Editorial

# An ace in the hole for hepatocellular carcinoma: yttrium-90 radioembolization

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Hepatocellular carcinoma (HCC) is currently the second most common cause of cancer related death (1). Assuming that the radical treatment as surgical resection and liver transplantation (LT) achieve better results and are increasingly employed even in HCC patients with intermediate and advanced diseases (2), locoregional treatment (LRT) are successfully applied in patients not candidates to curative therapies (3). In the last 5 years, Yttrium-90 radioembolization (Y90-RE) for HCC has been described as a safe procedure, and appears to be as well-tolerated and effective for the elderly as it is for younger patients with unresectable HCC patients with cirrhosis (4). LRT may be used as well to bridge or downstaging to LT and Y90-RE has been described to be safe as well in this setting (5,6).

Furthermore, Y90-RE has been described to have a better response rate compared to transarterial chemoembolization (TACE) in patients with advanced BCLC stage (7). However, until today no study have compared the time to progression (TTP) in patients treated with Y90-RE *vs*. TACE.

Salem *et al*. (8) have successfully analyzed the TTP in patients treated with Y90-RE or TACE in a prospective, randomized phase 2 study. The authors named the study as a Prospective Randomized Study Of Chemoembolization versus Radioembolization For The Treatment Of Hepatocellular Carcinoma (PREMIERE). This is a good way to emphasize, with the study name, which is the first prospective study for Y90-RE *vs*. TACE to compare TTP.

From October 2009 to October 2015, 45 patients were enrolled into the study after randomization. In the Y90-RE group 24 patients were analyzed and 13 of them were transplanted after LRT. In the TACE group of 21 allocated patients, 19 were analyzed and 7 were transplanted. The ultimate intent of treatment of these patients was LT.

The first observed difference between the two groups is the longer time to start the treatment for Y90-RE due to the planning angiography necessary in these patients (P<0.001). It is an important data; Y90-RE centers may need dedicated team equipment to decrease the loss of time between the multidisciplinary indication and the beginning therapy. At 30-day of the LRT, no mortality was observed in the two groups. Morbidity was higher in the TACE group with more diarrhea (P=0.031) and more hypoalbuminemia (P<0.001). Authors observed a median TTP of 6.8 months in the TACE group and superior to 26 months for the Y90-RE group (P=0.0012). TACE demonstrated significantly minor TTP compared to Y90-RE. These important results validated the first end point of the authors study. The role of radiological response to loco-regional therapies has been recently shown to be important selection criteria for the risk of intention-to-treat death and recurrence (9). If we consider the LT as the ultimate point for these patients, 13 were transplanted in Y90-RE group and 7 in TACE group. In case of longer waiting-time list for HCC patient there is an important risk of drop-out due to the tumor progression beyond the LT criteria. Therefore, a longer TTP will decreasing the dropout risk in patients treated with Y90-RE. We think that according to the authors study this is a complete revolutionary message. In case of HCC patients

in a LT setting a bridge therapy should be performed with Y90-RE when necessary. Authors presented a rate of 87% of LT in patients treated with Y90-RE. Nonetheless, authors described a change in local practice according to the study results and nowadays, patients bridged to LT receive Y90-RE. We fully agree with this practice and applied in both bridge and downstaging patients (5,6).

In conclusion, the study of Salem *et al*. (8) successfully compared the effectiveness of Y90-RE *vs*. TACE for HCC in an intention to treat cohort. The important results of a longer TTP after Y90-RE open a new horizon for HCC bridge and downstaging therapy. We have a new ace in the hole for HCC.

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## References

1. Torre LA, Bray F, Siegel RL, et al. Global cancer statistics, 2012. CA Cancer J Clin 2015;65:87-108.
2. Ettorre GM, Levi Sandri GB. Laparoscopic approach for hepatocellular carcinoma: where is the limit? Chin J Cancer Res 2014;26:222-3.
3. Guerra F, Levi Sandri GB. The problem of the most appropriate curative treatment for hepatocellular carcinoma. When to embolize? When to operate? J Hepatol 2015;63:280-1.
4. Golfieri R, Bilbao JI, Carpanese L, et al. Comparison of the survival and tolerability of radioembolization in elderly vs. younger patients with unresectable hepatocellular carcinoma. J Hepatol 2013;59:753-61.
5. Ettorre GM, Levi Sandri GB, Santoro R, et al. Bridging and downstaging to transplantation in hepatocellular carcinoma. Future Oncol 2014;10:61-3.
6. Ettorre GM, Levi Sandri GB, Laurenzi A, et al. Yttrium-90 Radioembolization for Hepatocellular Carcinoma Prior to Liver Transplantation. World J Surg 2016. [Epub ahead of print].
7. Sangro B, Carpanese L, Cianni R, et al. Survival after yttrium-90 resin microsphere radioembolization of hepatocellular carcinoma across Barcelona clinic liver cancer stages: a European evaluation. Hepatology 2011;54:868-78.
8. Salem R, Gordon AC, Mouli S, et al. Y90 Radioembolization Significantly Prolongs Time to Progression Compared With Chemoembolization in Patients With Hepatocellular Carcinoma. Gastroenterology 2016. [Epub ahead of print].
9. Lai Q, Nicolini D, Inostroza Nunez M, et al. A Novel Prognostic Index in Patients With Hepatocellular Cancer Waiting for Liver Transplantation: Time-Radiological-response-Alpha-fetoprotein-INflammation (TRAIN) Score. Ann Surg 2016;264:787-796.

 