

Con il patrocinio di:



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Betania

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X Edizione

L'EPATOLOGIA NEL III MILLENNIO: EPATOLOGIA SOSTENIBILE

I percorsi tra bisogni del paziente
e sostenibilità del sistema



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25 - 26
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RELATORE: **Francesco Fiore**
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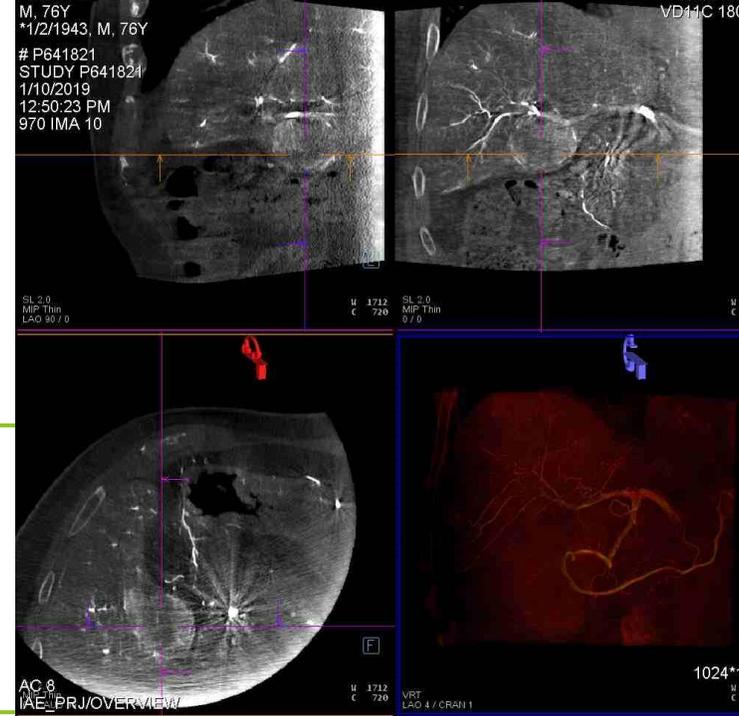
TITOLO: **Downstaging HCC**

Downstaging HCC

C-arm CBCT, Fusion Imaging, Navigation system, CEUS



Downstaging HCC



Cone Beam Computed Tomography

The advent of flat panel detectors has facilitated the ability of a fluoroscopy unit to double as a CT scanner.

Multiple radiographic images are obtained while the fluoroscopy unit rotates around the patient, and are then reconstructed into three-dimensional (3D) CT-like datasets known as a cone beam CT (CBCT) in as little as 5 seconds.



Downstaging HCC

Locoregional Therapies for HCC

INTRA-VASCULAR:

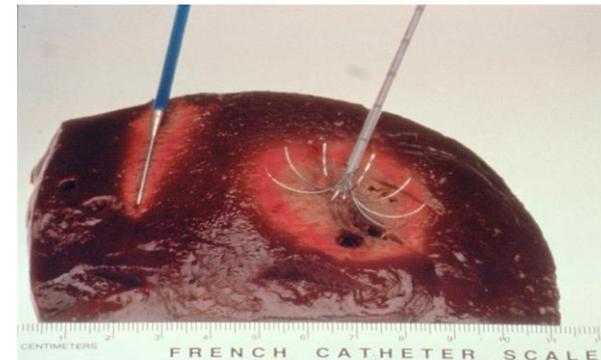
- cTACE
- Drug Eluting Transarterial Chemoembolization (DEBIRI)
- Transarterial Bland Embolization (TAE)
- Radio-Embolization (TARE)
- Hepatic Arterial Infusion (HAIP)

PERCUTANEOUS:

