglutaminase 5 enzyme in normal and defective human epidermis, we generated a rat antihuman transglutaminase 5 antiserum elicited against a purified active recombinant protein expressed in the baculovirus system. By use of Western blotting and immunofluorescence methods, the immunospecificity of the antibodies for transglutaminase 5 was tested; no crossreactivity with other transglutaminases (types 1, 2, and 3) was observed, thus allowing histochemistry studies. By indirect immunofluorescence analysis the antibodies decorated the upper layers of normal human epidermis, with consistent staining in the spinous and granular layers. We evaluated transglutaminase 5 expression in comparison with proliferating (keratin 14) and differentiating (transglutaminase 3) markers in different diseases, such as psoriasis, ichthyosis vulgaris, lamellar ichthyosis, and Darier's disease. We observed that transglutaminase 5 contributes, as a secondary effect, to the hyperkeratotic phenotype in ichthyosis (both vulgaris and lamellar) and in psoriasis. In Darier's disease, transglutaminase 5 expression, as well as transglutaminase 3, is completely missregulated, being overexpressed or totally absent in different areas of the same lesion.

Measuring cancer prevalence in Europe: the EUROPREVAL project.

CAPOCACCIA R., COLONNA M., CORAZZIARI I., DE ANGELIS R., FRANCISCI S., MICHELI A., MUGNO E., CONTI E.M.S., AND EUROPREVAL WORKING GROUP.

Ann. Oncol., 13(6), p.831-9, 2002

Cancer prevalence is the proportion of individuals in a population who at some stage during their lifetime have been diagnosed with cancer, irrespective of the date of diagnosis. Cancer prevalence statistics have generally been provided by a limited number of well established cancer registries that have been in existence for several decades. The advent of systematic follow-up of life status of incident cases and the availability of new statistical methodologies, now makes it possible for reg-

istries established during the 1970s or 1980s to provide prevalence data. The main problems encountered in the estimation of prevalence are the inclusion of: (I) cases lost to follow-up; (II) cases known only from their death certificate; (III) cases diagnosed before the start of registration; and (IV) the treatment of multiple tumours and migrations. The main aim of this paper was to review these problems and discuss, through the experience gained with EUROPREVAL, how they can be overcome. A method is presented for the calculation of prevalence of all cancers combined in the populations covered by the 45 cancer registries participating in EUROPREVAL. Prevalence of cancer is estimated to be 2% on average, with the highest values (3%) in Sweden and the lowest in Eastern Europe, with a minimum of approximately 1% in Poland.

Loss of pRb2/p130 Expression is Associated With Unfavorable Clinical Outcome in Lung Cancer.

CAPUTI M., GROEGER A.M., ESPOSITO V., DE LUCA A., MASCIULLO V., MANCINI A., BALDI F., WOLNER E., GIORDANO A.

Clin. Cancer Res., 8(12), p.3850-6, 2002

Altered expression of cell cycle regulators represents a frequent event in both small cell and non-small cell lung cancer (NSCLC). Despite several studies that reported involvement of tumor suppressor genes, such as p53 and pRb, in the development and progression of lung cancer, contrasting opinions exist about the prognostic role of this protein in this neoplasm. We developed an immunohistochemical assay suitable for the detection of pRb2/p130, the last discovered member of the retinoblastoma gene family, on formalin-fixed and paraffin-embedded sections. We evaluated the immunohistochemical expression of pRb2/p130 in 135 lung cancer specimens, and performed Western blot analysis in a subset of 30 corresponding tumor lysates. A high correlation between immunohistochemical data and Western blot results ($P = 0.0004$) was found. We statistically analyzed the relationship between overall survival (OS) time and pRb2/p130 expression according to the different histological types in 105 patients. We did not find any correlation between pRb2/p130 expression and OS in small cell lung cancers, whereas in NSCLCs a direct relationship between pRb2 and OS was found in both adenocarcinoma ($P = 0.0002$) and squamous cell carcinoma ($P = 0.0002$) histotypes. According to univariate analysis, pRb2/p130 was a prognostic factor of which the lost or reduced expression correlated with a shorter OS ($P < 0.0000$). At multivariate analysis, pRb2/p130 expression was an independent predictor of OS ($P = 0.0001$) when considered together with histotype. This study demonstrates for the first time the potential independent prognostic value of pRb2/p130 expression on formalin-fixed, paraffin-embedded sections from lung cancer patients. pRb2/p130 immunoreactivity can be used to predict OS in patients with NSCLC and, therefore, may represent a new prognostic marker.

Nuove tecnologie in neurochirurgia: il ruolo della chirurgia nel trattamento del gliomi di basso grado.

CARAPELLA C.M.

Neurol. Sci., 23:, p.S7-S9, 2002

No abstract available

Biomonitoring of exposure to urban air pollutants: analysis of sister chromatid exchanges and DNA lesions in peripheral lymphocytes of traffic policemen.

CARERE A., ANDREOLI C., GALATI R., LEOPARDI P., MARCON F., ROSATI M.V., ROSSI S., TOMEI F., VERDINA A., ZIJNO A., CREBELLI R.

Mutat. Res., 25,518(2), p.215-24, 2002

In order to elucidate the health effects of occupational exposure to traffic fumes, a few biomarkers of early genetic effect were investigated in Rome traffic policemen. One hundred and ninety healthy subjects engaged in traffic control (133 subjects) or in office work (57 subjects) participated the study. For all subjects, detailed information on smoking habits and other potential confounders were recorded by questionnaires. Average exposure of the study groups to benzene and other aromatic hydrocarbons was evaluated in a parallel exposure survey. All workers were genotyped for the following metabolic polymorphisms: CYP1A1 (m1, m2, and m4 variants), CYP2E1 (PstI and RsaI), NQO1

(Hinf1), GSTM1 and GSTT1 (null variants). In this paper, the results of the analysis of sister chromatid exchanges (SCE) in peripheral lymphocytes, and DNA damage by alkaline (pH 13) comet assay in mononuclear blood cells are reported. No statistically significant difference in the frequency of SCE or high frequency cells (HFC) was observed between traffic wardens and office workers (controls), despite the significantly higher exposure to benzene of the former (average group exposure 9.5 versus 3.8microg/m(3), 7h TWA). Conversely, both SCE per cell and HFC were highly significantly ($P<0.001$) increased in smokers compared to nonsmokers, showing a significant correlation ($P<0.001$) with the number of cigarettes per day. Multiple regression analyses of data, with metabolic polymorphisms, smoking habits, alcohol consumption, age, gender, and family history of cancer as independent variables, showed that smoking habits, and possibly the CYP2E1 variant genotypes, were the main factors explaining the variance of both SCE and HFC. Within smokers, an association of borderline significance between the CYP1A1 variant genotypes and increased SCE ($P=0.050$) and HFC ($P=0.090$) was found. This effect was mainly observed in light smokers (<15 cigarettes per day). The analysis of DNA damage by comet assay did not highlight any statistically significant difference between the exposed and control workers. Moreover, no significant model explaining tail moment variance was obtained by multiple regression analysis using the independent variables shown above. On the whole, these results indicate that exposure to moderate air pollution levels does not result in a detectable increase of genetic damage in blood cells. This evidence does not rule out any possibility of adverse effects, but strongly suggests that in urban residents life-style related factors, such as tobacco smoking, give the prevailing contribution to individual genotoxic burden.

Sentinel node in gastric cancer surgery.

CARLINI M., CARBONI F., PETRIC M., SANTORO R., GUADAGNI F., MARANDINO F., CASTELLI M., SANTORO E.

J. Exp. Clin. Cancer Res., 21(4), p.469-73, 2002

Sentinel Node (SN) biopsy studies have been recently applied to gastric cancer. In this series, 40 selected patients operated for gastric adenocarcinoma located in the lesser curvature and/or anterior wall of the body and antrum, underwent an intraoperative dye lymphography. The lymphatic ducts and nodes were visualized and a SN was evidenced in all cases. This was removed and a frozen section examined. In all cases a radical D2-3 gastrectomy was performed and histology, molecular biology, RT-PCR research of micrometastases (CEA-mRNA), were determined on the specimens. Correlations between T and histological status of SN and regional nodes were done. In 16 cases the SN was negative and all the resected regional nodes were negative too. In 15 cases the SN node was positive and other nodes in other stations were found to be positive as well. In 2 cases the SN was negative but other nodes, in the same stations and in others, were positive (false negative = 5%). In 7 cases the SN was the only node in which metastases occurred, 3 demonstrated by conventional histology and 4 detected by RT-PCR. In these 7 cases the SN was the only involved node out of all resected nodes, thus demonstrating to be the real first node along the lymphatic routes from the tumour. This experience seems to confirm the existence of a Sentinel Node and that each gastric adenocarcinoma has its own lymphatic basin in which metastasis can occur. Although a prudent attitude towards the indications resulting from these observations is required, in selected cases a controlled and tailored lymphoadenectomy could be adopted.

Transhiatal surgical resection for adenocarcinoma of the cardia.

CARLINI M., LONARDO M.T., CARBONI F., PETRIC M., LEPIANE P., SANTORO E.

J. Exp. Clin. Cancer Res., 21(1), p.15-21, 2002

Aim of this study is to define feasibility and effectiveness of the transhiatal esophagogastric resection in cardia adenocarcinoma. From 1981 to 2001, we submitted to surgery 85 patients affected by cardia adenocarcinoma. Since 1994, 34 patients, in consideration of clinical, anatomosurgical (Siewert II-III) and pathologic (T1-3, cN mediastinal negative) findings, underwent transhiatal esophagogastric resection according to Pinotti's technique. This consisted in the midline opening of the central tendon of the diaphragm, ligature and section of the left inferior phrenic vessels, exposure and anterior retraction of the pericardium. The approach allowed in all cases a satisfactory esophageal mobilization and a good dissection of the inferior mediastinal structures avoiding thoracotomy. Postoperative complications were observed in 8 patients (24%). In 4 cases the complications were

medical (11.8%) and in 4 cases surgical (11.8%). Death occurred in 4 cases (11.8%): in 3 patients (8.8%) for local complications (2 anastomotic leaks and 1 hemorrage) and in 1 (2.9%) for cardiac failure. The 26 non complicated cases had an uneventful postoperative course and were discharged 12 days after surgery. Middle and long term results were evaluated in terms of locoregional recurrence rate and actuarial survival. At 1 and 2 years locoregional recurrence occurred in 8.8% and 11.8% of cases respectively. Five-year overall survival was 22.5%. In selected cases (Siewert type II-III, T1-3 tumors with clinically negative mediastinal lymphnodes) the procedure in study appears technically feasible, it provides a satisfactory volume of esophageal exeresis and an adequate extension of mediastinal lymphadenectomy, representing a safe and effective alternative to thoracotomy in cardia cancer surgery.

Liver metastases from breast cancer. Results of surgical resection.

CARLINI M., LONARDO M.T., CARBONI F., PETRIC M., VITUCCI C., SANTORO R., LEPIANE P., ETTORRE G.M., SANTORO E.

Hepato-gastroenterology, 49, p.1597-1601, 2002

Background/Aims: Purpose of this study is to define the effectiveness of surgical resection of liver metastases from operated breast cancer.

Methodology: Nineteen patients underwent surgical exploration to resect liver metastases from previously operated breast carcinoma. Seventeen patients were resected: 15 patients had unique metastases and were submitted to a wedge liver resection while 2 had multiple lesions; in these cases a V-VI segmentectomy and a right hepatectomy was required. After liver resection 11 patients received chemotherapy, 2 chemotherapy plus hormone therapy, 2 hormone therapy alone and in the remaining 2 no adjuvant treatment was done.

Results: Postoperative mortality was nil and morbidity consisted of 1 subphrenic abscess and 1 pleural effusion. Actuarial 5-year survival rate was 46%. Eight patients are still alive, 7 of whom are disease-free. Nine patients died for neoplastic progression.

Conclusions: Surgical resection of liver metastases from breast cancer seems to be able to improve long-term survival in selected patients with unique and isolated lesions especially in association to systemic chemotherapy and hormone therapy.

Anti-peptide antibodies that recognize conformational differences of HLA class I intracytoplasmic domains.

CHERSI A., GALATI R., OGINO T., BUTLER R.H., TANIGAKI N.

Hum. Immunol., 63(9), p.731, 2002

Rabbit antibodies were raised against both long and short peptides derived from exon 7 sequences of human leukocyte antigen (HLA) class I alpha chains; anti-A/B against a 13-mer shared by most HLA-A alpha and HLA-B alpha chains, anti-C against a 15-mer characteristic of HLA-C alpha chains, anti-ACT against a 6-mer specific to HLA-A alpha chains, and anti-CCT against a 5-mer specific to HLA-C alpha chains. Binding activity of the antibodies was determined with peptides by enzyme-linked immunoabsorbent assay (ELISA) and with HLA class I transfectants and the parental cells by FACS analysis. Anti-A/B and anti-C were to a greater or lesser extent crossreactive with the long and short peptides, whereas anti-ACT and anti-CCT were specific to the corresponding short peptides. No binding was seen for anti-ACT and anti-CCT with HLA class I transfectants, C1R-A2, C1R-B7, and 221-Cw1 and the parental cells, C1R (Cw4, E) and 721.221 (E, F). Anti-A/B and anti-C were substantially protein-reactive and the binding order was C1R-B7 > C1R-A2, 721.221 > C1R, 221-Cw1 for anti-A/B, and C1R-B7 > 721.221 > C1R, 221-Cw1, C1R-A2 for anti-C. Thus, anti-A/B and anti-C bound better to HLA-B and HLA-E rather than to HLA-A and HLA-C. Computer modeling of the three-dimensional structure of the intracytoplasmic domains demonstrated that this may be due to structural differences despite the sequence similarities.

Contribution of fluorescence in situ hybridization to immunohistochemistry for the evaluation of HER-2 in breast cancer.

Cianciulli A.M., Botti C., Coletta A.M., Buglioni S., Marzano R., Benevolo M., Cione A., Mottolese M.

Cancer Genet. Cytogenet., 133(1), p.66-71, 2002

The main focus of the present study was to assess the efficacy of interphase cytogenetics using fluorescence in situ hybridization (FISH) as a valid alternative to immunohistochemistry (IHC) in paraffin-embedded tissue sections and/or the efficacy of the combination of the two methods, while, at the same time, aiming to provide additional information on the use of the two methods. For this study, selected breast cancer patients (n=66) were tested for HER-2 gene amplification by FISH. The probe contains DNA sequences specific for the HER-2 human gene locus and hybridizes to the 17q11.2 through q12 region of human chromosome 17. The same samples were tested previously for HER-2 overexpression by two monoclonal antibodies (300G9 and CB11), recognizing an extracellular and an internal domain of gp185(Her-2), respectively. HER-2 overexpression also was evaluated using the HerceptTest Kit (Dako, Milan, Italy). The HerceptTest was performed according to the manufacturer's standard procedures, and results were scored on a 0 to 3+ scale. A total of 34 (51%) of 66 breast tumors enrolled in this study were positive by FISH. Of the 34 cases amplified by FISH, 9 were negative by IHC using both monoclonal antibody (MoAb) 300G9 and MoAb CB11, with a concordance rate from 80.3% to 83.3%. A higher concordance was verified (92.4%) when we used the HerceptTest Kit. Of the 32 cases found negative with the HerceptTest, FISH analysis identified HER-2 gene amplification in more than 10%. Our results indicate that with the combined use of both methods, several amplified samples classified negative by IHC can be used thus improving therapeutic planning for specific therapy with the monoclonal antibody trastuzumab.

ZD1839 (IRESSA), an EGFR-selective tyrosine kinase inhibitor, enhances taxane activity in bcl-2 overexpressing, multidrug-resistant MCF-7 ADR human breast cancer cells.

Ciardiello F., Caputo R., Borriello G., Del Bufalo D., Biroccio A., Zupi G., Bianco A.R., Tortora G.

Int. J. Cancer, 20,98(3), p.463-9, 2002

Constitutive bcl-2 overexpression increases the tumorigenic and metastatic potential of doxorubicin-resistant, estrogen-independent, MCF-7 ADR human breast cancer cells. We evaluated the sensitivity to taxanes (paclitaxel, docetaxel and IDN 5109) of 2 bcl-2-overexpressing MCF-7 ADR clones and control neomycin-transfected MCF-7 ADR neo cells. The 2 bcl-2-overexpressing MCF-7 ADR clones were relatively resistant to all 3 taxanes, whereas the MCF-7 ADR neo cells were relatively resistant to paclitaxel and docetaxel, but sensitive to IDN 5109. We found that both MCF-7 ADR neo and bcl-2-overexpressing MCF-7 ADR clones express high levels of the epidermal growth factor receptor (EGFR) and its ligand, transforming growth factor-alpha (TGF-alpha). Therefore, we tested the growth inhibitory effect of ZD1839 (Iressa, AstraZeneca, Macclesfield, UK), an orally active, selective EGFR tyrosine kinase inhibitor (EGFR-TKI) that is in clinical development. ZD1839 inhibited the growth in soft agar of all 3 clones in a dose-dependent manner (IC(50) of approximately 0.1 microm). This effect was accompanied by a dose-dependent inhibition of EGFR tyrosine autophosphorylation and of the production of TGF-alpha, basic fibroblast growth factor (bFGF) and vascular endothelial growth factor (VEGF). To determine whether the blockade of EGFR signaling might affect the sensitivity of bcl-2-overexpressing MCF-7 ADR cells to taxanes, cells were treated with ZD1839 in combination with paclitaxel, docetaxel or IDN 5109, and dose-dependent cooperative growth inhibition as well as apoptosis potentiation were observed. Combined treatment with IDN 5109 and ZD1839 also resulted in a significant inhibition of bcl-2 expression in bcl-2-overexpressing MCF-7 ADR cells. These results demonstrate the ability of ZD1839 to overcome taxane resistance in a model of hormone-independent, multidrug-resistant, human breast cancer. Copyright 2002 Wiley-Liss, Inc.

Brief report: transient mutism following posterior fossa surgery studied by single photon emission computed tomography (SPECT).

CLERICO A., SORDI A., RAGNI G., FESTA A., CAPPELLI C., MAINI C.L.

Med. Pediatr. Oncol., 38(6), p.445-8, 2002

No abstract available.

Gemcitabine alone or with cisplatin for the treatment of patients with locally advanced and/or metastatic pancreatic carcinoma: a prospective, randomized phase III study of the Gruppo Oncologia dell'Italia Meridionale.

COLUCCI G., GIULIANI F., GEBBIA V., BIGLIETTO M., RABITTI P., UOMO G., CIGOLARI S., TESTA A., MAIELLO E., LOPEZ M.

Cancer, 15,94(4), p.902-10, 2002

Background: A prospective, randomized Phase III trial was performed to determine whether, compared with gemcitabine (GEM) alone, the addition of cisplatin (CDDP) to GEM was able to improve the time to disease progression and the clinical benefit rate in patients with advanced pancreatic adenocarcinoma. The objective response rate, overall survival rate, and toxicity patterns of patients in the two treatment arms were evaluated as secondary end points.

Methods: Patients with measurable, locally advanced and/or metastatic pancreatic adenocarcinoma were randomized to receive GEM (Arm A) or a combination of GEM and CDDP (Arm B). In Arm A, a dose of 1000 mg/m(2) GEM per week was administered for 7 consecutive weeks, and, after a 2-week rest, treatment was resumed on Days 1, 8, and 15 of a 28-day cycle for 2 cycles. In Arm B, CDDP was given at a dose of 25 mg/m(2) per week 1 hour before GEM at the same dose that was used in Arm A. On Day 22, only GEM was administered. Patients were restaged after the first 7 weeks of therapy and then again after the other 2 cycles.

Results: A total of 107 patients entered the trial: Fifty-four patients were randomized to Arm A, and 53 patients were randomized to Arm B. The median time to disease progression was 8 weeks in Arm A and 20 weeks in Arm B; this difference was statistically significant (P = 0.048). In Arm A, one complete response and four partial responses were recorded on the basis of an intent-to-treat analysis, with an overall response rate of 9.2% (95% confidence interval [95%CI], 3-20%). In Arm B, there were no complete responses, whereas 14 partial responses were achieved, with an overall response rate of 26.4% (95%CI, 15-40%). This difference in the overall response rates was statistically significant (P = 0.02). The tumor growth control rate (i.e., total number of patients who achieved complete responses, partial responses, and stable disease) was 42.6% (95%CI, 29-57%) in Arm A and 56.6% (95%CI, 42-70%) in Arm B. A clinical benefit was observed in 21 of 43 patients (49%) in Arm A and in 20 of 38 patients (52.6%) in Arm B without any significant difference. The median overall survival was 20 weeks for patients in Arm A and 30 weeks for patients in Arm B (P = 0.43). Toxicity was mild in both treatment arms, with no significant differences between the two groups except for the statistically higher incidence of Grade 1-2 asthenia in Arm B (P = 0.046).

Conclusions: The addition of CDDP to GEM significantly improved the median time to disease progression and the overall response rate compared with GEM alone. The clinical benefit rate was similar in both arms, whereas the median overall survival rate was more favorable for Arm B, although the difference did not attain statistical significance. The authors conclude that the combination of CDDP and GEM currently may be considered as an optimal treatment for patients with locally advanced and/or metastatic adenocarcinoma of the pancreas.

Interlaboratory reproducibility of the immunocytochemical assessment of oestrogen and progesterone receptors and proliferative activity in fine needle aspiration of breast cancer.

Confortini M., Carozzi F., Bozzola L., Miccinesi G., Mirri F., Mottolese M., Noferini D., Nizzoli R., Tinacci G., Vocaturo A., Zappa M., Maddau C.

Cytopathology, 13(2), p.92-100, 2002

The purpose of this study was to establish the interlaboratory reproducibility of immunocytochemical analysis of oestrogen (ER) and progesterone (PR) expression and Mib1 growth fraction on fine needle aspiration (FNA) smears. A set of 44 immunostained slides for ER, PR and Mib1 were randomly selected from the archives of the Center for the Study and Prevention of Cancer (CSPO) of Florence, Italy, and submitted for reading to 6 Italian laboratories. The generalized kappa statistic was used as an indicator of agreement among the six laboratories. A good correlation for ER and PR was evident. For Mib1 the results showed some discrepancies. In addition to adequate standardization of procedures, these data confirm that the reliability of the immunocytochemistry is strictly linked to accurate analysis of the results.

The alpha-like RNA polymerase II core subunit 3 (RPB3) is involved in tissue-specific transcription and muscle differentiation via interaction with the myogenic factor myogenin.

Corbi N., Di Padova M., De Angelis R., Bruno T., Libri V., Iezzi S., Floridi A., Fanciulli M., Passananti C.

FASEB J., 16(12), p.1639-41, 2002

RNA polymerase II core subunit 3 (RPB3) is an a-like core subunit of RNA polymerase II (pol II). It is selectively downregulated upon treatment with doxorubicin (dox). Due to the failure of skeletal muscle cells to differentiate when exposed to dox, we hypothesized that RPB3 is involved in muscle differentiation. To this end, we have isolated human muscle RPB3-interacting proteins by using yeast two-hybrid screening. It is of interest that an interaction between RPB3 and the myogenic transcription factor myogenin was identified. This interaction involves a specific region of RPB3 protein that is not homologous to the prokaryotic a subunit. Although RPB3 contacts the basic helix-loop-helix (HLH) region of myogenin, it does not bind other HLH myogenic factors such as MyoD, Myf5, and MRF4. Coimmunoprecipitation experiments indicate that myogenin contacts the pol II complex and that the RPB3 subunit is responsible for this interaction. We show that RPB3 expression is regulated during muscle differentiation. Exogenous expression of RPB3 slightly promotes myogenin transactivation activity and muscle differentiation, whereas the region of RPB3 that contacts myogenin, when used as a dominant negative molecule (Sud), counteracts these effects. These results indicate for the first time that the RPB3 pol II subunit is involved in the regulation of tissue-specific transcription.

DNA damage-dependent acetylation of p73 dictates the selective activation of apoptotic target genes.

Costanzo A., Merlo P., Pediconi N., Fulco M., Sartorelli V., Cole P.A., Fontemaggi G., Fanciulli M., Schiltz L., Blandino G., Balsano C., Levrero M.

Mol. Cell., 9(1), p.175-86, 2002

The tumor suppressor p53 and its close relative p73 are activated in response to DNA damage resulting in either cell cycle arrest or apoptosis. Here, we show that DNA damage induces the acetylation of p73 by the acetyltransferase p300. Inhibiting the enzymatic activity of p300 hampers apoptosis in a p53(-/-) background. Furthermore, a nonacetylatable p73 is defective in activating transcription of the proapoptotic p53AIP1 gene but retains an intact ability to regulate other targets such as p21. Finally, p300-mediated acetylation of p73 requires the protooncogene c-abl. Our results suggest that DNA damage-induced acetylation potentiates the apoptotic function of p73 by enhancing the ability of p73 to selectively activate the transcription of proapoptotic target genes.

Body size indices at different ages and epithelial ovarian cancer risk.

Dal Maso L., Franceschi S., Negri E., Conti E., Montella M., Vaccarella S., Canzonieri V., Parazzini F., La Vecchia C.

Eur. J. Cancer, 38(13), p.1769, 2002

The relationship between body mass measures at diagnosis and/or at different ages and ovarian cancer risk was investigated using an Italian multicentre case-control study. The study, conducted between 1992 and 1999, included 1031 cases of incident, histologically-confirmed epithelial ovarian cancer and 2411 controls admitted to the same network of hos-

pitals for acute non-neoplastic conditions. Odds ratios (OR) and 95% confidence intervals (CI) were obtained using unconditional multiple logistic regression analyses. Weight and body mass index (BMI, kg/m(2)) 1 year prior to diagnosis/interview were not associated with ovarian cancer risk. A direct association emerged with waist-to-hip ratio (W/H) (OR=1.45 in the highest category), particularly among women with stage I-II cancers. Cases also had a higher BMI at age 30 years (OR=1.22). Conversely, cases had lower weight gain between age 30 years and the year prior to diagnosis/interview, both for cases with stage I-II and those with stage III-IV cancers.

Alcohol drinking outside meals and cancers of the upper aero-digestive tract.

Dal Maso L., La Vecchia C., Polesel J., Talamini R., Levi F., Conti E., Zambon P., Negri E., Franceschi S.

Int. J. Cancer, 1,102(4), p.435-7, 2002

In our integrated series of case-control studies conducted in Italy and Switzerland (324 oral, 397 pharyngeal, 271 oesophageal, 506 laryngeal cancers and 3,263 controls), individuals who also drank alcoholic beverages outside meals showed an increased risk compared to those who drank at meals only. At any alcohol intake level, subjects also drinking between meals showed a more elevated risk of developing an upper aero-digestive tract cancer than subjects drinking only at meals. After adjustment for potential covariates, and, after allowance for the number of daily drinks to adjust for different alcohol-intake levels, the odds ratios for subjects reporting drinking outside meals were 1.5 (95% confidence interval [CI]: 1.0-2.2) for oral, 1.8 (95% CI: 1.3-2.5) for pharyngeal, 1.7 (95% CI: 1.2-2.5) for oesophageal and 1.2 (95% CI: 0.9-1.7) for laryngeal cancers. Our findings show that drinking pattern with respect to food consumption may influence alcohol carcinogenesis in the upper digestive and respiratory tract. An "alcohol washing effect" by chewing and swallowing is suggested.

Deletion of the mental retardation gene Gdi1 impairs associative memory and alters social behavior in mice.

D'Adamo P., Welzl H., Papadimitriou S., Raffaele di Barletta M., Tiveron C., Tatangelo L., Pozzi L., Chapman P.F., Knevett S.G., Ramsay M.F., Valtorta F., Leoni C., Menegon A., Wolfer D.P., Lipp H.P., Toniolo D.

Hum. Mol. Genet., 1,11(21), p.2567-80, 2002

Non-specific mental retardation (NSMR) is a common human disorder characterized by mental handicap as the only clinical symptom. Among the recently identified MR genes is GDI1, which encodes alpha Gdi, one of the proteins controlling the activity of the small GTPases of the Rab family in vesicle fusion and intracellular trafficking. We report the cognitive and behavioral characterization of mice carrying a deletion of Gdi1. The Gdi1-deficient mice are fertile and anatomically normal. They appear normal also in many tasks to assess spatial and episodic memory and emotional behavior. Gdi1-deficient mice are impaired in tasks requiring formation of short-term temporal associations, suggesting a defect in short-term memory. In addition, they show lowered aggression and altered social behavior. In mice, as in humans, lack of Gdi1 spares most central nervous system functions and preferentially impairs only a few forebrain functions required to form temporal associations. The general similarity to human mental retardation is striking, and suggests that the Gdi1 mutants may provide insights into the human defect and into the molecular mechanisms important for development of cognitive functions.

Epithelioid hemangioendothelioma of the liver: case report and review of the literature.

D'Annibale M., Piovanello P., Carlini P., Del Nonno F., Sciarretta F., Rossi M., Berloco P., Iappelli M., Lonardo M.T., Perrone Donnorso R.

Transplant Proc., 34(4), p.1248-51, 2002

No abstract available.

Endothelin-B (ET(B)) receptor distribution in tissues of the lizard *Podarcis sicula*.

De Falco M., Laforgia V., Fedele V., Russo T., De Luca L., Cottone G., Varano L., De Luca A.

Cell. Tissue Res., 309(3), p.381-6, 2002

Although the structural and pharmacological properties of endothelin (ET) receptors have been studied, little is known concerning their physiological significance, even if each subtype is supposed to have a distinct physiological action. Thus, to further elucidate the physiological function of this receptor, we examined the presence and distribution of the endothelin-B receptor (ET(B)) subtype in tissues of the lizard Podarcis sicula, using immunoblotting and immunohistochemistry. Immunoblotting indicated that, although the ET(B) receptor appears to be ubiquitous, it is present at different levels in the tissues examined. Furthermore, immunohistochemistry showed that this receptor is very abundant in endothelial cells of all tissues, suggesting that there is an ET(B)-mediated autocrine system of endothelin, which plays an important role in the regulation of endothelial cell function. On the other hand, the presence of ET(B) immunoreactivity also in endocrine systems such as adrenal and thyroid glands suggests an involvement also in the paracrine system of these organs.

Bcl-2 has differing effects on the sensitivity of breast cancer cells depending on the antineoplastic drug used.

Del Bufalo D., Biroccio A., Trisciuoglio D., Bruno T., Floridi A., Aquino A., Zupi G.

Eur. J. Cancer, 38(18), p.2455-62, 2002

The aim of this paper was to evaluate the role of bcl-2 in the susceptibility of the MCF7 ADR human breast carcinoma line overexpressing the P-170 glycoprotein (P-170) to various drugs. The sensitivity to four multidrug resistance (MDR)-related drugs (doxorubicin (ADR), vincristine (VCR), vinblastine (VBL), actinomycin D (ACTD)) and three MDR-non-related drugs (cisplatin (DDP), bischloroethylnitrosourea (BCNU), 5-fluorouracil (5-FU)) was evaluated by the 3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide (MTT) assay in three bcl-2-overexpressing clones obtained from the MCF7 ADR line. We found that the bcl-2-overexpressing clones show increased resistance to DDP and BCNU, while no difference to 5-FU were observed between the control cells and bcl-2 transfectants. Surprisingly, bcl-2-overexpressing clones displayed an increased sensitivity compared with the control cells to the MDR-related drugs ADR, VCR, VBL and ACTD. Focusing on DDP and ADR, we found that the increased resistance of the bcl-2 transfectants to DDP was correlated to their ability to prevent apoptosis, while the enhanced sensitivity to ADR was associated with an increased ADR accumulation and a decreased ADR efflux. Moreover, while bcl-2 overexpression does not induce changes in P-170 glycoprotein expression, it did induce a reduction of the adenosine triphosphate (ATP) levels and basal protein kinase C (PKC) activity, both of which have a crucial role in the regulation of the MDR phenotype. In conclusion, the effect of bcl-2 on antineoplastic sensitivity observed in this study underscores the idea that bcl-2 may have distinct biological effects depending on the anticancer drug used.

Endothelin-1 acts as a survival factor in ovarian carcinoma cells.

Del Bufalo D., Di Castro V., Biroccio A., Salani D., Rosano L., Spinella F., Bagnato A.

Clin. Sci. (Lond), 103(48), p.302S-305S, 2002

The aim of this study was to evaluate the role of endothelin-1 (ET-1) in the sensitivity of ovarian carcinoma to paclitaxel, one of the most common drugs used for the management of this tumour histotype. ET-1 is a powerful mitogenic peptide produced by ovarian carcinomas and it acts as an autocrine growth factor, selectively through ET(A) receptor (ET(A)R), which is predominantly expressed in this tumour. OVCA 433 and HEY, two ovarian carcinoma cell lines, which produce elevated amounts of ET-1 and express abundantly high-affinity ET(A)Rs, were used. As demonstrated by sub-G(1) peak in DNA content histograms and terminal transferase deoxytidyl uridine end labelling assay, we found that paclitaxel induces cytotoxic effect through the activation of apoptosis in both cell lines. When the treatment with paclitaxel was performed in association with ET-1, paclitaxel-induced apoptosis was inhibited. In order to evaluate which ET-1 receptor mediated the effect of ET-1 on protection from paclitaxel-induced apoptosis, we performed experiments using two selective antagonists for ET(A)R (BQ-123) and for

ET(B)R (BQ-788). We showed that ET(A)R blockade inhibits the ET-1-induced survival activity against paclitaxel-mediated apoptosis. However, no effect was observed on blocking ET(B)R with BQ-788. Our results establish a novel role for ET-1 in determining survival of ovarian carcinoma cells and suggest that pharmacological ET(A)R blockade using a specific ET(A)R antagonist may provide a novel approach to the treatment of ovarian carcinoma in combination therapy.

Endothelin-1 protects ovarian carcinoma cells against paclitaxel-induced apoptosis: requirement for Akt activation.

Del Bufalo D., Di Castro V., Biroccio A., Varmi M., Salani D., Rosanò L., Trisciuoglio D., Spinella F., Bagnato A.

