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**2013 is the year of the formal establishment of the multidisciplinary HPV unit (which was officially approved in 2012, with IFO resolution n.551).**

**MISSION:**

Formalizing an organizational model of a "unified and coordinated space" in which originate jointly initiatives related to the topic of HPV: clinical management (diagnosis, treatment guidelines, facilitated routes and more), and scientific matching (creation of "ad hoc" database, sharing of researches and more). This organizational model is a tool to inform, train and network both patients and health workers involved in HPV-related pathologies, from gynecological area to the skin, comprising ENT, urological and proctologic diseases. Finally, HPV-Unit is organized to deliver HPV vaccines to women and men.

**Formation/Information Activities**

Scientific activities of HPV-UNIT were focused on developing strategies for permanent professional training and information addressed to the citizens. Organization of "ad hoc" Meetings as part of the formation/information activity: a meeting organized in Rome (03-25-2017) "10 Anni di Vaccinazione HPV" was really a success with the partnership of the Italian Society for Virology as well as the International HPV Awareness Day (4th March of each year). HPV Unit is already committed to organize a main event for the 2019 International HPV Awareness Day campaign. In parallel, HPV-Unit is constantly carrying out a large activity of user's information by upgrading the dedicated internet site (www.hpvunit.it), by telephone, and by email that are the preferred way of communication of users. After almost five years of activity, we have seen a constant increase of about 40% in the overall number of contacts (up to the mean of 80 persons / week) at the dedicated email, phone and website for any kind of consultation regarding HPV.

Part of formation/information activity is granted by Italian Interior Ministry - Progetto Bando FAMI.

**Clinical Activities**

The main purpose of HPV-UNIT is the multi-discipline involvement of IRE/ISG specialists. The primary activity is focused on coordinating diagnostic interventions by clinical interpretation of molecular data from assay tests, advice in evaluation of clinical cases by clinical teams, outpatients counseling and advising in preventive actions like individual screening or HPV vaccination. In addition, HPV UNIT is actively engaged in second level diagnosis of virus-associated cancers, especially HPV-related in skin, oral cavity, and genital/perianal areas.

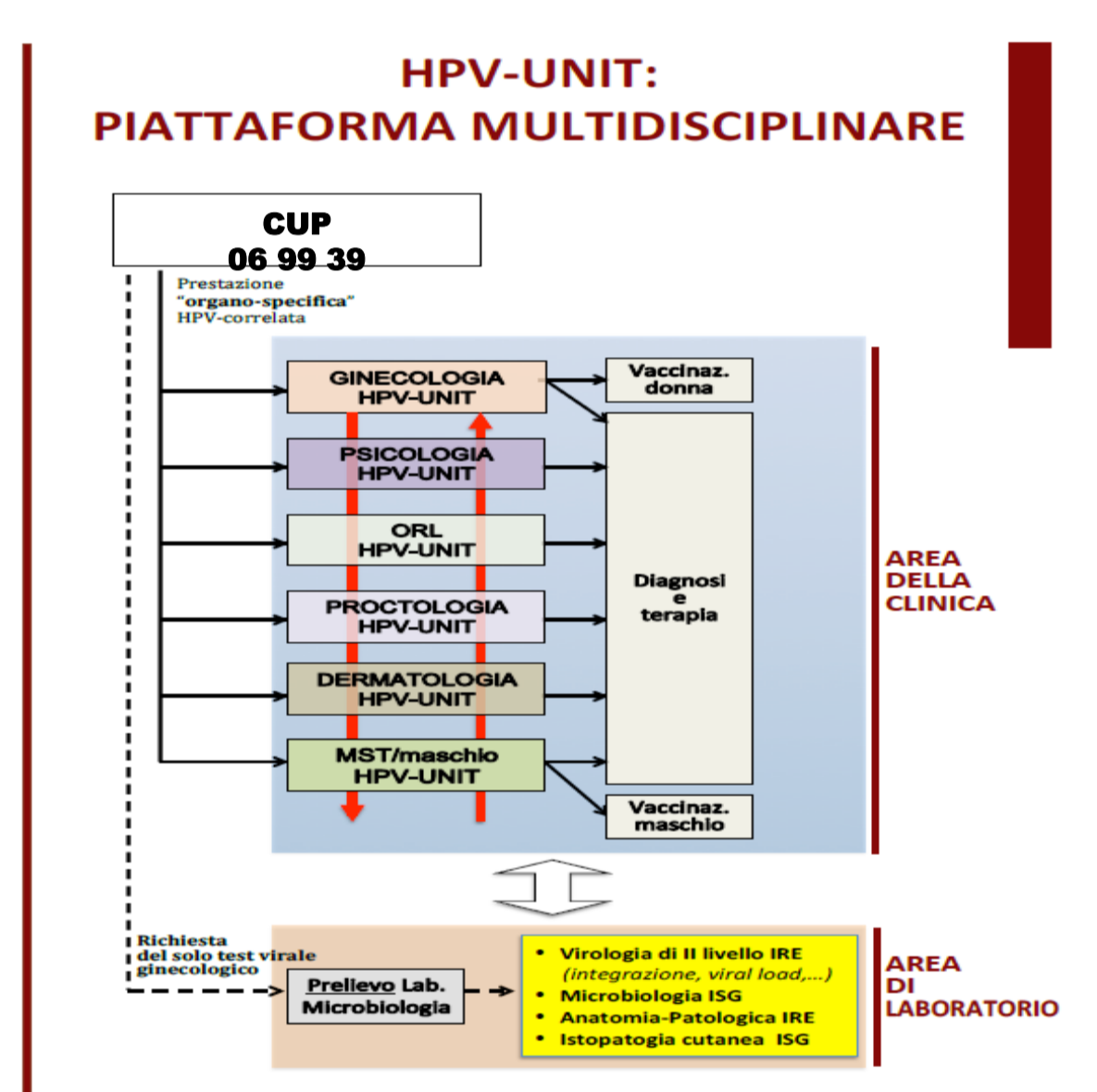
Regarding HPV prevention, HPV vaccination, that is a program already started in 2014 for female, up to 45 years old, and later on extended to male, is fully operating with a constant rise in number of administrated doses (more than 150 globally for male and female). This program was implemented by offering HPV vaccination to women as adjuvant prevention therapy after conization. An interim analysis of these patients seems to indicate that vaccination after conization is effective in reducing re-infection by HPVs that are included in vaccine formulation.

