Society of Medical Education & Research

2026, Volume 6, Issue 1, Page No: 78-90

ISSN: 3108-4834

Archive of International Journal of Cancer and Allied Science

Clinical Outcomes of Transarterial Radioembolization in Hepatocellular Carcinoma: A Comparison of Bridging Therapy and Palliative Intent Treatment

Mateo Alvarez[1]*, Sofia Herrera[2], Diego Cruz[1], Andres Castro[3]

[1]Department of HCC and Transarterial Radioembolization, Faculty of Medicine, National University of Colombia, Bogota, Colombia.
[2]Department of Bridging and Palliative Therapy, Faculty of Medicine, University of Chile, Santiago, Chile.
[3]Department of Interventional Oncology Clinical Outcomes, Faculty of Medicine, University of Antioquia, Medellin, Colombia.

***E-mail** ✉ mateo.alvarez@unal.edu.co

Abstract

The current analysis evaluated the application of transarterial radioembolization (TARE) in hepatocellular carcinoma (HCC) both for palliation and as a bridge to liver transplantation. In total, 167 patients underwent 245 TARE sessions, comprising 50 patients in the bridging cohort and 117 in the palliative cohort. Fourteen of these individuals later received liver transplantation (LT). Those who advanced to LT showed significantly better progression-free survival (PFS) than patients who received bridging TARE without subsequent transplantation (P = 0.033). In contrast, no meaningful difference in PFS was observed between the bridging without transplant group and the palliative group (P = 0.116). Following TARE, the median overall survival (OS) reached 16.6 months, with actuarial OS rates of 82.0% at 6 months and 60.5% at 12 months. LT recipients had markedly superior OS compared with the bridging without transplant subgroup (P = 0.001). Outcomes were comparable between the bridging without transplant and palliative cohorts. These observations highlight the clear advantage of LT over alternative approaches. TARE emerged as a valuable tool in cases that did not proceed to transplantation, enabling further lines of therapy. Overall, the study captures the diverse and multifaceted clinical challenges in HCC management and stresses the importance of continued research to optimize integrated multimodal treatment protocols.

Keywords: Hepatic carcinoma, Hepatocellular carcinoma, Radioembolization, Liver transplantation, Bridging therapies

Introduction

Hepatocellular carcinoma (HCC) constitutes the predominant primary liver cancer on a global scale. It occupies the sixth position among the most commonly diagnosed malignancies and ranks third in cancer-related deaths for both men and women worldwide [1]. Liver transplantation (LT) is unique in its capacity to remove the cancer entirely while simultaneously treating the coexisting cirrhosis. Across Europe, the interval between listing and organ receipt from deceased donors typically spans 6 to over 12 months, influenced by priority status and donor availability [2]. A considerable fraction of listed patients are delisted during this time due to disease progression or declining health [3]. Consequently, locoregional therapies are generally recommended to bridge the waiting period for transplant candidates [4, 5]. Beyond simply controlling tumor growth, the response to these bridging interventions provides essential information on tumor biology. This process helps identify and exclude more aggressive neoplasms, refining the selection of patients who ultimately benefit most from transplantation [6-8]. Patients continue to

Access this article online https://smerpub.com/

Received: 14 December 2025; **Accepted:** 27 February 2026

How to cite this article: Alvarez M, Herrera S, Cruz D, Castro A. Clinical Outcomes of Transarterial Radioembolization in Hepatocellular Carcinoma: A Comparison of Bridging Therapy and Palliative Intent Treatment. Arch Int J Cancer Allied Sci. 2026;6(1):78-90. https://doi.org/10.51847/KvnO8R8rJY

receive active care irrespective of whether transplantation ultimately occurs.

Transarterial radioembolization (TARE), commonly termed selective internal radiation therapy (SIRT), is an established locoregional approach for primary liver tumors and secondary hepatic metastases. The method capitalizes on the preferential arterial perfusion of neoplastic tissue relative to normal liver parenchyma. Delivery of radionuclide-loaded microspheres via microcatheter into tumor-feeding arteries results in substantially greater radiation exposure to malignant lesions than to adjacent healthy tissue [9, 10]. In addition to its established palliative indications, TARE is increasingly used as a bridging therapy to delay hepatic tumor progression, thereby preserving patient eligibility for LT throughout the waiting phase [11, 12].

Three microsphere platforms are currently approved for locoregional HCC therapy:

- ^{90}Y-containing resin microspheres (SirSpheres®, Sirtex Medical, Woburn, MA, USA);
- ^{90}Y-containing glass microspheres (TheraSphere®, Boston Scientific, Marlborough, MA, USA);
- ^{166}Ho-containing poly-l-lactic acid (PLLA) microspheres (QuiremSpheres®, Terumo, Leuven, Belgium).

This study primarily aimed to provide a detailed evaluation of clinical outcomes among patients receiving TARE as a bridging therapy before transplantation at our institution. A secondary objective was to compare outcomes between patients who completed bridging TARE but did not undergo LT and those treated with TARE for palliative intent only.

Materials and Methods

The institutional ethics committee approved this investigation under registration number 2020-1908. Written informed consent for the anonymous application of their medical data in scientific research was obtained from all patients upon admission to our facility.