Mol. Pharmacol., 61(3), p.524-32, 2002

Endothelin-1 (ET-1) is a powerful mitogenic peptide produced by different tumors. In ovarian carcinoma cells, ET-1 acts as an autocrine growth factor, selectively through ET(A) receptor (ET(A)R), which is predominantly expressed in tumor cells. The aim of this study was to examine whether ET-1 plays a role in the sensitivity of three ovarian carcinoma cell lines (OVCA 433, HEY, and SK-OV-3) to apoptosis induced by two different stimuli. Our results demonstrated that the addition of ET-1 markedly inhibited serum withdrawal and paclitaxel-induced apoptosis in a concentration-dependent manner, as demonstrated by Annexin-V assay, sub-G(1) peak in DNA content histograms, internucleosomal DNA fragmentation, and terminal deoxynucleotidyl transferase-mediated dUTP biotin nick-end labeling method. Pretreatment of the cells with an ET(A)R antagonist, BQ 123, reversed the ET-1-induced protective effect. Paclitaxel-induced apoptosis resulted in the phosphorylation of Bcl-2 that was suppressed by the addition of ET-1. Further analysis of the signaling pathway demonstrated that ET-1 stimulated Akt activation. The phosphatidylinositol 3-kinase (PI3-K) inhibitor wortmannin blocked ET-1-induced Akt phosphorylation. Inhibition of ET-1-stimulated mitogen-activated protein kinase activity did not affect ET-1 protection from paclitaxel-mediated apoptosis. Moreover, BQ 123 blocked the Akt-mediated pathway activated by ET-1, sensitizing ovarian carcinoma cells to paclitaxel treatment. These results establish a novel role for ET-1 in determining protection of ovarian carcinoma cells against paclitaxel-induced apoptosis through Bcl-2-dependent and PI3-K-mediated Akt pathways and suggest that ET-1 and ET(A)R could represent important targets for anticancer therapy.

The 78 kDa glucose-regulated protein (GRP78/BIP) is expressed on the cell membrane, is released into cell culture medium and is also present in human peripheral circulation.

Delpino A., and Castelli M.

Bioscience Reports, 22(3-4), p.12-16, 2002

In human rabdomiosarcoma cells (TE671/RD) chronic exposure to 500 nM thapsigargin (a powerful inhibitor of the endoplasmic reticulum Ca2+-ATPases) resulted in the induction of the stress protein GRP78/BIP. Making use of the surface biotinylation method, followed by the isolation of the GRP78 using ATP-agarose affinity chromatography, it was found that a fraction of the thapsigargin-induced GRP78 is expressed on the cell surface. The presence of GRP78 on the membrane of thapsigargin-treated cells was confirmed by fractionation of cell lysates into a soluble and a membrane fraction, followed by Western blot analysis with an anti-GRP78 antibody. It was also found that conspicuous amounts of GRP78 are present in the culture medium collected from thapsigargin-treated cultures. This extracellular GRP78 originates mostly by an active release from intact cells and does not result solely from the leakage of proteins from dead cells. Moreover, small amounts of circulating, free GRP78 and naturally-occurring anti-GRP78 autoantibodies were detected in the peripheral circulation of healthy human individuals.

Cyclin T: Three forms for different roles in physiological and pathological functions.

De Luca A., De Falco M., Baldi A., Paggi M.G.

J. Cell. Physiol., 194(2), p.101-7, 2003

Cyclins are members of family of proteins involved in the cell cycle regulation. They are regulatory subunits of complexes with proteins called cyclin-dependent kinases (CDKs). There are three forms of cyclin T: cyclin T1, cyclin T2a, and T2b. All cyclin T contain an N-terminal "cyclin homology box," the most conserved region among different members of the cyclin

family that serves to bind CDK9. In addition to the N-terminal cyclin domain, cyclin T contains a putative coiled-coil motif, a His-rich motif, and a C-terminal PEST sequence. The CDK9/cyclin T complex is able to activate gene expression in a catalytic-dependent manner, phosphorylating the carboxy-terminal domain (CTD) of RNA polymerase II. In addition, only cyclin T1 supports interactions between Tat and TAR. The interaction of Tat with cyclin T1 alters the conformation of Tat to enhance the affinity and specificity of the Tat:TAR interaction. On the other hand, CDK9/cyclin T2 complexes are involved in the regulation of terminal differentiation in muscle cells. Copyright 2002 Wiley-Liss, Inc.

Cytotoxicity of dopamine-derived tetrahydroisoquinolines on melanoma cells.

De Marco F., Perluigi M., Marcante M.L., Coccia R., Foppoli C., Blarzino C., Rosei M.A.

Biochem. Pharmacol., 15,64(10), p.1503-12, 2002

Tetrahydroisoquinolines (TIQs) are endogenous alkaloid compounds detected in urine, central nervous system and some peripheral tissues in Mammalia. No data are at present available on TIQ levels in skin, although in vitro biochemical evidences indicate that they may undergo auto-oxidation with production of reactive oxygen species or may be enzymatically converted into melanin pigments. The effect of two catechol-bearing TIQs, salsolinol (SAL) and tetrahydropapaveroline (THP), on the viability of melanotic or amelanotic melanoma cell lines was investigated. Both SAL and THP were well tolerated up to roughly 30 microM and became overtly toxic at higher concentrations, with SAL being better tolerated than THP. Intracellular activity of some antioxidant enzymes, tyrosinase and alpha-ketoglutarate dehydrogenase was also evaluated to assess the cell response to oxidative and metabolic challenge of TIQs treatment. Catalase and superoxide dismutase pretreatment only partially prevented TIQs toxicity while a complete protection was obtained with N-acetylcysteine and GSH. TIQs were able to provoke upregulation of the scavenging enzymes catalase and DT-diaphorase and to determine a decrease of the alpha-ketoglutarate dehydrogenase activity. SAL and THP enhanced tyrosinase activity and melanin production, suggesting that they were indeed tyrosinase substrates leading to melanin formation. The results support the evidence that TIQs were toxic toward melanoma cells, leading to their death by necrosis. TIQs toxicity was likely due to increased oxidative stress by generation of reactive oxygen species and oxidative metabolites. Our study represents an intent to furnish an additional contribution for the comprehension of catechol cytotoxicity.

Hyperthermic-antiblastic perfusion in the treatment of tumor of the extremities.

Di Filippo F., Cavaliere F., Anzà M., Garinei R., Rossi C.R., Deraco M., Perri P., Botti C., Cigna E.

Tumori, 1(3), p.S35-S37, 2002

No abstract available.

Cyclooxygenase-2 (COX-2), epidermal growth factor receptor (EGFR), and Her-2/neu expression in ovarian cancer.

Ferrandina G., Ranelletti F.O., Lauriola L., Fanfani F., Legge F., Mottolese M., Nicotra M.R., Natali P.G., Zakut V.H., Scambia G.

Gynecol. Oncol., 85(2), p.305-10, 2002

Purpose: To investigate whether cyclooxygenase-2 (COX-2) could be a marker of clinical outcome in cervical cancer patients undergoing concomitant chemoradiation plus surgery.

Methods and materials: The study included 33 locally advanced cervical cancer patients; all underwent neoadjuvant chemoradiation, and responsive patients underwent radical surgery. Immunohistochemistry was performed with rabbit antiserum against COX-2.

Results: COX-2 integrated density values (IDVs) in the tumor component ranged from 1.4 to 72.3 (median 15.0); in stromal inflammatory cells, COX-2 IDVs ranged from 1.4 to 96.0 (median 16.0). A statistically significant inverse relation was found between the COX-2 IDVs of the tumor vs. the stromal inflammatory component ($r = -0.52$, $p = 0.0017$). When the ratio between COX-2 IDV in the tumor vs. the stromal compartment was <or=1, it was considered to indicate cervical tumor with COX-2 expression in

the tumor component lower or equivalent to COX-2 expression in the stroma. According to the chosen cutoff value, 17 (51.5%) of 33 were scored as having a high (>1) tumor/stroma COX-2 IDV ratio. Patients with a high tumor/stroma COX-2 IDV ratio had a shorter disease-free survival than did those with a low tumor/stroma COX-2 IDV ratio (p = 0.030). Similarly, those with a high tumor/stroma COX-2 IDV ratio had a shorter overall survival (p = 0.033).

Conclusion: The assessment of COX-2 status in both the tumor and the stromal compartment could provide additional information in the prognostic characterization of cervical cancer patients administered concomitant chemoradiation plus surgery.

Re: Mastectomy and oophorectomy by menstrual cycle phase in women with operable breast cancer.

FERRETTI G., DI COSIMO S., CARLINI P., PAPALDO P., FABI A., COGNETTI F.

Corrispondence. J. Natl. Cancer Inst., 20,94(22), p.1720, 2002

No abstract available

Expression of RALT, a feedback inhibitor of ErbB receptors, is subjected to an integrated transcriptional and post-translational control.

FIORINI M., BALLARO C., SALA G., FALCONE G., ALEMA S., SEGATTO O.

Oncogene, 19,21(42), p.6530-9, 2002

Over-expression studies have demonstrated that RALT (receptor associated late transducer) is a feedback inhibitor of ErbB-2 mitogenic and transforming signals. In growth-arrested cells, expression of endogenous RALT is induced by mitogenic stimuli, is high throughout mid to late G1 and returns to baseline as cells move into S phase. Here, we show that physiological levels of RALT effectively suppress ErbB-2 mitogenic signals. We also investigate the regulatory mechanisms that preside to the control of RALT expression. We demonstrate that pharmacological ablation of extracellular signal-regulated kinase (ERK) activation leads to blockade of RALT expression, unlike genetic and/or pharmacological interference with the activities of PKC, Src family kinases, p38 SAPK and PI-3K. Tamoxifen-dependent activation of an inducible Raf : ER chimera was sufficient to induce RALT expression. Thus, activation of the Ras-Raf-ERK pathway is necessary and sufficient to drive RALT expression. The RALT protein is labile and was found to accumulate robustly upon pharmacological inhibition of the proteasome. We were able to detect ubiquitin-conjugated RALT species in living cells, suggesting that ubiquitinylation targets RALT for proteasome-dependent degradation. Such an integrated transcriptional and post-translational control is likely to provide RALT with the ability to fluctuate timely in order to tune ErbB signals.

Identification of direct p73 target genes combining DNA microarray and chromatin immunoprecipitation analyses.

FONTEMAGGI G., KELA I., AMARIGLIO N., RECHAVI G., KRISHNAMURTHY J., STRANO S., SACCHI A., GIVOL D., BLANDINO G.

J. Biol. Chem., 277, p.43359-43368, 2002

The newly discovered p53 family member, p73, has a striking homology to p53 in both sequence and modular structure. Ectopic expression of p73 promotes transcription of p53 target genes and recapitulates the most characterized p53 biological effects such as growth arrest, apoptosis, and differentiation. Unlike p53-deficient mice that develop normally but are subject to spontaneous tumor formation, p73-deficient mice exhibit severe defects in the development of central nervous system and suffer from inflammation but are not prone to tumor development. These phenotypes suggest different biological activities mediated by p53 and p73 that might reflect activation of specific sets of target genes. Here, we have analyzed the gene expression profile of H1299 cells after p73alpha or p53 activation using oligonucleotide microarrays capable of detecting approximately 11,000 mRNA species. Our results indicate that p73alpha and p53 activate both common and distinct groups of genes. We found 141 and 320 genes whose expression is modulated by p73alpha and p53, respectively. p73alpha up-regulates 85 genes, whereas p53 induces 153 genes, of which 27 are in common

with p73alpha. Functional classification of these genes reveals that they are involved in many aspects of cell function ranging from cell cycle and apoptosis to DNA repair. Furthermore, we report that some of the up-regulated genes are directly activated by p73alpha or p53.

Plant-derived human papillomavirus 16 E7 oncoprotein induces immune response and specific tumor protection.

Franconi R., Di Bonito P., Dibello F., Accardi L., Muller A., Cirilli A., Simeone (I) P., Dona M.G., Venuti A., Giorgi C.

Cancer Res., 1,62(13), p.3654-8, 2002

Vaccine strategies for treatment of human papillomavirus-induced cervical cancer are based on either the recombinant E7 fusion oncoprotein or E7 CTL peptides. The therapeutic potential of the E7-based vaccine depends on the use of different adjuvants. In this study, we describe for the first time the expression of the human papillomavirus 16 E7 protein in Nicotiana benthamiana plant using a potato virus X-derived vector. C57BL/6 mice immunized with E7-containing crude foliar extracts developed both humoral and cell-mediated immune responses and were protected from tumor development after challenge with the E7-expressing C3 tumoral cell line. Our data support the possibility of producing a cost-effective anticancer vaccine in plant with intrinsic adjuvant-like properties.

MDMX stability is regulated by p53-induced caspase cleavage in NIH3T3 mouse fibroblasts.

Gentiletti F., Mancini F., D'Angelo M., Sacchi A., Pontecorvi A., Jochemsen A.G., Moretti F.

Oncogene, 31,21(6), p.867-77, 2002

MDMX is a p53 binding protein, which shares a high degree of homology with MDM2, a negative regulator of the tumor suppressor p53. MDMX has been shown to counteract MDM2-dependent p53 degradation and to stabilize p53 in its inactive form. In this study: we identify two MDMX proteolytic pathways that control its intracellular levels, and show that MDMX post-translational processing may be regulated by p53. Mouse MDMX is cleaved in vitro and in vivo by caspase activity, between aminoacids 358 and 361, producing a p54 minor form. In addition, MDMX is subjected to proteasome-mediated degradation, which concurs to MDMX proteolysis mainly through degradation of p54. A D361A-MDMX mutant, resistant to caspase cleavage, exhibits prolonged intracellular lifetime in comparison to wild-type protein, indicating that caspase cleavage affects stability of MDMX protein probably by modulating its further degradation. Overexpression of exogenous p53 increases the intracellular levels of p54 product. Similarly, activation of endogenous p53 by adriamycin enhances MDMX cleavage and produces a marked decrease of its intracellular levels, while not affecting the D361A-MDMX mutant. In addition, the D361A-MDMX mutant lacks the ability to inhibit p53 transactivation in respect to wild-type MDMX, suggesting that MDMX caspase cleavage play an important functional role. In conclusion, our results demonstrate that, in analogy to MDM2, MDMX may be subjected to proteolytic modifications that regulate its intracellular levels. Moreover, decrease of MDMX protein levels following p53 activation suggests a p53-dependent regulatory feedback of MDMX function.

Circadian optimisation of irinotecan and oxaliplatin efficacy in mice with Glasgow osteosarcoma.

Granda T.G., D'Attino R.M., Filipski E., Vrignaud P., Garufi C., Terzoli E., Bissery M.C., Levi F.

Br. J. Cancer, 18,86(6), p.999-1005, 2002

The relevance of circadian rhythms in irinotecan and oxaliplatin tolerability was investigated with regard to antitumour activity. Mice bearing Glasgow osteosarcoma (GOS) received single agent irinotecan (50 or 60 mg kg(-1) per day) or oxaliplatin (4 or 5.25 mg kg(-1) per day) at one of six dosing times expressed in hours after light onset (3, 7, 11, 15, 19 or 23 hours after light onset). Irinotecan (50 mg kg(-1) per day) and oxaliplatin (4 or 5.25 mg kg(-1) per day) were given 1 min apart at 7 or 15 hours after light onset, or at their respective times of best tolerability (7 hours after light onset for irinotecan and 15 hours after light onset for oxaliplatin) or worst tolerability (15 hours after light onset for irinotecan and 7 hours after light onset for oxaliplatin). Tumour growth rate was nearly halved and per cent increase in estimated life span (% ILS) was - doubled in the mice receiving irinotecan at 7 hours after

light onset as compared to 15 hours after light onset (P<0.05). Results of similar magnitude were obtained with oxaliplatin for both endpoints, yet with 7 hours after light onset corresponding to least efficacy and 15 hours after light onset to best efficacy (P<0.05). Irinotecan addition to oxaliplatin proved therapeutic benefit only if the schedule consisted of irinotecan administration at 7 hours after light onset and oxaliplatin delivery at 15 hours after light onset, i.e. when both drugs were given near their respective "best" circadian times. These would correspond to the middle of the night for irinotecan and the middle of the day for oxaliplatin in humans. Copyright 2002 Cancer Research UK

Tracking regional endoscopy activity.

No abstract available

GRASSI A.

Gastrointest. Endosc., 55(2), p.298-300, 2002

Mammary implants: laboratory simulation of recreational diving conditions.

GRIPPAUDO F.R., MINASI P., ROCCO M., BRUNO A., SARACCA E., MURATORI L.

Br. J. Plast. Surg., 55(2), p.120-3, 2002

To ascertain whether mammary implants are prone to changes in conformation or structure if they are submitted to recreational dives, eight mammary implants were submitted to 40 simulated dives to imitate an average recreational diving schedule. Matching implants were used as a control group. Photographs were taken before and after completion of the protocol. All implants were observed for changes in volume and checked for integrity. Variations in density were evaluated using a Tc scan. No changes in volume occurred after each dive. None of the implants showed ruptures, and Tc scanning failed to reveal any differences in density between tested and control implants. Cohesive-gel implants submitted to the simulated dives showed some morphological alterations. This study indicates that the mammary implants tested could be implanted in a sports diver, but raises concern about whether the increased exposure to stress could negatively affect their durability. Copyright 2002 The British Association of Plastic Surgeons.

Seizures in paediatric Chiari type I malformation: the role of single-photon emission computed tomography.

IANNETTI P., SPALICE A., DE FELICE CICCOLI C., BRUNI O., FESTA A., MAINI C.L.

Acta Paediatr., 91(3), p.313-7, 2002

Chiari type I malformation is one of the posterior fossa maldevelopments with which different clinical manifestations have been associated. Seizures have only recently been associated with Chiari type I malformation. This study reports on 4 children with epilepsy (2M, 2F; age range 8-15 y) diagnosed with Chiari type I malformation by brain magnetic resonance imaging (MRI), in whom no cortical structural involvement was observed. In these patients an interictal ethylcysteinate-dimer-single-photon emission computed tomographic (ECD-SPECT) study was performed to define more precisely the relationship between Chiari type I malformation and seizures. In these patients the hypoperfusion area correlated with electroencephalographic (EEG) focal abnormalities. These hypoperfusions may represent the functional aspect of a cerebral microdysgenesis; seizures and EEG epileptic anomalies may also be linked to the complex network connection between cortices and cerebellar hemispheres. A cerebellar hypoperfusion was also detected in two of the four examined patients, indicating a functional or structural involvement.

Conclusion: Interictal SPECT scans are helpful for the clarification of seizures in patients with Chiari type I malformation.

Bcl-2 overexpression in human melanoma cells increases angiogenesis through VEGF mRNA stabilization and HIF-1-mediated transcriptional activity.

Iervolino A., Trisciuoglio D., Ribatti D., Candiloro A., Biroccio A., Zupi G., Del Bufalo D.

FASEB J., 16(11), p.1453-5, 2002

The aim of this paper was to study the molecular mechanisms by which bcl-2 increases hypoxia-induced vascular endothelial growth factor (VEGF) expression. We demonstrated that bcl-2 overexpression in M14 human melanoma cell line enhances hypoxia-induced VEGF mRNA stability and promoter activation. In particular, the half-life of the message was longer in bcl-2 transfectants (approximately 330 min) than in control cells (approximately 180 min). In addition, bcl-2 overexpression increased VEGF promoter activity through the hypoxia-inducible factor-1 (HIF-1) transcription factor. Increased HIF-1a protein expression and DNA binding activity were detected in bcl-2 overexpressing cells compared with control cells. An enhanced functional activity of secreted VEGF was found both in in vitro and in vivo angiogenic assays, and the use of VEGF specific antibodies validated the role of VEGF on bcl-2-induced angiogenesis. Taken together our results indicate that bcl-2 plays an important role in melanoma angiogenesis, and that VEGF mRNA stabilization and HIF-1-mediated transcriptional activity are two important control points in bcl-2/hypoxia-induced VEGF expression.

Carcinoembryonic antigen as a target for specific antitumor immunotherapy of head and neck cancer.

Kass E.S., Greiner J.W., Kantor J.A., Tsang K.Y., Guadagni F., Chen Z., Clark B., De Pascalis R., Schlom J., Van Waes C.

Cancer Res., 1,62(17), p.5049-57, 2002

Human carcinoembryonic antigen (CEA) is an oncofetal glycoprotein overexpression of which by gastrointestinal carcinomas is well known. Expression of CEA in head and neck cancer (HNC) is not widely recognized. It is important to note that most of these studies used polyclonal antibodies that may have cross-reactivity with CEA-related antigens. Currently, CEA is being evaluated in preclinical and clinical studies as a target for specific immunotherapy against gastrointestinal adenocarcinomas that express the antigen. This study was conducted to evaluate CEA as a potential target for specific immunotherapy against HNC. Immunohistochemical analysis of tumor tissue from 69 cases of squamous cell carcinoma (SCC) of the head and neck using a CEA-specific monoclonal antibody (COL-1) showed the majority to be positive for CEA. Tumor cell lines derived from human HNC were screened for CEA transcripts using nested reverse transcription-PCR. Constitutive expression of CEA mRNA was detected in 7 of 10 HNC lines. CEA protein was detectable in lysates from all 7 of the lines by quantitative fluoroimmunometry. SDS-PAGE/Western blot analysis of cell lysates from these lines showed a COL-1 immunoreactive product with a molecular weight equivalent to that of CEA. Cell surface expression of CEA was low for the SCC lines; however, there was moderate to strong cytoplasmic staining intensity for all of the CEA(+) HNC lines by immunocytochemistry. Additional supportive evidence for CEA as a target was demonstrated by the presence of cytolytic activity of an HLA-A2-restricted/CEA-epitope-specific human CTL against a CEA-overexpressing HNC-derived SCC line. These results suggest that CEA may be considered as a possible target for specific vaccine-mediated immunotherapy against HNCs.

Electroretinographic abnormalities in parents of patients with Leber congenital maurosis who have heterozygous GUCY2D mutations.

Koenekoop R.K., Fishman G.A., Iannaccone A., Ezzeldin H., Ciccarelli M.L., Baldi A., Sunness J.S., Lotery A.J., Jablonski M.M., Pittler S.J., Maumenee I.

Arch. Ophthalmol., 120(10), p.1325-30, 2002

Background: Leber congenital amaurosis (LCA) is an infrequently encountered congenital form of retinitis pigmentosa with marked genetic and clinical heterogeneity. Thus far, 10 genes have been identified in this disorder since 1996. In the future, LCA may become treatable by gene and/or pharmacological intervention, and these therapies will likely be gene specific, giving major significance to rapid gene identification and gene-phenotype studies.

Objective: To test the hypothesis that parents of patients with LCA have identifiable electroretinographic and psychophysical changes.

Subjects, materials, and methods: Complete eye examinations and electroretinographic

studies were performed on 2 sets of parents whose offspring were diagnosed as having LCA and who were found to carry a mutation in 1 of the 10 LCA genes-GUCY2D. One set of parents also underwent static perimetry threshold measurements.

Results: We found that single flash-light-adapted a- and b-wave amplitudes, 30-Hz flicker, or both cone signals were significantly decreased in amplitude in 4 heterozygotes, while 2 parents showed delayed 30-Hz flicker implicit times. Electroretinographic rod-mediated signals were normal in 2 of the heterozygotes, but subnormal in 2. Static perimetry testing showed normal thresholds in the 2 heterozygotes tested.

Main outcome measures: Single flash-light-adapted a- and b-wave amplitudes and implicit times, 30- or 32-Hz flicker amplitudes and implicit times, rod-mediated signals, and dark-adapted, rod-mediated thresholds.

Conclusions: Some carrier parents of patients with LCA and a GUCY2D mutation develop measurable, cone and possibly rod abnormalities most consistent with a mild cone-rod dysfunction. This correlates well with the known retinal expression pattern of GUCY2D, which is considerably higher in cone compared with rod photoreceptor cells.

Palliative treatment of esophageal tumors.

LAPENTA R., ASSISI D., GRASSI A., LAURIA V., STIGLIANO V., CASALE V.

J. Exp. Clin. Cancer Res., 21(4), p.503-507, 2002

In malignant dysphagia expandable metal stents are commonly used as palliative treatment, but early and late complications and the improvement of dysphagia have not been well described. This report summarizes our experience with expandable metal stents for malignant dysphagia. From 1995 to 2000, we placed 38 metal stents in 36 patients with malignant dysphagia from unresectable esophageal cancer (94.4%). Dysphagia scores, complications and modality of reintervention were evaluated. Dysphagia scores decreased from 3.2 before the stent placement to 2. Immediate complications occured in one patient because of severe pain, it was not possible to perform endoscopic treatments. Other complications included tracheoesophageal fistula (2 patients), tumor overgrowth (5 patients), new stent placements (2 patients), dislocation (2 patients). In conclusions expandable metal stents are safe and effective in the treatment of malignant dysphagia.

Conservative treatment for patients over 80 years with acute myelogenous leukemia.

LATAGLIATA R., ALIMENA G., CARMOSINO I., BRECCIA M., BORZA P.A., BONGARZONI V., COPIA C., SPADEA A., PINAZZI B., FRATTARELLI N., FERRARA F., PETTI M.C., MANDELLI F.

Am. J. Hematol., 71(4), p.256-9, 2002

In order to evaluate the best treatment of very elderly patients with AML, we have retrospectively analyzed 60 cases of patients aged more than 80 years, with a diagnosis of AML and observed from January 1988 to December 1998. Six of these patients were subsequently referred to other centers; of the remaining 54 patients, 20 (37%) received only supportive care, whereas 34 (63%) required palliative chemotherapy to control leukocytosis, after a median time from diagnosis of 9 days (range 0-253). Median overall survival was 13 weeks (range 1-105): 21 (39%) and 6 (11%) patients survived more than 6 and 12 months, respectively. Twenty-eight patients (51.8%) died from progressive disease, 19 (35.1%) died from AML-related or unrelated causes in the phase of stable disease, while in 7 patients the cause of death was unknown. In univariate analysis, PS > 2 and WBC > 50 x 10(9)/L had an adverse prognostic significance on survival. Our results, as compared with those reported in the literature for patients over 80 years treated with intensive chemotherapy, support the idea that intensive chemotherapy is usually not indicated in very elderly patients with AML, and that conservative treatment and the primary strategy of "watch-and-wait" presently seems to be the best choice.

Therapy-related myelodysplastic syndrome-acute myelogenous leukemia in patients treated for acute promyelocytic leukemia: an emerging problem.

LATAGLIATA R., PETTI M.C., FENU S., MANCINI M., SPIRITI M.A., BRECCIA M., BRUNETTI G.A., AVVISATI G., LO COCO F., MANDELLI F.

Blood, 199(3), p.822-4, 2002

The use of all-trans retinoic acid (ATRA) in combination with chemotherapy has markedly improved the prognosis for patients with acute promyelocytic leukemia (APL); the higher complete remission (CR) and survival rates now reported in this disease almost approach those obtained for other highly curable hematologic malignancies. Of 77 patients with APL who were consecutively treated at a single institution and who achieved CR after induction and consolidation therapy, 5 (6.5%) acquired therapy-related myelodysplasia (tMDS), acute myelogenous leukemia (AML), or both (tMDS-AML). Of these, 3 of 46 (6.5%) patients received front-line chemotherapy with or without ATRA and acquired tMDS-AML while in first remission of APL. Two underwent repeated chemotherapy cycles with ATRA because of APL relapse and acquired tMDS-AML while in the second or third remission of APL. In 2 patients, clinical and biologic characteristics of tMDS-AML were as expected for postalkylating forms (long latency, MDS phase preceding AML, karyotypic aberrations involving chromosomes 5 or 7), even though one of them had not previously received alkylating drugs. Three of the 5 patients died shortly after tMDS-AML diagnosis, one is alive with tMDS, and one is alive and in CR after allogeneic bone marrow transplantation. The occurrence of tMDS-AML after successful therapy for APL is an emerging problem. The availability of prognostic score systems at initial diagnosis and monitoring of residual disease by polymerase chain reaction might allow better tailoring of treatment intensity in APL to spare unnecessary toxicity and to minimize the risk for tMDS-AML in patients who are presumably cured.

Monoclonal antibodies raised against Xenopus p53 interact with human p73.

LE BRAS M., DELATTRE V., BENSAAD K., BLANDINO G., SOUSSI T.

Oncogene, 14,21(8), p.1304-8, 2002

The p53 tumor suppressor gene belongs to a multigene family that includes two paralogues, p63 and p73. The structure of the p63 and p73 genes is quite similar, but both have common activities with p53, such as DNA binding and transactivation. Both p53 and p73 bind to mdm2, but only p53 is degraded through the activity of mdm2. p63 neither binds to nor is degraded by mdm2 despite important conservation in the key interacting residues. Using a panel of monoclonal antibodies raised against human and Xenopus p53, we have been able to find several antibodies that cross-react strongly with human p73. These antibodies react both with exogenous p73 expressed in mammalian cells and with endogenous p73. Interestingly, all these antibodies react with the same epitope localized in the amino-terminus of p53, but have no cross-reaction with p63. This epitope corresponds to the exact mdm2 binding site to p53. These antibodies inhibit the interaction between either p53 or p73 and mdm2, and may be useful tools for the study of these proteins. Furthermore, our studies suggest that there exist specific spatial requirements for the interaction between p53 or p73 and mdm2.

Increasing single epirubicin doses in advanced soft tissue sarcomas.

LOPEZ M., VICI P., DI LAURO L., CARPANO S.

J. Clin. Oncol., 1,20(5), p.1329-34, 2002

Purpose: To evaluate the maximum-tolerated dose and the clinical efficacy of epirubicin in patients with advanced soft tissue sarcoma.

Patients and methods: Sixty-one patients were treated at three different epirubicin dose levels: 140 mg/m(2) (six patients), 160 mg/m(2) (52 patients), and 180 mg/m(2) (three patients). Cycles were repeated every 3 weeks for a maximum of eight cycles. The first two dose levels proved to be feasible and safe without dose-limiting toxicity (DLT). Because the first three patients entering the third dose level experienced DLT, subsequent patients received the next lower dose level.

Results: The overall response rate was 44% (95% confidence interval, +/- 12%), with six complete (10%) and 21 partial (34%) responses. Responses seemed related to epirubicin dose level, because the response rate was 17%, 44%, and 100% for the three dose levels (chi(2) test for

trend, P =.02). Median response duration, median time to progression, and median overall survival were 10, 8, and 15 months, respectively. Myelosuppression was the most frequent side effect, with grade 3 or 4 neutropenia occurring in 79% of the patients; 31% of patients were febrile. Nonhematologic toxicity was mainly grades 1 and 2. The mean epirubicin dose-intensity was 49 mg/m(2) per week.

Conclusion: The third epirubicin dose level (180 mg/m(2)) was the maximum-tolerated dose. The recommended drug dose for clinical use is 160 mg/m(2) every 3 weeks with hematopoietic support. Single high-dose epirubicin is effective as first-line treatment and should be preferentially used whenever a high response rate is important to allow the resection of an otherwise unresectable disease or whenever it might result in a significant symptomatic benefit.

Hepatic intra-arterial chemotherapy in the treatment of non-resectable colorectal liver metastasis: personal experience

MANCINI R., GARUFI C., PUGLIESE P., PERRONE M., CATERINO M., GIUNTA S., COSIMELLI M.

Tumori, 1(3), p.S30-S32, 2002

No abstract available.

Mxi1 inhibits the proliferation of U87 glioma cells through down-regulation of cyclin B1 gene expression.

MANNI I., TUNICI P., CIRENEI N., ALBAROSA R., COLOMBO B.M., ROZ L., SACCHI A., PIAGGIO G., FINOCCHIARO G.

Br. J. Cancer, 1,86(3), p.477-84, 2002

Mxi1 is a Mad family member that plays a role in cell proliferation and differentiation. To test the role of Mxi1 on tumorigenesis of glioma cells we transfected a CMV-driven MXI1 cDNA in U87 human glioblastoma cells. Two clones were isolated expressing MXI1 levels 18- and 3.5-fold higher than wild-type U87 cells (clone U87.Mxi1.14 and U87.Mxi1.22, respectively). In vivo, U87.Mxi1.14 cells were not tumorigenic in nude mice and delayed development of tumours was observed with U87.Mxi1.22 cells. In vitro, the proliferation rate was partially and strongly inhibited in U87.Mxi1.22 and U87.Mxi1.14 cells respectively. The cell cycle analysis revealed a relevant accumulation of U87.Mxi1.14 cells in the G(2)/M phase. Interestingly, the expression of cyclin B1 was inhibited to about 60% in U87.Mxi1.14 cells. This inhibition occurs at the transcriptional level and depends, at least in part, on the E-box present on the cyclin B1 promoter. Consistent with this, the endogenous Mxi1 binds this E-box in vitro. Thus, our findings indicate that Mxi1 can act as a tumour suppressor in human glioblastomas through a molecular mechanism involving the transcriptional down-regulation of cyclin B1 gene expression. Copyright 2002 The Cancer Research Campaign.

Vulvar vestibulitis syndrome: an overview of non-surgical treatment.

MARIANI L.

Eur. J. Obstet. Gynecol. Reprod. Biol., 101, p.109-112, 2002

Vulvar vestibulitis syndrome, which represents one of the major cause of dyspareunia, is a puzzling clinical entity. Although many treatment options have been employed, a rationale therapeutic strategy is still not stated. The present article reviews the most popular medical approaches of such entity (biofeedback, tricyclic antidepressants, interferon psychologic-behavioural therapy, diet modification), as well as those to avoid. Tricyclic antidepressants and biofeedback of the pelvic floor muscles represents the first line effective therapy. Moreover, psychological counselling must support any treatment options.

Minimal sentinel node procedure for staging early breast cancer.

Mariotti S., Buonomo O., Guadagni F., Spila A., Schiaroli S., Cipriani C., Simonetti G., Felici A., Granal A.V., Bellotti A., Cabassi A., Casciani C.U., Roselli M.

Tumori, 88(3), p.S45-7, 2002

Aims and background: Sentinel lymph node dissection (SLND) has recently been evaluated as a new staging technique for early breast cancer. To minimize the extent of surgery, the feasibility of eradicating primary breast lesions and the relative sentinel lymph nodes (SLN) under regional anesthesia was evaluated in this study.

Methods and study design: A selected population of 76 patients with suspected operable breast cancer and no clinically palpable lymph nodes was enrolled in the study. Intra- and perilesional administration of a radiotracer was performed. Lymphoscintigraphy was carried out to confirm the drainage pathway and locate the SLN. The following day, after inducing a nervous block induction of the ipsilateral intercostal nerves, we performed the surgical procedure with the help of a hand-held gamma-detecting probe. In case the primary lesion was diagnosed as invasive carcinoma by frozen section, the SLN and the remaining axillary lymph nodes (non-SLNs) were removed. The status of SLN and non-SLNs was compared.