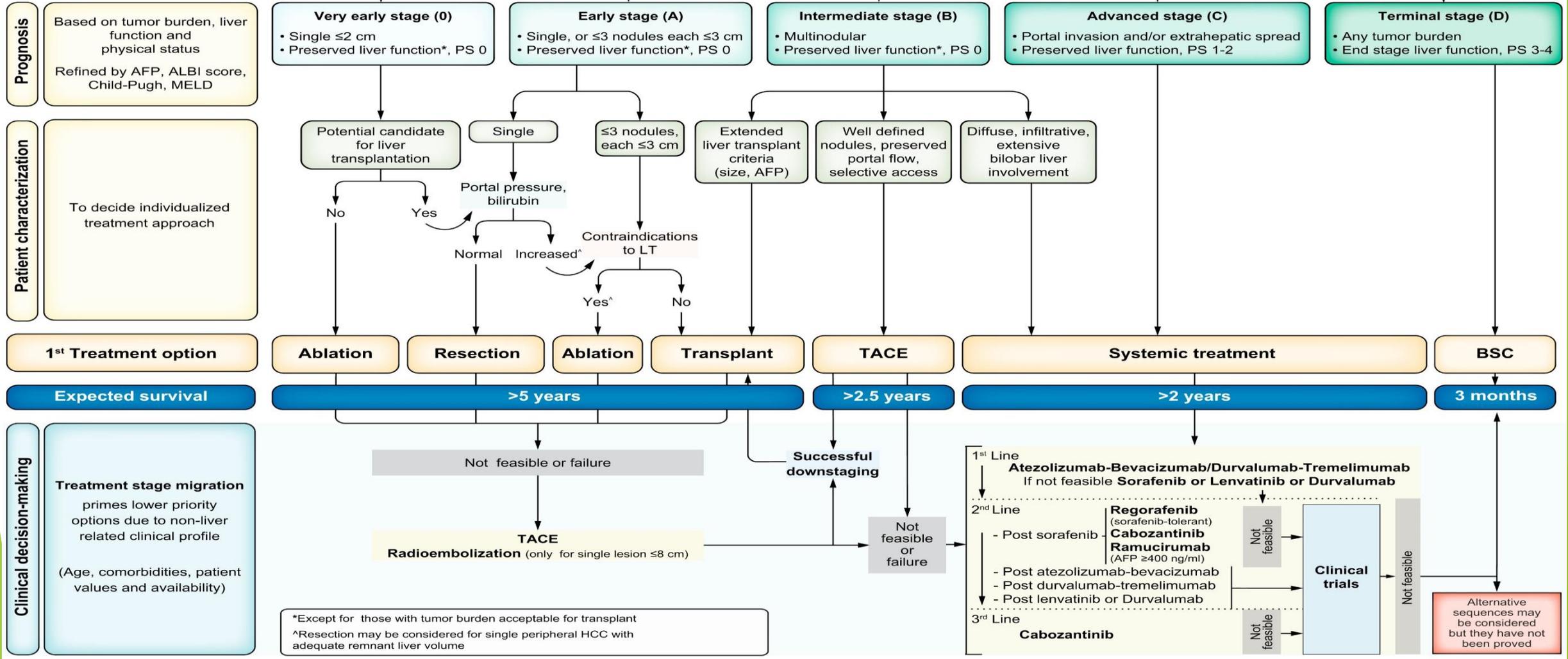
Thermoablation (RFA o MWA)