Inclusion criteria and patient characteristics

The cohort included every patient diagnosed with HCC who sequentially received TARE at our center from the implementation of this technique in 2011 through 2020. Decisions regarding the clinical use of TARE, patient suitability for liver transplantation, and the application of bridging therapy were made collectively by a multidisciplinary tumor board (MDT).

Relevant demographic and clinical details were gathered, covering tumor features, coexisting medical conditions, therapies administered before and after TARE, and longitudinal follow-up data with associated imaging. These records enabled evaluation of progression-free survival (PFS) and overall survival (OS). Imaging-based disease progression was classified according to the modified Response Evaluation Criteria in Solid Tumors (mRECIST) [13]. Surveillance continued for 12 months following the enrollment of the final participant or until the patient died for all previously included cases. Results were contrasted with those observed in patients undergoing TARE exclusively for palliative purposes.

TARE procedures

TARE interventions adhered strictly to manufacturer protocols and involved hepatic vascular angiography, planar scintigraphy covering the thorax and abdomen, and SPECT/CT imaging of the abdomen [14-16]. Pretreatment simulation utilized 99mTc-labeled human serum albumin (HSA) B20 microspheres (ROTOP, Dresden, Germany) to map activity distribution inside and outside the liver and to measure the lung shunt fraction. Actual treatment sessions were scheduled 1–2 weeks after the simulation. For 90Y-resin microspheres, administered activity was computed via the multi-compartment/modified body surface area (BSA) approach [16]. Activity calculations for 90Y-glass and 166Ho-PLLA microspheres followed their respective single-compartment equations [14, 15].

Follow-up

After each intervention, patients remained under observation in the nuclear medicine department for 24 hours following planning procedures or 48 hours after therapeutic administration. Repeat scintigraphy and SPECT/CT scans were conducted to verify microsphere localization. The initial imaging evaluation was performed three months after the final TARE session(s) and guided ongoing management and monitoring strategies.

Outcome evaluation and statistics

Overall survival (OS) was defined as the period from the first TARE procedure to death or last contact for patients who remained alive. Progression-free survival (PFS) was defined as the time from the initial TARE treatment to

radiographic disease progression, death, or completion of follow-up.

Intergroup differences in continuous parameters were assessed using t-tests, whereas chi-square tests were applied to categorical variables. Survival probabilities were estimated with the Kaplan–Meier approach. Analyses were conducted using SPSS Statistics (IBM, Armonk, NY, USA) and Stata/IC (StataCorp, College Station, TX, USA). A threshold of $P < 0.05$ was adopted to indicate statistical significance.

Results and Discussion

Clinical characteristics and indications for TARE treatment

Throughout the study period, the multidisciplinary tumor board (MDT) endorsed TARE therapy for 204 patients with HCC **(Figure 1)**. Ultimately, 37 patients (18.1%) did not receive the planned intervention. Reasons for exclusion included insufficient microsphere accumulation within tumor sites (n = 13), extrahepatic deposition (n = 6), elevated lung shunt fraction (n = 5), worsening hepatic function in the interim (n = 7), or unsuitable vascular architecture (n = 6).

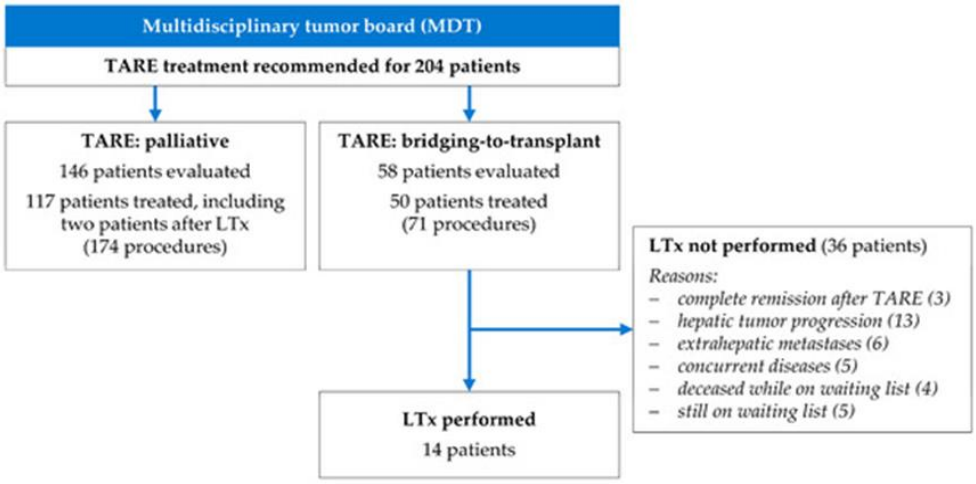

Figure 1. Indications for TARE utilized either palliatively or as bridging therapy before transplantation.

The analysis ultimately involved 167 patients who received a combined total of 245 TARE sessions **(Table 1)**. Bridging to LT was the goal in 50 cases (29.9%), while 117 patients (70.1%), judged ineligible for transplantation by the MDT, were treated with palliative intent.