Results: The primary breast lesion was located and excised in all cases (identification rate: 100%). Lymphoscintigraphy positively identified SLNs in 40/45 (89%) patients; in five patients no lymphatic drainage was detected. In 38 cases an average of 1.5 SLNs and 14 non-SLNs per patient were removed and pathologically analyzed; the remaining two patients showed SLNs in the internal mammary chain, which were not excised. Twenty-nine percent of the patients showed metastatic disease in the lymph nodes examined. Of all patients with affected nodes, 55% had cancer cells only in the SLN. No false negatives (skip metastases) were found. No immediate or long-term anesthesia-related complications (e.g., pleural lesions, intravascular injection) were observed.

Conclusions: Our data confirm the feasibility of single radiotracer administration for both occult lesion and SLN localization as well as the usefulness of SLND in staging early breast cancer. Regional anesthesia resulted in easy management and good patient compliance. This time-saving procedure allowed the completion of the whole surgical plan, reducing the recovery time without modifying the effectiveness of surgery.

Amitriptyline in neuropathic cancer pain in patients on morphine therapy: a randomized placebo-controlled, double-blind crossover study.

Mercadante S., Arcuri E., Tirelli W., Villari P., Casuccio A.

Tumori, 88(3), p.239-42, 2002

Aims and background: Amitriptyline is the most common analgesic adjuvant used in cancer patients with neuropathic pain, even though no specific studies have demonstrated a benefit. A randomized placebo-controlled, double-blind crossover study was designed to evidence the effects of amitriptyline in patients with neuropathic cancer pain.

Methods: Sixteen advanced cancer patients with neuropathic pain on systemic morphine therapy, no longer receiving oncologic treatment, presenting moderate pain (about 4 or more, but less than 7, on a numerical scale of 0-10) in the last week, and given a stable morphine dose in the last 2 days were admitted to the study. During the first week of study, patients were administered 25 mg of amitriptyline or equivalent drops of placebo at night for 3 days and 50 mg for the following 4 days. Doses for patients aged more than 65 years were 15 mg (first 3 days) and 30 mg (3 days after). After a week, a crossover took place for the second week, with the other treatment at an inverse sequence. Opioid consumption, pain intensity, symptoms and adverse effects, mood, sleep, patient's preference, quality of life before starting the study, the first week after and the second week after were recorded.

Results: No significant benefits in analgesia were found in the global pain intensity of the previous week of treatment, the least pain intensity or the pain evaluated just after a week of treatment, at the moment of the visit, when amitriptyline was compared with placebo. A significant difference was evidenced for the worst pain ($P < 0.035$). No differences in opioid doses during the period of study were found. Drowsiness, confusion and dry mouth were significantly more intense with amitriptyline than with placebo ($P < 0.036$, 0.003, and 0.034, respectively). There were no substantial differences between the two treatments in Spitzer's quality of life

score and for each item. No differences in patients' preference for the two treatment periods were found. The analgesic effects of amitriptyline were slight and associated with adverse effects.

Conclusions: In light of the results obtained in the study, the extensive use of the drug for cancer pain should be questioned.

The synergistic activity of thyroid transcription factor 1 and Pax 8 relies on the promoter/enhancer interplay.

MICCADEI S., DE LEO R., ZAMMARCHI E., NATALI P.G., CIVITAREALE D.

Mol. Endocrinol., 16(4), p.837-46, 2002

The transcription factors, thyroid transcription factor 1 (TTF-1) and Pax 8, play a pivotal role in the transcriptional regulation of the thyroid differentiation marker genes and in the differentiation of the thyroid follicular cells. They have a very restricted tissue distribution, and the thyrocyte is the only cell type with the simultaneous expression of these factors. Here we show that TTF-1 and Pax 8 cooperatively activate their target genes and that their synergistic activity requires the cross-talk between enhancer and gene promoter. We have characterized the cis and trans requirements of the TTF1/Pax 8 synergistic activity on the thyroperoxidase gene. We show that their synergy is also important for thyroglobulin gene transcription.

Cancer prevalence in European registry areas.

MICHELI A., MUGNO E., KROGH V., QUINN M.J., COLEMAN M., HAKULINEN T., GATTA G., BERRINO F., CAPOCACCIA R., CONTI E.M.S. AND EUROPREVAL WORKING GROUP.

Ann. Oncol., 13(6), p.840-65, 2002

Background: Information on cancer prevalence is of major importance for health planning and resource allocation. However, systematic information on cancer prevalence is largely unavailable.

Materials and methods: Thirty-eight population-based cancer registries from 17 European countries, participating in EUROPREVAL, provided data on almost 3 million cancer patients diagnosed from 1970 to 1992. Standardised data collection and validation procedures were used and the whole data set was analysed using proven methodology. The prevalence of stomach, colon, rectum, lung, breast, cervix uteri, corpus uteri and prostate cancer, as well as of melanoma of skin, Hodgkin's disease, leukaemia and all malignant neoplasms combined, were estimated for the end of 1992.

Results: There were large differences between countries in the prevalence of all cancers combined; estimates ranged from 1170 per 100000 in the Polish cancer registration areas to 3050 per 100000 in southern Sweden. For most cancers, the Swedish, Swiss, German and Italian areas had high prevalence, and the Polish, Estonian, Slovakian and Slovenian areas had low prevalence. Of the total prevalent cases, 61% were women and 57% were 65 years of age or older. Cases diagnosed within 2 years of the reference date formed 22% of all prevalent cases. Breast cancer accounted for 34% of all prevalent cancers in females and colorectal cancer for 15% in males. Prevalence tended to be high where cancer incidence was high, but the prevalence was highest in countries where survival was also high. Prevalence was low where general mortality was high (correlation between general mortality and the prevalence of all cancers = -0.64) and high where gross domestic product was high (correlation = +0.79). Thus, the richer areas of Europe had higher prevalence, suggesting that prevalence will increase with economic development.

Conclusions: EUROPREVAL is the largest project on prevalence conducted to date. It has provided complete and accurate estimates of cancer prevalence in Europe, constituting essential information for cancer management. The expected increases in prevalence with economic development will require more resources; allocation to primary prevention should therefore be prioritised.

The human integrin beta4B and beta4C variants are not expressed in a tissue-specific manner.

MICHELONI A., FALCIONI R., ZAMBRUNO G., D'ALESSIO M.

FEBS Lett., 22,519(1-3), p.238-9, 2002

No abstract available.

Re: Mastectomy and oophorectomy by menstrual cycle phase in women with operable breast cancer.

MILELLA M., GIANNARELLI D., FERRARESI V., MOTTOLESE M., BOTTI C., NISTICÒ C.

Corrispondence. J. Natl. Cancer Inst., 20,94(22), p.1719-1720, 2002

No abstract available.

Clinicoprognostic implications of increased serum levels of vascular endothelial growth factor and basic fibroblastic growth factor in early B-cell chronic lymphocytic leukaemia.

MOLICA S.,VITELLI G., LEVATO D., RICCIOTTI A., DIGIESI G.

Br. J. Cancer, 7,86(1), p.31-5, 2002

To assess the relative merit of increased serum levels of vascular endothelial growth factor and basic fibroblastic growth factor in predicting the risk of disease progression of patients with early B-cell chronic lymphocytic leukaemia we analyzed 81 Binet stage A patients whose sera were taken at the time of diagnosis and evaluated for the presence of vascular endothelial growth factor and basic fibroblast growth factor using an enzyme-linked immunosorbent assay. Serum levels of vascular endothelial growth factor positively correlated with Rai sub-stages (P=0.03), peripheral blood lymphocytosis (P=0.03), bone marrow histology (P=0.04) and beta2-microglobulin (beta2-m) (P=0.006). When dealing with basic fibroblast growth factor only a correlation with Rai sub-stages (P=0.02) could be found. Different cut-offs set on the basis of a stratification in quartiles, failed to demonstrate any correlation between serum levels of basic fibroblast growth factor and disease progression. In contrast, patients with increased serum levels of vascular endothelial growth factor (above median value, 203 pg ml(-1)) had a three times increased risk of disease progression, although, in multivariate analysis only Rai sub-stages (P=0.0001) and lymphocyte doubling time (P=0.002) retained their prognostic significance. Low levels of vascular endothelial growth factor were indicative of good clinical outcome in the subgroup of patients with either low (P=0.02) or high (P=0.03) beta2-m concentration. Finally, the highest prognostic power was obtained when serum vascular endothelial growth factor and beta2-m were examined in combination. Median of progression-free survival of patients who had both serum vascular endothelial growth factor and beta2-m higher than median value was only 13 months, in contrast median progression-free survival of patients with one marker increased (i.e. above the 50th percentile) was 40 months. Patients with both markers below the median experienced the best clinical outcome (median progression-free survival not reached at 40 months). In conclusion, serum levels of either vascular endothelial growth factor or basic fibroblast growth factor are high in patients with early chronic lymphocytic leukaemia, however, only vascular endothelial growth factor predicts behaviour of disease and helps to refine the prognosis of stage A patients.

Expression of the beta 4 integrin subunit induces monocytic differentiation of 32D/v-Abl cells.

MORENA A., RICCIONI S., MARCHETTI A., POLCINI A.T., MERCURIO A.M., BLANDINO G., SACCHI A., FALCIONI R.

Blood, 1,100(1), p.96-106, 2002

The alpha 6 beta 4 integrin is the receptor for various laminin isoforms and is a component of the hemidesmosome. Increased expression levels of this integrin correlate with the aggressive phenotype of many epithelial tumors compared with surrounding normal tissue. Furthermore, the long cytoplasmic tail of the beta 4 integrin subunit has been implicated in several signal transduction pathways that are involved not only in invasion, but also in proliferation and apoptosis. Here we report that the exogenous expression of beta 4 integrin in 32D/v-abl-transformed cells reduces tumor ag-

gressiveness in vivo and strongly inhibits cell proliferation in vitro by inducing monocytic differentiation. These effects are accompanied by growth arrest and p73 protein accumulation. The hypothesis that the inhibition of v-Abl oncogenic capacity could allow the activation of the endogenous c-Abl was tested in RKO cells. The results clearly demonstrated a strong increase of c-Abl phosphorylation that is accompanied by its association with p73 protein. Overall, the reported findings indicate that alpha 6 beta 4 integrin promotes growth arrest and differentiation by modulating Abl kinases and p73 protein pathway(s).

Crystallization and preliminary X-ray analysis of substrate complexes of leucine dehydrogenase from Thermoactinomyces intermedius.

MURANOVA T.A., RUZHEINIKOV S.N., SEDELNIKOVA S.E., BAKER P.J., PASQUO A., GALKIN A., ESAKI N., OHSHIMA T., SODA K., RICE D.W.

Acta Crystallogr. D. Biol. Crystallogr., 58(Pt 6 Pt 2), p.1059-62, 2002

Leucine dehydrogenase is an octameric enzyme which belongs to the superfamily of amino-acid dehydrogenases and catalyses the reversible oxidative deamination of leucine to 2-ketoisocaproate, with the corresponding reduction of the co-factor NAD(+). Catalysis by this enzyme is thought to involve a large-scale motion of the enzyme's two domains between an 'open' and 'closed' form, with the latter representing a conformation of the enzyme in which the partners involved in the hydride-transfer reaction are appropriately positioned for catalysis. Whilst a structure for the open form of the enzyme has been determined, the nature of the closed form has yet to be observed. In order to trap a closed form, crystals of the complexes of leucine dehydrogenase from Thermoactinomyces intermedius with 2-ketoisocaproate and with 2-ketoisocaproate and NAD(+) have been obtained by the hanging-drop vapour-diffusion method using PEG 4000 as a precipitant. The crystals of the binary complex with 2-ketoisocaproate belong to space group P2(1)2(1)2(1), with approximate unit-cell parameters a = 106, b = 118, c = 320 A and an octamer in the asymmetric unit, corresponding to a V(M) of 3.1 A(3) Da(-1). The crystals of the non-productive ternary complex belong to space group P6(1) or P6(5), with approximate unit-cell parameters a = b = 117, c = 502 A and an octamer in the asymmetric unit, corresponding to a V(M) of 3.0 A(3) Da(-1). These crystals diffract X-rays on a synchrotron-radiation source to at least 2.8 and 3.3 A resolution, respectively, and are suitable for a full structure determination.

Signaling through estrogen receptors modulates telomerase activity in human prostate cancer.

NANNI S., NARDUCCI M., DELLA PIETRA L., MORETTI F., GRASSELLI A., DE CARLI P., SACCHI A., PONTECORVI A., FARSETTI A.

J. Clin. Invest., 110(2), p.219-27, 2002

Sex steroid hormone receptors play a central role in all stages of prostate cancer. Here, we tested whether estrogen receptor (ER) signaling contributes to telomerase activation, an early event in prostate tumorigenesis. Following 17beta-estradiol (E(2)) treatment, both mRNA encoding the catalytic subunit of human telomerase (hTERT) and telomerase activity were promptly induced in human prostate normal epithelial cells, fresh explants from benign prostate hyperplasia, and prostate cancer explants and cell lines. Reporter expression studies and in vivo chromatin immunoprecipitation assays revealed E(2)-dependent hTERT promoter induction and showed that both ERalpha and ERbeta bound this sequence. Crucially, addition of the anti-estrogen 4-hydroxytamoxifen caused a differential recruitment in vivo of ERalpha and ERbeta onto the hTERT promoter and inhibited telomerase activity. Treatment with the aromatase inhibitor letrozole, which prevented testosterone-mediated interaction between ER and the hTERT estrogen response element, resulted in a negative regulation of telomerase activity. Thus, intracellular conversion of androgens to estrogens may contribute to the etiopathogenesis of prostate cancer. Given the present evidence for direct control of hTERT gene expression and telomerase activity in the prostate by the ER, we suggest that this transcriptional regulator represents a possible therapeutic target in prostate cancer.

Mice overexpressing placenta growth factor exhibit increased vascularization and vessel permeability.

Odorisio T., Schietroma C., Zaccaria M.L., Cianfarani F., Tiveron C., Tatangelo L., Failla C.M., Zambruno G.

J. Cell. Sci., 15,115(12), p.2559-67, 2002

Placenta growth factor (PlGF) is a member of the vascular endothelial growth factor (VEGF) family, comprising at least five cytokines specifically involved in the regulation of vascular and/or lymphatic endothelium differentiation. Several lines of evidence indicate a role for PlGF in monocyte chemotaxis and in potentiating the activity of VEGF, but the exact function of this cytokine is not fully understood. To define the biological role of PlGF in vivo, we have produced a transgenic mouse model overexpressing this factor in the skin by using a keratin 14 promoter cassette. Our data indicate that PlGF has strong angiogenic properties in both fetal and adult life. PlGF overexpression results in a substantial increase in the number, branching and size of dermal blood vessels as well as in enhanced vascular permeability. Indeed, intradermally injected recombinant PlGF was able to induce vessel permeability in wild-type mice. The analysis of vascular endothelial growth factor receptor 1/flt-1 and vascular endothelial growth factor receptor 2/flk-1 indicates that the two receptors are induced in the skin endothelium of transgenic mice suggesting that both are involved in mediating the effect of overexpressed PlGF.

Molecular stability of DNA typing short tandem repeats in the mammary tree of patients with breast cancer.

Orlandi F., Barucca A., Biagini G., Pasqui G., Mottolese M., Botti C., Bracalenti C., Cardarelli M.A., Concetti A., Venanzi FM.

Diagn. Mol. Pathol., 11(1), p.41-6, 2002

Archival pathologic specimens are a rich source for the studies of hereditary diseases, cancer genetics, and identification cases in forensic science. In this study, the intraindividual consistency of eight identifying microsatellite polymorphisms (i.e., HMTH01, vWFA31, F13A, MITMH26, FES-FPS, CD4, TPOX, CSF1PO)in a cohort of 40 patients with invasive breast carcinoma were analyzed. Nests of cancer and adjacent morphologically normal ductal-lobular structures (TDLUs) were microdissected as discrete regions from hematoxylin-eosin-stained slides. As controls for each case, DNA templates were prepared from TDLUs located in nontumor quadrants and from unaffected breast skin. Over 1,400 carefully controlled PCR reactions were reviewed, and no evidence was found for microsatellite mismatches among intraindividual cancer and control DNAs. The negative results, supported by validation experiments, strongly argue that alterations of simple repeats are rare somatic events during the onset and progression of breast cancer. This study suggests that PCR artifacts may be a relevant cause of misdiagnosis of microsatellite instability in human sporadic cancer.

Griseofulvin induces mitotic delay and aneuploidy in bone marrow cells of orally treated mice.

Pacchierotti F., Bassani B., Marchetti F., Tiveron C.

Mutagenesis, 17(3), p.219-22, 2002

Griseofulvin (GF) is a fungicide drug well characterized for its aneugenic activity in vitro. In vivo strong evidence of aneuploidy and polyploidy induction has been obtained in germ cells, especially in oocytes. More controversial are the data on the aneugenicity of griseofulvin in somatic cells. In this paper we provide evidence that GF induces non-disjunction and cell cycle delay in bone marrow cells of orally treated mice. Adult female mice were administered olive oil suspensions of 200, 666 or 2000 mg/kg GF by gavage and killed 18 or 24 h later. To minimize animal-to-animal variation in the absorption and distribution of GF, mice were fasted from the time of GF administration to the time of killing. Two hours before treatment the animals were s.c. implanted with a bromodeoxyuridine tablet to obtain differential chromatid staining and to determine the number of divisions after GF treatment for each metaphase. Mitostatic effects of GF were assessed by the relative proportions of first, second and third generation metaphases and the average generation time (AGT) method. A statistically significant increase with respect to the control AGT value was observed after treatment with 666 and 2000 mg/kg, suggesting that GF, as already shown in meiosis, interfered with cell cycle progression. Hyperploidy was scored in second generation metaphases. Eighteen hours after treatment, the frequencies of hyperploid cells were significantly ($P < 0.05$) higher in all GF-treated groups than in their matched control group. The effect was not dose-dependent. No further increase in aneuploidy

was observed at 24 h, suggesting that cells overcoming mitotic arrest did not have a higher rate of non-disjunction. No induction of polyploidy was demonstrated. We conclude that GF induces mitotic delay and aneuploidy in mouse bone marrow and suggest that the protocol used to formulate the gavage suspensions and the after-treatment fasting of the animals enhanced the bioavailability of GF to bone marrow cells.

Expression of human epileptic temporal lobe neurotransmitter receptors in Xenopus oocytes: An innovative approach to study epilepsy.

Palma E., Esposito V., Mileo A.M., Di Gennaro G., Quarato P., Giangaspero F., Scoppetta C., Onorati P., Trettel F., Miledi R., Eusebi F.

Proc. Natl. Acad. Sci. USA, 12,99(23), p.15078-83, 2002

Poly(A(+)) RNA was extracted from the temporal lobe (TL) of medically intractable epileptic patients which underwent surgical TL resection. Injection of this mRNA into Xenopus oocytes led to the expression of ionotropic receptors for gamma-aminobutyric acid (GABA), kainate (KAI) and alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA). Membrane currents elicited by GABA inverted polarity at -15 mV, close to the oocyte's chloride equilibrium potential, were inhibited by bicuculline, and were potentiated by pentobarbital and flunitrazepam. These basic characteristics were also displayed by GABA currents elicited in oocytes injected with mRNAs isolated from human TL glioma (TLG) or from mouse TL. However, the GABA receptors expressed by the epileptic TL mRNA exhibited some unusual properties, consisting in a rapid current run-down after repetitive GABA applications and a large EC(50) (125 microM). AMPA alone evoked very small or nil currents, whereas KAI induced larger currents. Nevertheless, upon cyclothiazide treatment, AMPA elicited substantial currents that, like the KAI currents, were inhibited by 6-cyano-7-nitroquinoxaline-2,3-dione (CNQX). Furthermore, the glutamate receptor 5 (GluR5) agonist, ATPA, failed to evoke an obvious current although both RT-PCR and Western blot analyses showed GluR5 expression in the epileptic TL. Oocytes injected with mouse TL or human TLG mRNAs generated KAI and AMPA currents similar to those evoked in oocytes injected with epileptic TL mRNA but, in contrast to these, the mouse TL and human TLG oocytes were also responsive to ATPA. Our findings are in accord with the concept that both a depression of GABA inhibition and a dysfunction of the KAI-receptor system maintain a high neuronal excitability that results in epileptic seizures.

Some properties of human neuronal alpha 7 nicotinic acetylcholine receptors fused to the green fluorescent protein.

Palma E., Mileo A.M., Martinez-Torres A., Eusebi F., Miledi R.

Proc. Natl. Acad. Sci. USA, 19,99(6), p.3950-5, 2002

The functional properties and cellular localization of the human neuronal alpha7 nicotinic acetylcholine (AcCho) receptor (alpha7 AcChoR) and its L248T mutated (mut) form were investigated by expressing them alone or as gene fusions with the enhanced version of the green fluorescent protein (GFP). Xenopus oocytes injected with wild-type (wt), mutalpha7, or the chimeric subunit cDNAs expressed receptors that gated membrane currents when exposed to AcCho. As already known, AcCho currents generated by wtalpha7 receptors decay much faster than those elicited by the mutalpha7 receptors. Unexpectedly, the fusion of GFP to the wt and mutated alpha7 receptors led to opposite results: the AcCho-current decay of the wt receptors became slower, whereas that of the mutated receptors was accelerated. Furthermore, repetitive applications of AcCho led to a considerable "run-down" of the AcCho currents generated by mutalpha7-GFP receptors, whereas those of the wtalpha7-GFP receptors remained stable or increased in amplitude. The AcCho-current run-down of mutalpha7-GFP oocytes was accompanied by a marked decrease of alpha-bungarotoxin binding activity. Fluorescence, caused by the chimeric receptors expressed, was seen over the whole oocyte surface but was more intense and abundant in the animal hemisphere, whereas it was much weaker in the vegetal hemisphere. We conclude that fusion of GFP to wtalpha7 and mutalpha7 receptors provides powerful tools to study the distribution and function of alpha7 receptors. We also conclude that fused genes do not necessarily recapitulate all of the properties of the original receptors. This fact must be borne close in mind whenever reporter genes are attached to proteins.

Anastrozole alone in combination with Tamoxifen versus tamoxifen alone for treatment of postmenopausal women with early breast cancer: first results of the ATAC randomised trial.

Papaldo P., Cognetti F., the ATAC Trialist' Group. Arimidex, Tamoxifen Alone or in Combination.

Lancet, 22,359(9324), p.2126-7, 2002

No abstract available.

Quality control for biomarker determination in oncology: the experience of the Italian Network for Quality Assessment of Tumor Biomarkers (INQAT).

Paradiso A., Volpe S., Iacobacci A., Marubini E., Verderio P., Costa A., Daidone M.G., Marchetti A., Mottolese M., Amadori D., et al.

Int. J. Biol. Markers, 17(3), p.201-14, 2002

Biomarker analysis and evaluation in oncology is the product of a number of processes (including managerial, technical and interpretation steps) which need to be monitored and controlled to prevent and correct errors and guarantee a satisfactory level of quality. Several biomarkers have recently moved to clinical validation studies and successively to clinical practice without any definition of standard procedures and/or quality control (QC) schemes necessary to guarantee the reproducibility of the laboratory information. In Italy several national scientific societies and single researchers have activated -- often on a pilot level -- specific external quality assessment protocols, thereby potentially jeopardizing the clinical reality even further. In view of the seriousness of the problem, in 1998 the Italian Ministry of Health sponsored a National Survey Project to coordinate and standardize the procedures and to develop QC programs for the analysis of cancer biomarkers of potential clinical relevance. Twelve QC programs focused on biomarkers and concerning morphological, immunohistochemical, biochemical, molecular, and immunoenzymatic assays were coordinated and implemented. Specifically, external QC programs for the analytical phase of immunohistochemical p53, Bcl-2, c-erb-2/neu/HER2, and microvessel density determination, of morphological evaluation of tumor differentiation grade, and of molecular p53 analysis were activated for the first time within the project. Several hundreds of Italian laboratories took part in these QC programs, the results of which are available on the web site of the Network (www.cqlaboncologico.it). Financial support from the Italian Government and the National Research Council (CNR) will guarantee the pursuit of activities that will be extended to new biomarkers, to preanalytical phases of the assays, and to revision of the criteria of clinical usefulness for evaluating the cost/benefit ratio.

Complete remission through blast cell differentiation in PLZF/RARalpha-positive acute promyelocytic leukemia: in vitro and in vivo studies.

Petti M.C., Fazi F., Gentile M., Diverio D., De Fabritiis P., De Propris M.S., Fiorini R., Spiriti M.A., Padula F., Pelicci P.G., Nervi C., Lo Coco F.

Blood, 1,100(3), p.1065-7, 2002

Acute leukemia with the t(11;17) expressing the PLZF-RARalpha gene fusion is a rare variant of acute promyelocytic leukemia (APL) that has been associated with poor clinical response to all-trans retinoic acid (ATRA) treatment. However, some recent reports have put into question the absolute refractoriness of this leukemia to ATRA. We describe here a patient with PLZF/RARalpha APL who was treated at relapse with ATRA and low-dose hydroxyurea. Complete hematologic remission was obtained through differentiation of leukemic blasts, as proven by morphologic, immunophenophenotypic, and genetic studies carried out in sequential bone marrow samples. Moreover, in vitro studies indicated that blast differentiation was potentiated by the addition of the histone deacetylase inhibitor tricostatin A, but not of hydroxyurea, to ATRA. Our findings indicate that the maturation block may be overcome and terminal differentiation obtained in this leukemia subset and support the view that sensitivity/refractoriness of this form to ATRA should be revisited.

Melphalan treatment in patients with myelofibrosis with myeloid metaplasia.

PETTI M.C., LATAGLIATA R., SPADEA T., SPADEA A., MONTEFUSCO E., ALOE SPIRITI M.A., AVVISATI G., BRECCIA M., PESCARMONA E., MANDELLI F.

Br. J. Haematol., 116(3), p.576-81, 2002

Between January 1985 and December 1992, 104 consecutive patients with symptomatic myelofibrosis with myeloid metaplasia (MMM) [splenic enlargement >5 cm and/or transfusional requirement or Hb < 10 g/dl and/or white blood cell (WBC) count >20 x 10(9)/l and/or platelets >1.0 x 10(9)/l] received low-dose Melphalan (2.5 mg/3 times/week) to evaluate the efficacy and toxicity of this approach. Among 99 evaluable patients, 66 (66.7%) achieved a response after a median time of 6.7 months: 26 (26.3%) had a normalization of all clinical and haematological parameters (complete response, CR) and 40 (40.4%) showed an improvement >50% (partial response, PR). Thirty-three patients (33.3%) were resistant. Reversible haematological toxicity was the most common complication. Median durations of CR and PR were 28.4 and 26 months respectively: median survival of CR + PR patients was 71.2 months (95%CI: 33.8-108.7) versus 36.5 months (95%CI: 24.5-48.5) for the non-responders (log-rank test, P =0.002). In the multivariate analysis, the following variables were significantly associated with a shorter survival: anaemia [hazard risk (HR) = 2.7], WBC count >20 x 10(9)/l (HR = 2.4) and not achieving any type of response, either partial or complete (HR = 3.9). In conclusion, Melphalan could be a promising first-line option for MMM patients with clinical or haematological symptoms requiring treatment.

Antimicrobial action of nitens® mouthwash (cetyltrimethylammonium naproxenate) on multiple isolates of pharyngeal microbes: a controlled study against chlorhexidine, benzydamine, hexetidine, amoxicillin, amoxicillin-clavulanate, clarithromycin, and cefaclor.

PILLONI A.P., BUTTINI G., GIANNARELLI D., GIORDANO B., IOVENE M.R., MONTELLA F., DI SALVO R., COLANTUONO R., LALLI G., TUFANO M.A.

Chemotherapy, 48(4), p.168-73, 2002

Background: Acute oropharyngeal and respiratory tract infections are due to a wide spectrum of microorganisms. The aim of this study was to compare and evaluate the in vitro activity of four antiseptics (cetyltrimethylammonium naproxenate, chlorhexidine, benzydamine, hexetidine) to four antibiotics (amoxicillin, amoxicillin-clavulanate, clarithromycin, cefaclor) on strains of Haemophilus influenzae, Moraxella catarrhalis, Streptococcus pyogenes and Streptococcus pneumoniae.

Methods: Susceptibility tests were performed on 90, aerobic and anaerobic, bacterial strains, isolated from nasopharyngeal swabs and sputum. Minimum inhibitory concentrations (by microdilution) and minimum bactericidal concentrations were determined and compared.

Results: Our selected panel of bacteria was highly susceptible to the antiseptics, particularly to chlorhexidine and naproxenate, even more so than two of the most frequently used antibiotics. Data were statistically significant ($p < 0.005$).

Conclusions: In view of their bactericidal and anti-inflammatory properties, these antiseptics may be effective in controlling the transitory colonization of the oral cavity by microbes that cause or worsen disease in patients with mild infections.

The Italian multi-centre project on evaluation of MRI and other imaging modalities in early detection of breast cancer in subjects at high genetic risk.

PODO F., SARDANELLI F., CANESE R., D'AGNOLO G., NATALI P.G., CRECCO M., GRANDINETTI M.L, ET AL.

J. Exp. Clin. Cancer Res., 21,3, p.115-124, 2002

This report presents the preliminary results of the first phase (21 months) of a multi-centre, non-randomised, prospective study, aimed at evaluating the effectiveness of contrast-enhanced magnetic resonance imaging (MRI), X-ray mammography (XM) and ultrasound (US) in early diagnosis of breast cancer (BC) in subjects at high genetic risk. This Italian national trial (coordinated by the Istituto Superiore di Sanita, Rome) so far recruited 105 women (mean age 46.0 years; median age 51.0; age range 25-77 years), who were either proven BRCA1 or BRCA2 mutation carriers or had a 1 in 2 probability of being carriers (40/105 with a previous personal history of BC). Eight cases of breast carcinomas were detected in the trial (mean age 55.3 years, median age 52.5; age range 35-70 years; five with previous personal history of BC). All trial-detected BC cases (8/8) were identified by MRI, while XM and US correctly classified only one. MRI had one false posi-

tive case, XM and US none. Seven "MRI-only" detected cancers (4 invasive, 3 in situ) occurred in both pre- (n = 2) and post-menopausal (n = 5) women. With respect to the current XM screening programmes addressed to women in the age range 50-69 years, the global incidence of BC in the trial (7.6%) was over ten-fold higher. The cost per "MRI-only" detected cancer in this particular category of subjects at high genetic risk was substantially lower than that of an XM-detected cancer in the general women population. These preliminary results confirmed that MRI is a very useful tool to screen subjects at high genetic risk for breast carcinoma, not only in pre-, but also in post-menopausal age, with a low probability of false positive cases.

"Misura" project: a retrospective survey on the use of 5fluorouracil in the treatment of colorectal cancer in 24 Italian clinical centers.

Poletti P., Pinotti G., Rosati G., Luppi G., Ibrahim T., Marinozzi C., Pucci F., Pancera G., Biasco G., Barni S., Garufi C., Martignoni G., Visona G., Labianca R.

Tumori, 88(2), p.104-9, 2002

The "Misura" project is a retrospective survey, with the aim to evaluate how 5FU is used in the treatment of colorectal cancer in clinical practice in Italian oncology departments. Twenty-four centers participated. Patients seen in the second half of 1998 with colorectal cancer and treated with 5FU were analyzed. Observed patients were 664, 45.9% of patients presented metastatic disease. Biochemical modulation with folinic acid and bolus 5FU was the most used schedule (59%). The De Gramont (LV 5FU2) regimen, alone or with other cytotoxic drugs, was the second most chosen schedule (14%). The most frequent side effect observed was gastrointestinal toxicity. No hematological toxicity was demonstrated in 68.8% of patients. Cutaneous toxicity occurred in 21.1% of patients. 5FU is widely used independently by the stage of disease. In palliative treatment a variety of schedules were administered by the Italian centers, lacking a standard therapy. There are very few surveys investigating oncology clinical practice. A larger survey on this issue is auspicable.

Asymptomatic esophageal perforation caused by late screw migration after anterior cervical plating: report of a case and review of relevant literature.

Pompili A., Canitano S., Caroli F., Caterino M., Crecco M., Raus L., Occhipinti E.

Spine, 1,27(23), p.499-502, 2002

Study design: This report documents a case of asymptomatic esophageal perforation, secondary to a dislocated and then migrated cervical screw after anterior plating, and reviews the relevant Western literature.

Objectives: To report a rare and potentially dangerous complication and suggest mechanisms of asymptomatic esophageal perforation and healing.

Summary of background data: Anterior surgical approaches to the cervical spine have become popular and safer during the past decade. Materials and devices for anterior stabilization have improved in quality and safety. Nevertheless, failure of the devices may occur either because of technical mistakes or rupture. Reoperation is not always necessary, as spontaneous recovery is possible.

Methods: Our patient was operated on for severe cervical spondylotic myelopathy. One year after surgery, one of the screws migrated and was found anteriorly to the spine. Six months later, the screw could no longer be identified, and we concluded that an esophageal perforation had occurred and that the screw had been eliminated through the intestinal tract. The results of esophagoscopy were normal.

Results: The neurologic conditions of our patient improved constantly, and his spine alignment was maintained despite the missing screw.

Conclusions: This case demonstrates that a serious complication may not need any treatment. Each case of screw displacement in anterior cervical spine surgery should be evaluated separately in conjunction with the clinical symptoms of the patient, as spontaneous resolution is possible.

Quality-of-life assessment in patients who had been surgically treated for cerebellar pilocytic astrocytoma in childhood.

Pompili A., Caperle M., Pace A., Ramazzotti V., Raus L., Jandolo B., Occhipinti E.

J. Neurosurg., 96(2), p.229-34, 2002

Object: After radical surgery for childhood cerebellar astrocytomas, patients are considered to be cured. Long-term follow up demonstrates that these patients survive, with most of them leading a normal life. The study reported here was aimed at assessing the quality of life (QOL) of these adults, which is defined as a person's sense of well-being, as derived from his or her current experience of life as a whole.