COMBINED THERAPIES

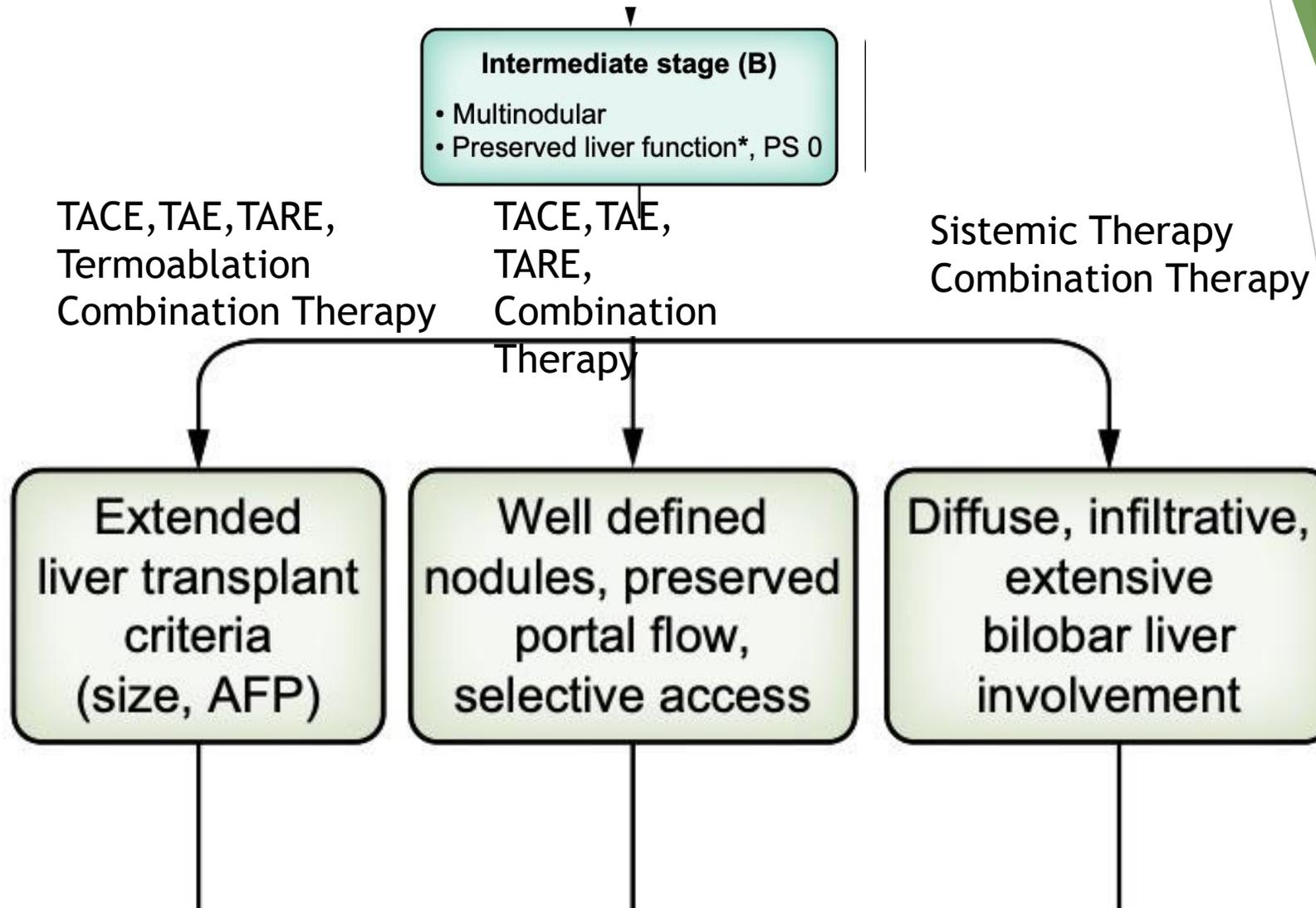
Thermo+TACE



Downstaging HCC



Downstaging HCC



Downstaging HCC

Overall, the place of TACE in BCLC B is somewhat restricted and TARE is not even mentioned.

Reig M. et al.: BCLC strategy for prognosis prediction and treatment recommendation:
The 2022 update Journal of Hepatology 2022 vol. 76 681-693

Lucatelli P et Guiu B : 2022 Update of BCLC Treatment Algorithm of HCC: What's New for Interventional Radiologists? Cardiovasc Intervent Radiol (2022) 45:275-276

Downstaging HCC

BCLC 2022 : omissions

- It does not differentiate the treatment in consideration of biological aggression
- It does not include combined techniques



Downstaging HCC

Milan criteria

Single lesion \leq 5 cm
or up to three separate lesions,
none larger than 3 cm

Mazzaferro V, et al Liver transplantation for the treatment of small hepatocellular carcinomas in patients with cirrhosis. N Engl J Med 1996; 334: 693-699

Downstaging HCC

Treatments for Bridging and Downstaging

- ▶ Milan criteria have consistently demonstrated 5 year overall survival of approximately 70%