Table 1. Baseline patient profiles and pre-TARE interventions.

Variable	p value**	TARE as palliative treatment (n=117)			TARE as bridging to liver transplantation (LT) (n=50)	Overall cohort (n=167)
			LT not performed (n=36)	LT performed (n=14)	All bridging cases	All patients
Number of patients		117	36	14	50	167
Sex	0.616					
Male		101 (86.3%)	31 (86.1%)	14 (100.0%)	45 (90.0%)	146 (87.4%)
Female		16 (13.7%)	5 (13.9%)	0	5 (10.0%)	21 (12.6%)
Age at TARE (years)	<0.001					
Mean ± SD		69.6 ± 8.7	62.3 ± 5.0	63.4 ± 2.5	62.6 ± 4.5	67.5 ± 8.4
Median (range)		72.0 (45.7–85.5)	62.6 (50.6–70.7)	63.0 (59.4–69.0)	62.6 (50.6–70.7)	66.6 (45.7–85.5)
Interval from HCC diagnosis to TARE (months)	0.509					
Mean ± SD		13.8 ± 25.4	11.1 ± 13.4	9.9 ± 10.1	10.8 ± 12.7	12.9 ± 22.4

Median (range)		4.9 (1.3–177.5)	5.5 (1.5–54.3)	5.7 (1.3–40.3)	5.5 (1.3–54.3)	5.3 (1.3–177.5)
Previous HCC-directed treatments before TARE*						
None	0.613	60 (51.3%)	17 (47.2%)	6 (42.9%)	23 (46.0%)	83 (49.7%)
Surgical resection	0.399	21 (17.9%)	10 (27.8%)	2 (14.3%)	12 (24.0%)	33 (19.8%)
Transarterial chemoembolization	0.861	42 (35.9%)	11 (30.6%)	6 (42.9%)	17 (34.0%)	59 (35.3%)
Percutaneous radiation therapy	0.318	4 (3.4%)	0	0	0	4 (2.4%)
Systemic therapy	1.000	9 (7.7%)	2 (5.6%)	1 (7.1%)	3 (6.0%)	12 (7.2%)
Previous liver transplantation	1.000	2 (1.7%)	0	0	0	2 (1.2%)
HCC stage	0.647					
IA		1 (0.9%)	0	0	0	1 (0.6%)
IB		5 (4.3%)	0	0	0	5 (3.0%)
II		64 (54.7%)	22 (61.1%)	8 (57.1%)	30 (60.0%)	94 (56.3%)
IIIA		34 (29.1%)	10 (27.8%)	3 (21.4%)	13 (26.0%)	47 (28.1%)
IIIB		7 (6.0%)	3 (8.3%)	3 (21.4%)	6 (12.0%)	13 (7.8%)
IVA		6 (5.1%)	1 (2.8%)	0	1 (2.0%)	7 (4.2%)
Child–Pugh classification	0.253					
A5		29 (24.8%)	13 (36.1%)	5 (35.7%)	18 (36.0%)	47 (28.1%)
A6		75 (64.1%)	20 (55.6%)	9 (64.3%)	29 (58.0%)	104 (62.3%)
B7		12 (10.3%)	2 (5.6%)	0	2 (4.0%)	14 (8.4%)
B8		1 (0.9%)	1 (2.8%)	0	1 (2.0%)	2 (1.2%)

Abbreviations: HCC, hepatocellular carcinoma; LT, liver transplantation; TARE, transarterial radioembolization; SD, standard deviation. Multiple interventions per patient possible; Comparison between bridging (column 3) and palliative (column 6) groups.

Table 1 outlines the pretreatment characteristics across both cohorts. Patients selected for bridging to transplantation were notably younger (median age 62.6 years) compared with those managed palliatively (median age 72.0 years). The groups were otherwise comparable with respect to additional clinical variables, disease stage, and Child–Pugh scores. Prior treatment patterns were heterogeneous: TARE functioned as first-line therapy in 46.0% of the bridging group and 51.3% of the palliative group. Surgical resection and transarterial chemoembolization (TACE) represented the most frequent preceding interventions.

TARE interventional procedures

Overall, 245 TARE interventions were executed over 209 separate treatment cycles **(Table 2)**. Whole-liver treatment was performed in 36 cycles (72 procedures) using a sequential bilobar technique, with each lobe addressed in separate sessions spaced 5–6 weeks apart. The majority of cycles (173) targeted only one hepatic lobe. Microsphere selection comprised 113 procedures (64.5%) with 90Y-glass, 51 procedures (34.3%) with 90Y-resin, and 3 procedures (1.2%) with 166Ho-PLLA microspheres.

Table 2. Procedural details of TARE sessions.