Methods: Twenty patients who had undergone surgery between 1970 and 1985 were enrolled in the study. In four patients ventriculoperitoneal shunts were in place; two of these patients had required more than six shunt revisions. At present, all patients have clear neuroimaging studies and their Karnofsky Performance Scale (KPS) scores are as follows: 70 in three, 80 in seven, 90 in six, and 100 in four. A QOL questionnaire was administered to the patients and to a control group consisting of 20 healthy volunteers of matching age and sex. The chi-square test was applied to compare patients and controls. Traditional questions on the level of education, work, whether the patients have their own families, and whether they possessed a driver's license were asked at the end of the questionnaire. In all the dimensions assessed except one (sex life), the difference between patients and control volunteers was significant, socializing and adolescence being the most striking ones. This was also true when the three patients with the lowest KPS scores and the worst QOL results were excluded.

Conclusions: By traditional standards, these patients appear to fare quite well. Nevertheless, their self-reported life experience is unsatisfying when compared with the control group. The authors conclude that psychosocial factors are critical to complete recovery and the QOL of children who undergo successful operations for benign cerebellar astrocytoma.

Pharmacological modulation of carcinoembryonic antigen in human cancer cells: studies with staurosporine.

Prete S.P., Cappelletti D., Baier S., Nasuti P., Guadagni F., De Vecchis L., Greiner J.W., Bonmassar E., Graziani G., Aquino A.

Int. Immunopharmacol., 2(5), p.641-51, 2002

Preliminary studies, performed in our laboratory, showed that staurosporine (ST), a protein-kinase (PK) inhibitor, increases the expression of the carcinoembryonic antigen (CEA) in a human colon cancer cell line. The present study explores the cellular and molecular effects of ST on the CEA expression in breast cancer MCF-7 line and in a number of colon cancer cell lines characterized by the different basal levels of the antigen, including two cloned sublines (i.e. C22.20 and C6.6, expressing low and high CEA levels, respectively). In all cases, increase of the CEA expression was observed at drug concentrations devoid of marked cytostatic effects (e.g. 5 nM) and was accompanied by the enhanced CEA shedding in the supernatant. Moreover, the increase of the CEA levels both occurred in the cell membranes and in the cytosolic compartments and appeared to be the result of the enhanced CEA gene transcription. Similar results have been previously obtained with interferon-gamma. However, ST treatment, different from interferon-gamma, did not up-regulate the level of the HLA class I molecules. A preliminary investigation also showed that other PKC inhibitors did not substantially modulate the CEA expression. Therefore, the biochemical mechanism underlying the effect of ST should not be correlated with that involved in the PKC inhibition. The present study suggests that ST and, presumably, its analogs used in the cancer treatment could enhance the CEA expression on neoplastic cells in patients affected by the CEA-positive malignancies. This appears to be of potential clinical interest for the development of new immunotherapeutic or diagnostic approaches based on the pharmacological modulation of this antigenic marker.

Quality of life and chronotherapy.

Pugliese P., Garufi C., Perrone M., Aschelter A.M., Zappalà A., Terzoli E.

Chronobiol. Int., 19(1), p.299-312, 2002

The importance of evaluating patient's quality of life (QoL) in clinical practice and research is recognized clearly in oncology. In the advanced phase of disease such an evaluation represents an endpoint as important as survival. Quality of life is both a subjective and multidimensional concept evaluated mainly by validated questionnaires. In colorectal trials involv-

ing advanced stage disease the effects of different chemotherapy treatments on QoL were evaluated. Almost all the studies found no deterioration in QoL during chemotherapy. The European Organization for the Research and Treatment of Cancer (EORTC) Chronotherapy Study Group utilized three different approaches to assess QoL. The first centered on the stability of QoL during a 6mon treatment period in patients undergoing chronotherapy. The second centered on research of the biological and clinical determinants of QoL involving features of the circadian activity rhythm and patient survival and the relationship between QoL and patient performance status, response to therapy, and psychosocial variables as well as drug-induced toxicity. The third centered on the clinical effectiveness of psychological intervention on patients undergoing chronotherapy to improve psychosocial status during treatment. This papers reviews the results of EORTC Chronotherapy Group studies on QoL.

Clinical end points for the assessment of cytostatic agents.

RINALDI M.

Lung Cancer, 38(1), p.S37, 2002

No abstract available.

Endothelin-1 promotes proteolytic activity of ovarian carcinoma.

ROSANÒ L., SALANI D., DI CASTRO V., SPINELLA F., NATALI P.G., BAGNATO A.

Clin. Sci. (Lond), 103,48, p.306S-309S, 2002

Endothelin-1 (ET-1) is a potent mitogenic and angiogenic factor for ovarian carcinoma cell lines, which acts selectively through the ET(A) receptor (ET(A)R). A previous study demonstrated that ET-1 is present at high concentrations in ovarian cancer ascites, indicating a direct role in the progression and metastasis of ovarian carcinoma. In this study, we investigated whether ET-1 could induce production and activation of tumour-associated proteinases in ovarian carcinoma cells. As demonstrated by ELISA, we found that the secretion of matrix metalloproteinase (MMP)-2 and MMP-9, urokinase-type plasminogen activator and plasminogen activator inhibitor type-1 and -2 was upregulated by ET-1 in a dose-dependent manner in the HEY cell line. In addition, the MMPs in ET-1-treated cells are consistently active, as shown by MMP gelatinase activity assay. Finally, we demonstrated that BQ-123, an antagonist of ET(A)R, inhibited the ET-1-induced tumour protease secretion and activity, suggesting that ET-1/ET(A)R may play an important role in the progression and metastasis of ovarian carcinoma, activating multiple proteinase cascades.

Soluble selectin levels in patients with lung cancer.

ROSELLI M., MINEO T.C., MARTINI F., MARIOTTI S., AMBROGI V., SPILA A., D'ALESSANDRO R., BASILI S., GUADAGNI F., FERRONI P.

Int. J. Biol. Markers, 17(1), p.56-62, 2002

Increased expression of selectins has been found on endothelial cells of venules and capillaries in the tumor stroma of non-small cell lung cancer, suggesting their functional role in the process of chemotaxis for tumor cells. The present study was aimed at analyzing the role of both soluble (s)P-selectin and sE-selectin levels in association with clinico-pathological variables in 116 patients with lung cancer, 38 patients with benign diseases and 59 healthy donors. The results obtained showed that sP-selectin and sE-selectin levels were higher in patients with lung cancer compared to normal donors ($p<0.02$ and $p<0.005$, respectively). No differences were observed among patients with various benign diseases for both selectins. Increased levels of sP-selectin and sE-selectin were significantly associated with squamous lung cancer at late stages ($p<0.05$), but not adenocarcinoma. Both sP- and sE-selectin were independently related to the stage of squamous lung cancer by stepwise regression analysis ($p<0.02$ and $p<0.03$, respectively), while only sE-selectin was independently related to the presence of distant metastasis in the same histotype ($p<0.02$). These results suggest that measurement of plasma soluble selectins might represent a useful laboratory parameter in the management of patients with squamous lung cancer.

Hyperthermic intraoperative intraperitoneal chemotherapy with cisplatin and doxorubicin in patients who undergo cytoreductive surgery for peritoneal carcinomatosis and sarcomatosis: phase I study.

ROSSI C.R., FOLETTO M., MOCELLIN S., PILATI P., DE S.M., DERACO M., CAVALIERE F., PALATINI P., GUASTI F., SCALERTA R., LISE M.

Cancer, 15,94(2), p.492-9, 2002

Background: Hyperthermic intraperitoneal intraoperative chemotherapy (HIIC) combined with cytoreductive surgery (CS) has been proposed as a new multimodal treatment mainly for carcinomatosis of gastrointestinal origin. To evaluate whether this regimen could be used for other tumor types, the authors conducted a Phase I study on HIIC with doxorubicin and cisplatin in patients with peritoneal carcinomatosis or sarcomatosis.

Patients and methods: Thirty-one patients with peritoneal carcinomatosis or sarcomatosis (PCS) were enrolled for the study. After completion of CS, HIIC was administered with drug doses that were increased for each consecutive cohort following a three-patient cohort scheme. Thereafter, the accrual was stopped when Grade 4 locoregional or systemic toxicity was observed. The maximum tolerated dose (MTD) was considered the dose in the previous triplet. Drug pharmacokinetics and procedure costs also were analyzed.

Results: After CS, residual tumors were not present or measured less than or equal to 3 mm (in dimension) in all cases. Maximum tolerated dose was 15.25 and 43.00 mg L(-1) for doxorubicin and cisplatin, respectively. The perfusate/plasma area under the curve ratios were favorable for both drugs, at 162+/-113 and 20.6+/-6.0, respectively, for doxorubicin and cisplatin. Doxorubicin levels in the peritoneum were higher than in tumor or normal tissue samples. There were no postoperative deaths. Surgery-related complications were observed in 25% of cases. Findings at cost analysis showed that the length of stay in the operation room and intensive care unit were the major cost drivers.

Conclusions: Cytoreductive surgery combined with HIIC is an expensive but feasible therapeutic approach for locally advanced abdominal tumors. Because our preliminary findings for local disease control are encouraging, a Phase II study is now advisable to verify the activity of this promising treatment.

ABT-627, a potent endothelin receptor A antagonist, inhibits ovarian carcinoma growth in vitro.

SALANI D., ROSANÒ L., DI CASTRO V., SPINELLA F., VENUTI A., PADLEY R.J., NICOTRA M.R., NATALI P.G., BAGNATO A.

Clin. Sci. (Lond), 1,103(1), p.318S-21S, 2002

Endothelin-1 (ET-1) is present at high concentrations in ovarian cancer ascites and is overexpressed in primary and metastatic ovarian carcinomas. In these tumours the presence of ET-1 is associated with enhanced neovascularization and with vascular endothelial growth factor (VEGF) expression. In these tumour cells, ET-1 acts as an autocrine growth factor selectively through the receptor ET(A), which is predominantly expressed in tumour cells. Furthermore, ET-1 produced by ovarian tumour cells stimulates VEGF production and VEGF-mediated angiogenic effects through ET(A) binding. These results demonstrate that activation of the ET(A) in ovarian carcinoma cells promotes cell proliferation, neovascularization and invasion, which are the principal hallmarks of malignant transformation. The present study was designed to investigate the effects of the ET(A)-selective antagonist ABT-627 on the ET-1-induced mitogenic effect in both primary cultures (PMOV1 and PMOV2) and cell lines (OVCA 433 and HEY) of ovarian carcinoma. All tumour cells express the components of the ET-1 system and secrete ET-1. ET(A) blockade by ABT-627 inhibits ET-1-induced mitogenic effects. The ET(B) antagonist BQ-788 is ineffective although all cell lines express both ET(A) and ET(B) mRNAs. In conclusion, our results demonstrate that ABT-627 is capable of inhibiting the proliferative activity of ET-1, suggesting that this potent ET(A) antagonist may provide a novel approach to the multidisciplinary treatment of ovarian carcinoma.

Free flap reconstruction of the sole of the foot with or without sensory nerve coaptation.

SANTANELLI F., TENNA S., PACE A., SCUDERI N.

Plast. Reconstr. Surg., 109(7), p.2314-22, discussion 2323-4, 2002

The authors present a retrospective study on major plantar foot reconstruction to evaluate the role of the free fasciocutaneous flap and the importance of sensory nerve reconstruction in improving long-term results. Between 1995 and 1999, 20 patients with major defects of the sole of the foot underwent free forearm flap reconstruction performed by the senior author (F.S.). Sensory nerve reconstruction was added to this technique in 1997. The age and sex of the patients and the cause, location, and dimensions of their defects were recorded. The patients were clinically and neurophysiologically evaluated at 3, 6, and 12 months after the procedure for the following parameters: flap contour, flap stability, load capacity, walking ability, touch sensation, pain sensation, static two-point discrimination, and thermal sensibility. Dermatomic somatosensory-evoked potentials were also tested at 12 months. Follow-up ranged from 1 to 5 years. Patients were divided into two groups according to sensory nerve reconstruction. Group A consisted of 11 patients with nerve repair, and group B consisted of nine patients without nerve repair. One patient from group A who had an idiopathic neuropathy was excluded from the study because of interference with the reinnervation process. Five more patients (three from group A and two from group B) were lost at follow-up and excluded from the study. The final sample size in each group was seven. Data from both groups were compared and statistically analyzed with the Mann-Whitney test and the Fisher exact test. Long-term results confirmed in all reconstructions long-lasting stability. During the first postoperative year, patients with sensory nerve reconstruction showed better sensibility. The statistical analyses confirmed significant differences between the two groups to be dependent upon surgical technique at 3 and 6 months. Two-point discrimination and dermatomic somatosensory-evoked potentials were recorded. After 12 months, flaps without surgical nerve repair showed progressive improvement of sensitive thresholds, achieving a good protective sensibility, similar to that of the other group, but these flaps never regained two-point discrimination or dermatomic somatosensory-evoked potentials.

Perspectives of BRCA mutations carriers in the clinical management.

SAVARESE A. AND COGNETTI F.

J. Exp. Clin. Cancer Res., 21,2, p.487-491, 2002

The recent identification of the breast cancer-associated genes BRCA1 and BRCA2 is changing the clinical care provided to women at high-risk of breast cancer. We briefly review what is currently known about the clinical management of individuals who bear (or are suspected of bearing) genes mutations and which are the prevention strategies that would reduce the incidence and mortality of breast cancer in this subset of women.

Phase III randomized trial comparing three platinum-based doublets in advanced non-small-cell lung cancer.

SCAGLIOTTI G.V., DE MARINIS F., RINALDI M., CRINO L., GRIDELLI C., RICCI S., MATANO E., BONI C., MARANGOLO M., FAILLA G., ALTAVILLA G., ADAMO V., CERIBELLI A., ET AL.

J. Clin. Oncol., 1,20(21), p.4285-91, 2002

Purpose: To evaluate whether two commonly used newer platinum-based regimens offer any advantage over vinorelbine-cisplatin (reference regimen) in response rate for patients with advanced non-small-cell lung cancer (NSCLC).

Patients and methods: Chemotherapy-naive patients were randomized to receive gemcitabine 1,250 mg/m(2) days 1 and 8 plus cisplatin 75 mg/m(2) day 2 every 21 days (GC arm), or paclitaxel 225 mg/m(2) (3-hour infusion) then carboplatin (area under the concentration-time curve of 6 mg/mL x min), both on day 1 every 21 days (PCb arm), or vinorelbine 25 mg/m(2)/wk for 12 weeks then every other week plus cisplatin 100 mg/m(2) day 1 every 28 days (VC arm). RESULTS: Six hundred twelve patients were randomized to treatment (205 GC, 204 PCb, and 203 VC). Overall response rates for the GC (30%) and PCb (32%) arms were not significantly different from that of the VC arm (30%). There were no differences in overall survival, time to disease progression, or time to treatment failure. Median survival for the GC, PCb, and VC groups was 9.8, 9.9, and 9.5 months, respectively. Neutropenia was significantly higher on the VC arm (GC 17% or PCb 35% v VC 43% of cycles,

P <.001), as was thrombocytopenia on the GC arm (GC 16% v VC 0.1% of cycles, P <.001). Alopecia and peripheral neurotoxicity were most common on the PCb arm, as was nausea/vomiting on the VC arm (P <.05).

Conclusion: Efficacy end points were not significantly different between experimental and reference arms, although toxicities showed differences. These findings suggest that chemotherapy in NSCLC has reached a therapeutic plateau.

Cloning of the mouse insulin receptor substrate-3 (mIRS-3) promoter, and its regulation by p53.

Sciacchitano S., Orecchio A., Lavra L., Misiti S., Giacchini A., Zani M., Danese D., Gurtner A., Soddu S., Di Mario U., Andreoli M.

Mol. Endocrinol., 16(7), p.1577-89, 2002

The insulin receptor susbtrate-3 (IRS-3) is a member of a family of intermediate adapter proteins that function as major intracellular targets for phosphorylation by the activated insulin and IGF-I receptors. Among the four IRS proteins identified so far, IRS-3 exhibits a rather peculiar expression pattern during both the embryonic development and adult life, suggesting a different mechanism of regulation of its expression. In this study, we cloned the 5' flanking region of the mIRS-3 gene and analyzed its promoter activity. The mIRS-3 promoter is inhibited by wild-type p53, and this effect is completely abolished by cotransfection of a dominant negative p53. Tumor-derived p53 mutants show variable, but lower suppressing capability than wt p53. In addition, treatment with doxorubicin inhibits endogenous expression of mIRS-3 mRNA in C2C12 and 3T3-L1 cells. The DNA region spanning from nucleotides -287 and -178 in the mIRS-3 promoter is responsible for a 32.2% reduction of the mouse double minute 2 (MDM2) promoter activity, suggesting its involvement in the p53-mediated inhibitory effect. In conclusion, our study demonstrates that the mIRS-3 promoter is regulated by p53 at the transcriptional level. The inhibition of mIRS-3 promoter by wild-type p53, and its de-repression by tumor-derived p53 mutants, appears to be similar to that previously reported for the IGF-I receptor promoter, suggesting a common role of these two genes in p53-mediated cell growth and differentiation.

Effects of low-dose cisplatin on 89Sr therapy for painful bone metastases from prostate cancer: a randomized clinical trial.

Sciuto R., Festa A., Rea S., Pasqualoni R., Bergomi S., Petrilli G., Maini C.L.

J. Nucl. Med., 43(1), p.79-86, 2002

This study evaluated the effects of low-dose cisplatin plus 89Sr versus 89Sr alone in the treatment of painful bone metastases from prostate cancer, addressing both pain palliation and cytostatic effects.

Methods: Seventy patients with metastatic hormone-refractory prostate cancer were randomized into 2 groups: One group (arm A) received 148 MBq 89Sr plus 50 mg/m(2) cisplatin, and the other group (arm B) received 148 MBq 89Sr plus placebo. After treatment, the patients were followed up until death to evaluate the outcome variables: grade and duration of pain palliation, onset of new painful sites, changes in bone disease, global survival, serum prostate-specific antigen and alkaline phosphatase changes, and hematologic toxicity.

Results: Overall pain relief occurred in 91% of patients in arm A and 63% of patients in arm B (P < 0.01), with a median duration of 120 d in arm A and 60 d in arm B (P = 0.002). New painful sites on previously asymptomatic bone metastases appeared in 14% of patients in arm A and in 30% of patients in arm B (P = 0.18). The median survival without new painful sites was 4 mo in arm A and 2 mo in arm B (P = 0.04). Bone disease progression was observed in 27% of patients in arm A and in 64% of patients in arm B (P = 0.01). Median global survival after therapy was 9 mo in arm A and 6 mo in arm B (P = 0.30). Transient and moderate hematologic toxicity, as determined by World Health Organization criteria, was apparent in both arms without significant differences.

Conclusion: The addition of a low dose of cisplatin enhances the effect of a standard dose of 89Sr without significant side effects, producing a significant improvement in pain palliation and a cytostatic effect on bone disease.

Prognostic value of (99m)Tc-sestamibi washout in predicting response of locally advanced breast cancer to neoadjuvant chemotherapy.

Sciuto R., Pasqualoni R., Bergomi S., Petrilli G., Vici P., Belli F., Botti C., Mottolese M., Maini C.L.

J. Nucl. Med., 43(6), p.745-51, 2002

This study evaluated the role of (99m)Tc-sestamibi washout in the prediction of pathologic tumor response to neoadjuvant chemotherapy in 30 patients with locally advanced breast cancer.

Methods: Two (99m)Tc-sestamibi studies were performed before and after chemotherapy for each patient. Early (10 min) and delayed (240 min) planar breast views were acquired after a 740-MBq (99m)Tc-sestamibi intravenous injection, and the washout rate (WOR) was computed. All patients underwent radical mastectomy with pathologic evaluation of the residual tumor size.

Results: The pretherapy (99m)Tc-sestamibi WOR ranged from 14% to 92% (mean +/- SD, 50% +/- 18%). At pathologic examination, 15 patients showed no tumor response to chemotherapy and 15 patients showed an objective response to chemotherapy. The pretherapy (99m)Tc-sestamibi study predicted chemoresistance (WOR > 45%) in 18 of 30 patients and no chemoresistance (WOR < or = 45%) in 12 of 30 patients. When the WOR cutoff was set at >45%, the prognostic performance of the test was indicated by a sensitivity of 100%; a specificity of 80%; positive and negative predictive values of 83% and 100%, respectively; and a likelihood ratio of 5. The repeatability of the test was good, with 80%-93% interreader agreement (kappa = 0.57-0.85). Posttherapy (99m)Tc-sestamibi studies confirmed the pretherapy study prediction in 29 of 30 patients.

Conclusion: (99m)Tc-Sestamibi WOR is a reliable test for predicting tumor response to neoadjuvant chemotherapy. In fact, negative findings (WOR < or = 45%) rule out chemoresistance and positive findings (WOR > 45%) indicate a high risk of chemoresistance.

Salvage chemotherapy for advanced sarcoma patients: a single-institution experience survey.

Serrone L., Nardoni C., Gelibter A., Felici A., Cognetti F.

J. Exp. Clin. Cancer Res., 21(2), p.181-4, 2002

There is no standard salvage chemotherapy for patients with recurrent sarcoma following a first-line chemotherapy. A few therapeutic options are available and of limited efficacy. The objective of this study was to determine the activity and toxicity of salvage therapies in advanced sarcoma patients in our experience. A retrospective analysis of 41 case records of patients with recurrent sarcoma treated at our division between May 1995 and October 2000 was conducted. Several different therapy regimens were employed: dacarbazine (DTIC) in 16 patients; carboplatin (CBDCA) plus gemcitabine (GEM) in 9 patients; ifosfamide (IFO) in 10 patients; other regimens in 6 patients. A total of 153 cycles of chemotherapy were delivered (median, 3 cycles). Among 38 evaluable patients, seven partial responses were obtained (RR 18.4%). Treatment-related responses were: 2/15 in DTIC group; 1/8 in CBDCA/GEM group; 3/9 in IFO group; 1/6 in other regimens. Stable disease was obtained in 10 patients. Median time to treatment failure and median survival time were 5 months and 4.5 months, respectively. The main treatment-related toxicities were hematologic and gastrointestinal. Most of salvage chemotherapies for recurrent sarcoma patients have an unacceptably high treatment failure rate and do not appear to offer any quality of life advantages. Future clinical trials with high dose ifosfamide seem appropriate even if the use of investigational new drugs and novel strategies in these patients should be considered.

Abdominal wall recurrences after colorectal resection for cancer: results of the Italian registry of laparoscopic colorectal surgery.

Silecchia G., Perrotta N., Giraudo G., Salval M., Parini U., Feliciotti F., Lezoche E., Morino M., Melotti G., Carlini M., Rosato P., Basso N.

Dis. Colon Rectum, 45(9), p.1172-7, p.1177, 2002

Purpose: The purpose of the present study was to evaluate prospectively the abdominal wall recurrence rate after laparoscopic resection for colorectal cancer, to analyze the impact of the learning curve on abdominal wall recurrence, and to assess the outcome of those patients.

Methods: The Italian Registry of Laparoscopic Colorectal Surgery database was analyzed to obtain data on cancer patients with abdominal wall recurrence, concomitant local or distant metastases, and interval between initial surgery and diagnosis of trocar site or minilaparotomy recurrences. The records of the initial procedures and the technique of specimen removal were reviewed.

Results: From January 1992 to July 2000, 2,583 patients (1,753 cases of carcinomas and 830 cases of benign diseases) were recorded. The malignant lesions were located on the right colon in 19 percent, the left colon in 48.8 percent, and rectum in 32.2 percent. Sixteen patients with histologic evidence of colorectal adenocarcinoma recurrences at the abdominal wall were observed (0.9 percent). Ten patients presented an advanced stage (III for 7 patients and IV for 3 patients). Eleven cases occurred during the learning curve period (the first 50 consecutive cases). The median survival time after abdominal wall recurrence diagnosis was 16 (range, 12-60) months. By July 2000 only two patients were alive.

Conclusions: The results of the Italian prospective Registry of Laparoscopic Colorectal Surgery confirm that the incidence of abdominal wall recurrences is similar to that reported in open studies (<1 percent). Most abdominal wall recurrences occurred in the learning curve period, suggesting that surgical experience may play a role in the development of this outcome. The prognosis of these patients is very poor.

Verapamil reverts resistance to drug-induced apoptosis in Ki-ras-transformed cells by altering the cell membrane and the mitochondrial transmembrane potentials.

Spalletti-Cernia D., D'Agnano I., Sorrentino R., Zupi G., Vecchio G., Portella G., Laccetti P.

Oncol. Res., 13(1), p.25-35, 2002

We have previously shown that in vivo ras-transformed cell lines display natural doxorubicin resistance compared with the normal cells and that such resistance is accompanied by a plasma membrane depolarization. In this article we first extend the analysis of doxorubicin effect to other ras-transformed cell lines, which are characterized by an increasing degree of malignant phenotype. Rat thyroid ras-transformed cells are markedly resistant to doxorubicin and the degree of drug resistance correlates with the degree of cell malignancy. The lower amount of drug accumulated inside the malignant and resistant cells is a consequence of their constitutive depolarized membrane potential and may account for their lack of drug-induced apoptosis. Verapamil, a known modulator of drug resistance, is able to decrease the resistance of all the malignant cell lines, initially causing a higher incorporation of doxorubicin as a consequence of its ability to hyperpolarize the membrane potential. In resistant cells, verapamil is also able to alter the mitochondrial membrane potential allowing apoptosis. In conclusion, these studies demonstrate that ras transformation induces the natural resistance to doxorubicin of the malignant cells. We suggest that the most malignant and resistant cells, of metastatic origin, could be preferentially destroyed by manipulation of their membrane properties, and we confirm the possibility of overcoming drug resistance by the administration of verapamil also in P-gp170-nonexpressing cells.

Endothelin-1 induces vascular endothelial growth factor by increasing hypoxia-inducible factor-1alpha in ovarian carcinoma cells.

Spinella F., Rosanò L., Di Castro V., Natali P.G., Bagnato A.

J. Biol. Chem., 2,277(31), p.27850-5, 2002

Angiogenesis is an essential prerequisite for tumor growth, invasion, and metastasis. In ovarian carcinoma cells, endothelin-1 (ET-1) stimulates the secretion of vascular endothelial growth factor (VEGF), a major mediator of tumor angiogenesis. In OVCA 433 and HEY ovarian carcinoma cell lines, ET-1 treatment increases VEGF mRNA expression and induces VEGF protein levels in a time- and dose-dependent fashion, and do so to a greater extent under hypoxic conditions. ET-1 also increases hypoxia-inducible factor-1alpha (HIF-1alpha) accumulation and activates the HIF-1 transcription complex under both normoxic and hypoxic conditions, suggesting a role for HIF-1 in the induction of VEGF expression. These effects are inhibited by the selective ET(A) receptor (ET(A)R) antagonist, BQ123. The ET-1-induced increase in HIF-1alpha protein levels is due to the enhanced HIF-1alpha stabilization. These results implicate HIF-1alpha in the induction of VEGF expression in ET-1-stimulated ovarian carcinoma cells, and provide a mechanism whereby ET-1 acting selectively through ET(A)R can interact with the HIF-1alpha-dependent machinery of angiogenesis. Our results suggest that new therapeutic strategies using specific ET(A)R antagonists could provide an additional approach to the treatment of ovarian carcinoma by inhibiting neovascularization as well as tumor cell growth.

Use of hyaluronidase for the treatment of extravasation of chemotherapeutic agents in six dogs.

SPUGNINI E.P.

J. Am. Vet. Med. Assoc., 221(10), p.1437-40, 2002

Six dogs had perivascular extravasation of antineoplastic agents during IV administration. Treatment with 300 units of hyaluronidase injected locally in the affected site was initiated following the extravasation event. Injections were repeated weekly until signs of toxic effects within the tissues resolved satisfactorily. All dogs recovered within 6 weeks, and residual fibrosis at the extravasation sites most was considered minimal. Many chemotherapeutic agents cause severe cytotoxic reactions when extravasated during cycles of chemotherapy, resulting in tissue necrosis with ulceration and sloughing of skin during the following weeks. Surgical treatments and skin grafting are often necessary to achieve healing. The sequelae of extravasation may result in discontinuation of chemotherapy or euthanasia of the animal. Hyaluronidase appears to be a safe treatment for the adverse effects of extravasation of various chemotherapeutic agents and may be used effectively to reduce the severity of cutaneous toxicosis.

Sustained response to recombinant human erythropoietin and intermittent all-trans retinoic acid in patients with myelodysplastic syndromes.

STASI R., BRUNETTI M., TERZOLI E., AMADORI S.

Blood, 1,99(5), p.1578-84, 2002

In vitro studies suggest that all-trans retinoic acid (ATRA) synergizes with erythropoietin (EPO) for the stimulation of hematopoiesis in patients with myelodysplastic syndrome (MDS). A clinical trial was performed to evaluate whether a combination of these agents was effective in relieving the cytopenias associated with MDS. Twenty-seven patients with low- or intermediate-risk MDS were enrolled in a 12-week study. ATRA was administered orally at the dose of 80 mg/m(2) per day in 2 divided doses for 7 consecutive days every other week. Recombinant human EPO was given subcutaneously 3 times a week. The EPO dose was initiated at 150 U/kg and was increased to 300 U/kg if after 6 weeks there was no or there was suboptimal erythroid response. Patients who responded to therapy were continued on ATRA and EPO at the same doses for 6 additional months (extension phase). Further treatment was given to patients with a continued response. Clinically significant erythroid responses with increases of hemoglobin levels of at least 1 g/dL or reduction of transfusion needs were seen in 13 (48%) patients, with 4 showing improved responses after dose escalation of EPO. Ten (37%) patients displayed continued responses during 6 months of extended treatment, and 7 (26%) are still responsive after a follow-up period of 13 months. Neutrophil responses were observed in 5 of 12 patients with neutropenia, and platelet responses were observed in 6 of 9 patients with thrombocytopenia. Three patients displayed trilineage responses that were sustained during continuation therapy. Side effects were observed in all patients but were of mild entity and did not require discontinuation of therapy. It is concluded that the combination ATRA + EPO is an effective and well-tolerated treatment for patients with low- and intermediate-risk MDS. The optimal ATRA and EPO schedule and the role of maintenance treatment remain to be determined and warrant further investigation.

Physical interaction with human tumor-derived p53 mutants inhibits p63 activities.

STRANO S., FONTEMAGGI G., COSTANZO A., RIZZO M.G., MONTI O., BACCARINI A., DEL SAL G., LEVRERO M., SACCHI A., OREN M., BLANDINO G.

J. Biol. Chem., 24,277(21), p.18817-26, 2002

The p53 tumor suppressor gene is the most frequent target for genetic alterations in human cancers, whereas the recently discovered homologues p73 and p63 are rarely mutated. We and others have previously reported that human tumor-derived p53 mutants can engage in a physical association with different isoforms of p73, inhibiting their transcriptional activity. Here, we report that human tumor-derived p53 mutants can associate in vitro and in vivo with p63 through their respective core domains. We show that the interaction with mutant p53 impairs in vitro and in vivo sequence-specific DNA binding of p63 and consequently affects its transcriptional activity. We also report that in cells carrying endogenous mutant p53, such as T47D cells, p63 is unable to recruit some of its target gene promoters. Unlike wild-type p53, the binding to specific p53 mutants markedly counteracts p63-induced growth inhibition. This effect is, at least par-

tially, mediated by the core domain of mutant p53. Thus, inactivation of p53 family members may contribute to the biological properties of specific p53 mutants in promoting tumorigenesis and in conferring selective survival advantage to cancer cells.

Differential expression of UN1, early thymocyte-associated sialoglycoprotein, in breast normal tissue, benign disease and carcinomas.

TASSONE P., BONELLI P., TUCCILLO F., BOND H.M., D'ARMIENTO F.P., GALEA E., PALMIERI C., TAGLIAFERRI P., NATALI P.G., VENUTA S.

Anticancer Res., 22(4), p.2333-40, 2002

Background: The UNI antigen (Ag) is a 120 kDa sialoglycoprotein which has been primarily found in human undifferentiated CD3dim thymocytes and leukemic T-cell lines, but subsequently also detected in solid tumors. We studied the expression of this Ag in a panel of normal and pathological breast tissues.

Materials and methods: Analysis of UN1 Ag expression on tissue specimens was performed by immunohistochemistry and Western blotting.

Results: No Ag expression was found in 14 sections of normal tissue and 10 sections of benign nonproliferative lesions. Progressively increasing levels of UN1 Ag expression were found in fibroadenomas (24 positive out of 27 cases), proliferative lesions (9 cases), in situ (17 cases) and invasive carcinomas (56 cases). Finally, the highest expression was observed in 10 metastatic lesions.

Conclusion: These data suggest that UN1 Ag is a promising marker of potential value for immunophenotyping studies and therapeutic applications in breast diseases.

Combined treatment with temozolomide and poly(ADP-ribose) polymerase inhibitor enhances survival of mice bearing hematologic malignancy at the central nervous system site.

TENTORI L., LEONETTI C., SCARSELLA M., D'AMATI G., PORTARENA I., ZUPI G., BONMASSAR E., GRAZIANI G.

Blood, 15,99(6), p.2241-4, 2002

Temozolomide (TZM) is a DNA-methylating agent that has recently been introduced into various clinical trials for treatment of solid or hematologic neoplasias, including brain lymphomas. In the current study, we have investigated whether the antitumor activity of TZM could be selectively enhanced at the central nervous system (CNS) site by intracerebral injection of a poly(ADP-ribose) polymerase (PARP) inhibitor. Mice were injected intracranially with lymphoma cells. The PARP inhibitor NU1025 (1 mg/animal) was delivered intracerebrally, whereas TZM was given as a single or a fractionated dose of 200 mg/kg by intraperitoneal administration. Results indicated that this drug combination significantly enhanced the survival of tumor-bearing mice and that this fractionated modality of treatment was the most effective schedule. Increased survival time was related to a marked reduction of tumor growth, as evidenced by histologic studies. Treatment with TZM alone was ineffective. This is the first report exploring in vivo the combination of TZM with PARP inhibitor for intracerebral neoplasias.

Does downstaging predict improved outcome after preoperative chemoradiation for extraperitoneal locally advanced rectal cancer? A long-term analysis of 165 patients.

VALENTINI V., COCO C., PICCIOCCHI A., MORGANTI A.G., TRODELLA L., CIABATTONI A., CELLINI F., BARBARO B., COGLIANDOLO S., NUZZO G., DOGLIETTO G.B., AMBESI-IMPIOMBATO F., COSIMELLI M.

