IMPACT OF PERSONALIZED TREATMENT IN HCC PATIENTS TREATED WITH RESIN 90Y-MICROSPHERES: a randomized clinical trial.

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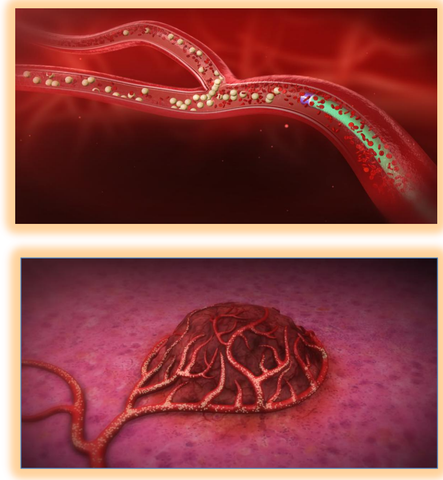
BACKGROUND

- Selective internal treatment **SIRT** or radioembolization -RE with Yttrium-90 microspheres is an effective treatment in unresectable hepatocellular carcinoma (HCC) due to differential tumor / normal liver flow
- IRE experience on SIRT in HCC is the one of the largest in Europe, with nearly 1000 treatment performed until today.
- Unfortunately the treatment is still under optimized being most studies based on non-dosimetric method approach, i.e. semi-empiric method named Body Surface Area (BSA).
- Recently, a **SPECT/CT** scanner with a **quantitative tool** has been installed in our Institute allowing an accurate **3D dosimetry**. Accordingly, the selection of a personalized activity of Y90-resin-microspheres - dosimetry based - and the predictive role of biomarker has been investigated to evaluate the impact on treatment efficacy and toxicity



SIRT is a catheter-based infusion of ^{90}Y microspheres into the hepatic arterial circulation, from which approximately 80 -100% of liver tumor blood flow derives, owing to high intratumoral ^{90}Y radiation dose delivered,

Design of study

RCT- Double blind

comparing

- STANDARD TREATMENT - BSA *(Arm A : 70 pts)*

against

- PERSONALIZED TREATMENT by 3D DOSIMETRY *(Arm 2 : 70 pts)*

AIM

to demonstrate a **survival benefit** when a dosimetric- based patient-specific activity is administered compared to a standard treatment with BSA method in a sample of **140 unresectable HCC** elegible to SIRT .

Duration of the study : 5 years

PRIMARY ENDPOINT

Evaluate **two years OS** differences between two Arms

SECUNDARY ENDPOINT

Evaluate following differences between two Arms:

- liver progression free survival
- time to progresssion lesion based
- rate of 3 months objective response
- type of response (% of RC, RP)
- time to response
- biomarkers modifications (AFP, PIVKA)
- dosimetric data

METHODS

ENROLLMENT

TREATMENT INDICATION — LIVER TUMOR BOARD

ELIGIBILITY EVALUATION — IRE SIRT TEAM

ANSWER THE QUESTION

1. TREAMENT in the SPECIFIC TUMOR TYPE and SETTING IS SUPPORTED by EVIDENCE ?
2. WHAT ARE TREATMENT GOALS: downstaging /potentially cure / tumor control or palliation
3. WHAT ARE (*if any*) TREATMENT OPTIONS and PREDICTED RISK/BENEFIT

EVALUATE

1. PATIENT CONDITION: Liver , Renal, Hematological Function
2. TUMOR FEATURES : CT /MRI / PET (< 1 months)

VERIFY

Inclusion - esclusion criteria

LIVER TUMOR BOARD CONCLUSION
^{90}Y-RE MAY BE INDICATED

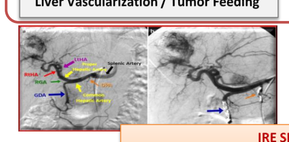
IRE SIRT TEAM CONCLUSION
PATIENT ELIGIBLE

PRE- TREATMENT PROCEDURES

Angiography Suite — Nuclear Medicine

HEPATIC ANGIOGRAPHY
Liver Vascularization / Tumor Feeding

MAA IMAGING
Lung Shunt/ GI Shunt / MAA Distribution



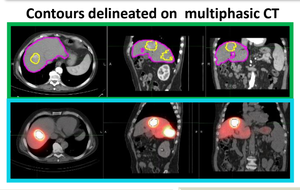
IRE SIRT TEAM CONCLUSION
TREATMENT FEASIBILITY CONFIRM

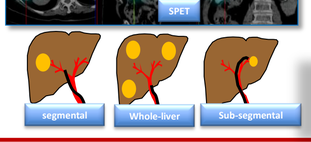
MULTIMODALITY IMAGING INTEGRATION MULTIDISCIPLINARY THERAPY PLAN

CHOICE
TARGET VOLUME / STRATEGY OF ADMINISTRATION:

CALCULATE ^{90}Y ACTIVITY TO BE ADMINISTERED:
with both methods: BSA , 3D DOSIMETRY in each pt.