Variable	**p value****	**TARE as palliative treatment**			**TARE as bridging to liver transplantation (LT)**	**Overall cohort**
			LT not performed	LT performed	All bridging cases	All procedures/patients
Number of TARE procedures		174	55	16	71	245
Distribution of treated liver lobes	0.649					
Right lobe		119 (68.4%)	40 (72.7%)	11 (68.8%)	51 (71.8%)	170 (69.4%)
Left lobe		55 (31.6%)	15 (27.3%)	5 (31.2%)	20 (28.2%)	75 (30.6%)
Treatment cycles	0.999					
Total cycles		148	47	14	61	209

Monolobar treatment		122 (82.4%)	39 (83.0%)	12 (86.7%)	51 (83.6%)	173 (82.8%)
Sequential bilobar treatment		26 (17.6%)	8 (17.0%)	2 (14.3%)	10 (16.4%)	36 (17.2%)
Number of TARE procedures per patient	0.763					
One procedure		71 (60.7%)	18 (50.0%)	12 (85.7%)	30 (60.0%)	101 (60.5%)
Two procedures		38 (32.5%)	17 (47.2%)	2 (14.3%)	19 (38.0%)	57 (34.1%)
Three procedures		5 (4.3%)	1 (2.8%)	0	1 (2.0%)	6 (3.6%)
Four procedures		3 (2.6%)	0	0	0	3 (1.8%)
Tumor burden within treated volume (%)	0.013					
Mean ± SD		20.2 ± 23.2	13.5 ± 21.4	10.4 ± 11.4	12.7 ± 19.1	18.0 ± 22.2
Median (range)		8.8 (1.7–100.0)	6.2 (1.9–100.0)	5.3 (1.7–37.6)	5.6 (1.7–100.0)	7.4 (1.7–100)
Type of microsphere used	0.814					
^{90}Y glass microspheres		111 (63.8%)	36 (65.5%)	11 (68.8%)	48 (66.2%)	158 (64.5%)
^{90}Y resin microspheres		60 (34.5%)	19 (34.5%)	5 (31.2%)	26 (33.8%)	84 (34.3%)
^{166}Ho PLLA microspheres		3 (1.7%)	0	0	0	3 (1.2%)
Prescribed activity (GBq), median (range)						
^{90}Y glass	0.697	2.2 (0.4–7.1)	2.1 (0.6–7.7)	1.9 (0.6–4.3)	2.1 (0.6–7.7)	2.1 (0.4–7.7)
^{90}Y resin	0.881	1.0 (0.3–3.1)	1.0 (0.6–2.0)	0.85 (0.6–1.4)	1.0 (0.6–2.0)	1.0 (0.3–3.1)
^{166}Ho PLLA	–	1.8 (1.4–5.6)	–	–	–	1.8 (1.4–5.6)

Abbreviations: LT, liver transplantation; TARE, transarterial radioembolization; SD, standard deviation; PLLA, poly-L-lactic acid. **Comparison between bridging (column 3) and palliative (column 6) groups.

Tumor load in the treated liver volume was markedly lower in the bridging cohort (median 5.6%) than in the palliative cohort (median 8.8%). All other procedural aspects were statistically comparable between the groups.

Liver transplantation and TARE

Fourteen of the 50 patients (28%) who underwent successful bridging TARE advanced to liver transplantation **(Figure 1)**. The median interval between TARE and LT was 5.6 months, ranging from 0.5 to 25.5 months. Three patients received no additional locoregional therapy before transplantation. Median waiting-list time amounted to 7.3 months (range 0.9–21.6 months). Twelve procedures involved deceased donors and two involved living donors; all transplants were completed without technical complications.

Thirteen of the 14 transplanted patients were alive at the 12-month mark following surgery. By the conclusion of follow-up, 11 patients remained alive. One 61-year-old male recipient, transplanted 2.6 months after right-lobar TARE, succumbed 2.5 months postoperatively due to acute inferior vena cava thrombosis. A 71-year-old male died from sepsis complicated by hepatic abscesses 14.4 months after LT. A 62-year-old male experienced fatal extrahepatic tumor progression 31.3 months post-LT.

Thirty-six of the 50 bridging patients (72%) did not receive a transplant during the study **(Figure 1)**. Nineteen experienced local or distant tumor advancement, while five developed intercurrent illnesses precluding transplantation (such as newly identified gastric cancer, advancing coronary disease, repeated variceal bleeding, or renal failure accompanied by sepsis). In three patients (aged 56–67 years; two treated sequentially in both lobes and one in the right lobe; tumor burden 3–8%; all with 90Y-glass microspheres), CT imaging performed three months after TARE revealed complete resolution of HCC.

Two patients underwent TARE following prior living-donor liver transplantation. HCC recurrence was identified at 25.5 months and 40.9 months post-transplant, respectively. For the 71-year-old male, initial management consisted of radiofrequency ablation plus sorafenib. Upon subsequent progression, TARE of the allograft using 90Y-glass microspheres was administered, resulting in 8.9 months of progression-free

survival (PFS) before sorafenib was resumed. The 66-year-old male initially received transarterial chemoembolization (TACE) for a solitary recurrence; however, multifocal disease emerged 11 months later. Right-lobar TARE with 90Y-resin microspheres then yielded 7.7 months of PFS, after which further therapy was not pursued.