Int. J. Radiat. Oncol. Biol. Phys., 1,53(3), p.664-74, 2002

Purpose: To evaluate the impact of tumor response; tumor and nodal downstaging; and cTNM, yTNM (clinical stage after chemoradiation, based on preoperative imaging), and pTNM classifications on long-term outcome in patients with rectal cancer treated with preoperative 5-fluorouracil (5-FU)-based concurrent chemoradiation.

Methods and materials: Between January 1990 and March 1998, 165 consecutive patients with locally advanced extraperitoneal cancer of the rectum were treated with preoperative chemoradiation. Four patients had a cT2 lesion (2.5%), 120 had a cT3 lesion (74.5%), and 41 had a cT4 lesion (23%). The nodal involvement at combined imaging was cN0 in 21%, cN1 in 41%, cN2 in 34%, and cN3 in 4%. Preoperative chemoradiation was delivered according to 1 of 3 schedules: (1) FUMIR-T3 (from 1990 to 1995) for patients with cT3N0-2 or cT2N1-2 rectal carcinoma (82 patients): 37.8 Gy (1.8 Gy/fraction) plus 5-FU, 1 g/m(2)/d on Days 1-4, continuous infusion,

and mitomycin-C, 10 mg/m(2)/d on Day 1; (2) FUMIR-T4 (from 1990 to 1999) for patients with cT4N0-3 or cT3-4N3 rectal carcinoma (40 patients): 45 Gy (1.8 Gy/fraction) plus 5-FU, 1 g/m(2)/d on Days 1-4 and 29-32, continuous infusion, and mitomycin-C, 10 mg/m(2)/d on Days 1 and 29; and (3) PLAFUR-4 (from 1995 to 1998) for patients with cT3N0-2 or cT2N1-2 rectal carcinoma (42 patients): 50.4 Gy (1.8 Gy/fraction) plus 5-FU, 1 g/m(2)/d on Days 1-4 and 29-32, continuous infusion, and cisplatin, 60 mg/m(2)/d on Days 1 and 29. Four to five weeks after chemoradiation, patients were reevaluated for clinical response by imaging studies (CT scan, transrectal ultrasonography, barium enema, liver ultrasonography, chest X-rays) and restaged (yTNM). Surgery was performed 6-8 weeks after chemoradiation. Adjuvant chemotherapy (5-FU + l-folinic acid) was delivered to 26 patients in the FUMIR-T4 protocol group. Local control (LC), freedom from distant metastases (FDM), disease-free survival, and overall survival (OS) were evaluated according to the clinical response and cTNM, yTNM, and pTNM classification. The median follow-up was 67 months. RESULTS: The 5-year survival rate was 100% for cT2, 77% for cT3, and 62% for cT4 ($p = 0.0497$); after chemoradiation, it ranged between 81% and 91% for pT0-pT2 and dropped to 66% for pT3 and 47% for pT4 ($p = 0.014$). The 5-year local control rate was, at the first staging, 84% for cT3 and 72% for cT4; after chemoradiation, the pT stage correlated significantly with LC ($p = 0.0012$): 100% for pT0, 83% for pT1, 88% for pT2, 79% for pT3, and 46% for pT4. N stage was statistically significant in predicting FDM and OS at any staging step. A significant impact of tumor response, tumor downstaging, and nodal downstaging on LC, FDM, disease-free survival, and OS was also recorded. If the residual tumor, before surgery, had a tumor index <30 (i.e., width less than one-quarter of rectal circumference and length in its caudocranial axis < or =30 mm), the 5-year LC, FDM, disease-free survival, and OS rates were significantly higher at both the univariate and the multivariate analyses. The surgical procedure was tailored according to tumor downstaging, and thus the choice of sphincter-preserving surgery was based on the distance between the lower pole of the tumor and the anorectal ring "after" chemoradiation. In 36 patients with the lower pole of the lesion in the range of 0-30 mm from the anorectal ring, 16 patients (44%) underwent a sphincter-saving procedure. All clinical outcomes were similar compared with 20 patients with tumor located at the same rectum level who received an abdominoperineal resection.

Conclusion: After preoperative chemoradiation, clinical response and tumor/nodal pathologic downstaging showed a close correlation with improved outcomes. The better 5-year survival and local control in pT0-2 patients regardless of their initial stage seems to confirm a heterogeneity in rectal cancer patients. The responder population showed a behavior similar to rectal cancer diagnosed at Stage cT1-2 and treated with conservative surgery alone. Additional studies aimed at improving local tumor response seem justified. Trials of sphincter-saving surgery after a major response are warranted.

Endothelin receptor blockade inhibits the growth of human papillomavirus-associated cervical carcinoma.

VENUTI A., SALANI D., CIRILLI A., SIMEONE P., MULLER A., FLAMINI S., PADLEY R., BAGNATO A.

Clin. Sci. (Lond), 1,103(1), p.310S-3S, 2002

Human papillomaviruses (HPVs) are associated with cervical cancer and interact with growth factors that may enhance malignant transformation of cervical carcinoma cells. Endothelin-1 (ET-1) is released from HPV-transfected keratinocytes and induces increased growth response in these cell lines in comparison with normal cells. HPV-positive cancer cells secrete ET-1 and express mRNA for ET-1 and its receptors, whereas HPV-negative carcinoma cell lines express only the ET(B) receptor (ET(B)R) mRNA and do not secrete ET-1. In HPV-positive cancer cells, ET(A)R mediates the ET-1-induced mitogenic effect and sustains the basal growth rate of unstimulated cervical tumour cells. Therefore, ET-1 may be involved in the neoplastic growth of HPV-associated cervical carcinoma, where the increased ET-1 autocrine loop can be targeted for antitumour therapy. In the present work, the action of specific antagonists of ET(A)R (BQ-123 and ABT-627), was analysed in CaSki and C33A cells that are derived from human cervical carcinoma. CaSki cells are HPV-16-positive, produce ET-1 and possess ET(A)R and ET(B)R, whereas the C33A line is HPV-negative, does not secrete ET-1 and has no ET(A)R. In HPV-positive cancer cells ABT-627 strongly inhibited the proliferation induced by ET-1 and substantially reduced the basal growth rate of unstimulated cer-

vical tumour cells, whereas the ET(B)R antagonist had no effect. These results demonstrate that ET-1 participates in the progression of neoplastic growth in HPV-associated carcinoma, in which ET(A)R expression is increased and could be targeted for antitumour therapy. In conclusion, an ET-1 autocrine loop is involved in tumour cell proliferation via ET(A)R, and ABT-627 is effective in controlling proliferation of cervical carcinoma cells.

Search of anti-adriamycin antibodies in serum of cancer patients under chemotherapic treatment.

VERDINA A., TONACHELLA R., COLELLA E., FALASCA G., GALATI R.

J. Exp. Clin. Cancer Res., 21(3), p.337-40, 2002

The exposure to DNA reactive carcinogens is known to elicit a specific humoral immunological response, with the production of antibodies towards the carcinogen adducts. In analogy to chemical carcinogens, any chemotherapic, like Adriamycin, undergoes the same adduct formation, and for this reason could elicit specific antibodies. In this case we can suppose that an eventual immunological response could influence the efficacy of chemotherapy. The aim of this study was to verify if adriamycin adducted to DNA or transport proteins can elicit an immunological response of specific anti-adriamycin (ADM) antibodies in sera of 43 cancer patients treated with the drug. No specific antibodies were detected in these individuals. The lack of anti-adriamycin antibodies suggests that the therapeutic exposure to the drug does not elicit a specific immunological response.

First-line treatment with epirubicin and vinorelbine in metastatic breast cancer.

VICI P., COLUCCI G., GEBBIA V., AMODIO A., GIOTTA F., BELLI F., CONTI F., GEBBIA N., PEZZELLA G., VALERIO M.R., BRANDI M., PISCONTI S., DURINI E., GIANNARELLI D., LOPEZ M.

J. Clin. Oncol., 20(11), p.2689-94, 2002

Purpose: This phase II multicenter trial was aimed at investigating the activity of epirubicin-vinorelbine combination as first-line chemotherapy in metastatic breast cancer patients.

Patients and methods: Ninety-seven patients with metastatic breast cancer and no prior exposure to anthracyclines received the following regimen: epirubicin 100 mg/m(2) by intravenous (IV) bolus infusion on day 1 plus vinorelbine 25 mg/m(2) by 30-minute IV infusion on days 1 and 5, every 3 weeks for up to eight cycles. All patients also received granulocyte colony-stimulating factor (G- CSF) on days 7 to 12 of every cycle.

Results: Objective responses, confirmed at least 4 weeks after the first documentation, were observed in 65 out of 92 assessable patients (70.6%; 95% CI, 62% to 80%). Disease remained stable in 17 patients (18.5%). Responses were observed in all disease sites, being 94% in soft tissue, 60% in bone, and 66% in visceral disease. Median time to response, median duration of response, median time to progression, and median overall survival were 2, 9, 10, and 26 months, respectively. The dose-limiting toxicity was neutropenia, which was grade 4 in 36% of the patients, and was accompanied by fever in 26% of the cases. Grade 3 to 4 mucositis was encountered in 28% of the patients. Other toxicities were mild to moderate. No cardiotoxicity was observed.

Conclusion: The epirubicin-vinorelbine combination with G-CSF support has been shown in this study to be highly active as first-line treatment of metastatic breast cancer patients, with significant although transient toxicity. This justifies further evaluation in the neoadjuvant setting and in early-stage breast cancer.

Role and prognostic significance of CD44s expression in colorectal cancer.

VISCA P., DEL NONNO F., BOTTI C., MARANDINO F., SEBASTIANI V., DI TONDO U., PERRONE DONNORSO R., TROMBETTA G., FILIPPI S., AND ALO P.

Anticancer Res., 22(5), p.2671-5, 2002

The purpose of this study was to clarify the role and the predictive strength of the adhesion molecule CD44s (standard isoform) in colorectal carcinogenesis.

Materials and methods: CD44s immunohistochemical expression was evaluated in 100 patients with colon adenoma and 100 patients with colon adenocarcinoma and adjacent non-neoplastic mucosa (ANNM). The patients were followed-up for five years.

Results: CD44s immunoreactivity was expressed in low-moderate-high-grade dysplasia ade-

nomas and associated with adenocarcinoma (p = 0.01), ANNM (p = 0.05) and pTNM stage (p = 0.00001). Univariate analysis revealed that CD44s expression was associated with overall survival (OS) in carcinomas (p = 0.01) and ANNM (p = 0.05). Bivariate analysis revealed that CD44s was associated with OS in stages I and II patients (p = 0.03). Multivariate analysis revealed that stage (p = 0.0001) and CD44s expression (p = 0.05) were independent predictors of OS.

Conclusion: CD44s is involved in colon carcinogenesis and is associated with aggressive carcinomas. The immunohistochemical expression of CD44s may reveal cells that have lost their adhesion ability and therefore detect carcinomas with high metastatic power.

Colourimetric signal amplification of in situ hybridization assay for human papillomavirus DNA detection in cytological samples.

VOCATURO A., MARANDINO E., CELATA E., CAFFO A., MOAURO M., VOCATURO G., PERRONE DONNORSO R.

J. Exp. Clin. Cancer Res., 21(2), p.239-46, 2002

Signal amplification of In Situ Hybridization (ISH) can be obtained by Catalyzed Reporter Deposition (CARD), the catalyzed deposition of biotinylated tyramide at the location of the labelled probe. We analyzed 156 cervico/vaginal samples in order to evaluate whether ISH-CARD improves conventional ISH technique in detecting Human Papillomavirus (HPV) on cytological smears and can be used in clinical practice. 126 patients were clinically suspected to have a squamous intraepithelial lesions (SIL) and 30 were negative control-patients. We performed a HPV test screening on these 156 patients with both methods. The screening positive cases were tested for the presence of subtypes of HPV: 6/11, 31/33/51 and 16/18, using only the ISH-CARD. We found a significant increase of positivity with the amplified system, ISH: positive = 50 cases, ISH-CARD: positive = 120 cases, even in many cases cytologically negative. Many cases showed coinfections with different types of HPV. We observed overlapping results in some cell lines harbouring specific HPV subtypes (SiHa, CaSki and HeLa cells), whereas there was no reaction in the C33A cells, negative for HPV presence. This method enables the detection and the typing of HPV in cytological smears, represents a useful tool for clinical purposes and even identifies occult HPV infections.

Transcription and alternative splicing of telomerase reverse transcriptase in benign and malignant breast tumours and in adjacent mammary glandular tissues: implications for telomerase activity.

ZAFFARONI N., DELLA PORTA C., VILLA R., BOTTI C., BUGLIONI S., MOTTOLESE M., GRAZIA DAIDONE M.

J. Pathol., 198(1), p.37-46, 2002

Telomerase activity was determined in 15 breast cancers, 24 benign breast lesions, and 36 breast tissues adjacent to benign or malignant tumours. A positive TRAP (telomeric repeat amplification protocol) signal was detected in 67% of carcinomas and 29% of benign tumours. In five of ten cases, non-invaded breast tissues adjacent to telomerase-positive carcinomas also displayed telomerase activity. Conversely, in peritumoural specimens adjacent to benign lesions, telomerase activity was never detected. To investigate the regulatory mechanisms of telomerase activity in breast tissues, the expression of telomerase subunits was assessed, as well as the presence of alternatively spliced variants of human telomerase reverse transcriptase (hTERT). The presence of the hTERT full-length transcript appeared necessary for telomerase activity in breast carcinomas. Specifically, all telomerase-positive carcinomas expressed the hTERT full-length message, together with different combinations of alternatively spliced variants, whereas in telomerase-negative cancers, the hTERT full-length transcript was not detectable, or its abundance was markedly lower than that of alternatively spliced variants. Results obtained in benign tumours and normal tissues surrounding carcinomas instead showed that the presence of hTERT full-length transcript was not sufficient to determine telomerase activity. These findings suggest that in non-neoplastic tissues there are other mechanisms that suppress telomerase activity downstream from hTERT transcription and mRNA splicing and that such mechanisms have been lost during neoplastic transformation.

The prolyl isomerase Pin1 reveals a mechanism to control p53 functions after genotoxic insults.

ZACCHI P., GOSTISSA M., UCHIDA T., SALVAGNO C., AVOLIO F., VOLINIA S., RONAI Z., BLANDINO G., SCHNEIDER C., DEL SAL G.

Nature, 24,419(6909), p.853-7, 2002

The tumour suppressor p53 is important in the cell decision to either arrest cell cycle progression or induce apoptosis in response to a variety of stimuli. p53 post-translational modifications and association with other proteins have been implicated in the regulation of its stability and transcriptional activities. Here we report that, on DNA damage, p53 interacts with Pin1, a peptidyl-prolyl isomerase, which regulates the function of many proteins involved in cell cycle control and apoptosis. The interaction is strictly dependent on p53 phosphorylation, and requires Ser 33, Thr 81 and Ser 315. On binding, Pin1 generates conformational changes in p53, enhancing its transactivation activity. Stabilization of p53 is impaired in UV-treated Pin1(-/-) cells owing to its inability to efficiently dissociate from Mdm2. As a consequence, a reduced p53-dependent response was detected in Pin1(-/-) cells, and this correlates with a diminished transcriptional activation of some p53-regulated genes. Our results suggest that, following stress-induced phosphorylation, p53 needs to form a complex with Pin1 and to undergo a conformational change to fulfil its biological roles.

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XLII Congresso Nazionale della Società dei Neurologi, Neurochirurghi e Neuroradiologi Ospedalieri (SNO). Catania, 22-25 Maggio 2002

35. Gelibter A., Ceribelli A., Milella M., Mottolese M., Cognetti F.

Clinically meaningful response to EGFR inhibition in NSCLC.

IV Congresso Nazionale AIOM. Torino, 28 Settembre - 1 Ottobre 2002. Ann. Oncol., 3(3), p.21, 2002

36. Giorda E., Sibilio L., Fraioli R., Martayan A., Moretti S., Venturo I., Mottolese M., Ferrara G.B., Cappellacci S., Grammatico P., Catricalà C. and Giacomini P.

The assembly line of HLA-A, -B, -C molecules: linked patterns of coordinate gene expression in neoplastic cells.

XXIX Symposium of the Italian Cancer Society SIC. Genova, 27-30 Ottobre 2002

37. Grassi A., Assisi D.

Chronic atrophic gastritis with intestinal metaplasia: Methylene blue chromoendoscopy in the clinical practice.

Dig. Liver Dis., 34, A 113, 2002

38. Greco C., Cosimelli M., Casale V., Vona R., Assisi D., Matarrese P., Straface E., Scordati P., et al.

Comparative analysis of Ki-Ras codon 12 mutation and expression of CD44/v6 and Galectin-3 in the adenoma-carcinoma sequence of the colorectal tract.

Congresso Italiano di Patologia e Diagnostica Molecolare. Pisa, 25-28 Settembre 2002

39. Jandolo B.

Complicanze della chemioterapia.

Atti del Corso Complicanze Neurologiche delle Neoplasie e delle Terapie Antineoplastiche. Torino, 12 Dicembre 2002

40. Leonetti C., Scarsella M., D'Angelo C., Cianfriglia M., Molinari A., Semple S.C., Zupi G.

Encapsulation in liposome is able to overcome the in vivo resistance to vincristine of human solid tumors.

XXIX Symposium of the Italian Cancer Society SIC. Genova, 27-30 Ottobre 2002

41. Lepiane P., Carlini M., Carboni F., Lonardo M.T., Scardamaglia F., Petric M., Santoro E.

L'adenocarcinoma del cardias: resezione esofagogastrica transiatale.

XV Congresso Nazionale SPIGC. Vibo Valentia, 23-25 Giugno 2002.
Minerva Chirurgica, 57(1), p.130, 2002

42. Mancini R., Garufi C., Pugliese P., Perrone M., Caterino M., Giunta S., Cosimelli M.

Chemioterapia endoarteriosa epatica (E.A.E.) nel trattamento delle metastasi epatiche colorettali non resecabili: esperienza personale.

XXIX Symposium of the Italian Cancer Society SIC. Genova, 27-30 Ottobre 2002.
Tumori, 3(1), p.S30-S32, 2002

43. Mancini R., Graziano F., Buglioni S., D'alessandro R., Biroccio A., Piperno G., Sperduti I., Cosimelli M.

Impatto clinico della stadiazione biologica nel cancro del colon-retto stadio B2 di Astler-Coller.

XXIX Symposium of the Italian Cancer Society SIC. Genova, 27-30 Ottobre 2002.
Tumori, 3(1), p.S103, 2002

44. Mancini R., Graziano F., Piperno G., Ambesi-Impiombato F., Sperduti I., Cosimelli M.

La chirurgia del carcinoma rettale nei pazienti ultrasettantenni: esperienza dell'Istituto "Regina Elena" di Roma.

104° Congresso Società Italiana di Chirurgia

45. Manni I., Caretti G., Frontini M., Mantovani R., Sacchi A. and Piaggio G.

Mechanisms regulating NF-Y Expression: Role for Acetylation.

IV Convegno Federazione Italiana Scienze della Vita. Riva Del Garda, 20-23 Settembre 2002

46. Marzano R., Cosimelli M., Graziano F., Merola R., Leonardo G., Cianciulli A.M.

Cytogenetic aberrations in colorectal adenocarcinomas and their correlation with clinicopathologic features.

XXIX Symposium of the Italian Cancer Society SIC. Genova, 27-30 Ottobre, 2002. Tumori, 3(1), p.106-107, 2002

47. Maschio M., Pietrangeli A., Pace A., Angelici A., Galiè E., Jandolo B., et al.

Involvement of peripheral nervous system after influenza virus infection: presentation of an unusual case.

XXXIII Congresso Nazionale della Società Italiana di Neurologia (SIN). Napoli, 17 Settembre 2002. Neurol. Sci., 23, 2002

48. Mattioni M., Spila A., D'Alessandro R., Sacchi A., Guadagni F.

Serum p53 antibody as a useful marker for monitoring gastric carcinoma.

XXIX Symposium of the Italian Cancer Society SIC. Genova, 27-30 Ottobre 2002

49. Milella M.

Intermedi citoplasmatici di segnalazione (MAPK-PI3K).

Simposio Scientifico: Le Terapie Target-Oriented. IV Congresso Nazionale AIOM. Torino, 28 Settembre - 1 Ottobre 2002

50. Milella M.

IV Congresso Nazionale AIOM. Intervento pubblicato sul Volume Educazionale, p.235. Torino, 28 Settembre - 1 Ottobre 2002

51. Milella M.

Inibitori della traduzione del segnale ed induttori di apoptosi nel modello leucemico.

Congresso Interdisciplinare S.Lc.D. - S.LT., Attualità in Terapia Biomolecolare, intervento pubblicato sul Volume dei Riassunti. Torino, 28-30 Novembre 2002

52. Morrone A., Franco G., Toma L., Latini O., Mariani L.

Le mutilazioni genitali femminili: esperienza dell'Istituto San Gallicano.

78° Congresso Nazionale della SIGO. Perugia 9-13 Novembre 2002

53. Nadasi E., Botti C., Giannarelli D., Buglioli S., Benevolo M., Del Monte G., Venturo I., Marandino F., Perrone Donnorso R., Scordati P., Natali P.G., Mottolese M.

COX-2 expression in high risk breast cancer patients treated with adjuvant anthracycline-based therapy.

XXIX Symposium of the Italian Cancer Society SIC. Genova, 27-30 Ottobre 2002

54. Nisticò C., Bria E., Carpino A., Vanni B., Vitelli G., D'Ottavio A.M., Colella E., Tropea F., Aschelter A.M., Garufi C., Izzo F., Casali A., Scapati A. and Terzoli E.

Cardiological toxicity of weekly administration of epirubicin and paclitaxel in untreated advanced breast cancer patients.

IV Congresso Nazionale AIOM. Torino, 28 Settembre - 1 Ottobre 2002

55. Oppido P.A., Antenucci P., Piola P., Conti L., Carapella C.M., Occhipinti E.

La cinetica cellulare nella valutazione prognostica dei pazienti affetti da meningioma intracranico.

51° Congresso Nazionale SINch. Bolzano, 18-21 Settembre 2002

56. Pace A., Maschio M.

XXXIII Congresso della Società Italiana di Neurologia SIN. Napoli, 17 Settembre 2002. Neurol. Sci., 23, p.S629-633, 2002

57. Pace A., Vidiri A., Cattani F., Galiè E., Maschio M., Occhipinti E., Jandolo B., Carapella C.M.

Temozolomide chemotherapy for progressive low grade glioma.

XLII Congresso Nazionale SNO. Catania, 22-25 Maggio 2002

58. Paggi M.G.

Novel molecular approaches in the therapy of the human melanoma.

VI Congresso Nazionale GOIM. Napoli, 11-15 Giugno 2002

59. Papaldo A., Fabi A., Ruggeri E.M., Cognetti F.

Clinical benefit (cb) from using anastrozole (anz) followed by formestane (for) in metastatic breast cancer (mbc).

IV Congresso Nazionale AIOM. Torino, 28 Settembre - 1 Ottobre 2002

60. Piantelli M., Caltagirone S., Rossi C., Aiello F.B., Iacobelli S., Natali P.G.

Flavonoids inhibit melanoma lung metastasis by imparing tumor cell-endothelium interactions.

XXIX Symposium of the Italian Cancer Society SIC. Genova, 27-30 Ottobre 2002

61. Pietrangeli A., Galiè E., Pugliese P., Perrone M., Cusumano G., Graziano F., Cosimelli M., Jandolo B.

Impotenza sessuale come complicanza neurologica della chirurgia del carcinoma del retto.

Congresso di Elettrofisiologia in Riabilitazione. Roma, 18 Ottobre 2002

62. Pizzi G., Vidimi A., Carpanese L., Caterino M., Crecco M.

Ricerche di metastasi epatiche con Levovist: comparazione con l'utilizzo di mdc paramagnetici epatospecifici in Risonanza Magnetica.

40° Congresso Nazionale SIRM. Rimini, 24-28 Maggio 2002.
La Radiologia Medica, 103(3), p.215, 2002

63. Poggiali F., Ambrosio V., Borzacchiello G., Roperto S., Tsirimonakis E., Campo S.M., Roperto F., Marcante M.L., Venuti A.

First evidence of BPV-4 presence in continental Europe.

II Congresso Nazionale di Virologia. Cortona, 13-14 Settembre 2002

64. Riccioni S., Blandino G., Sacchi A., Falcioni R.

Expression of integrin subunit in 32D/v-Abl cell induces monocytic differentiation.

"Meccanismi di trasduzione del segnale in adesione e differenziamento cellulare". ABCD Torino, 10-11 Maggio 2002

65. Rosanò L., Spinella F., Di Castro V., Nicotra M.R., Natali P.G., Bagnato A.

Role of endothelin-1 and its receptor in proliferation and invasive behavior of Kaposi's sarcoma.

XXIX Symposium of the Italian Cancer Society SIC. Genova, 27-30 Ottobre 2002

66. Scardamaglia F., Ettorre G.M., Vennarecci G., Carboni F., Lonardo M.T., Petric M., Santoro R., Lepiane P., Carlini M., Santoro E.

Liver Hanging Maneuver, per un'epatectomia destra sicura.

XV Congresso Nazionale SPIGC. Vibo Valentia, 23-25 Giugno 2002.
Minerva Chirurgica, 57(1), p.85, 2002

67. Simeone P., De Marco F., Venuti A., Muller A., Flamini S., Romdhane K.B., Marcante M.L.

"Human Papillomavirus presence in genital tumours of Tunisian women". Poggiali F.

XXIX Symposium of the Italian Cancer Society SIC. Genova, 27-30 Ottobre 2002

68. Soddu S., Cecchinelli B., Prodosmo A., Di Stefano V., D'Orazi G.

Functional role of the HIPK2/P53 interaction in differentiation and development.

Comitato Telethon Fondazione Onlus, Scientific. Riva del Garda, 24-26 Novembre 2002

69. Spinella F., Rosanò L., Elia G., Di Castro V., Nicotra M.R., Natali P.G., Bagnato A.

Regulation of connexin-43gap junctional intercellular communication by endothelin-1: possible involvement of the mitogen-activated protein kinase and phosphatidylinositil 3-kinase.

XXIX Symposium of the Italian Cancer Society SIC. Genova, 27-30 Ottobre 2002

70. Spriano G., Ruscito P., Morello R., Appetecchia M.

Analisi dei fattori di rischio di metastasi linfatiche locoregionali ed a distanza nel carcinoma differenziato della tiroide.

XX Giornate Italiane della Tiroide. Pisa, 5-7 Dicembre 2002

71. Venuti A., Cirilli A., Salani D., Simeone P., Muller A., Nicotra M.R., Natali P.G., Bagnato A.

Targeted therapy of HPV associated cervical carcinoma: endothelin A receptor antagonists.

XXIX Symposium of the Italian Cancer Society SIC. Genova, 27-30 Ottobre 2002

72. Vidiri A., Carapella C.M., Caterino M., Pace A., Crecco M.

La Risonanza Magnetica precoce nella valutazione dei gliomi sottoposti a chirurgia.

40° Congresso Nazionale SIRM. Rimini, 24-28 Maggio 2002.
La Radiologia Medica, 103(3), p.105, 2002

73. Vizza E., Corrado G., Galati G.M., Di Paola G., Sbiroli C.

Tumefazioni annessiali di grosso volume: approccio laparoscopico mediante S.A.N.D. Balloon Catheter.

II Corso: Dalla anatomia chirurgica alla chirurgia anatomica demolitiva
e ricostruttiva della pelvi femminile. Roma, 3-7 Giugno 2002

74. Vizza E., Galati G.M., Corrado G., Vincenzoni C., Quattrini M., Mariani L., Sbiroli C.

Carcinoma invasivo a cellule squamose della vulva in pazienti giovani: case report.

XVII Congresso Nazionale della Società Italiana di Colposcopia e Patologia Cervico Vaginale. Roma, 5-7 Dicembre 2002

75. Vocaturo A., Novelli F., Piperno G., Scordati P., Cianciulli A.M., Merla R., Marandino F., Giannarelli D., Benevolo M., Buglioli S., Botti C., Mottolese M.

HER-2 status evaluation in breast carcinoma by chromogenic in situ hybridization (CISH): correlation with immunohistochemical (ICH) and fluorescence in situ hybridization (FISH) analysis.

Congresso italiano di Patologia e Diagnostica Molecolare. Pisa, 25-28 Settembre 2002

Conferenze
Hosted Lectures

4 Gennaio — Dr. Giuseppe Trigiante, Ludwing Institute for Cancer Research, Imperial College St. Mary's Campus, London
ASPP proteins: apoptosis advisors of p5.

29 Gennaio — Dr.ssa Stella Zannini, Dipartimento di Biologia e Patologia Cellulare e Molecolare, Università degli Studi Federico II di Napoli
Pax8 agisce da master gene nel differenziamento tiroideo.

20 Febbraio — Dr. Salvatore Sciacchitano, Dipartimento di Medicina Sperimentale e Patologia, Università degli Studi "La Sapienza" di Roma
Analisi della perdita di eterozigosi in cellule neoplastiche tiroidee isolate mediante laser capture microdissection.

3 Aprile — Dr. Mauro Boiocchi, Centro di Riferimento Oncologico di Aviano
Linfomi HCV associati.

22 Aprile — Prof. Adriano Aguzzi, Istituto di Neuropatologia, Università di Zurigo
Molecular biology of prion diseases.

23 Maggio — Dr.ssa Mary Ellen Perry, McArdle Laboratory, University Wisconsin Medison, USA
Physiological Functions of MDM2.

7 Giugno — Dr. Simone Fulda, University Children's Hospital, Prittwitzstr, Germania
Apoptosis signaling pathways in cancer therapy.

11 Giugno — Prof.ssa Marina Konopleva, Department of Blood and Marrow Transplantation, University of Texas, M.D. Anderson Cancer Center
PPARgamma ligation by a triterpenoid CDDO as a novel therapy for leukemias.

14 Giugno — Prof. Antonio Giordano, lo Sbarro Institute for Cancer Research and Molecular Medicine
The retinoblastoma family genes in cell cycle and cancer.

21 Giugno — Dr. Claudio Sette, Dipartimento di Sanità Pubblica e Biologia Cellulare, Università degli Studi Tor Vergata, Roma
Meccanismi molecolari che regolano le transizioni del ciclo cellulare meiotico.

24 Giugno — Prof. Guido Forni, Dipartimento di Scienze Cliniche e Biologiche, Ospedale S. Luigi Gonzaga, Orbassano, Torino
Raffaele Tecce - 2° Memorial Lecture. Prevenzione immunologia dei tumori: una nuova prospettiva?

23 Luglio — Dr. Erik Knudsen, University of Cincinnati

Retinoblastoma tumor suppressor: trascriptional repression, targets and the cell cycle.

25 Settembre — Dr. James T. Kurnick, Associate Professor Department of Pathology, Massachusetts General Hospital and Harvard Medical School, USA

Restoring Antigen Expression in Melanomas: Implications for Immunotherapy.

7 Ottobre — Dr.ssa Maria Felice Brizzi, Ricercatore presso il Dipartimento di Medicina Interna, Università di Torino

STAT5 e neoangiogenesi patologica.

17 Ottobre — Dr. Steven J. Berberich, Department of Biochemistry and Molecular Biology, Wright State University, Dayton, Ohio

Comparing Mdmx to Mdm2.

18 Ottobre — Dr.ssa Keiko Ozato, Group Leader of Laboratory of Molecular Growth Regulation, NICHD, NIH, Bethesda

A novel bromodomain protein Brd4 interacts with chromatin and regulates cell growth.

22 Ottobre — Dr. Fabrizio Mainiero, Istituto di Patologia Generale dell'Università degli Studi "La Sapienza", Roma

Integrine e controllo dell'espressione di citochine e chemiochine della risposta immunitaria ed infiammatoria.

25 Ottobre — Dr. Ivan Dikic, M.D., Ph.D., Group Leader, Molecular Signaling Laboratory, Ludwig Institute for Cancer Research, Uppsala, Sweden

Regulation of EGF receptor degradation through Cbl and CIN85 dependent pathways.

6 Novembre — Prof. Renato Baserga, Kimmel Cancer Institute, Philadelphia, USA

IRS-1 nucleare e controllo della proliferazione.

13 Novembre — Dr. Cy Stein, Dept. Of Medicine, Columbia University, College of Physicians and Surgeons, New York

The second-largest biotech deal in history: an update on G3139 (Oblimersen).

20 Dicembre — Dr. Danilo Perrotti, Kimmel Cancer Center, Thomas Jefferson University, Philadelphia, Pennsylvania, USA

Genomics, Ribonomics and Proteomics: an Integrated Tree Level Study to Characterize the Effect of BCR/ABL on Mrna metabolism.

Seminari Intramurali C.R.S.
Intramural Seminars C.R.S.

15 Febbraio — MAP chinasi come target terapeutico nelle leucemie mieloidi acute
Milella M.

20 Marzo — E1A e Ran, la strana coppia
Paggi M.

27 Marzo — Meccanismi trascrizionali di regolazione del ciclo cellulare e del differenziamento
Piaggio G.

24 Aprile — Ruolo differenziale dei recettori nucleari estrogenici, ERalpha ed ERbeta, nella regolazione trascrizionale della subunità catalitica della telomerasi umana (hTERT) in cellule e tessuti ormono-dipendenti
Farsetti A.

8 Maggio — Controllo trascrizionale specifico dell'espressione genica in cellule follicolari della tiroide
Civitareale D.

22 Maggio — Meccanismi che regolano la funzione della integrina alpha6beta4 nei tumori
Falcioni R.

29 Maggio — p53 e MAPK nella regolazione del ciclo cellulare
Soddu S.

26 Giugno — Come le cellule neoplastiche eludono il sistema immune (ovvero: invadi senza dare nell'occhio)
Sibilio L.

10 Luglio — Caratterizzazione funzionale del gene Che-1
Fanciulli M.

9 Ottobre — Ruolo di Bcl2 nell'angiogenesi tumorale
Del Bufalo D.
Seminario accreditato

23 Ottobre — Regolazione dell'attività di p73 nei processi dell'apoptosi e il differenziamento
Blandino G.
Seminario accreditato

15 Novembre

Nuove strategie nel trattamento nei tumori solidi umani

Leonetti C.

Seminario accreditato

27 Novembre

Un nuovo gene umano, omologo alla famiglia di Ena/VASP, isolato mediante SEREX da un tumore primitivo della mammella

Di Modugno F.