- ▶ Kulik et al. *Hepatology* vol 67 n° 1 2018



Downstaging HCC

- ▶ Loco-regional treatments pursue tumor downstaging from outside Milan criteria to within criteria.
 - ▶ In case of partial response or complete response (CR), patients entered a non-intervention period of at least 3 months
 - ▶ The study demonstrates that neoadjuvant loco-regional therapies aimed at reduction of intra-hepatic tumor load may be proposed to any patient beyond Milan criteria.
 - ▶ The potential of complete tumor downstaging to eradicate HCC and spare transplantation in a subset of patients, emphasizes the role of response to neoadjuvant treatment as a key determinant of HCC management
-
- ▶ V. Mazzaferro et al: Liver transplantation in hepatocellular carcinoma after tumour downstaging (XXL): a randomised, controlled, phase 2b/3 trial
 - ▶ Lancet oncol.2020



Downstaging HCC

- ▶ Downstaging may serve as a screening tool to identify patients who might benefit from surgery.
- ▶ Resection after successful downstaging can improve prognosis.

- ▶ Chen et al. *Frontiers in oncology* 2021: Downstaging Therapies for Unresectable HCC



Downstaging HCC

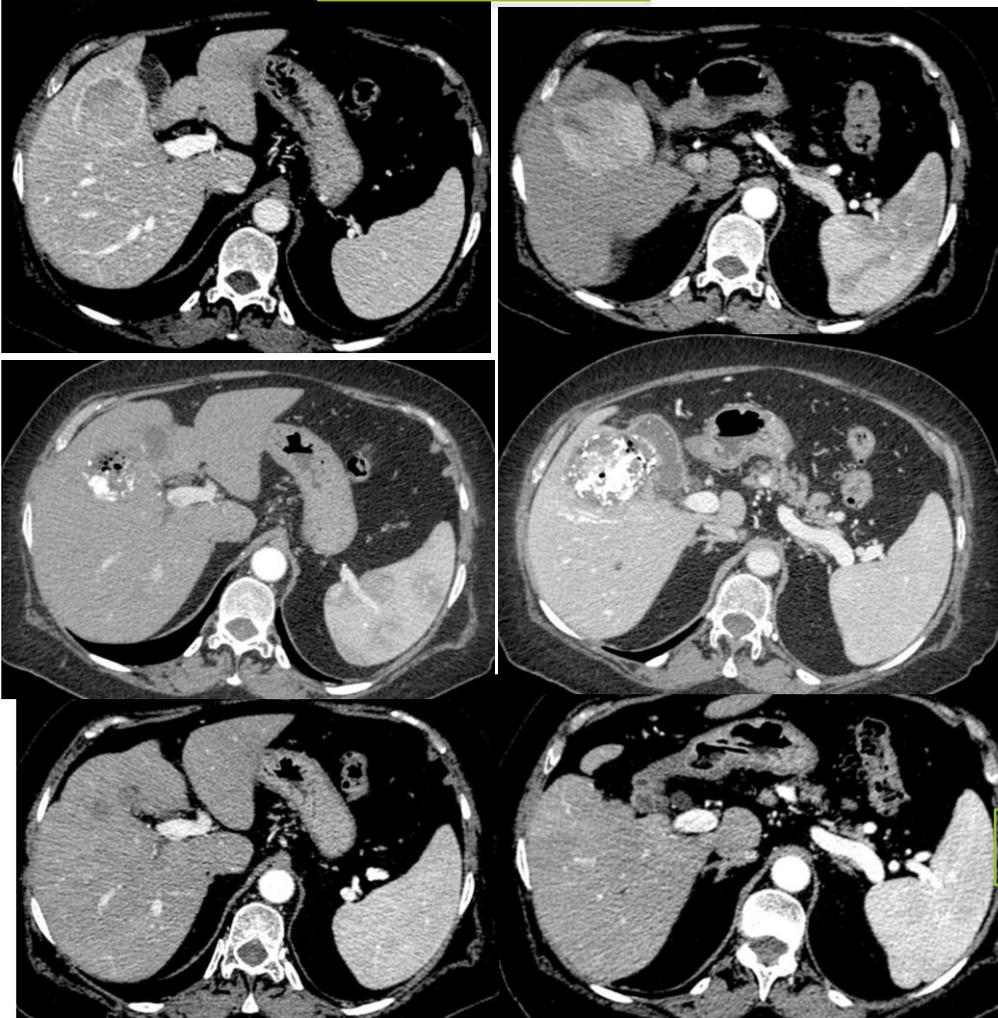
- ▶ Transarterial and ablative procedures are involved in treatment for curative-intent, disease control, bridging to surgery, downstaging for future treatment and palliation.
- ▶ Outcomes data reveal that locoregional therapies provide survival benefits in appropriately selected patients
- ▶ Locoregional therapies produce an immune response that can be augmented via immune checkpoint inhibition