Progression-free and overall survival

Median follow-up duration reached 14.5 months (range 0.9–112.6 months) from the date of initial TARE and 26.8 months (range 2.5–94.8 months) from the time of liver transplantation. Subsequent HCC-directed therapies were delivered to 39.5% of the study population after TARE, primarily through locoregional modalities such as TACE and percutaneous irradiation **(Table 3)**. Systemic agents were administered in 20.4% of cases.

Table 3. Post-TARE management strategies and observed outcomes.

Variable	p value**	TARE as palliative treatment			TARE as bridging to liver transplantation (LT)	Overall cohort
			LT not performed	LT performed	All bridging cases	All patients
Number of patients		117	36	14	50	167
Follow-up duration after TARE (months)	0.040					
Mean ± SD		19.1 ± 16.8	19.3 ± 14.8	45.7 ± 30.2	26.7 ± 23.5	21.3 ± 19.4
Median (range)		13.8 (0.9–112.6)	14.7 (1.4–70.7)	38.1 (5.0–100.6)	21.8 (1.4–100.6)	14.5 (0.9–112.6)
HCC-directed treatments after TARE*						
No additional treatment	<0.001	81 (69.2%)	20 (55.6%)	0	20 (40.0%)	101 (60.5%)
Transarterial chemoembolization	0.279	19 (16.2%)	8 (22.2%)	4 (28.6%)	12 (24.0%)	31 (18.6%)
Percutaneous radiation therapy	0.108	10 (8.5%)	6 (16.7%)	3 (21.4%)	9 (18.0%)	19 (11.4%)
Systemic therapy	0.294	21 (17.9%)	10 (27.8%)	3 (21.4%)	13 (26.0%)	34 (20.4%)
Surgical treatment (excluding LT)	0.999	3 (2.6%)	1 (2.8%)	0	1 (2.0%)	4 (2.4%)
Liver transplantation	<0.001	0	0	14 (100%)	14 (28.0%)	14 (8.4%)
Development of extrahepatic metastases	0.679	26 (22.2%)	6 (16.7%)	3 (21.4%)	9 (18.0%)	35 (21.0%)
Progression-free survival (PFS)	0.033					
Progression events (%)		75 (64.1%)	29 (80.6%)	5 (35.7%)	34 (68.0%)	109 (65.3%)
Median PFS (months, 95% CI)		11.4 (7.7–17.8)	9.2 (7.1–13.7)	– (4.3–.)	10.0 (7.2–16.3)	11.0 (8.9–15.1)
Estimated PFS rate at 6 months (95% CI)		74.8% (65.5–82.0%)	72.7% (54.0–84.8%)	71.4% (40.6–88.2%)	72.2% (56.9–82.8%)	74.0% (66.3–80.2%)
Estimated PFS rate at 12 months (95% CI)		47.5% (37.1–57.2%)	41.1% (24.2–57.2%)	63.5% (33.1–83.0%)	47.4% (32.4–61.0%)	47.5% (38.9–55.5%)
Overall survival (OS)	0.001					
Death events (%)		92 (78.6%)	30 (83.3%)	3 (21.4%)	33 (66.0%)	125 (74.9%)
Median OS (months, 95% CI)		13.9 (10.8–17.8)	19.8 (11.1–23.9)	–	23.1 (15.0–31.7)	16.6 (13.2–21.8)

Estimated survival rate at 6 months (95% CI)	80.3% (71.9–86.5%)	83.3% (66.6–92.1%)	92.9% (59.1–99.0%)	86.0% (72.9–93.1%)	82.0% (75.3–87.1%)
Estimated survival rate at 12 months (95% CI)	54.7% (45.3–63.2%)	66.7% (48.8–79.5%)	92.9% (59.1–99.0%)	74.0% (59.5–84.0%)	60.5% (52.6–67.4%)

Abbreviations: HCC, hepatocellular carcinoma; LT, liver transplantation; TARE, transarterial radioembolization; SD, standard deviation; CI, confidence interval. *Multiple interventions per patient possible; **Comparison between bridging (column 3) and palliative (column 6) groups.

Across the full cohort, median progression-free survival (PFS) was 11.0 months after TARE, accompanied by 6-month and 12-month PFS estimates of 73.4% and 47.1%, respectively **(Table 3 and Figure 2)**. Individuals proceeding to liver transplantation demonstrated substantially prolonged PFS relative to bridging patients who did not receive LT (p = 0.033; hazard ratio for LT not performed versus LT performed: 2.81 [CI 1.08–7.29]). Intrahepatic progression before transplantation was identified in four cases, with three occurring inside previously targeted segments and one in an untreated region. No intrahepatic HCC recurrences were noted following transplantation. Extrahepatic metastatic spread developed in three transplanted patients: abdominal wall involvement at 92 months post-TARE (79.1 months post-LT), adrenal/lung/lymph node disease at 17.3 months post-TARE (12.3 months post-LT), and peritoneal/lung metastases at 11.7 months post-TARE (5.9 months post-LT).