Seminario accreditato

4 Dicembre

Regolazione della funzione e della espressione del ligando di Fas, CD95L attraverso i recettori nucleari ormonali

Cippitelli M.

Seminario accreditato

18 Dicembre

Effetti biologici e meccanismi molecolari indotti dalla deregolazione dell'oncogene c-Myc nel melanoma umano

Biroccio A.

Seminario accreditato

Seminari Monotematici Multidisciplinari
Multidisciplinary Seminary

5 Marzo — Nuove chinasi nella regolazione dell'oncosoppressore p53: possibili applicazioni cliniche
Soddu A., Sacchi S.

2 Aprile — I Tumori neuroendocrini
Zeuli M., Perri P.

7 Maggio — I Tumori ereditari della mammella e del colon
Sega F., Guadagni F., Stigliano V.

4 Giugno — Ruolo della PET e della PET-TC in oncologia: possibili applicazioni cliniche
Maini C.M., Crecco M.

3 Luglio — Possibilità di potenziamento della chemioterapia: modelli pre-clinici
Zupi G., Leonetti F.

17 Settembre — Sarcomi delle parti molli
Lopez M., Di Filippo F.,Vidiri A.

8 Ottobre — Ruolo del personale infermieristico nello svolgimento della ricerca clinica
Nisticò C., Onesi E., Per Conti G.

5 Novembre — Farmacocinetica e modelli animali in oncologia
Citro G., Spugnino E., Carapella C.M.

3 Dicembre — Screening e trattamento locale dei tumori della prostata
Caperle M., Saracino B., Gallucci M.

Seminari Mattutini
Breakfast-Meetings

7 Febbraio — Polmone
Chairman: Guadagni F.
Giunta S.: Ruolo della TAC spirale low dose nella diagnosi precoce
Cilenti V.: Strategie contro il Tabagismo

14 Febbraio — Mammella
Article Review
Botti C.: Terapia ormonale neoadiuvante
Discussant: Papaldo P.

21 Febbraio — Mammella
Chairman: Terzoli E.
Carlini P.: Cross-resistenza degli inibitori delle aromatasi
Mottolese M.: Valore prognostico di FAS FAS/ligando

28 Febbraio — Biologia molecolare applicata alla clinica
Article Review
Milella M.: Inibitori della trasduzione del segnale: applicazioni cliniche
Discussant: Zupi G.

7 Marzo — Mammella
Chairman: Natali P.G.
Nisticò P.: Nuovi bersagli immunoterapeutici
Di Filippo F.: Impatto prognostico dei margini di resezione

14 Marzo — Colon-Retto
Article Review
Zeuli M.: Terapia Adiuvante nello stadio B2 Astler-Coller
Discussant: Paoletti G.

21 Marzo — Colon-Retto
Chairman: Arcangeli G.
Cosimelli M.: Dieci anni di RT-CT neoadiuvante nel carcinoma rettale
Guadagni F.: Micrometastasi circolanti: risultati preliminari

28 Marzo — Linfomi
Article Review
Ceribelli A.: Terapie di salvataggio nei LNH
Discussant: Petti M.C.

4 Aprile — Ricerca di base e biostatistica
Chairman: Zupi G.
Biroccio A.: Ruolo di c-myb e di bcl-x nel carcinoma colorettale
Giannarelli D.: Modelli sperimentali in biostatistica

11 Aprile — Fegato

Case Report

Ettorre G.: Trapianto

Discussant: Antonini M.

18 Aprile — Tumori

Chairman: Facciolo F.

Marino M.: Problemi diagnostici e classificativi dei tumori epiteliali

Carlini S.: Terapia chirurgica

9 Maggio — Genetica applicata alla clinica

Article Review

Cianciulli A.: Significato prognostico e predittivo della risposta alla terapia di alcuni marcatori genetici

Discussant: Lopez M.

16 Maggio — Tumori gliali

Chairman: Occhipinti E.

Vidiri A.: Ruolo della RMN precoce post-operatoria nella valutazione e prognosi

Pompili A.: Fattori prognostici e indicazioni terapeutiche

23 Maggio — Chirurgia plastica

Case Report

Pozzi M.: Nuove strategie ricostruttive in chirurgia mammaria

Discussant: Varanese A.

30 Maggio — Prevenzione della neurotossicità da chemioterapia

Chairman: Jandolo B.

Savarese A.: Ruolo della vitamina E

Pace A.: Ruolo del nerve-growth factor

6 Giugno — Cervice Uterina

Chairman: Sbiroli C.

Saracino M.: Trattamento integrato

Venuti A.: Nuove strategie terapeutiche

13 Giugno — Nuovi farmaci

Chairman: Natali P.G.

Bagnato A.: Il recettore della endotelina: un nuovo bersaglio terapeutico

Rinaldi M.: Efficacia dei nuovi farmaci biologici: criteri di valutazione

20 Giugno — Terapia del dolore

Chairman: Arcuri E.

Giovinazzo G.: Palliazione radioterapica

Sciuto V.: Terapia palliativa radiometabolica delle metastasi ossee

27 Giugno — Qualità di vita

Chairman: Pugliese P.

Perrone M.: Valutazione e miglioramento della qualità di vita

Pietrangeli A.: Impotenza sessuale nel retto operato

12 Settembre

Endometrio

Chairman: Sbiroli C.
Vizza E.: Morfodinamica 3D della trasformazione ed invasione neoplastica
Cianciulli A.: Aspetti genotipici e fenotipici della trasformazione ed invasione neoplastica

19 Settembre

Melanoma

Chairman: Di Filippo F.
Catricalà C.: La diagnosi precoce
Foggi P.: Chemioimmunoterapia

26 Settembre

Carcinoma esocrino del pancreas

Chairman: Santoro E.
Carpanese L.: Ruolo e limiti dello staging clinico
Carboni F.: Risultati della terapia chirurgica

3 Ottobre

Nutrizione artificiale in oncologia

Chairman: Casale V.
Assisi D.: Enterale
Centulio F.: Parenterale totale

10 Ottobre

Immunologia nei tumori solidi

Chairman: Natali P.G.
Giacomini P.: Strategie immunoevasive dei tumori solidi: modelli per svelarle, metodi per contrastarle
Mottolese M.: Ruolo degli anticorpi nella diagnosi e prognosi

17 Ottobre

Vescica

Chairman: Gallucci M.
Cantiani R.: Neovescica ortotopica
Ruggeri E.M.: Trattamento chemioterapico adiuvante

24 Ottobre

Epatocarcinoma

Article Review
Pizzi G.: Termoablazione: indicazioni e limiti
Discussant: Ettorre G.M.

7 Novembre

IORT

Chairman: Botti C.
Soriani A.: Aspetti di fisica sanitaria
Pinnarò P.: Nuove prospettive terapeutiche nel carcinoma mammario

14 Novembre

Cardiotossicità da chemioterapia e prevenzione

Case Report
Morace N.
Discussant: Vici P.

21 Novembre

Metastasi epatiche colorettali

Chairman: Cosimelli M.
Caterino M.: Nuovi criteri radiologici nella valutazione della risposta
Garufi C.: Chemioterapia neoadiuvante

28 Novembre

Il dolore post-operatorio

Article Review

Morace E.: Il controllo del dolore post-operatorio in chirurgia oncologica

Discussant: Aloe L.

5 Dicembre

Tiroide

Article Review

Marandino F.: Applicazione dell'immunoistochimica nel monitoraggio preoperatorio delle lesioni nodulari tiroidee

Discussant: Appetecchia M.L.

12 Dicembre

Metastasi cerebrali

Article Review

Raus L.: Trattamento integrato

Discussant: Carapella C.

19 Dicembre

Tumori cutanei

Chairman: Conti E.M.S.

Paggi M.G.: Identificazione e caratterizzazione di geni coinvolti nella trasformazione e progressione del melanoma umano

Ramazzotti V.: Prevenzione dei tumori cutanei nell'infanzia: distribuzione dei fattori di rischio

Organizzazione Seminari
Organization of Seminars and Meetings

Brescia 4-6 Marzo	Corso teorico-pratico AICC sulle "Tecniche di base per l'allestimento delle colture cellulari in vitro" (Dr. Leonetti C. in collaborazione con la Fondazione Iniziative Zooprofilattiche e Zootecniche e l'Istituto Zooprofilattico Sperimentale della Lombardia e dell'Emilia Romagna)
Cortona 11-13 Aprile	Convegno SIBBM 2002 Gruppo di Studio "Struttura e Funzione del Genoma" (Piaggio G., Tripodi M.)
Catania 22-25 Maggio	XLII Congresso Nazionale SNO (Società Neurologi Ospedalieri) (Dr. Jandolo B.)
Milano 30-31 Maggio	Convegno AICC (Dr. Leonetti C. in collaborazione con l'AISAL)
Roma 7 Giugno	Simposio Lap Group Roma (Dr. Carlini M.)
Roma 10-11 Giugno	P73/P63 Workshop 2002 Auditorium, I Clinica Medica Università di Roma "La Sapienza" (Dr. Blandino G.)
Roma 20-21 Giugno	Meeting "New approaches to diagnosis and treatment of non Hodgkin Lymphomas" (Dr.ssa Petti M.C., Dr.ssa Marino M.)
Napoli 17-23 Settembre	Congresso SIN (Dr. Jandolo B.: Sessione Neuro-Oncologia)
Firenze 7-10 Settembre	Congresso EANO (Dr. Jandolo B., Dr. Carapella C.M.)
Bolzano 18 Settembre	51° Congresso Nazionale SINch II Simposio Satellite SPIGC (Dr. Oppido P.A.)
Frascati (RM) 3-5 Ottobre	II International Workshop: "Making decision in G1" (Dr. Blandino G., Dr. Segatto O.)
Roma 7-9 Novembre	II Seminario Internazionale di chirurgia digestiva in oncologia (Prof. Santoro E.)

Brescia 11-13 Novembre	Corso avanzato di formazione teorico-pratico AICC sulla "Applicazione delle colture cellulari in vitro" (Dr. Leonetti C. in collaborazione con la Fondazione Iniziative Zooprofilattiche e Zootecniche e l'Istituto Zooprofilattico Sperimentale della Lombardia e dell'Emilia Romagna)
Roma 14 Novembre	Convegno: "Sì al Sole ma non da soli" (Dr. Conti E. M. S.)
Roma 16 Novembre	Convegno: "Morbo di Cushing: aspetti diagnostici e terapeutici" (Dr.ssa Appetecchia M.)
Roma 18 Novembre	Seminario: "Sarcomi dei tessuti molli" (Prof. Lopez M.)
Roma 29-30 Novembre	Seminario: "Tecnologie e problematiche della radioterapia conformazionale 3D" (Prof. Arcangeli G., Dr. Benassi M.)
Milano 2-3 Dicembre	Convegno Annuale AICC in collaborazione con l'Istituto Nazionale per lo Studio e la Cura dei Tumori di Milano: "Combinazione tra farmaci: basi farmacologiche, modelli e valutazioni in vitro e in vivo" (Dr. Leonetti C.)
Roma 5 Dicembre	Corso: "Statistiche Sanitarie relative ai Tumori della Pelle" (Dr.ssa Roscioni S.)
Roma 10 Dicembre	Meet the professor. Il medico di base e lo specialista. (Dr. Carlini M.)
Roma 12 Dicembre	Corso: "Fattori di rischio collegati all'alimentazione e sviluppo dei tumori" (Dr. Conti E.M.S.)
Roma 19 Dicembre	Corso: "Il tumore della pelle, i melanomi: misure di prevenzione della popolazione giovanile" (Dr.ssa Cercato M.C.)

Corsi
Teaching Courses

Corso per volontari ARVAS, anno 2002

54° Corso di formazione per Assistenti Volontari AMSO, anno 2002

II Corso Satellite di Informatica per neurochirurgia Endoscopica
(Dr. Oppido P. A.)
Bologna, 10-11 Maggio 2002

Corso teorico-pratico sul monitoraggio della pressione endocranica
(Dr. Oppido P. A.)
Roma, IRE, 23 Ottobre 2002

Corso Residenziale - Scuola Superiore di Oncologia e Scienze Biomediche: Thoracic Cancer: From bench to bedside
(Dr.ssa Ceribelli A.)
Roma, 12-13 Aprile 2002

Corso permanente per medici di medicina generale
(Dr. Casale V.)
Roma, anno 2002

Corso biennale in psicologia oncologica
(Dr. Pugliese P.)
Roma, anno 2002

Corso "Metodi di calcolo per IMRT"
Scuola superiore di oncologia e di scienze biomediche
(Dr. Benassi M.)
Napoli, Genova, Torino, Roma, anno 2002

Corso di aggiornamento AIOM Lazio/AIRO Lazio-Abruzzo
"L'integrazione terapeutica nelle neoplasie della mammella: dai consensus alla pratica clinica"
(Prof Terzoli. E., Prof. Arcangeli G.)
Roma, 10 Maggio 2002

Corso di aggiornamento AIOM Lazio/AIRO Lazio-Abruzzo
"L'integrazione terapeutica nelle neoplasie del retto: cosa è standard e cosa è da definire"
(Prof Terzoli. E., Prof. Arcangeli G.)
Roma, 14 Giugno 2002

Corso di Aggiornamento AIOM/Lazio AIRO/Lazio-Abruzzo
"L'integrazione terapeutica nelle neoplasie del polmone: dalla ricerca clinica alla pratica terapeutica"
(Prof. Terzoli E., Prof. Arcangeli G.)
Roma, 22 Novembre 2002

Corso di formazione ANDOS
(Prof. Terzoli E.)
Roma, 24-25 e 28-30 Ottobre 2002

Corso di scuola mediterranea di oncologia
(Dr. Garufi C.)
Roma, anno 2002

Corso Residenziale dell'Accademia Nazionale di Medicina.
"Terapie innovative in oncologia: targets molecolari e nuovi farmaci"
(Dr.ssa Biroccio A.M.)
Roma, 6-7 Giugno 2002

Corso dermatoscopia romana
(Dr. Frascione P.)
Roma, 11 Maggio 2002

Corso AMDO (Associazione Nazionale Medici Direzione Ospedaliera):
"Bisogni informativi e letteratura biomedica: il medico di fronte all'informazione su supporto elettronico: saper cercare, saper trovare"
(Dr.ssa Cognetti G.)
Roma, 20 Aprile 2002

Corso di aggiornamento: "La Caposala in Oncologia"
(Dr. Conti E.M.S.)
Sabaudia, 27-28 Settembre 2002

Corso di aggiornamento: "Caposala in Chirurgia"
(Dr. Carlini M.)
Sabaudia, 27-28 Settembre 2002

Corsi e sedi per scuole di specializzazione post-laurea
Post Graduate Specialization Courses and Venues

Anatomia Patologica

Pathology

Università degli Studi "Tor Vergata", Roma

Insegnamenti: Tecnica e Diagnostica delle Autopsie, Anatomia Patologica del Tratto Gastro-Digerente, Statistica

Anestesia e Rianimazione

Anaesthesiology and Intensive Care

Università "Campus Biomedico", Roma

Insegnamenti: Terapia del dolore

Chirurgia Generale

General Surgery

Università degli Studi "La Sapienza", Roma.

Insegnamenti: Patologia Mammaria e Melanomi, Chirurgia Oncologica, Terapie Parachirurgiche, Chirurgia Toracica

Università degli Studi "Tor Vergata", Roma

Insegnamenti: Chirurgia Oncologica

Chirurgia Plastica

Plastic and reconstructive Surgery

Università degli Studi "La Sapienza", Roma

Insegnamenti: Chirurgia Oncologica

Chirurgia Toracica

Thoracic Surgery

Università degli Studi "La Sapienza", Roma

Insegnamenti: Endoscopia Toracica

Chirurgia Vascolare

Vascular Surgery

Università degli Studi "La Sapienza", Roma

Insegnamenti: Accessi vascolari in Chirurgia Oncologica

Dermatologia e Venereologia

Dermathology

Università degli Studi "Tor Vergata" Roma

Insegnamenti: Dermatologia Clinica

Ematologia

Emathology

Università degli Studi "La Sapienza", Roma

Insegnamenti: Manifestazioni cliniche delle emopatie

Endocrinologia e malattie metaboliche

Endocrinology and Metabolic Diseases

Università degli Studi "La Sapienza", Roma

Insegnamenti: Endocrinologia, Andrologia, Malattie del Ricambio

Fisica Sanitaria

Medical Physics

Università degli Studi "Tor Vergata", Roma

Insegnamenti: Strumentazione Ospedaliera II, Risonanza Magnetica, Brachiterapia, Garanzia della qualità in Radiodiagnostica, Aspetti operativi dei controlli di qualità

Gastroenterologia

Gastroenterology

Università degli Studi "La Sapienza", Roma

Insegnamenti: Endoscopia digestiva, Ematologia

Geriatria

Geriatric

Università degli Studi "La Sapienza", Roma

Insegnamenti: Terapia del dolore, La patologia oncoematologica dell'anziano

Medicina Nucleare

Nuclear Medicine

Università degli Studi "La Sapienza", Roma

Insegnamenti: Indagini medico-nucleari in oncologia

Università Cattolica del Sacro Cuore, Roma

Insegnamenti: Struttura ed organizzazione dei Servizi di Medicina Nucleare

Neurochirurgia

Neurosurgery

Università degli Studi "Tor Vergata", Roma

Insegnamenti: Neurochirurgia III, Neurochirurgia Stereotassica e Funzionale, Neurofisiologia

Neurologia

Neurology

Università degli Studi "La Sapienza", Roma

Insegnamenti: Patologia Elettromiografica ed Elettroneurografica

Oncologia

Oncology

Università degli Studi "La Sapienza", Roma

Insegnamenti: Endoscopia digestiva, Epidemiologia, Biologia Molecolare, Terapia del dolore, Oncologia Medica, Chirurgia toracica oncologica, Determinazioni dei Recettori e loro Implicazione Terapeutica, Immunologia, Biologia Molecolare

Università degli Studi "Tor Vergata", Roma

Insegnamenti: Oncologia Medica, Anticorpi monoclonali in Oncologia: Nuove Prospettive, Chirurgia dei tumori del sistema endocrino, Chirurgia Generale I, Farmacoresistenza, Ruolo della terapia radiante nel carcinoma rettale

Università Cattolica del S. Cuore, Roma

Insegnamenti: Immunologia

Università degli studi, L'Aquila

Insegnamenti: Patologia Molecolare

Ostetricia e Ginecologia

Obstetries and gynecology

Università degli studi, Palermo

Insegnamenti: Tecnica chirurgica in Ginecologia Oncologica

Università degli studi G. D'Annunzio, Chieti

Insegnamenti: Storia naturale di principali tumori umani, terapie integrate (trial clinici)

Patologia Clinica

Clinical Pathology

Università degli Studi "La Sapienza", Roma.

Insegnamenti: Elementi di Indagini Citodiagnostiche, Patologia Generale, Tecniche analitiche II

Tisiologia e malattie apparato respiratorio

Pulmonary diseases

Università degli Studi "La Sapienza", Roma

Insegnamenti: Chirurgia Toracica

Urologia

Urology

Università degli Studi "La Sapienza", Roma

Insegnamenti: Urologia d'urgenza, Endourologia

Insegnamenti
Teaching Courses

Corso di Perfezionamento in Oncobiologia
Università degli Studi, Palermo
Insegnamenti: Biotecnologie nella diagnostica oncologica di laboratorio, Controllo di qualità in oncobiopatologia

Corso di Laurea breve per Tecnici di Neurofisiopatologia
Università degli Studi "Tor Vergata", Roma
Insegnamenti: Tecniche di Registrazione Elettromiografiche

Scuola per terapisti della Riabilitazione
Università di Bologna
Insegnamenti: Servizi sociali e relazioni umane

I Corso Istituzionale Terapie Locoregionali della Società Italiana di Terapie integrate Locoregionali in Oncologia (S.I.T.I.L.O.)
Insegnamenti: Fisiopatologia della disseminazione peritoneale

Scuola Medica Ospedaliera di Roma e della Regione Lazio
Insegnamenti: Prevenzione, diagnosi e terapia chirurgica dei tumori del colon-retto

Corso di perfezionamento in oncologia per infermieri professionali
Università G. D'Annunzio, Chieti
Insegnamenti: trattamenti infusionali in oncologia

Corso Teorico-Pratico di Aggiornamento Professionale in Citopatologia Cervico-Vaginale e in Biologia Molecolare Applicata
Società Italiana di Citologia
Insegnamenti: Citopatologia ed Istopatologia

Corso di Laurea in Scienze motorie
Università Cattolica del Sacro Cuore, Milano
Insegnamenti: Endocrinologia

Corso Avanzato di Chirurgia in Ostetricia e Ginecologia.
Accademia dell'Arte Sanitaria, Roma

Corso di Perfezionamento in Psicologia oncologica
Università degli Studi "La Sapienza", Roma
Insegnamenti: Aspetti psicologici dei pazienti con cancro

Corso di Aggiornamento Specialistico
Ordine dei Medici, Roma
Insegnamenti: Terapia Delle Malattie Endocrine e Metaboliche

Corso di Laurea in Medicina e Chirurgia
Università Campus Biomedico, Roma
Insegnamenti: Urologia

Stage all'estero
Overseas Training and Experience

Dr.ssa Alessandra Felici, S.C. Oncologia Medica A
(1 marzo - 31 ottobre 2002)
Erasmus Medical Centre, Daniel Den Hoed Hospital, Rotterdam, Dipartimento di Farmacologia

Dr. Alain Gelibter, S.C. Oncologia Medica A, Fellowship as Medical Doctor at Sheba Medical Center (Tel Aviv, Israel)
(agosto 2002 - gennaio 2003)
Department of Medical Oncology and Laboratory of molecular Cytogenetic

Dr. Michele Milella, S.C. Oncologia Medica A
(4-19 ottobre 2002)
University of Texas M.D. and Anderson Cancer Center Houston, Texas

Dr.ssa Mirella Marino, S.C. Anatomia e Istologia Patologica e Citodiagnostica
(18-27 marzo 2002)
Istituto Patologia dell'Università di Wuerzburg, Germania

Dr.ssa Mirella Marino, S.C. Anatomia e Istologia Patologica e Citodiagnostica
(2-25 settembre 2002)
Istituto Patologia dell'Università di Wuerzburg, Germania

Dr.ssa Valeria Landoni, S.C. Fisica Medica e sistemi esperti, "Eclipse Application corse"
(30 settembre - 3 ottobre 2002)
Switzerland

Dr. Giuseppe Iaccarino, S.C. Fisica Medica e sistemi esperti, "Configurazione del sistema per piani di trattamento Eclipse"
(2-6 agosto 2002)
Switzerland

Dr.ssa Simona Marzi, S.C. Fisica Medica e sistemi esperti
(12-15 marzo 2002)
IMRT School Physicist Berlino

Dr. Giuseppe Maria Ettorre, S.C. Chirurgia Digestiva, Hospital Beaujon Service de Chirurgie Hepatique et transplantation
(1-3 luglio 2002)
Prof. J. Belghiti

Dr. Maurizio Fanciulli, S.C. Laboratorio B
(21 febbraio - 2 aprile 2002)
Laboratory of Physical Biology of National Institutes of Health di Bethesda diretto dal Dr. Vittorio Sartorelli, Bethesda, Washington, USA

Dr. Oreste Segatto, S.C. Immunologia
Borsa UICC e FIRC per stage (1 febbraio -15 agosto 2002)
Buck Institute for Age Research, Program of Cancer and Developmental Therapeutics

Brevetti
Patents

Subunit vaccines and processes for the production thereof

Brevetto Internazionale: PCT/IT/02/00354

Inventori: Marcante M.L.- Venuti A.

Partecipazione a Compilazione Linee Guida
Participation to Definition of Guidelines

Presidente Comitato Internazionale di valutazione per l'indagine sui rischi sanitari dell'esposizione ai campi elettrici, magnetici ed elettromagnetici (CEM).
Istituito dai Ministeri dell'Ambiente e della Tutela del Territorio, della Salute e delle Telecomunicazioni nel dicembre 2001.
Dichiarazione del Comitato (Linee Guida) pubblicata nel settembre 2002.

Prof. Cognetti Francesco

"Garanzia di qualità in Radioterapia. Linee Guida in relazione agli aspetti clinici e tecnologici". Rapporti Istituto Superiore Sanità 02/20.

Prof. Benassi Marcello

Attività dello Stabilimento Allevatore Fornitore Utilizzatore (S.A.F.U.)

Laboratory Animal Center: for breeding, care and experimentation

L'attività che si svolge nel servizio è prevalentemente di supporto alle unità operative dell'Ente afferenti ai dipartimenti sia clinici che sperimentali, che utilizzano modelli animali per lo sviluppo dei progetti di ricerca corrente e finalizzata.
Le collaborazioni esterne in corso attualmente sono:

Università degli Studi "La Sapienza", Roma

Dipartimento Clinica Medica
Dipartimento Scienze Biomediche
Dipartimento Ortopedia e Traumatologia
Cattedra di Endocrinologia II
Istituto di Farmacologia Medica

II Università Tor Vergata, Roma

Dipartimento Medicina Sperimentale e Scienze Biomediche
Dipartimento Biologia

C.N.R., Roma

Istituto di Neurobiologia e Medicina Molecolare

Fondazione Telethon

Lo stabilimento ospita il Transgenic Mice Service Center finanziato dalla Fondazione Telethon per la produzione di topi transgenici e knock-out.

Università della Tuscia, Viterbo

Dipartimento Scienze Ambientali

Ditta BIO-D, Bari

Progetti di Ricerca Finalizzata
Research Projects

Finanziamenti Associazione Italiana per la Ricerca sul Cancro (AIRC)

Endothelin-1 receptor blockade as therapeutical target in ovarian carcinoma.
Responsabile: Anna Bagnato

P53 family interactions as determinants for tumor response to anti-neoplastic treatment.
Responsabile: Giovanni Blandino

Impact of Biological Profile, Chemoradiation and Surgery of Rectal Cancer on Downstaging and Quality of Life.
Responsabile: Maurizio Cosimelli

Study of the mechanisms by which bcl-2 modulates angiogenesis.
Responsabile: Donatella Del Bufalo

Mechanisms that regulate the function of alpha6beta4 integrin during tumor progression.
Responsabile: Rita Falcioni

Molecular characterization of the mechanisms by which Che-1 affects Rb activity.
Responsabile: Maurizio Fanciulli

Altered HLA phenotypes in tumors and their correction.
Responsabile: Patrizio Giacomini

Molecular changes in peritumoral non-involved breast tissue: implications for early diagnosis of cancer.
Responsabile: Marcella Mottolese

SEREX-defined antigens in breast cancer: characterization of their immunogenicity in breast cancer patients.
Responsabile: Paola Nisticò

Peptides interfering with the cell cycle machinery. A hypothesis for targeted cancer therapy.
Responsabile: Marco Giorgio Paggi

Biological role of the transcription factor NF-Y in cell growth and transformation.
Responsabile: Giulia Piaggio

Identification of genes activated/repressed by p53 family members using microarrays: implications for prognosis and therapy.
Responsabile: Ada Sacchi

Negative regulation of signals propagated by Erb-B receptors.
Responsabile: Oreste Segatto

Role of the p53 onco-suppressor in the differentiation of normal and tumor cells: dissection of moleculare mechanisms (N.U.S.U.G.).
Responsabile: Silvia Soddu

New therapeutic strategies against cervix carcinoma: ET-1 receptor antagonist and vaccines against the HPV.

Responsabile: Aldo Venuti

Study of intracellular redox-state and telomerase involvement in c-Myc mediated apoptosis to design effective therapeutic strategies in melanoma.

Responsabile: Gabriella Zupi

Finanziamenti CNR-MIUR

Ruolo dell'endotelina-1 nella progressione del carcinoma ovarico: nuove prospettive terapeutiche.

Responsabile: Anna Bagnato

Monitoraggio biochimico del marker di attività angiogenica VEGF: Implicazioni prognostiche e terapeutiche nel melanoma cutaneo.

Responsabile: Francesco Cognetti

Terapie adiuvanti basate sul profilo biologico del carcinoma colorettale curabile.

Responsabile: Maurizio Cosimelli

Studio multicentrico di fase II volto a testare in modo formale l'attività del regime TNF/adriamicina in termini di risposte patologiche complete in pazienti affetti da sarcoma delle parti molli localmente avanzato.

Responsabile: Franco Di Filippo

Identificazioni di nuovi antigeni nel carcinoma della mammella: definizione di nuovi protocolli immunoterapeutici e ruolo della risposta immune nell'andamento clinico della malattia.

Responsabile: Paola Nisticò

Differenziazione p53 e p73 - Dipendente nella terapia del cancro.

Responsabile: Ada Sacchi

Modulazione del trattamento antineoplastico in relazione all'espressione di alcuni geni coinvolti nel processo apoptotico e nella farmacoresistenza.

Responsabile: Gabriella Zupi

Finanziamenti Istituto Superiore Sanità

Il valore predittivo del test "extreme drug resistance" in pazienti con carcinoma ovarico refrattario sottoposte a chemioterapia test-selezionata confrontata con chemioterapia non test-selezionata.

Responsabile: Francesco Cognetti

Infezione della cervice uterina da HPV.

Responsabile: Carlo Sbiroli

Finanziamenti Ministero della Salute

Profili di espressione dei geni p53-relati p73/p63 in cellule normali e trasformate: identificazione di nuovi bersagli terapeutici.

Responsabile: Giovanni Blandino

Sviluppo di modelli animali transgenici per gli oncogeni c-Myc, Ret ed il gene oncosoppressore Fhit.

Responsabile: Gennaro Citro

Controllo neuroendocrino della crescita a modulazione immunitaria nei tumori epiteliali del timo.

Responsabile: Franco Facciolo

Ruolo del microambiente e ricerca di nuovi target terapeutici nel carcinoma prostatico.

Responsabile: Michele Gallucci

Caratterizzazione funzionale e molecolare degli effetti di farmaci interferenti con la trasduzione del segnale e la trascrizione.

Responsabile: Michele Millela

Identificazione e caratterizzazione funzionale di nuovi antigeni nel carcinoma della mammella.

Responsabile: Paola Nisticò

Valutazione dell'impatto clinico, psicologico e socio-sanitario del ricovero temporaneo in Hospice di pazienti in Cure Palliative.

Responsabile: Edmondo Terzoli

Determinants of prognosis and treatment response.

Responsabile: Anna Biroccio; Capofila: M.G. Daidone - INT-Milano

Progetto sulla dissezione molecolare delle vie di trasduzione del segnale che convergono sui regolatori del ciclo cellulare.

Responsabile: M. Luisa Appetecchia; Capofila: N. Mozzillo, N.T. Pascale - Napoli

Marcatori molecolari ed immunoterapia genica per la diagnosi ed il trattamento dei gliomi diffusi.

Responsabile: Carmine Carapella; Capofila: F. Giangaspero - Neuromed- IS

Uso di tecnologie innovative per l'identificazione di bersagli molecolari nelle patologie neoplastiche sporadiche ed ereditarie.

Responsabile: Francesco Cognetti; Capofila: S. Giunta - Università Catanzaro

Studio dei meccanismi di controllo del sistema Redox intracellulare come possibile target di terapie innovative nel melanoma.

Responsabile:Virginia Ferraresi; Capofila:Vittoria Maresca - ISG-Roma

Sviluppo di nuove strategie di immunoterapia e terapie combinate contro i tumori.

Responsabile: Fiorella Guadagni; Capofila: Enrico Proietti - ISS-Roma

Studi di protocolli preclinici di vaccinazioni a DNA antitumorale orientati al trasferimento clinico.

Responsabile: Fiorella Guadagni; Capofila:V.M. Fazio - "Casa Sollievo Della Sofferenza" - SGR

Nuove strategie terapeutiche di combinazione: ipometilazione del DNA e bioimmunoterapia.

Responsabile: Marcella Mottolese; Capofila: M. Maio - CRO - Aviano

Studio dei meccanismi di controllo del sistema Redox intracellulare come possibile target di terapie innovative nel melanoma.

Responsabile: Marco Giorgio Paggi; Capofila: Vittoria Maresca - ISG-Roma

Approccio proteomico allo studio della malattia neoplastica.

Responsabile: Silvia Soddu; Capofila: Mario Crescenzi - ISS-Roma

Apoptosis in tumor growth and treatment: identification and characterization of novel regulatory mechanism.

Responsabile: Silvia Soddu; Capofila: Kristian Helin - IEO-Milano

Strategie di immunoterapia contro genotipi di HPV oncogeni e non oncogeni.

Responsabile: Aldo Venuti; Capofila: Aldo Di Carlo - ISG-Roma

Finanziamenti Commissione Europea

Quit & Win! - Smetti di fumare e vinci.

Responsabile: Vincenzo Cilenti

Finanziamenti Alleanza Contro il Cancro

Progetto Globale per la valutazione e il miglioramento della QoL nei pazienti oncologici a lunga aspettativa di vita.

Responsabile: Francesco Cognetti

Network per l'analisi epidemiologica, etiopatogenetica ed economico-sanitaria della popolazione con tumore della tiroide e patologia tiroidea d'interesse neoplastico afferente agli IRCCS.

Responsabile: Ettore Maria Salvatore Conti

Classificazione molecolare per migliorare la diagnosi, prognosi e cura dei tumori.

Responsabili: Ada Sacchi, Massimo Loda

Progetto AZALEA: Biblioteca virtuale in oncologia.

Responsabile: Gaetana Cognetti

Finanziamenti Ministero Affari Esteri

Prevenzione tumori della cervice uterina.

Responsabile: Maria Luisa Marcante

Finanziamenti Regione Lazio

Programma di prevenzione dei tumori della cute nei bambini delle scuole materne della Regione Lazio.

Responsabile: Ettore Maria Salvatore Conti

Finanziamenti Compagnia di S. Paolo

Tumori testa-collo: identificazione di targets molecolari per diagnosi precoce e terapia.

Responsabili: Maria Luisa Marcante, Aldo Venuti

Borse di studio
Fellowships

FIRC

Amodei Sarah (S.C. Lab. "A" Chemioterapia Sperimentale)

Ruolo della telomerasi nella risposta ai farmaci antineoplastici in linee di melanoma umano.

Benassi Barbara (S.C. Lab. "A" Chemioterapia Sperimentale)

Studio del ruolo dell'oncogene c-myc nella risposta ai farmaci antineoplastici.