**HPV vaccination after conization**

ID	HPV test pre-conization	Year of conization	Histology	HPV test pre-vaccine	HPV test at 6 months	HPV test at 12 months
41186	HR+	2013	CIN3	n	n	neg
29528	89	2013	CIN3	89	n	n
30915	HR+	2009	CIN2	n	n	n
27413	54,58,82,16	2015	CIN2	n	16,45,53	45, 53
31719	HR+	2014	CIN3	n	n	n
27576	16+	2012	CIN2	n	n	n
31369	66	2014	CIN2	n	n	n
29924	16, 18	2014	CIN2	n	n	n
31345	HR+	2015	CIN2	n	n	n
26079	HR+	2013	CIN2	HR+	HR+	n
26945	18	2015	CIN2	n	n	n
33733	HR+	2014	CIN2	n	n	n
29022	66	2013	CIN3	n	n	n
22896	18	2013	CIN2	n	31+	n
31980	HR+	2014	CIN2	HR+	n	n
26076	18	2013	CIN3	n	n	n
33621	16	2015	CIN3	n	n	n
30696	18	2015	CIN2	39+	39,51,56,89	n
25875	HR-positivo	2014	CIN3	n	n	n
31259	6-42-52-84-89	2013	CIN2	n	n	n

Patients were analyzed for HPV before conization, before vaccination (Gardasil 4), and thereafter at 6 and 12 months, respectively. Only one patient was still HPV positive at 12 months but HPV types were not in the vaccine preparation.

**Information leaflet of HPV Unit platform**



**Information leaflet of HPV vaccination in males**

**HPV-Unit in translational researches.**

**Molecular carcinogenesis.** All available data of high risk HPV E5 protein were collected to highlight how this oncogene interacts with many different pathways during the viral life cycle to create an environment favorable to viral replication and cell transformation (de Freitas et al. hrHPV E5 oncoprotein: immune evasion and related immunotherapies. J Exp Clin Cancer Res. 2017)