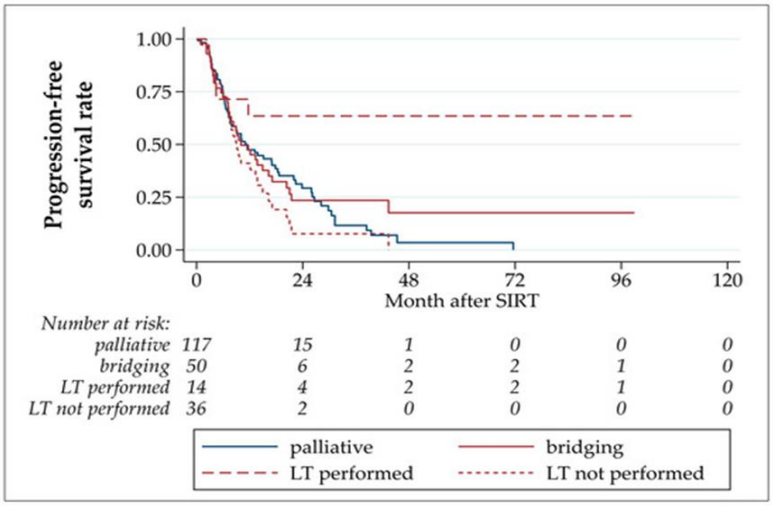

Figure 2. Progression-free survival following TARE.

PFS did not differ significantly between bridging patients who remained without transplantation and those managed palliatively (P = 0.116; hazard ratio for LT not performed versus palliative: 1.40 [CI 0.92–2.13]). Likewise, no difference was found when comparing palliative cases against the complete bridging TARE population (P = 0.932; hazard ratio for palliative versus bridging: 1.02 [CI 0.67–1.54]).

Median overall survival (OS) after TARE stood at 16.6 months in the entire study group, with 6-month and 12-month survival probabilities of 82.0% and 60.5%, respectively **(Table 3 and Figure 3)**. Survival was markedly prolonged among patients who received LT compared with those who did not undergo transplantation (P = 0.001; hazard ratio for LT not performed versus LT performed: 7.68 [CI 2.30–25.61]). No significant OS distinction appeared between the bridging-without-transplant and palliative cohorts (P = 0.9666; hazard ratio for LT not performed versus palliative: 0.99 [CI 0.68–1.45]). However, a statistically significant advantage emerged when contrasting palliative patients with the full bridging TARE group (p = 0.029; hazard ratio for palliative versus bridging: 1.55 [CI 1.05–2.30]), driven primarily by the excellent results observed in the subset that advanced to LT.

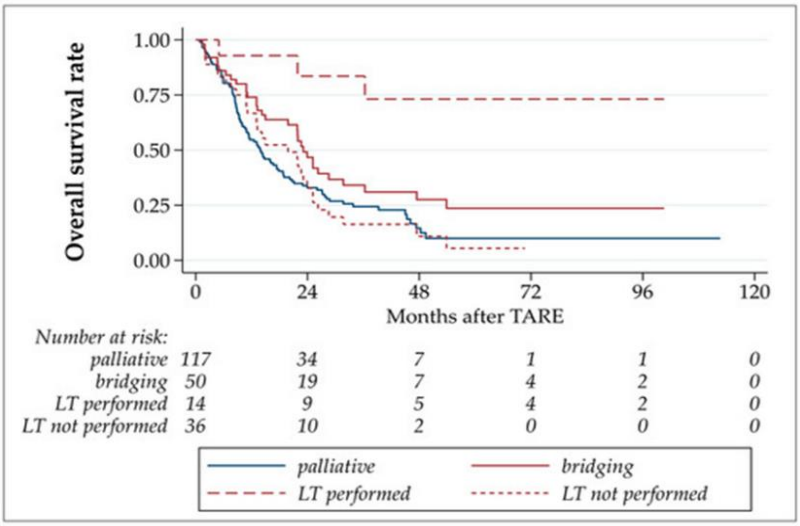

Figure 3. Overall survival following TARE.

Transarterial radioembolization (TARE) has gradually become a well-established treatment option in the overall management of hepatocellular carcinoma (HCC). Functioning as a locoregional approach, it serves as an intermediate strategy situated between potentially curative surgery, other localized interventions (including transarterial chemoembolization (TACE) and radiofrequency ablation (RFA)), and systemic therapies. TARE is particularly suitable when patients present with extensive or numerous HCC lesions that cannot be targeted individually and when no clinically significant extrahepatic metastases are present.

Individualized treatment decisions are made through discussion at multidisciplinary tumor boards (MDT). Experts from multiple specialties work together to develop integrated care plans informed by expert consensus, contemporary clinical guidelines, and available scientific evidence. Liver function represents a key determinant when selecting the most appropriate intervention. Depending on the clinical situation, patients with HCC may receive either curative or palliative treatment, or palliative measures may be used to prepare for a later curative procedure. Bridging therapy with TARE before liver transplantation (LT) exemplifies this strategy. The value of such locoregional neoadjuvant approaches in this context is supported by numerous published studies [5, 6, 11, 17-25]. Direct comparative trials between TARE and TACE have shown advantages for TARE, including higher rates of disease control, markedly improved overall and intrahepatic progression-free survival, and superior survival even among patients with advanced-stage disease [19, 20]. Additional benefits of TARE include its ability to promote hypertrophy of the untreated liver lobe and its suitability for use in individuals with portal vein thrombosis (PVT) [18, 19]. According to a recent review, TARE offers a practical bridging option to LT when standard eligibility criteria are fulfilled [12]. The three studies within that review addressing bridging to transplantation reported encouraging results [26-28].