Di Padova Monica (S.C. Lab. "B" Aggregato)

Caratterizzazione di Che-1 un nuovo gene umano che interagisce con la proteina retinoblastoma e con la subunità 11 della RNA polimerasi II.

Fiorini Monia (S.C. Lab. "B" Immunologia)

Analisi delle relazioni struttura-funzione di RALT, un regolatore negativo dell'attività fitogenica e trasformante del recettore ErbB-2.

Fontemaggi Giulia (S.C. Lab. "C" Oncogenesi Molecolare)

Espressione di p73: meccanismi regolativi e possibili applicazioni per una terapia differenziativa.

Gabellini Chiara (S.C. Lab. "A" Chemioterapia Sperimentale)

Role of the retinoblastoma gene pRb2/p130 and putative related genes in the apoptosis induced by antineoplastic agents.

Gasbarri Alessandra (S.C. Lab. "B" Immunologia)

Dall'alterazione genetica specifica del sarcoma sinoviale alla ricerca di potenziali nuovi marcatori diagnostico-terapeutici per le neoplasie umane.

Gurtner Aymone (S.C. Lab. "C" Oncogenesi Molecolare)

Studio in vivo dell'attività di legame al DNA del fattore trascrizionale NF-Y nel ciclo cellulare, nel differenziamento e nella senescenza. Caratterizzazione della sua espressione in tessuti adulti normali e trasformati.

Iervolino Angela (S.C. Lab. "A" Chemioterapia Sperimentale)

Studio del ruolo di bcl-2 nel fenotipo angiogenico di diversi istotipi tumorali.

Porrello Alessandro (S.C. Lab. "C" Oncogenesi Molecolare)

Studio delle attività di mutazioni del gene TP53: analisi in vivo, in vitro ed attraverso modelli matematici.

Rosanò Laura (S.C. Lab. "A" Aggregato)

Ruolo dell'Endotelina-1 nella crescita e nella progressione del carcinoma ovarico.

Severino Anna (S.C. Lab. "C" Aggregato)

Identificazione e caratterizzazione di nuovi partner cellulari delle oncoproteine virali E1A di Adenovirus e E7 di HPV-16.

Spinella Francesca (S.C. Lab. "B" Immunologia)

Ruolo dell'Endotelina-1 nei meccanismi che regolano le comunicazioni intercellulari coinvolte nella migrazione e nell'invasione cellulare del carcinoma ovarico.

Trisciuoglio Daniela (S.C. Lab. "A" Chemioterapia Sperimentale)

Ruolo di Bcl-2, c-myc e hTERT nel fenotipo angiogenico del melanoma.

Scholarship FIRC

De Luca Antonio (S.C. Lab. "C" Aggregato)

The effects of pRb2/p130 and E1a-associated proteins on cell cycle regulation and neoplastic transformation.

Borse di Studio C.E. - Marie Curie Training Site Fellowships

Artificial Regulation of Cell Cycle in Cancer Cells and its Potential Clinical Applications.

Dr.ssa Funny De La Igliesia Lopez (S.C. Lab. "B" Immunologia)

Dr. Martin Mojzisek (S.C. Lab. "B" Immunologia)

Dr.ssa Edit Andrea Nàdasi (S.C. Lab. "B" Immunologia)

Dr.ssa Ioana Tuduce (S.C. Patologia Clinica)

Dr. Alvaro Avivar Valderas (S.C. Lab. "C" Aggregato)

Fondazione "Telethon"

Tatangelo Laura (Stabulario)

Produzione di animali transgenici e "Knock-out".

Tiveron Cecilia (Stabulario)

Produzione di animali transgenici e "Knock-out".

Rhone Poulenc Rorer

Pacetti Umberto (S.C. Oncologia Medica "B")

Nuove opportunità terapeutiche per il trattamento adiuvante del carcinoma della mammella in fase avanzata.

Aventis Pharma

Capomolla Elisabetta (S.C. Oncologia Medica "B")

Di Giorgi Silvia (S.C. Oncologia Medica "B")

Epirubicina e Ciclosfamide vs Taxotere seguito da Epirubicina e Ciclosfamide nel trattamento adiuvante nel carcinoma mammario con linfonodi ascellari positivi.

Sperimentazione Matritech

Pascucci Anna Lisa (S.C. Patologia Clinica)

Contratti di consulenza
Consultants

Dr. Vincenzo Giusti
S.C. Laboratorio "C" Oncogenesi Molecolare

Dr.ssa Laura Pozzi
S.A.F.U.

Dr. Enrico Spugnini
S.C. Laboratorio "C" Oncogenesi Molecolare

Contratti di Collaborazione di Ricerca
Research Contracts

Personale laureato
Post-graduate Contract Researchers

Nominativi *Name*	Ente Erogatore *Fund granted by:*	Strutture Complesse/SSD/SSO *Assignement*
Acquadro Francesco	MIN. SALUTE 01	Chemioterapia Sperimentale
Aloe Simona	MIN. SALUTE 00	Patologia Clinica
Anastasi Sergio	AIRC 00	Immunologia
Baccarini Alessia	AIRC 01	Oncogenesi Molecolare
Battisti Francesca	CNR-MIUR 02	Chemioterapia Sperimentale
Bon Giulia	CNR-MIUR	Oncogenesi Molecolare
Calcioli Simona	CNR-MIUR	Immunologia
Carone Daniela	MIN. SALUTE 00	Patologia Clinica
Ciuffini Laura	MIN. SALUTE 00	Oncogenesi Molecolare
Coletta Angela Maria	MIN. SALUTE 01	Patologia Clinica
D'Alessandro Roberta	MIN. SALUTE 00	Patologia Clinica
D'Andrea Marco	IORT-ENEA	Fisica Medica
D'Avenia Paola	IORT-ENEA	Fisica Medica
D'Eletto Manuela	Mc Master University	Oncogenesi Molecolare
De Angelis Roberta	MIN. SALUTE 01	Lab. "B" Aggregato
Del Bello Duilia	AIRC 01	Immunologia
Felici Alessandra	Ricerca Corrente	Oncologia Medica A
Filomeni Giuseppe	INEX	Chemioterapia Sperimentale
Gabellini Chiara	AIRC 01	Chemioterapia Sperimentale
Giovanelli Morena	REGIONE LAZIO 00	Neurochirurgia
Gradi Alessandra	AIRC 00	Oncogenesi Molecolare
Lo Nardo Maria Teresa	MIN. SALUTE 01	Chirurgia Generale B
Lucarelli Enrico	AIRC NUSUG	Oncogenesi Molecolare
Maggini Alda	MIN. SALUTE 01	Patologia Clinica
Manghi Enrico	IORT-ENEA	Fisica Medica
Martegani Paolo	AIRC 99/00	Oncogenesi Molecolare
Martayan Aline	MIN. SALUTE 01	Immunologia
Miceli Roberto	IORT-ENEA	Fisica Medica
Monti Olimpia	AIRC 01	Oncogenesi Molecolare
Novelli Flavia	MIN. SALUTE 99	Anatomia Patologia
Pacilio Massimiliano	I.S.S. protoni 00	Fisica Medica
Pasquo Alessandra	AIRC 00	Oncogenesi Molecolare
Pellicciotta Mario	Contributo ELI LILLY	Direzione Scientifica
Petricca Adele	AIRC 01	Chemioterapia Sperimentale
Piovanello Paolo	MIN. SALUTE 00	Chirurgia Toracica
Piperno Giulia	MIN. SALUTE RF 00	Anatomia Patologica
Poggiali Federica	CNR	Virologia
Riccioni Sabrina	Ricerca Corrente	Oncogenesi Molecolare

Romano Luisa	MIN. SALUTE 00	Medicina Nucleare
Sala Gianluca	AIRC 99	Immunologia
Salis Patrizia	REGIONE LAZIO 00	Neurochirugia
Sibilio Leonardo	MIN. SALUTE 01	Immunologia
Simeone Paola	MIN. SALUTE 00	Virologia
Sperduti Isabella	Contrib. ELI LILLY	Direzione Scientifica
Spila Antonella	MIN. SALUTE 01	Patologia Clinica
Strano Sabrina	QLG1-99-00273	Oncogenesi Molecolare
Vallati Ilaria	AIRC –FRC	Direzione Scientifica

Personale non laureato
Non Graduated Contract Researchers

Nominativi *Names*	Ente Erogatore *Funds Granted by:*	Strutture Complesse/SSD/SSO *Assignement*
Antonucci Alessia	IORT-ENEA	Fisica Medica
Bernardi Roberto	CNR 01	Immunologia
Bona Daniela	AIRC 01	Oncogenesi Molecolare
Bonaventura Fabrizio	AIRC 00	Chemioterapia Sperimentale
Bruno Teresa	Aeroporti Rm - ENEL 00	Radiologia
Bruno Tiziana	MIN. SALUTE 01	Lab. "B" Aggregato
Caffo Angela	MIN. SALUTE RF00-207	Anatomia Patologica
Cassani Stefania	MIN. SALUTE 00	Chirurgia Toracica
Catalini Alessandro	MIN. SALUTE 00	Patologia Clinica
Cialfi Alessaia	MIN. SALUTE 01	Patologia Clinica
Cutazzo Valter Roberto	MURST	Radiologia
D'Angelo Marc	QLG1-99-00273	Oncogenesi Molecolare
Del Prete Fabrizio	AIRC 99	Immunologia
Elia Giacomo	AIRC 98	Lab. "A" Aggregato
Fonsi Maria Assunta	MIN. SALUTE 00	Anatomia Patologica
Gioffrè Giuseppina	MIN. SALUTE 99	Chirurgia Generale B
Giommi Simone	MIN. SALUTE 01	Patologia Clinica
Giorda Ezio	AIRC 01	Immunologia
Matrascia Barbara	Contrib. Eli Lilly/ M. SALUTE 00	Dir. Scientifica, Chirg. A
Merola Roberta	MIN. SALUTE 01	Patologia Clinica
Miele Paola	MIN. SALUTE 00	Oncogenesi Molecolare
Parasecoli Cristina	Contrib. Rhone Poulenc Rorer	Oncologia Medica B
Parisi Cristiano	REGIONE LAZIO 00	Neurochirurgia-Neurologia
Pecci Andrea	AIRC 99	Chemioterapia Sperimentale
Perrotta Gioia	MIN. SALUTE 00	Patologia Clinica
Piccoli Marzia	REGIONE LAZIO 00	Neurochirurgia-Neurologia
Piccolo Tiziana	MIN. SALUTE 00	Chirurgia Generale A
Polidori Daniele	AIRC 00	Lab. "C" Aggregato
Ranieri Alessandra	SIGMA-TAU	Immunologia
Sarcone M.Vincenza	AIRC 99	Immunologia
Scarsella Marco	MIN. SALUTE 00	Chemioterapia Sperimentale
Scordati Patrizia	CNR 00	Anatomia Patologica
Zizzari Alessia	REGIONE LAZIO 00	Neurochirurgia

Frequenze
Visiting Researchers

Aggiornamento professionale
Professional Updating

Personale laureato – *Visiting Post-graduate Researchers*

Nominativi	Strutture Complesse/SSD
Albino Giuseppe	Urologia
Alfano Alessandra	Rianimazione, Terapia Intensiva…
Aliotta Nicoletta	Oncogenesi Molecolare
Antonelli Serena	Rianimazione, Terapia Intensiva…
Antoniadou Kristallia	Chirurgia Plastica e Ricostruttiva
Barletta Tiziana	Patologia Clinica
Biscotti Mario	Oncologia Medica "A"
Bratta Massimo	Oncologia Medica "A"
Brun Stefano	Chirurgia Toracica
Buoncristiano Nicola	Fisica Medica e sistemi esperti
Bussolotti Federico	Psicologia
Carriero Elena	ORL e Chirurgia Cervico Facciale
Cauchi Carolina	Oncologia Medica "B"
Cerasoli Virna	Chirurgia Toracica
Cerere Lucia	Biblioteca
Chilelli Mario Giovanni	Oncologia Medica "A"
Corvino Carmela	Biblioteca
Dalfino Maria Giovanna	Oncologia Medica "B"
De Angelis Enzo	Chirurgia "A"
Della Pietra Linda	Oncogenesi Molecolare
D'Orazi Gabriella	Oncogenesi Molecolare
Diacono Fabrizio	Endocrinologia
Di Stefano Valeria	Oncogenesi Molecolare
Fabroni Stefano	Rianimazione, Terapia Intensiva…
Falcone Sonia	Radioterapia
Fantozzi Iole	Fisica Medica e sistemi esperti
Ferrari Francesca	Patologia Clinica
Gaia Gallo	Lab. "C" Aggregato
Galati Gregorio Marco	Ginecologia
Gallì Benedetta	Rianimazione, Terapia Intensiva…
Gargano Francesco	Chirurgia Plastica e Ricostruttiva
Giacinti Laura	Oncologia Medica "B"
Ginobbi Patrizia	Rianimazione, Terapia Intensiva…
Greco Olga	Lab. "C" Aggregato
Gullo Pier Paolo	Chirurgia Plastica e Ricostruttiva
Lemme Carmelita	Patologia Clinica
Longo Roberto	Chirurgia "A"

Marcelli M. Elena	Rianimazione, Terapia Intensiva…
Marchesi Paolo	ORL e Chirurgia Cervico Facciale
Mastroianni Santo	Neurologia
Mattei Alessia	Rianimazione, Terapia Intensiva…
Merola Roberta	Patologia Clinica
Mollo Mara	Fisica Medica e sistemi esperti
Moretti Fabiola	Oncogenesi Molecolare
Nanni Simona	Oncogenesi Molecolare
Napoli Anna	Anatomia ed Istologia Patologica e Citodiagnostica
Ombricolo Emilia	Fisiopatologia Respiratoria
Pacetti Umberto	Oncologia Medica "A"
Parretta Teresa	Radioterapia
Pasquali Antonello	Oncologia Medica "C"
Pellicciotta Mario	Oncologia Medica "A"
Perdonato Bruno	Chirurgia "B"
Perrone Maria	Psicologia
Piemonte Paolo	Dermatologia Oncologica
Piovanello Paolo	Chirurgia Toracica
Pizzini Emma	Oncologia Medica "C"
Postumi Katia	Neurologia
Pompei Eugenia	Fisica Medica e sistemi esperti
Priolo Carmen	Oncologia Medica "A" (Oncogenesi Molecolare)
Prodosmo Andrea	Oncogenesi Molecolare
Quaresima Tiziana	Rianimazione, Terapia Intensiva…
Rogliano Marco	Chirurgia Plastica e Ricostruttiva
Ruscio Giusy	Oncogenesi Molecolare
Salerno Manuela	Patologia Clinica
Scarcello Giovanna	Endocrinologia
Scarcia Stefano	Neurologia
Serra Emanuela	Farmacia
Serraino Filiberto	Radioterapia
Stringari Lidia	Fisica Medica e sistemi esperti
Suriano Maria	ORL e Chirurgia Cervico Facciale
Teodoli Stefania	Fisica Medica e sistemi esperti
Tirelli Walter	Rianimazione,Terapia Intensiva…
Trimarco Anna	Chirurgia Plastica e Ricostruttiva
Urban Cicero	Chirurgia "A"
Uricchio Emanuela	Neurologia
Vona Rosa	Patologia Clinica

Personale non laureato – *Non-graduated Visiting Researchers*

Nominativi	Strutture Complesse/SSD
Aceti Gianluca	Biblioteca
Armezzani Alessia	Oncogenesi Molecolare
Cirilli Alessia	Virologia
Folgiero Valentina	Oncogenesi Molecolare
Garroni Marta	ORL e Chirurgia Cervico Facciale
Sergi Domenico	Oncologia Medica "B"
Solieri Angela	Patologia Clinica
Tynes Hrefna	Oncologia Medica "B"
Veltri Francesco	Patologia Clinica

Svolgimento tesi di laurea
Degree Thesis

Nominativi	Strutture Complesse/SSD
Campioni Mara	Lab. "C" Aggregato
Carlino Claudia	Dip. Oncologia Sperimentale
Cottone Giuliano	Lab. "C" Aggregato
Di Berto Claudia	Oncogenesi Molecolare
Emiliozzi Velia	Oncogenesi Molecolare
Fiorini Francesca	Lab. "C" Aggregato
Folgiero Valentina	Dip. Oncologia Sperimentale
Grasselli Annalisa	Oncogenesi Molecolare
Iacovelli Stefano	Oncogenesi Molecolare
Inzillo Simone	Chemioterapia Sperimentale
Lucini Fabiana	Immunologia
Marzano Pasqualina	Virologia
Pensieroso Simone	Dip. Oncologia Sperimentale
Ricci Rolando	S.C. Lab. "A" Aggregato

Tirocinio post-laurea
Post-graduate Training

Nominativi	Strutture Complesse/SSD
Bon Giulia	Oncogenesi Molecolare
Del Bravo Jessica	Chemioterapia Sperimentale
Iodice Marcello	Immunologia
Mancini Francesca	Oncogenesi Molecolare
Monti Olimpia	Oncogenesi Molecolare
Omerovic Jasmink	Immunologia
Zacharia Athina	Immunologia

Dottorati
Doctorates

Nominativi	Strutture Complesse/SSD
Bronzi Giovanna	Immunologia
Cecchinelli Barbara	Oncogenesi Molecolare
De Angelis Roberta	S.C. Lab. "B" Aggregato
De Nicola Francesca	S.C. Lab. "C" Aggregato
Della Pietra Linda	Oncogenesi Molecolare
Gentiletti Francesca	Oncogenesi Molecolare

Collaborazione scientifica
Scientific Cooperation

Nominativi	Strutture Complesse/SSD
Alimandi Maurizio	Immunologia
Belloni Laura	Dip. Oncologia Sperimentale
Farsetti Antonella	Oncogenesi Molecolare
Chiara Romano	Oncogenesi Molecolare
Cippitelli Marco	Dip. Oncologia Sperimentale
Civitareale Donato	S.C. Lab. "A" Aggregato
Cristiano Simone	Oncogenesi Molecolare
Farsetti Antonella	Oncogenesi Molecolare
Fionda Cinzia	Dip. Oncologia Sperimentale
Forcales Sonia	Dip. Oncologia Sperimentale
Giorgini Angela	Oncogenesi Molecolare
Guerrieri Francesca	Dip. Oncologia Sperimentale
Latella Lucia	Dip. Oncologia Sperimentale
Levrero Massimo	Dip. Oncologia Sperimentale
Lombardi Daniela	S.C. Lab. "C" Aggregato
Napolitano Silvia	Immunologia
Narducci Michela	Oncogenesi Molecolare
Pagano Sabrina	Oncogenesi Molecolare
Palescandolo Emanuele	Dip. Oncologia Sperimentale
Pediconi Natalia	Dip. Oncologia Sperimentale
Piombino Emanuela	Dip. Oncologia Sperimentale
Pollicino Teresa	Dip. Oncologia Sperimentale
Pontecorvi Alfredo	Oncogenesi Molecolare
Puggioni Eleonora	Immunologia
Romano Chiara	Dip. Oncologia Sperimentale
Santoni Angela	Dip. Oncologia Sperimentale
Serra Carlo	Dip. Oncologia Sperimentale
Simone Cristiano	Dip. Oncologia Sperimentale
Velotti Francesca	Dip. Oncologia Sperimentale
Vossio Stefania	Dip. Oncologia Sperimentale

Ospitalità a ricercatori esterni
Hosted foreign researchers

Edit Nadasi
Departimento di Medicine Preventiva, Università de Pécs, Ungheria
Periodo: 21 Gennaio 2002 - 21 Maggio 2002

Nowrasteh Ghodratollah
Departimento di Medicine Preventiva, Università de Pécs, Ungheria
Periodo: 1 Ottobre 2002 - 31 Ottobre 2002

Fanny De La Iglesia Lopez
Facoltà di Medicina dell'Università di Saragoza, España
Periodo: 15 Maggio 2002 - Dicembre 2002 (continua nel 2003)

Magdalena Gonzales Quiros
Hospital Universitario "Marques de Valdecilla", Santander, España
Periodo: Settembre - Novembre 2002

Ioana Laura Tuduce
Provenienza: West University from Timisoara, Romania
Periodo: 18 Novembre 2002 - Dicembre 2002

Claudia Palena
Laboratory of Tumor Immunology and Biology, National Cancer Institute, National Institutes of Health, Bethesda, MD, USA
Periodo: Settembre 2002

Ling C.
Memorial Sloan Kettering Cancer Center, 2002

Ridha Khelifa
Istituto di Cancerologia Salaz Aizez di Tunisi
Programma per l'assistenza scientifica e tecnologica
Periodo: Maggio - Giugno 2002

Silvana Celiku
University hospital "Mother Theresa" Tirana
Progetto: "La prevenzione del tumore della cervice uterina"
Periodo: Novembre 2002

Marzia Perluigi
Dipartimento di Scienze Biochimiche dell'Università degli studi di Roma "La Sapienza"
Periodo: 1 Gennaio - 31 Dicembre 2002

Giuseppe Borzacchiello
Istituto di Patologia Generale Facoltà di Medicina Veterinaria Università di Napoli Federico II
Periodo: Aprile - Giugno 2002

Corrado Cutrufo
Dipartimento di Farmacologia della Menarini Ricerche di Pomezia
Periodo: Novembre 2001 - Luglio 2002

Luca Ruggiero
Università di Napoli "Federico II" Dipartimento di Genetica e Biologia Molecolare
Periodo: 12-20 Dicembre 2002

Ospitalità a Ricercatori ITBM CNR
Hosted Foreign Researchers IBMT CNR

Nominativi	Strutture Complesse/SSD
Nicotra M. Rita	Immunologia

Reviewing and Editorial Board Membership in indexed journal

- America Journal Pathology (Bagnato A., Falcioni R.)
- Annals of Oncology (Cognetti F.)
- Anticancer Research (Guadagni F.)
- British Journal of Cancer (Bagnato A., Badaracco G. Sacchi A.)
- Cancer Research (Blandino G., Farsetti A., Segatto G., Sacchi A.)
- Cell and Tissue Research (Bagnato A.)
- Cell Death and Differentiation (Blandino G., Sacchi A.)
- Cell Growth and Differentiation (Sacchi A.)
- Cell Proliferation (Zupi G.)
- Cellular and Molecular Biology (Sacchi A.)
- Cytotechnology (Sacchi A.)
- EMBO Journal (Blandino G.)
- Endoscopy (Grassi A.)
- European Journal of Biochemistry (Sacchi A.)
- European Journal of Cancer (Bagnato A., Leonetti C., Zupi G.)
- Experimental Cell Research (Sacchi A.)
- FEBS (Blandino G.)
- Hepatogastroenterology (Santoro E.)
- Human Gene Therapy (Sacchi A.)
- Hystology and Histopathology (Natali P.G.)
- International Journal of Biological Markers (Castelli M.,Guadagni F., Natali P.G.)
- International Journal of Cancer (Bagnato A., Natali P.G., Zupi G.)
- In vivo (Guadagni F.)
- Journal Immunotherapy (Nisticò P.)
- Journal of Cellular Physiology (Paggi M.G.)
- Journal of Experimental and Clinical Cancer Research (Bagnato A., Benassi M., Blandino G., Carlini M., Castelli M., Conti E.M.S., Falcioni R., Jandolo B., Leonetti C., Mariani L., Natali P.G., Paggi M.G., Pontecorvi A., Rizzo M.G., Santoro E., Sega M., Stigliano M.G.,Venuti A.)
- Journal of Nuclear Medicine (Sciuto R.)
- Melanoma Research (Natali P.G.)
- Molecular and Cellular Biochemistry (Sacchi A.)
- Mutation Research (Del Bufalo D.)
- Neurological Sciences (Jandolo B.)
- Oncogene (Blandino G., Farsetti A., Paggi M.G., Sacchi A.)
- Oncology (Zupi G.)
- Tumor Biology (Guadagni F.)
- Tumori (Natali P.G.)

Reviewing di Progetti Finalizzati
Research Project Review

- A.I.R.C. (Blandino G., Zupi G.)
- C.N.R. (Sacchi A., Zupi G.)
- Dutch Cancer Society (Falcioni R.)
- European Community Projects (Oppido P.A.)
- F.I.R.C. (Zupi G., Del Bufalo D., Leonetti C., Biroccio A.)
- La Campagna per la Ricerca sul Cancro (Sacchi A.)
- M.I.U.R. (Benassi M., Blandino G., Zupi G.)
- Referee Nazionale EMC (Santoro E.)
- The Israel Science Foundation (Sacchi A.)
- UICC TCRF (Venuti A.)

Incarichi nell'ambito di Fondazioni, Società, Associazioni
Appointments to Foundations, Societies, Associations

Arcuri E.
- Fondazione Federico Calabresi: *Membro del Comitato Scientifico*
- Centro di Ascolto "Gigi Ghirotti" Associazione ONLUS: *Consulente Scientifico per la Terapia del Dolore e Assistenza Domiciliare*

Carapella C.M.
- Associazione Italiana di Neuro-Oncologia - AINO: *Segretario*
- European Association of Neuro-Oncology - Executive Committee: *President*
- EORTC - Brain Tumor Group: *Membro*

Carlini M.
- Lap Group Roma - Gruppo Laparoscopico Romano: *Segretario*

Castelli M.
- Associazione Promozione Studi Immunologia dei Tumori - APSIT: *Presidente*

Cavaliere F.
- Consiglio Direttivo della Società Polispecialistica Italiana dei Giovani Chirurghi (S.P.I.G.C.): *Consigliere*
- International Society Regional Cancer Treatment (I.S.R.C.T.): *Membro*

Cognetti F.
- AIOM - Associazione Italiana di Oncologia Medica: *Presidente*
- AIOM - Associazione Italiana di Oncologia Medica: *Chairman della Commissione Educazionale*
- FECS - Federation of the European Cancer Societies: *Membro del Membership Committee*
- EORTC - Head and Neck cooperative group: *Membro*
- Scuola Superiore di Oncologia: *Presidente consiglio scientifico*
- ESMO - European Society of Medical Oncology: *Membro executive and steering Committee*
- American Society of Clinical Oncology (ASCO): *Membro*
- Fondazione per la Ricerca Oncologica FO.R.O. ONLUS: *Presidente legale*
- Collegio Sindacale di "Galileo 2001 - Associazione per la libertà e la dignità della scienza": *Socio Fondatore e Sindaco Effettivo*

Cognetti G.
- Associazione Bibliotecari Documentalisti Sanità: *Presidente*

Cosimelli M.
- Consiglio Direttivo S.I.T.I.L.O. - Società Italiana di Terapie Integrate Locoregionali in Oncologia: *Consigliere*

Di Filippo F.
- Società Italiana Terapie Loco-Regionali in Oncologia (S.I.T.I.L.O.): *Presidente*
- Società Italiana di Chirurgia Oncologica (S.I.C.O.): *Coordinatore regionale per il Lazio*
- Italian Sarcoma Group: *Responsabile del trattamento delle forme avanzate degli arti*
- Italian Melanoma Intergroup: *Membro del Comitato Scientifico*

- WHO Melanoma Programme: *Membro*
- International Society of Regional Cancer Treatment: *Chairman of Membership Committee*
- European Society of Surgical Oncology: *Membro*

Garufi C.
- AIOM Lazio: *Consigliere Regionale*
- Board dell'EORTC Chronotherapy Group: *Membro*

Grassi A.
- Comitato Education and Training OMGE/OMED: *Membro*
- Comitato Terminology and Data Processing dell'OMED: *Membro*

Guadagni F.
- Comitato Scientifico del Gruppo per l'Applicazione delle Biotecnologie in Oncologia (ABO): *Membro*
- Comitato Scientifico Internazionale "Institute for Anticancer Research", Atene, Grecia: *Membro*
- Comitato Direttivo del Gruppo Italiano per lo Studio della Chirurgia Radioimmunoguidata e della Immunoscintigrafia (G.I.S.C.R.I.S.): *Vice-Presidente*
- Direttivo dell'"European Group of Tumor Marker" (E.G.T.M.): *Membro*

Jandolo B.
- Comitato dei Probi-Viri della Società Italiana di Neurologia (SIN): *Membro*
- Gruppo di Studio di Neuro-Oncologia della SIN: *Coordinatore*
- Consiglio Direttivo della SNO (Scienze Neurologiche Ospedaliere): *Membro in qualità di segretario del Comitato di redazione della Rivista di Neurobiologia*

Leonetti C.
- AICC - Associazione Italiana Colture Cellulari: *Segretario*

Lopez M.
- SIT - Società Italiana Tumori: *consigliere*
- GOIM - Gruppo Oncologico Italia Meridionale: *consigliere*

Mariani L.
- Official contributor del 25° FIGO Annual Report on the Results of Treatment in Gynaecological Cancer
- Rivista ONCOGYN, organo ufficiale della Società Italiana Oncologia Ginecologica: *Segretario scientifico*

Marino M.
- SIAPEC (Società Italiana di Anatomia Patologica e Citopatologia Diagnostica): *Consigliere Regione Lazio*

Natali P.G.
- Comitato AIRC Lazio: *Membro Scientifico*
- OECI: *Membro*
- SIC- Società Italiana di Cancerologia: *Past Presidente*
- American Academy of Microbiology: *Proctor*
- AACR: *Membro*
- World Alliance of Cancer Research Organization: *Membro International Steering Committee*
- Progetto Marie Curie Training Site: *Coordinatore*
- Hungarian Society of Molecular and Preventive Epidemiology: *Socio Fondatore*
- Comitato Premio G.Venosta, FIRC: *Membro*
- Commissione Scientifica Int. Conf. Anti Cancer Treatment (ICAT), Parigi: *Membro*

Paggi M.G.
- American Association for Cancer Research: *Active Member*

Perri P.
- European Society of Surgical Oncology (E.S.S.O.): *Membro*
- European Network for Endocrine Tumors (E.N.E.T.): *Membro*
- Società Italiana di Chirurgia Oncologica (S.I.C.O.): *Tesoriere Nazionale*
- Scientific Advisory Board of the International Institute of Anticancer Research: *Membro*

Perrone M.
- SIPO - Lazio: *Consigliere*
- AIOM - Lazio: *Socio*

Pugliese P.
- SIPO - Lazio: *Segretario regionale*

Sacchi A.
- Comitato Scientifico del programma cooperativo Italia-USA sulla terapia dei tumori, istituito presso l'Istituto Superiore di Sanità: *Membro*
- Comitato Tecnico Scientifico A.I.R.C.: *Membro*
- Comitato Scientifico della Fondazione Neuroblastoma: *Membro*

Santoro E.
- Consiglio Direttivo Lega Italiana Lotta contro i Tumori: *Consigliere*
- Consiglio Direttivo SIC: *Past-President*
- Consiglio Superiore di Sanità: *Membro*
- Accademia Romana di Chirurgia: *Accademico Reggente*
- Federchir: *Presidente*
- Società Italiana di Chirurgia: *Presidente Emerito*
- Lega Italiana Lotta contro i tumori: *Membro Consiglio Direttivo*
- IGCA: *Presidente Eletto*

Sega F. M.
- Roswell Park Surgical Society: *Membro*
- Associazione Promozione Studi Immunologia Tumori (A.P.S.I.T.): *Vicepresidente*

Stigliano V.
- AIGO: *Consigliere Regionale*

Terzoli E.
- Lega Italiana Tumori - Sez. Provincia di Roma: *Vicepresidente*

Zupi G.
- FIRC - Fondazione Italiana Ricerca sul Cancro: *Membro del Comitato Scientifico*
- SICCAB - Società Italiana Cinetica Cellulare Applicata e di Base: *Consigliere*
- SIC - Società Italiana di Cancerologia: *Consigliere*
- Fondazione Federico Calabresi: *Membro del Consiglio Direttivo*
- AICC - Associazione Italiana Colture Cellulari: *Socio Onorario*

Riconoscimenti e Premi
Awards

Dott.ssa Ada Sacchi e Dott.ssa Silvia Soddu

Premio "Golfo D'Oro" per la specifica attività di ricercatori nel campo della Oncogenesi Molecolare, individuando una proteina in grado di attivare "l'interruttore" delle cellule, il gene p53 chiave nella regolazione dei processi che portano alla formazione dei tumori

Accordi bilaterali
Bilateral Agreements

Italia - Albania (2002-2003)

La prevenzione del tumore della cervice uterina.

The Prevention Uterine Cancer.

Project Co-ordinators:

Prof.ssa Maria Luisa Marcante S.C. Lab. D di Virologia, Istituto Regina Elena, Roma, Italia.
"Institute of Public Health" di Tirana.

Italia-Canada (2000-2004)

Regolazione dell' attività telomerasica e dell' espressione della subunità catalitica della telomerasi umana (hTERT) in cellule epiteliali umane provenienti da espianti di prostata normale e tumorale.

Regulation of Telomerase Activity and Expression of Catalytic Telomerase Subunit (hTERT) in Human Epithelial Cells Derived from Normal and Tumoral Prostate Explants.

Project Co-ordinators:

Dr.ssa Ada Sacchi - Dr.ssa Antonella Farsetti, S.C. Lab. C Oncogenesi Molecolare, Istituto Regina Elena, Roma, Italia.

Prof.ssa Silvia Bacchetti, McMaster University Dept. of Pathology and Molecular Medicine, Hamilton ON, Canada.

Costruzione di nuovi vettori adenovirali per terapia genica.

Construction of New Adenoviral Vectors for Gene Therapy.

Project Co-ordinators:

Dr.ssa Ada Sacchi, S.C. Lab. C Oncogenesi Molecolare, Istituto Regina Elena, Roma, Italia.

Dr. Frank Graham, McMaster University, Department of Biology, Hamilton ON, Canada.

Sperimentazione dell'efficacia antitumorale di oligo antisenso c-myc in combinazione con il cisplatino nel melanoma umano su linee in vitro e su tumori impiantati in animali immunodepressi.

Pre-Clinical Evaluation of the Antitumoral Efficacy of C-myc Antisense Oligodeoxymucleotides in combination with Cisplatin in Human Melanoma Lines in vitro and in vivo.

Project Co-ordinators:

Dr.Ssa Gabriella Zupi, S.c. Lab. A Chemioterapia Sperimentale, Istituto Regina Elena, Roma, Italia.

Dr. Sean Semple, INEX Pharmaceuticals Corp., Burnaby, Canada.

Italia - Finlandia (2000-2005)

Valutazione di nuovi parametri diagnostici e prognostici nei pazienti affetti da cancro, con enfasi particolare alla potenziale applicazione di biotecnologie in ambiente di laboratorio, per una migliore definizione dei sotto gruppi di soggetti ad alto rischio.