- ▶ Makary MS et al. HCC locoregional therapies World J Gastroenterol 2021 November 21; 27(43)

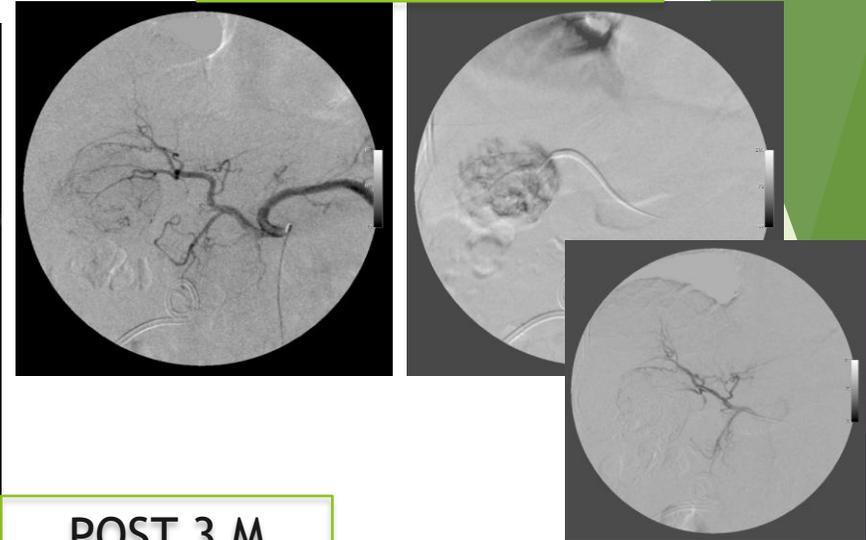


TAELE without chemotherapy

PRE



ANGIO E TAELE

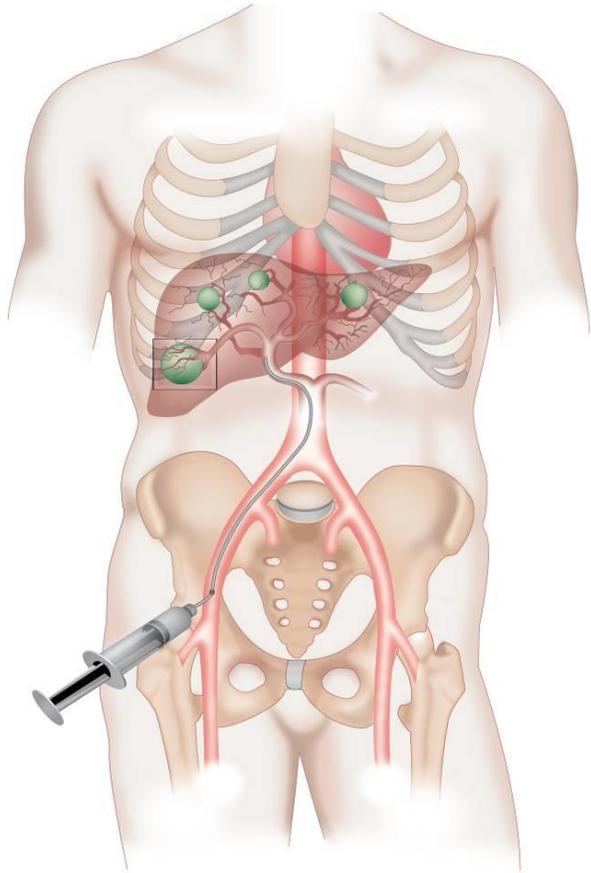


POST 3 M

POST 6 M

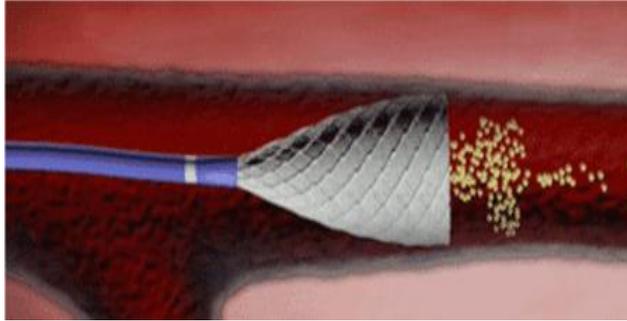
Downstaging HCC

Radioembolization o TARE



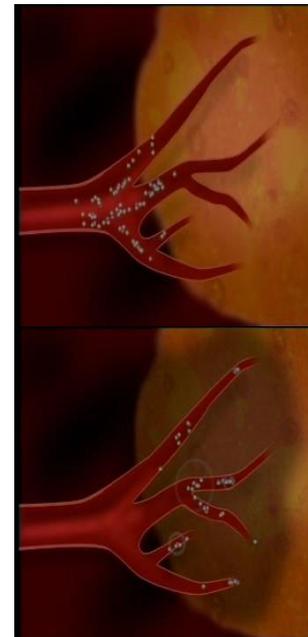
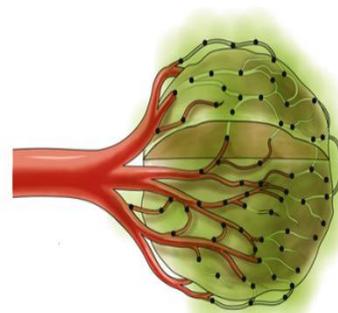
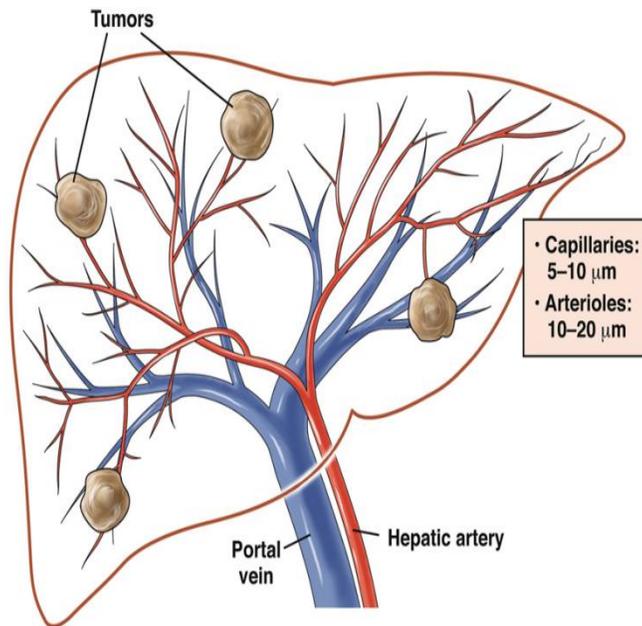
Downstaging HCC

TARE



20-60 μm
microspheres

Y-90



β -radiation

No more activity
over 8 mm
from sphere

RADIOEMBOLIZATION

- MECHANISM OF ACTION: Delivery of β -emitting microspheres that provide local, high dose tumor radiation. The radiation affects tissues 2.5-11 mm from the delivered microsphere (green).
- PARTICLE SIZE: 20-60 μm



Downstaging HCC

Several authors described their results of TARE in the treatment of HCC as a bridge therapy before resection or transplantation as compared to TACE.

TARE performed prior to LT reported that none of the 15 patients progressed from United Network for Organ Sharing T2 to T3 during the waiting time, and eight out of ten were downstaged from the T3 to the T2 stage.

Furthermore, at histology, 100% necrosis was found in 89% of the lesions ≤ 3 cm and 65% of the lesions 3-5 cm in size.