Contours delineated on multiphasic CT

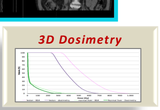




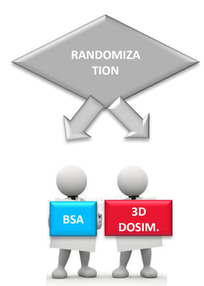
BSA method

$$\text{Activity (GBq)} = \text{BSA} - 0.2 + \left[\frac{\text{Tumor volume}}{\text{Total liver volume}}\right]$$

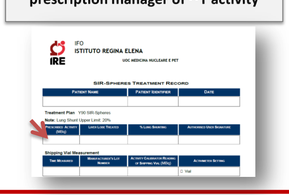
3D Dosimetry



RANDOMIZATION



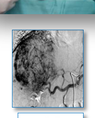
ARM ASSIGNMENT
is centralized and communicated only to the identified Nuclear Medicine prescription manager of ^{90}Y activity



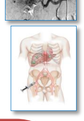
TREATMENT PROCEDURES

1. PREPARE
^{90}Y MICROSPHERE ACTIVITY and DELIVERY SET

2. CHECK
LIVER and TUMOR VASCULARIZATION before starting SIRT

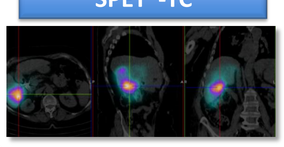


3. ADMINISTRATE
^{90}Y MICROSPHERE SLOWLY INTRA-HEPATIC ARTERY BRANCHES

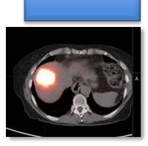


4. FINAL CHECK
CORRECT ADMINISTRATION with ^{90}Y PET / ^{90}Y SPET

^{90}Y Bremsstrahlung SPET -TC



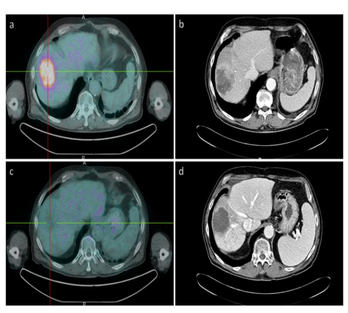
^{90}Y PET



FUP

EVALUATE from 1 mo to 2 years

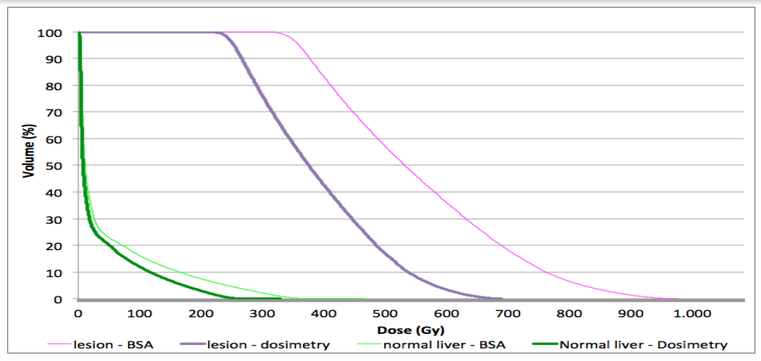
SAFETY : PATIENT CONDITION & LIVER FUNCTION
RESPONSE : CT /MRI (mRECIST) PET (PERCIST)
BIOMARKERS : AFP, PIVKA



BLINDING

PRELIMINARY RESULTS

Figure shows the cumulative Dose-Volume Histograms (DVHs) obtained using BSA or patient-specific dosimetry for tumor and normal liver for a representative patient.



- preliminary results show that dosimetry provide at least therapeutic dose to lesion (>120Gy) while sparing normal liver (<40Gy in all patients) and thus reducing the expected radiation induced effects.
- the administered activity widely varies between the two methods with a trend of significantly lower activity by usign the 3D dosimetric approach.
- multidisciplinary evaluation of integrated imaging and of therapy planning is mandatory to allow patient personalization and improve the predictive dose-effect models.

IRE ISTITUTO NAZIONALE TUMORI REGINA ELENA

15th Nov 2018

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