Evaluation of New Diagnostic and Prognostic Parameters in Cancer Patients, with Special Emphasis on the Potential Application of Biotechnologies in the Laboratory Setting for a Better Definition of High-Risk Subgroups of Subject.

Project Co-ordinators:

Dr.ssa Fiorella Guadagni, S.C. Patologia Clinica, Istituto Regina Elena, Roma, Italia.

Prof. Grènman Reidar, Department of Medical Biochemistry, University of Turku, Finland.

Molecole espresse da tumori umani di utilizzo clinico diagnostico terapeutico. Sviluppo di misure metodologiche in vitro e in vivo.

Molecules Expressed by Human Tumours for Clinical, Diagnostic and Therapeutic Use. Development of New in vitro and in vivo Methodologies.

Project Co-ordinators:

Dr. Pier Giorgio Natali, S.C. Lab. B Immunologia, Istituto Regina Elena, Roma, Italia.
Dr. Michele Maio, Advanced Immunotherapy Unit-CRO Aviano, Italia.
Dr. Kalevi Kairemo, Department of Nuclear Medicine-Helsinki University Central Hospital, Finland.

Italia-Tunisia (2000-2003)

Programma integrato per la valorizzazione del Sahara e del Sud della Tunisia.

Integrated Programme for the Improvement of Sahara and Southern Tunisia.

Project Co-ordinator:

Prof. Massimo Crespi, S.C. Servizio per la Promozione delle attività di prevenzione, istituzionali, delle relazioni estere, delle attività didattiche e formative, Istituto Regina Elena, Roma, Italia.
L'Accordo si è concretizzato in una convenzione tra il M.AA.EE.-DGCS/Università La Sapienza-CIRPS e il nostro Istituto per l'Assistenza Tecnica all'Ospedale Habib Thameur e all'Istituto di Cancerologia di Tunisi (Lotta ai Tumori Femminili).

Chirurgia plastica e ricostruttiva per pazienti oncologici con patologia del distretto testa-collo.

Plastic and Reconstructive Surgery for Oncological Patients with Head and Neck Pathologies.

Project Co-ordinators:

Dr. Lorenzo Palma, S.C. Otorinolaringoiatria, Istituto Regina Elena, Roma, Italia.

Prof. Ben Aved, Istituto Oncologico Salaz Azaiz, Tunisi, Tunisia.

Danno cutaneo e tumorigenesi da luce occupazionale: diagnosi e prevenzione del cancro cutaneo, esteso anche all'età scolare.

Skin Damage and Tumorigenesis caused by Occupational Light: Skin Cancer Diagnosis and Prevention, extended to School-Age Children.

Project Co-ordinators:

Dr. Ettore M.S. Conti, Sintesi (Servizio Integrato di Epidemiologia e Sistemi Informativi), Istituto Regina Elena, Roma, Italia.

Prof. Zahaf Abdel Majid, Facoltà di Medicina, Università di Sfax, Tunisia.

Italia-Ungheria (2000-2003)

Valutazione immunoistochimica di indicatori biologici associati alla prognosi del cancro nella fase iniziale.

Immunohistochemical Evaluation of Biological Indicators Associated to the early stage Prognosis of Cancer.

Project Co-ordinators:

Dr.ssa Marcella Mottolese, S.C. Anatomia ed Istologia Patologica, Istituto Regina Elena, Roma, Italia.

Dr. Ember Istvàn, Dep. of Public Health, University Medical School of Pècs, Hungary
Exchanges: Dr.ssa Ed/T A. Nàdasi (Ungheria-Italia 27/08-26/09/01).

Dr. Istvàn Ember (Ungheria-Italia 21/05-01/06/01).

Italia –Usa (2000-2002)

Molecular-Based technology for a better detection of micrometastatic neoplastic disease in human cancer patients.

Project Co-ordinators:

Dr.ssa Fiorella Guadagni, S.C. Patologia Clinica, Istituto Regina Elena, Roma, Italia.

Dr. Jeffrey Schlom, National Cancer Institute, Bethesda, MD, USA.

New approaches in surgical oncology for a better definition of cancer spreading. memorandum of understanding colorectal cancer and radioimmunoguided surgery (rigs) positive lymph nodes.

Project co-ordinators:

Dr.ssa Fiorella Guadagni, S.C. Patologia Clinica, Istituto Regina Elena, Roma, Italia.

Dr. Edward W. Martin, Comprehensive Cancer Center, Ohio State University, USA.

Evaluation of the clinical impact of serum tumor markers in cancer patients - a joint clinical effort.

Project Co-ordinators:

Dr.ssa Fiorella Guadagni, S.C. Patologia Clinica, Istituto Regina Elena, Roma, Italia.

Dr. Robert C. Knapp, Harvard Medical School, Boston, USA.

Screening Colonoscopy 'Once in life' for Colorectal Cancer Prevention. A Feasibility Trial.

Project Co-ordinators:

Prof. Massimo Crespi, S.C. Servizio per la Promozione delle attività di prevenzione,

istituzionali, delle relazioni estere, delle attività didattiche e formative, Istituto Regina Elena, Roma, Italia.
Memorial Sloan Kettering Cancer Centre, Gastrointestinal Unit, New York, Usa.

New Radioenhancing Drugs in the treatment of Malignant Brain Tumors.

Project Co-ordinators:

Dr. Carmine M. Carapella, S.C. Neurochirurgia, Istituto Regina Elena, Roma, Italia.

DR. Peter Mclaren Black, Dana Farber Cancer Institute-Harward Medical School, Boston, USA.

In vivo effect of Microencapsulated C-MYC Antisense ODNS on Human Melanoma and BCR-ABL Antisense ODNS on Leukemia.

Project Co-ordinators:

Dr. Carlo Leonetti, S.C. Lab. A Chemioterapia Sperimentale, Istituto Regina Elena, Roma, Italia.

Dr. Bruno Calabretta, Kimmel Cancer Institute, Thomas Jefferson University, Philadelphia, USA.

Transcriptional and Post-Translational Control of the Retinoblastoma Family Gens.

Dr. Marco Giorgio Paggi, S.C. Lab. C, Istituto Regina Elena, Roma, Italia.

Dr. Antonio Giordano, Thomas Jefferson University, Philadelphia, USA.

Biological Basic for Somatic Gene Therapy using p53 Oncosuppressor Gene.

Project Co-ordinators:

Dr.ssa Ada Sacchi, S.C. Lab. C Oncogenesi Molecolare, Istituto Regina Elena, Roma, Italia.

Prof. Renato Baserga, Kimmel Cancer Institute, Thomas Jefferson University, Philadelphia, USA.

Lista protocolli per patologia approvati dal comitato etico

Protocolli	*Random*	*Multicentrico*	*Attivaz.*	*Reclut.*
Colon-retto				
Casale V. Studio di fattibilità di screening per cancro colorettale: FOBT annuale vs RSCS "once in a lifetime".	No	Si	2002	in corso
Casale V. Efficacia e sicurezza di Celecoxib (SC 58635) nella prevenzione della poliposi adenomatosa del colon.	No	No	2001	chiuso
Cosimelli M. Valutazione dell'impatto che i profili biologici, il trattamento combinato radio-chemioterapico e la chirurgia esercitano nella sottostadiazione del carcinoma del retto e sulla qualità della vita dei pazienti.	No	Si	2002	in corso
Garufi C. Time finding study of chronomodulated irinotecan, 5-Fluoraucil, leucoverin and oxaliplatin as first line against metastatic colorectal cancer.	Si	Si	2002	in corso
Garufi C. First line infusional 5-fluorouracil folinic acid and oxaliplatin for metastatic colorectal cancer or loco-regional recurrency-role of chronomodulated delivery upon survival. A multicenter randomized phase III trial.	Si	Si	1999	chiuso
Izzo F. Multicenter phase III open label randomized comparing CPT-11 in combination with a 5FU/FA infusional regimen to the same 5FU/FA infusional regimen alone as adjuvant treatment of stage III colon cancer.	Si	Si	2000	chiuso
Lopez M. Studio randomizzato di fase III che compara capecitabina (RO 09-1978) con fluorouracile (5-FU) endovena bolo combinato con bassi dosaggi di leucovorin come terapia adiuvante in pazienti sottoposti ad intervento chirurgico per carcinoma del colon in stadio C di Dukes.	Si	Si	1999	in corso
Paoletti G. Multicenter phase III open label randomized comparing CPT-11 in combination with a 5FU/FA infusional regimen to the same 5FU/FA infusional regimen alone as adjuvant treatment of stage III colon cancer.	Si	Si	2000	chiuso
Paoletti G. A dose-finding study followed by a phase II trial of oral UFT and LV (Leucovorin) plus I.V. mitomycin in metastatic colorectal cancer.	No	Si	2001	in corso
Zeuli M. Multicenter phase III open label randomized comparing CPT-11 in combination with a 5FU/FA infusional re-	Si	Si	2000	chiuso

Protocolli	*Random*	*Multicentrico*	*Attivaz.*	*Reclut.*
gimen to the same 5FU/FA infusional regimen alone as adjuvant treatment of stage III colon cancer.				
ZEULI M. Studio di fase II di ZD1839 (IRESSA) in combinazione con oxaliplatino e capecitabina nel trattamento di prima linea di pazienti con carcinoma del colon-retto in stadio avanzato.	No	Si	2002	in corso
MAMMELLA				
CARLINI P. Terapia di mantenimento con anastrozolo (Arimidex) verso controllo in pazienti affetti da neoplasia mammaria metastatica, responsivi o in stabilità di malattia dopo chemioterapia antiblastica.	Si	Si	2000	in corso
CARLINI P. An open, randomized sequential study of endocrine therapy in postmenopausal patients with advanced breast cancer with estrogen and/or progesteron positive tumors.	Si	Si	2001	in corso
CARLINI P. Valutazione dei livelli sierici di VGEF (Vascular Endothelial Growth Factor) in pazienti affette da carcinoma della mammella metastatico trattate con ormonoterapia.	No	Si	2001	in corso
CARLINI P. Exemestane (Aromasin): ormonoterapia di mantenimento dopo chemioterapia di I linea nel trattamento del carcinoma mammario metastatico.	No	Si	2001	in corso
DI FILIPPO F. Studio multicentrico, prospettico, randomizzato di fase III: linfonodo sentinella +- linoadenectomia ascellare nel carcinoma della mammella allo stadio iniziale.	Si	Si	1999	in corso
FABI A. Associazione di doxorubicina liposomiale (caelix) e gemcitabine (gemzar) nel trattamento della neoplasia mammaria avanzata: studio di fase II .	No	Si	2002	in corso
IZZO F. Studio clinico in aperto per valutare l'efficacia e la tollerabilità dello zometa (Zolendronato) 4mg somministrato per via endovenosa a pazienti affetti da carcinoma mammario metastatico, in cui sia indicato il trattamento con bifosfonati.	No	Si	2001	in corso
MARIANI L. Studio internazionale, multicentrico, randomizzato, in doppio cieco, a gruppi paralleli, controllato verso placebo, per valutare efficacia e sicurezza del tibolone (Org OD14) in donne con sintomi climaterici e storia di cancro della mammella.	Si	Si	2002	in corso
NISTICÒ C. A multistep randomized phase II-III trial comparing oxaliplatino 5-Fluorouracil (-FU) to vinorelbine 5-FU in patients with metastatic breast cancer (MBC) after taxane/Anthracycline.	Si	Si	2000	chiuso

Protocolli	*Random*	*Multicentrico*	*Attivaz.*	*Reclut.*
NISTICÒ C. A phase III randomized study if sequential epidoxorubicin followed by CMF (arm A) vs sequential epidoxorubicin followed by docetaxel followed by CMF (arm B) vs sequential intensified epidoxorubicin followed by docetaxel followed by high-dose cyclophosphsmide (arm C) in eqrly breast cancer patients with positive axillary lymph nodes.	Si	Si	2000	chiuso
PAPALDO P. A randomized three-arm multicentre study comparing one year and two years of Herceptin vs Herceptin vs Herceptin in women with Her2 positive primary tbreast cancer who have completed adjuvant therapy.	No	Si	2002	in corso
PAPALDO P. Studio randomizzato di fase III con EC seguito da Paclitaxel verso FEC seguito da Paclitaxel, cicli somministrati ogni 3 settimane o 2 settimane con supporto di Pegfilgrastim, per pazienti con carcinoma della mammella con linfonodi ascellari positivi (Studio randomizzato di fase III con EC seguito da Paclitaxolo versus FEC seguito da Paclitaxolo in pazienti con neoplasia mammaria con linfonodi positivi).	Si	Si	2002	in corso
PAPALDO P. A phase II study of Epothilone analog BMS-247550 in patients with metastatic breast cancer previously treated with an antracycline.	Si	Si	2001	chiuso
PAPALDO P. A randomized phase II study of two different schedule of Caelix in metastatic breast cancer.	Si	Si	2001	chiuso
PAPALDO P. MOON - Metastasi Ossee Osservatorio Nazionale: metastasi ossee nel carcinoma mammario. Studio osservazionale per la valutazione dei pattern di presentazione, di evoluzione clinica e di modalità di trattamento.	No	No	1997	chiuso
PAPALDO P. A phase III randomized study if sequential epidoxorubicin followed by CMF (arm A) vs sequential epidoxorubicin followed by docetaxel followed by CMF (arm B) vs sequential intensified epidoxorubicin followed by docetaxel followed by high-dose cyclophosphsmide (arm C) in eqrly breast cancer patients with positive axillary lymph nodes	Si	Si	1997	chiuso
PAPALDO P. Studio comparativo, randomizzato, multicentrico, multinazionale, in aperto, di Herceptin in associazione a Docetaxel, come trattamento di prima linea in pazienti con tumore metastatico della mammella con iperespressione di HER-2 neu.	Si	Si	1999	chiuso
PAPALDO P. Studio di fase II con Vinorelbine orale nella chemioterapia prima linea del carcinoma mammario metastatico.	No	Si	2000	chiuso

Protocolli	*Random*	*Multicentrico*	*Attivaz.*	*Reclut.*
PAPALDO P. An open label randomized phase 2 study of Trastuzumab (Herceptin) given with weekly Paclitaxel (Taxol) versus weekly Paclitaxel as single agent in first-line therapy metastatic breast cancer (MBC) patients with HER-2/neu overexpression.	Si	Si	2000	in corso
PINNARÒ P. Studio prospettico e randomizzato di confronto tra quadrantectomia seguita da radioterapia esterna complementare e quadrantectomia associata a radioterapia intraoperatoria in pazienti affette da carcinoma mammario di piccole dimensioni e di età > a 48 anni in postmenopausa.	Si	No	2002	in corso
PINNARÒ P. Studio prospettico e randomizzato di fase III: RT dilazionata vs RT immediata in pazienti affette da ca mammario sottoposte a chirurgia conservativa, CMF adiuvante e RT complementare.	Si	No	1998	chiuso
SAVARESE A. /SEGA F. Consulenza integrata oncologica-genetica-psicooncologica (counselling genetico) nelle neoplasie mammarie ad incidenza familiare. Programma di sorveglianza per la identificazione e prevenzione dei tumori mammari in soggetti ad alto rischio genetico.	No	No	2001	in corso
TERZOLI E. An open, randomized sequential study of endocrine therapy in postmenopausal patients with advanced breast cancer .	Si	Si	2001	in corso
VICI P. An open, randomized sequential study of endocrine therapy in postmenopausal patients with advanced breast cancer with estrogen and/or progesteron positive tumors.	Si	Si	2001	in corso
VICI P. Epirubicina e ciclosfamide vs taxotere seguito da epirubicina e ciclosfamide nel trattamento adiuvante del carcinoma mammario con linfonodi ascellari positivi. Studio multicentrico randomizzato.	Si	Si	1999	in corso
VICI P. An open label randomized phase III study of Capecitabine in combination with exemestane compared with exemestane alone as maintaining therapy for metastatic hormonereceptor positive breast cancer.	Si	Si	2001	in corso
VICI P. Gemcitabina e docetaxel come terapia di prima linea nel carcinoma mammario metastatizzato. Studio multicentrico di fase II.	No	Si	2001	in corso
MELANOMA				
FERRARESI V. Post-operative adjuvant ganglioside GM2-KLH/QS-21 vaccinacion treatment vs observation after resection of	Si	Si	2002	in corso

Protocolli	*Random*	*Multicentrico*	*Attivaz.*	*Reclut.*
primary cutaneous melanoma (AJCC Stage II, T3-T4N0M0).				
FERRARESI V. Adjuvant PEG-Intron treatment in stage III melanoma (Trattamento adiuvante con PEG-Intron vs osservazione dopo linfoadenectomia regionale in pazienti affetti da melanoma stadio III: studio.	Si	Si	2001	in corso
FERRARESI V. Studio clinico di fase II, multicentrico, randomizzato, in aperto, per valutare l'efficacia del farmaco ST1472 in una terapia di combinazione con basse dosi di IFN+DTIC paragonata alla terapia ST1472+DTIC e alla terapia DTIC+IFN a basse dosi in pazienti affetti da melanoma maligno avanzato.	Si	Si	2002	in corso
ZEULI M. Studio multicentrico per la valutazione dell'attività di Temozolomide preceduta da radioterapia in pazienti affetti da metastasi cerebrali da melanoma maligno.	No	Si	2000	in corso
OVAIO				
SAVARESE A. A multicenter, randomized, phase III study comparing paclitaxel/carboplatin versus topotecan/paclitaxel/carboplatin in patients with stage III (residual tumor > 1cm after primary surgery) and IV ovarian cancer.	Si	Si	2002	in corso
PANCREAS				
CARLINI P. Gemcitabina vs gemcitabina + cisplatino nel trattamento del carcinoma del pancreas avanzato.	Si	Si	2002	in corso
IZZO F. A phase III trial of ALIMTA plus gemzar versus gemzar in patients with unresectable or metastatic cancer of the pancreas.	Si	Si	2001	in corso
LOPEZ M. Gemcitabina vs gemcitabina + cisplatino nel trattamento del carcinoma del pancreas avanzato.	Si	Si	2002	in corso
PIÙ PATOLOGIE				
CAVALIERE F. Trattamento integrato dello pseudomixoma peritonei da carcinoma appendicolare colorettale ed ovarico.	No	No	1999	in corso
GIOVINAZZO G. Studio prospettico e randomizzato tra due diversi schemi di radioterapia, in associazione o meno con Zolendronato, in pazienti affetti da metastasi ossee sintomatiche da carcinoma mammario e prostatico.	Si	Si	2002	in corso
ZEULI M. Trapianto allogenico non mieloablativo (mini-allotrapianto) di cellule staminali emopoietiche come terapia di salvataggio nei tumori solidi refrattari ai trattamenti convenzionali.	No	Si	2002	in corso

Protocolli	*Random*	*Multicentrico*	*Attivaz.*	*Reclut.*
POLMONE				
CERIBELLI A. Studio multicentrico randomizzato di fase II di ZD1839 in combinazione con gemcitabina e ZD1839 in combinazione con Vinorelbina nel trattamento di prima linea di pazienti anziani con carcinoma del polmone non a piccole cellule in stadio avanzato.	Si	Si	2002	in corso
CERIBELLI A. Studio multicentrico di fase II di Gemcitabina-oxaliplatino come prima linea di trattamento in pazienti con tumore polmonare non microcitoma (NSCLC) in stadio avanzato.	No	Si	2002	in corso
CERIBELLI A. A phase III trial of LY900003 plus gemcitabine and cisplatin versus gemcitabine and cisplatin in patients with advanced, previously untreated non-small cell lung cancer.	No	Si	2002	in corso
CERIBELLI A. Valutazione dell'attività e della tossicità della polichemioterapia con schemi a due farmaci contenenti Gemcitabina nel microcitoma polmonare esteso in pazienti anziani.	No	Si	2002	in corso
CERIBELLI A. A randomized phase III of surgery alone or surgery plus gemcitabine - cisplatin in clinical early stages (T2N0,T1, T3 N0 and T3N1) non small cell lung cancer (NSCLC).	Si	Si	2001	in corso
CERIBELLI A. Studio multicentrico randomizzato di chemioterapia vs radioterapia adiuvante nel carcinoma polmonare non a piccole cellule stadio IIIA-N2 dopo terapia primaria e resezione chirurgica.	Si	Si	2000	in corso
CERIBELLI A. Studio randomizzato di fase II multicentrico con due schede di Gemcitabina + Cisplatino nel tumore del polmone non a piccole cellule (NSCLC) stadio IIIB-IV.	Si	Si	2001	in corso
CERIBELLI A. Docetaxel ogni tre settimane verso docetaxel settimanale nel trattamento di seconda linea del carcinoma polmonare non a piccole cellule stadio IIIB-IV.	Si	Si	2001	chiuso
CERIBELLI A. Studio multicentrico, randomizzato, in aperto, comparativo, di fase III con Topotecan orale/Cisplatino verso Etoposide/Cisplatino somministrato come trattamento chemioterapico di prima linea in pazienti affetti da microcitoma polmonare.	Si	Si	2001	chiuso
GIUNTA S. La TAC spirale "low-dose" nella diagnosi precoce del cancro del polmone nei soggetti a rischio.	No	No	2000	in corso
LOPEZ M. Chemioterapia seguita da radioterapia standard vs che-	No	Si	2000	in corso

Protocolli	*Random*	*Multicentrico*	*Attivaz.*	*Reclut.*
mioterapia seguita da radio+chemioterapia concomitante nel trattamento del NSCLC inoperabile in stadio III.				
LOPEZ M. Efficacia clinica sulla sopravvivenza del trattamento con chemioterapia standard vs chemioterapia standard + modulo di attivazione linfocitaria con interleuchina-2 (IL-2) Tumore polmonare .	Si	Si	2000	in corso
RINALDI M. A randomized phase III of surgery alone or surgery plus gemcitabine - cisplatin in clinical early stages (T2N0,T1, T3 N0 and T3N1) non small cell lung cancer (NSCLC).	Si	Si	2000	in corso
RINALDI M. A phase III trial of ALIMTA versus docetaxel in patients with locally advanced or metastatic NSCLC who where previously treated with chemotherapy.	No	Si	2001	chiuso
RINALDI M. Studio multicentrico di fase II che valuta la fattibilità e l'attività di due diverse combinazioni di Docetaxel e Gemcitabina e del trattamento Gemcitabina Cisplatino seguito da Docetaxel in pz con carcinoma del polmone NSCLC localmente avanzato o metastatico che non abbiano ricevuto recedentemente trattamento chemioterapico.	Si	Si	2002	in corso
SAVARESE A. Chemioterapia seguita da radioterapia standard vs chemioterapia seguita da radio+chemioterapia concomitante nel trattamento del NSCLC inoperabile in stadio III.	Si	Si	2000	in corso
RINALDI M. Studio clinico di fase II nel carcinoma polmonare non a piccole cellule localmente avanzato relativo alla combinazione di vinorelbine orale (Navelbine) e cisplatino, somministrata come terapia d'induzione e contemporaneamente alla radioterapia.	No	Si	2002	in corso
RINALDI M. Studio multicentrico randomizzato di fase II di ZD1839 in combinazione con gemcitabina e ZD1839 in combinazione con Vinorelbina nel trattamento di prima linea di pazienti anziani con carcinoma del polmone non a piccole cellule in stadio avanzato.	Si	Si	2002	in corso
RINALDI M. Docetaxel ogni 3 settimane vs Docetaxel settimanale nel trattamento di II linea del carcinoma polmonare NSCLC di stadio IIIB-IV.	Si	Si	2002	in corso
PROSTATA				
ARCANGELI G. Studi paralleli di fase II con assegnazione randomizzata tra frazionamento convenzionale standard e ipofrazionamento nell'irradiamento del carcinoma prostatico a prognosi sfavorevole, in associazione a soppressione androgenica totale.	Si	Si	2002	in corso

Protocolli	*Random*	*Multicentrico*	*Attivaz.*	*Reclut.*
CARLINI P. Studio di fase II multicentrico, randomizzato, in doppio cieco, controllato con placebo, per valutare la sicurezza e l'attività di ZD1839 (IRESSA) nel migliorare il controllo del PSA e il decorso clinico del tumore alla prostata refrattario agli ormoni.	Si	Si	2002	in corso
CARLINI P. Studio osservazionale multicentrico e multinazionale per documentare il trattamento e lo standard di cura dei pazienti affetti da carcinoma metastatico della prostata refrattario al trattamento ormonale(W 01-381).	No	Si	2002	in corso
GIOVINAZZO G. Three dimensional conformal radiotherapy alone vs three dimensional conformal therapy plus adjuvant hormonal therapy in localized T1b-c, T2a, M0 prostatic carcinoma. A phase III randomized study.	Si	Si	2001	in corso
GIOVINAZZO G. Terapia ormonale adiuvante a lungo termine con analoghi LHRH versus trattamento nel carcinoma della prostata localmente avanzato. Trattamento con radioterapia esterna e blocco androgenico totale per 6.	No	No	2001	chiuso
VARIE				
ARCANGELI G. Studio clinico controllato sugli effetti della correzione dell'anemia in pazienti affetti da neoplasie del distretto cervico cefalico sottoposti a radioterapia.	No	Si	2000	chiuso
ARCURI E. Double blind, placebo controlled, randomized, multicenter study on the effect and safety of gabapentin (neurontin) as adjuvant in neuropathic pain in patients with malignancies.	Si	Si	2000	chiuso
ARCURI E. Studio clinico policentrico sull'utilizzo del tramadolo nel trattamento del dolore oncologico. Confronto tra due vie di somministrazione	Si	Si	2001	in corso
CASALE V. Comportamento della dispepsia funzionale dopo eradicazione dell'infezione da Helicobacter Pylori. Indagine conoscitiva in endoscopia digestiva.	No	No	1999	chiuso
CASALE V. Efficacy and tolerability of Pantoprazole (20mg u.i.d.) versus placebo in preventing the symptomatic relapses of mild gerd.	Si	Si	2000	chiuso
CASALE V. Comparison of the efficacy and tolerability of Pantoprazole (20mg u.i.d.) and ranitidine (150mg b.i.d.) in patients with mild gerd.	Si	Si	2000	chiuso
CASALE V. Study of the efficacy of rabeprazole in the curative (vs omeprazole) and maintenance (open) treatment of reflux oesophacities.	No	Si	2000	chiuso

Protocolli	*Random*	*Multicentrico*	*Attivaz.*	*Reclut.*
CASALE V. Butirrato di sodio per via topica nella prevenzione della proctite acuta da radiazioni. Studio multicentrico controllato a doppia cecità contro placebo.	No	Si	2000	in corso
CASALE V. Nexium nel trattamento a lungo termine della malattia da reflusso gastroesofageo (MRGE). Studio multicentrico, in aperto, randomizzato di confronto tra i costi generati da un trattamento di mantenimento della MRGE con Nexium 20mg al bisogno ed un trattamento di mantenimento con nexium 20 mg in maniera continuativa.	Si	Si	2002	in corso
CILENTI V. Studio clinico di 12 settimane, multicentrico, randomizzato, in doppio cieco, doppio placebo, a gruppi paralleli mirato a confrontare efficacia e tollerabilità della combinazione Salmeterolo/Fluticasone propinato 50/100 mcg (Seretide/Viane/Advair) assunta una volta al dì di sera mediante Diskus/Accuhaler e di Budesonide 400mcg assunto una volta al dì di sera mediante inalatore a polvere secca azionato tramite respiro quale terapia iniziale di mantenimento in soggetti con asma da lieve a moderato.	No	Si	2002	in corso
COGNETTI F. Progetto globale per l'identificazione ed il miglioramento della Qualità di vita nei pazienti oncologici a lunga aspettativa di vita.	No	Si	2002	in corso
FERRETTI G., FABI A. Profilo sierico di fattori angiogenici (VEGF), citochine e metalloproteinasi in pazienti affette da neoplasia mammaria con lesioni ossee e in trattamento con acido zoledronico (Zometa).	No	Si	2002	in corso
GRASSI A. Studio policentrico sulla prevalenza della metaplasia intestinale e displasia sulla giunzione esofagogastrica nei pazienti che si sottopongono a gastroscopia.	No	Si	2001	in corso
IZZO F. Anemia da cancro e terapia trasfusionale: studio osservazionale prospettico longitudinale multicentrico dell'epidemiologia, eziopatogenesi dell'anemia e dei costi sociali della gestione del suo trattamento mediante terapia trasfusionale in corso di chemio associata o meno a radioterapia.	No	Si	2001	chiuso
JANDOLO B. Studio randomizzato, crossover, in aperto con IC351 (LY450190) somministrato in pazienti con disfunzione erettile, per valutare la preferenza dei pazienti per uno schema di assunzione "a richiesta" o "predefinito".	Si	Si	2002	in corso
MARIANI L. Immunogenicità e sicurezza del vaccino tetravalente HPV L1 (tipo 6,11,16,18) costituito da particelle virus simili (VLP) in lotti differenti in donne di età tra i 16 ed i 23 aa ed immunogenicità del vaccino HPV 16 (VLP) e studio x valutare l'efficacia del vaccino HPV L1 tetra-	Si	Si	2002	in corso

Protocolli	*Random*	*Multicentrico*	*Attivaz.*	*Reclut.*
valente (tipo 6,11,16,18) costituito da particelle virus simili (VLP) nel ridurre CIN e VaIN correlati a HOV 6,11,16 e 18 e di lesioni verrucose genitali esterne eVIN correlate a HPV 6,11,16 e 18 in donne di età compresa tra i 16 ed i 23 aa.				
MIRRI M.A. Studio multicentrico (doppio cieco) comparativo su efficacia e tollerabilità del fluoconazolo versus placebo in pazienti sottoposti a radioterapia per tumore di testa e collo.	Si	Si	1999	chiuso
PACE A. Progetto di assistenza continuativa integrata e neuroriabilitazione a domicilio per pazienti affetti da tumori cerebrali.	No	Si	2002	in corso
PETTI M.C. Trattamento del mieloma multiplo alla diagnosi: confronto prospettico randomizzato di chemioterapia intensificata con supporto di progenitori emopoietici e melphalan alla dose di 100 mg/mq verso lo stesso tipo di trattamento con melphalan alla dose di 200 mg/mq.	Si	Si	2002	in corso
PETTI M.C. Valutazione clinica dell'effetto del mantenimento dei livelli di emoglobina con dosaggi settimanali di eprex/erypo (epoetina alfa) nei soggetti affetti da tumori linoidi maligni (malattia di hodgkin, linfonoma non-hodgkin, leucemia linfocitica cronica e mieloma multiplo.	No	Si	2002	in corso
PETTI M.C. Studio pros\co randomizzato nei linfonomi non-Hodgkin (LNH) aggressivi - NHLCSG: 1) VACOP-B e high dose sequential therapy (HDS) nei LNH in stadio avanzato; 2) anti-CD 20 nei linfonomi b/CD 20 + in prima remissione completa.	Si	No	2001	in corso
SANTORO E. Studio prospettico, multicentrico, in aperto, randomizzato, comparatico per valutare l'efficacia, la sicurezza e la tollerabilità di ertapenem (MK-826) verso ceftriaxone/metronidazolo nel trattamento delle infezioni intraaddominali negli adulti.	Si	Si	2002	in corso
SAVARESE A., JANDOLO B. Valutazione dell'efficacia e tollerabilità di L-cetilcarnitina nel prevenire o ridurre la polineuropatia indotta da trattamento con Taxolo in monoterapia o in associazione ad altri farmaci neurotossici e non. Studio multicentrico, randomizzato in doppio cieco controllato verso placebo.	Si	Si	2001	in corso
SAVARESE A. Anemia da cancro e terapia trasfusionale: studio osservazionale prospettico longitudinale multicentrico dell'epidemiologia, eziopatogenesi dell'anemia e dei costi sociali della gestione del suo trattamento mediante terapia trasfusionale in corso di chemio associata o meno a radioterapia.	No	Si	2001	chiuso

Protocolli	*Random*	*Multicentrico*	*Attivaz.*	*Reclut.*
SAVARESE A. Indagine di prevalenza sui comportamenti prescrittivi relativi alla prescrizione di farmaci antiemetici per la prevenzione ed il trattamento dell'emesi ritardata indotta da chemioterapia e loro efficacia e tossicità.	No	Si	2002	in corso
SAVARESE A. Livelli di emoglobina e qualità della vita in soggetti con tumore solido in trattamento con chemioterapia ed epoetina alfa 40k (40000UI) una volta alla settimana.	No	Si	2002	in corso
SAVARESE A. Studio di fase II randomizzato di due diverse schedule di ondansteron nella terapia di salvataggio dell'emesi indotta da chemioterapia ad alto e moderato potere emetogeno.	Si	Si	2002	in corso
SAVARESE A. Studio randomizzato, in aperto, di darbepoetin alfa (Nuova Proteina Stimolante l'Eritropoiesi, NESP) e rHuEPO per il trattamento dell'anemia in soggetti con neoplasie non-mieloidi che ricevono cicli multipli di chemioterapia.	Si	Si	2002	in corso
TERZOLI E. A randomized study to evaluate the effect of maintaining haemoglobin levels with epotin alfa, on anemia quality of life in breast cancer subjects receiving myelotoxic chemotherapy.	Si	Si	2001	chiuso
ZEULI M. STI571 (Glivec) in KIT-expressing gastrointestinal stromal tumors (GIST): a prospective, open-label, multicenter study on best clinical use in advanced disease.	No	Si	2002	in corso
ZEULI M. Studio clinico biologico multicentrico, randomizzato, in aperto, di fase III, per valutare l'equivalenza clinica di due formulazioni di lanreotide (SR 60 mg ed ATG 120 mg) in pazienti affetti da tumore neuroendocrino ben differenziato.	Si	Si	2002	in corso
VESCICA				
GALLUCCI M. Somministrazione endovescicale di gemcitabina nelle neoplasie superficiali della vescica: studio di fase II.	No	Si	2002	in corso
RUGGERI E.M. Chemioterapia adiuvante con Cisplatino/Gemcitabine in pz con carcinoma transizionale della vescica ad elevato rischio di recidiva dopo cistectomia radicale vs chemioterapia differita alla ripresa di malattia.	Si	Si	2001	in corso
RUGGERI E.M. 'Gemcitabine+Cisplatino vs Gemcitabina+Carboplatino nel carcinoma dell'urotelio metastatico o avanzato a cellule transizionali in uno schema terapeutico di 21 giorni. Studio randomizzato di fase II.	Si	Si	2000	chiuso

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