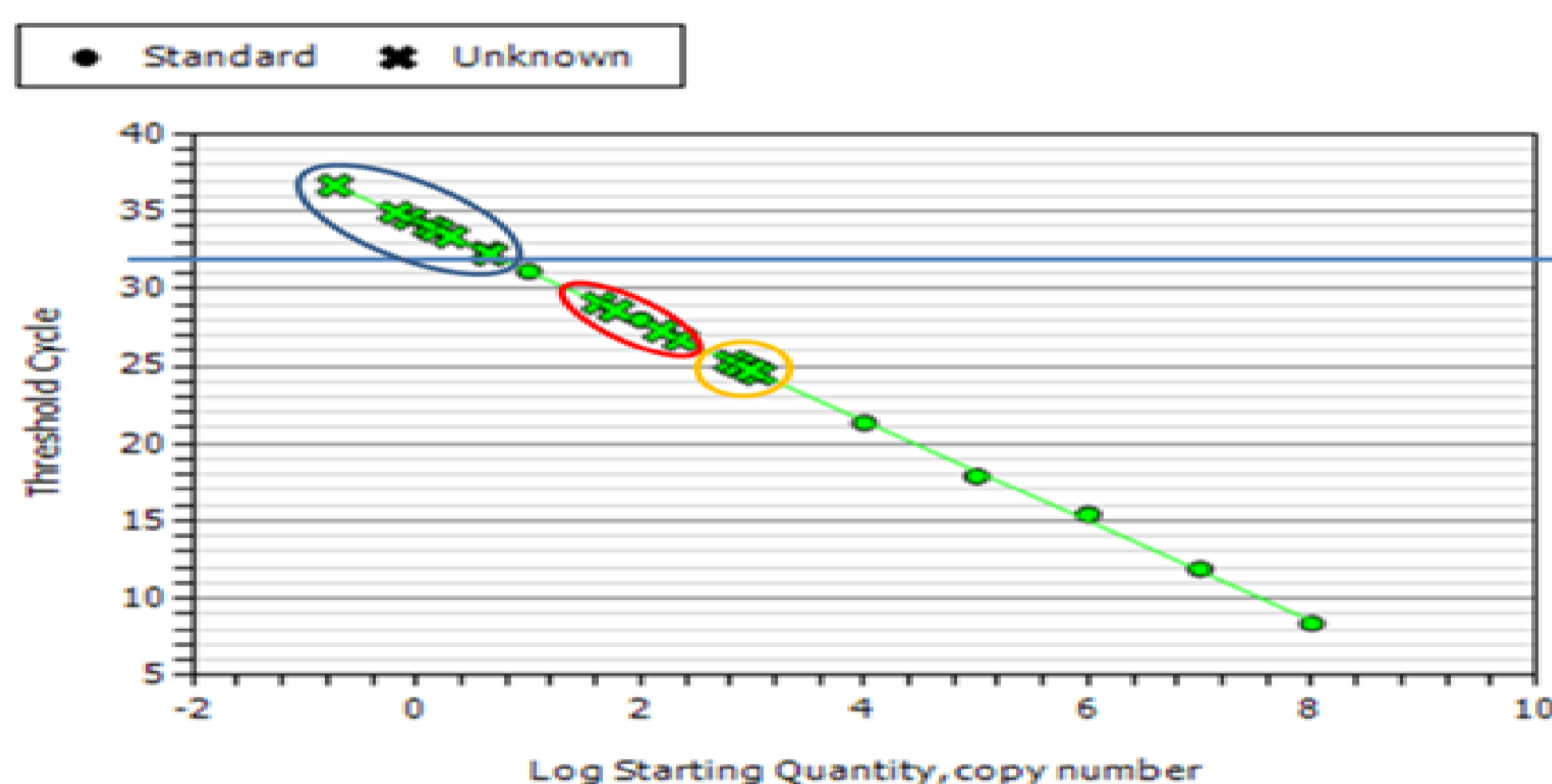
**Molecular epidemiology:**

1- Genital tumors. Benefits and potential issues of the 9valent HPV vaccine were overviewed together with data on the implementation of cervical screening after vaccination (Cordeiro et al. MN, Current research into novel therapeutic vaccines against cervical cancer. Expert Rev Anticancer Ther. 2018) . Bio-molecular follow-up of patients undertaken vaccination after conization is ongoing (see Table)

2- Extra-genital tumors. Presence and expression of HPV were demonstrated in pre-neoplastic lesions of skin, suggesting that HPV might be involved in skin carcinogenesis (Dianzani et al. Human papilloma virus expression in immunocompetent patients with actinic keratosis: A case series. J Am Acad Dermatol. 2017). HPV was detected in Merkel carcinoma together with MCPyV (Curzio et al. Merkel cell carcinoma: new insights into pathogenesis. Eur J Dermatol. 2017).

3- New real-time and digital PCR technologies are employed to detect differences in the level of circulating cell free (ccf) HPV DNA among patients treated with radiotherapy for oropharyngeal tumors (in collaboration with Prof. Sanguineti - UOC Radiotherapy).

**Preliminary results. Different levels of ccfHPV DNA in patient at baseline of radiotherapy.**



The figure shows the values of ccfDNA for HPV16 by real-time PCR on a standard curve of known concentrations of circular HPV-DNA. Patient plasma samples (from IRE Bio-Bank) were classified in three categories: negative (blue circle), positive at high (yellow circle), and positive at low (red circle) HPV copy number. Follow-up of these patients is ongoing.

4- New therapies of HPV-associated cancers. New therapeutic vaccines were produced, and tested in our mouse models demonstrating their high effectiveness in curing experimental tumors (SEE POSTER 58)

**Acknowledgment**

We apologize for not mentioning all the people working in the different UNITS at IRE and ISG (see information leaflet) that are essential for the activity of HPV functional Unit.