The same authors and others had previously analyzed similar data in patients treated with TACE prior to LT, showing 35%-57% complete necrosis in lesions ≤ 3 cm and 17%-42% in lesions 3-5 cm in size.

Riaz A, Kulik L, Lewandowski RJ, et al. Radiologic-pathologic correlation of hepatocellular carcinoma treated with internal radiation using yttrium-90 microspheres. *Hepatology*. 2009;49(4):1185-1193.

Lewandowski RJ, Kulik LM, Riaz A, et al. A comparative analysis of transarterial downstaging for hepatocellular carcinoma: chemoembolization versus radioembolization. *Am J Transplant*. 2009;9(8): 1920-1928

Ettorre GM, Laurenzi A, Vennarecci G. Downstaging Hepatocellular carcinoma with Yttrium-90 radioembolization: resection or transplantation? *Eur J Surg Oncol*. 2014;40(6):789-790.

Tohme S, Sukato D, Chen HW, et al. Yttrium-90 radioembolization as a bridge to liver transplantation: a single- institution experience. *J Vasc Interv Radiol*. 2013;24(11):1632-1638

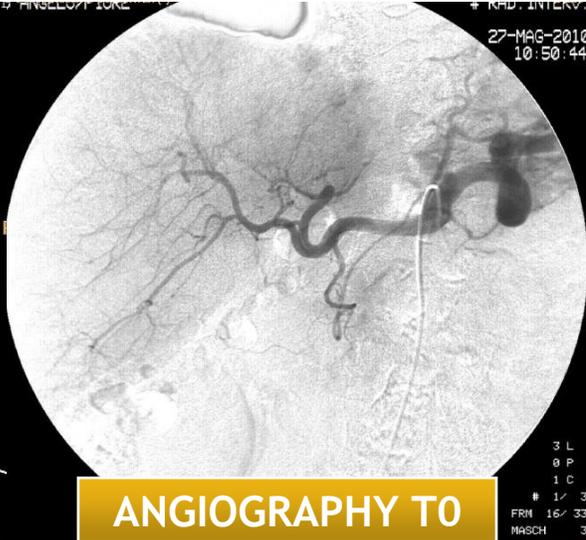
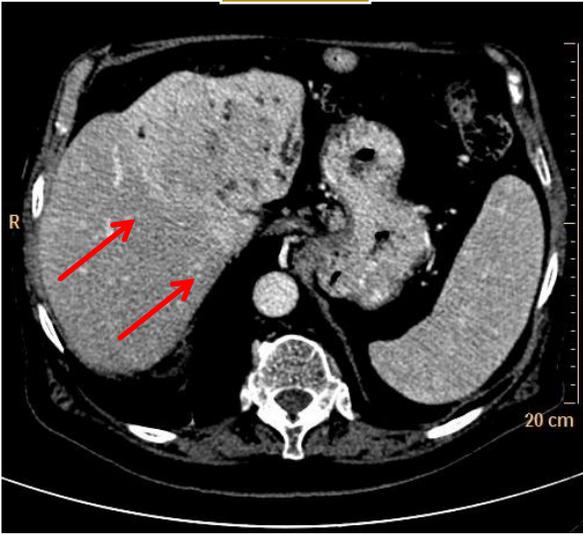
Downstaging HCC Pre resection