Clinical outcome

In the current cohort, estimated survival rates reached 82.0% at 6 months and 60.5% at 12 months post-TARE. These results are consistent with findings from other investigations involving patients with unresectable HCC, including the fraction of cases that advanced to LT after bridging therapy [11, 23, 24]. Despite operating within a dedicated liver transplantation facility, only about one-third (29.9%) of TARE procedures at our center were performed with bridging intent, and just 28% of those patients ultimately received a transplant. The primary reasons for not proceeding to transplantation included disease progression (intrahepatic or metastatic) or the emergence of comorbidities that disqualified patients from the waiting list. Analysis of prognostic variables revealed that increased tumor burden and elevated Child–Pugh scores were linked to inferior overall and progression-free survival. Conversely, the absence of underlying cirrhosis, tumor response, and curative therapy after TARE were associated with improved OS

and PFS, while tumor size independently influenced the likelihood of response [23]. A previous institutional study that partially overlapped with the present series compared LT recipients with and without prior bridging treatment (mainly TACE and RFA, with TARE used in only 8% of bridged cases) [17]. Five- and 10-year survival rates were 67% and 47%, respectively, in the bridging group, versus 56% and 46% in the non-bridging group. Tumor-specific 10-year survival differed significantly between the groups (81% versus 59%).

The use of 166Ho-PLLA microspheres for TARE was implemented at our hospital in 2019, and only 3 such cases were included in this analysis [29]. Holmium-166 has a shorter half-life than yttrium-90 (26.8 h vs. 64.1 h), resulting in higher tissue dose rates. The potential clinical benefit of this property for standard HCC or more aggressive variants remains to be clarified. In addition, no studies have yet directly compared the optimal timing of tumor response assessment between 166Ho-TARE and 90Y-TARE.

Comparison of bridging to palliative treatments

Patients assigned to the bridging-to-transplant group tended to be younger (median age 62.6 years versus 72.0 years) and presented with a smaller tumor load in the treated liver (median 5.6% versus 8.8%) than those receiving palliative TARE **(Tables 1 and 2)**. On this basis, superior outcomes were anticipated for both those who successfully underwent LT and those who completed bridging without transplantation. However, the lower tumor burden in the bridging cohort did not consistently produce better clinical results among patients who did not receive a transplant. In the bridging-without-LT subgroup, median PFS was slightly shorter (9.2 months vs. 11.4 months), whereas median OS was longer (19.8 months vs. 13.9 months); neither difference reached statistical significance. Within this series, neither patient age nor hepatic tumor burden at the time of TARE proved to be strong independent prognostic factors.

The bridging-to-transplant group had fewer patients with Child–Pugh score (CPS) stage B disease than the palliative group (6.0% versus 11.1%; difference not statistically significant), and none of the CPS stage B patients in the bridging arm proceeded to transplantation. Intra-arterial locoregional therapies are now frequently delivered in sequential or combined regimens alongside other locoregional or systemic agents. Tumor burden, disease dynamics, hepatic reserve, and comorbidities should guide treatment selection. The most favorable oncologic outcomes are achieved through a multimodal, multidisciplinary strategy in which TARE functions as a valuable adjunct rather than a rival to alternative therapies [22, 30]. Combination TACE with sorafenib has been shown to improve PFS compared with monotherapy [31]. Comparable advantages may exist for TARE-based combinations, potentially through synergistic effects between radiation and immune checkpoint blockade [32]. A phase 2 trial investigating 90Y-glass TARE followed by durvalumab plus tremelimumab for local tumor control in HCC is actively recruiting (ROWAN trial, NCT05063565). Given that any antecedent therapy can affect residual liver capacity, functional assessment must be performed with particular attention using standardized scoring tools [33]. Additional modalities such as the liver maximum capacity test (LiMAx) and hepatobiliary scintigraphy can further refine this evaluation [34, 35].

Although uncommon, TARE can be applied in cases of HCC recurrence after LT and has been documented as a safe and practical approach [36]. In the present series, two patients received 90Y-TARE following transplantation without adverse events, and their liver function parameters remained stable.

Outcome of patients undergoing liver transplantation

In our cohort of patients who received liver transplantation (LT), the estimated survival rate at 12 months reached 92.9%. Extrahepatic metastases represented the chief barrier to longer survival. Among the five individuals who had undergone bridging TARE before LT and later showed signs of tumor progression, three developed distant metastatic disease following transplantation. In two of these cases, intrahepatic tumor advancement had already taken place after TARE but before LT (one case involving previously treated liver segments and the other occurring in untreated portions of the liver). Notably, metastatic dissemination in one patient manifested more than five years after both TARE and LT, rendering any causal association uncertain. Published reports indicate that intrahepatic HCC recurrence occurs in 10–20% of liver transplant recipients, with the precise incidence influenced by the effectiveness of pre-transplant bridging interventions. Although the present series showed no HCC recurrences throughout the observation period, available evidence suggests that bridging approaches help mitigate the likelihood of post-transplant HCC relapse [18, 19]. A

separate investigation involving 207 patients treated with LT after 90Y-TARE demonstrated comparable long-term overall survival to transplantation performed for benign liver conditions. Gabr *et al*. [19] proposed that the reduced incidence of HCC recurrence may partly result from the biological impact of TARE.