RESULTS

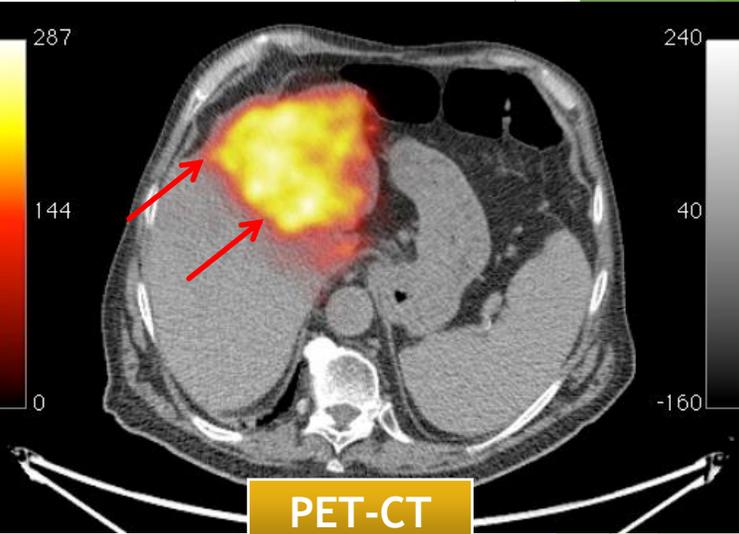
PRE-RESECTION

R. D. 44 y-o

T0



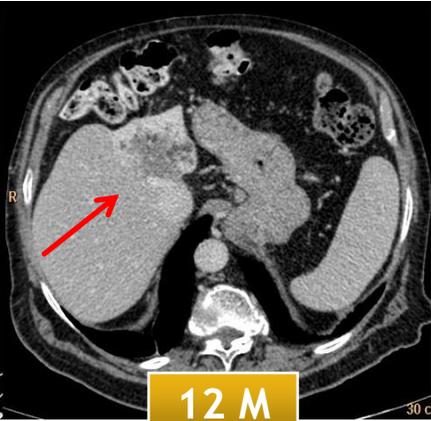
ANGIOGRAPHY T0



PET-CT



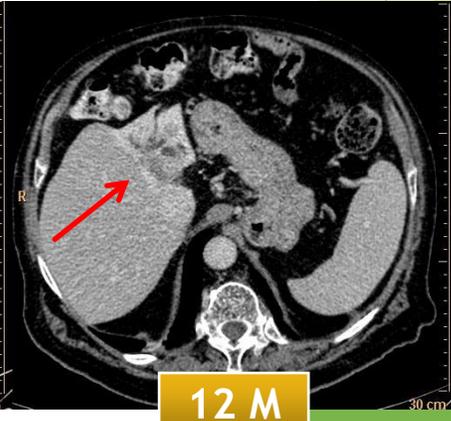
T0



12 M



T0



12 M

Advantages TARE

TARE seems a promising therapy in the downstaging setting:
to reduce the tumor burden within acceptable limits for LT,
to render “non-operable patients” operable,
or to simplify surgery,

Furthermore, the advantage of pre-LT downstaging is to recognize patients with a favorable tumor biology with a reduced risk of recurrence after transplantation.

Additionally, atrophy of the irradiated lobe after TARE and contralateral lobe hypertrophy as a result of lobar TARE, known as “radiation lobectomy” may contribute to resectability

Kulik, L.M.; et al. Safety and Efficacy of 90Y Radiotherapy for Hepatocellular Carcinoma with and without Portal Vein Thrombosis. *Hepatology* 2008, 47, 71-81.

Gordon, A.C.; et al. Radioembolization Super Survivors: Extended Survival in Non-Operative Hepatocellular Carcinoma. *Cardiovasc. Interv. Radiol.* 2018, 1-9.

Salem, R.; et al. Y90 Radioembolization Significantly Prolongs Time to Progression Compared With Chemoembolization in Patients With Hepatocellular Carcinoma. *Gastroenterology* 2016, 151, 1155-1163.e2.

Downstaging HCC

TACE is less effective in large tumors, especially in the presence of multiple satellite nodules, and these patients often experience severe post-embolization syndrome;

in this setting, TARE could be the first choice of treatment.

The higher cost of TARE and, on the other, the longer hospital stay and the cumulative charges involved in repeated TACE procedures.

Downstaging HCC

TARE Indications

Pre-resection (BCLC B1)

Pre-OLT (BCLC B 1)

Resistance to TACE (BCLC B2)

Elderly patients

Large HCC \leq 8 cm (BCLC A)

Portal thrombosis (BCLC C)



multidisciplinary team



The GOM must indicate the most correct therapeutic sequence for the individual patient, possibly using the combination of locoregional therapies and medical therapies (immunotherapy) even if not provided for by the guidelines

Neoadjuvant locoregional therapies in liver transplantation for HCC may become, as in other cancers, a standard that favors patient selection, waiting list management and post-operative survival.

Grazie per l'attenzione

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