Future perspectives

Image-guided locoregional therapies (LRTs) directed at primary hepatic malignancies must be evaluated against the backdrop of HCC's marked biological diversity, including its varied molecular subtypes and distinctive tumor microenvironments [37]. Rather than acting through direct molecular targeting, TARE exerts its effects via vascular delivery, administering radioactive material straight into the tumor or its feeding arterial branches. Consequently, such locoregional modalities are poised to continue playing a meaningful role in multimodal treatment algorithms, particularly when integrated with molecularly directed systemic agents that have markedly prolonged survival among individuals with advanced-stage disease [22]. At present, the preferred first-line regimen for advanced HCC combines immune checkpoint blockade with tyrosine kinase inhibition (e.g., atezolizumab plus bevacizumab). Nevertheless, optimal second-line strategies are increasingly viewed as integrated approaches merging locoregional and systemic treatments [38, 39].

By virtue of its selective capillary-level radiation deposition and consequent injury to endothelial structures, TARE appears especially well suited to impede the extension of tumor neovasculature into surrounding healthy parenchyma [21, 40]. This property may also underlie the comparatively low incidence of extrahepatic recurrence observed after TARE, possibly by diminishing the pool of viable circulating HCC cells. Additional research utilizing sensitive assays for circulating tumor cells and tumor-derived DNA will be essential to validate this concept. Ongoing efforts also explore radiosensitization strategies to downregulate PD-L1 and alleviate tumor hypoxia, as radiation exposure can induce PD-L1 upregulation, thereby constraining treatment efficacy. Nanoparticle-mediated delivery is being studied to facilitate intracellular accumulation of the cytotoxic compound lonidamine (LND) [41, 42]. The adoption of personalized TARE protocols employing multi-compartment voxel-based dosimetry is expected to enhance therapeutic results by enabling accurate prediction of absorbed doses in different tissues and permitting patient-specific dose tailoring. Dose–response data have already been defined for 90Y-glass microsphere treatment of HCC and for 166Ho-PLLA microsphere therapy of colorectal liver metastases [43, 44]. A clinical trial investigating optimal 166Ho-TARE dosing in early-stage HCC is in progress [45]. Standardized procedural recommendations covering dosimetry planning, tumor dose targets, and sparing of non-tumorous liver tissue are available for all three microsphere platforms [46-48]. However, these guidelines rest predominantly on retrospective analyses, underscoring the need for prospective studies to establish context-specific dose thresholds across diverse clinical settings.

An important evolution beyond the bridging-to-transplant paradigm is the expanded application of TARE to selected patients with early- or intermediate-stage HCC [39]. Current recommendations endorse TARE when surgical resection, ablation, or transplantation prove unfeasible or ineffective. Drawing on findings from the LEGACY trial, TARE is now also advised for solitary HCC tumors measuring up to 8 cm [49]. These refinements, which have yet to be reflected in the AASLD and EASL clinical practice guidelines [4, 50], mark a fundamental departure from earlier views of TARE as a salvage option reserved for cases in which all other modalities have failed. During treatment planning, greater emphasis must now be placed on safeguarding residual liver function to avoid compromising eligibility for subsequent therapies, especially the rapidly expanding repertoire of systemic agents. When an ideal tumor-to-liver activity ratio proves unattainable, priority should be assigned to restricting radiation exposure of healthy parenchyma rather than pursuing maximal tumor dosing. This strategy helps maintain the feasibility of repeat TARE sessions and adequate hepatic reserve throughout the patient's disease trajectory [33, 51]. De novo HCC foci may arise in previously unaffected liver segments, often requiring further interventions that could incrementally impair liver function.

Limitations of the study

The chief drawback of this investigation is its retrospective, single-center design, which captured the considerable heterogeneity of real-world oncologic treatment pathways in HCC but lacked the rigor of a prospective controlled trial. Outcome assessment was anchored in the evaluation of TARE interventions and therefore emphasizes the nuclear medicine and

interventional radiology standpoint. Given that most participants received multiple lines of therapy before and/or after TARE, it is not possible to attribute clinical effects to any individual modality. Owing to the wide diversity of treatment sequences, survival metrics were calculated from the time of TARE administration. A comparative analysis with other locoregional approaches (e.g., TACE or percutaneous radiation therapy) was not conducted.

Conclusion

This study examined the clinical outcomes of TARE performed at our center as part of liver transplantation for HCC. Multidisciplinary team consensus determined the use of TARE for bridging or palliative purposes. Analyses of progression-free and overall survival, together with inter-group comparisons among bridging-with-transplant, bridging-without-transplant, and palliative cohorts, substantiated the superior outcomes associated with LT. In patients who did not proceed to transplantation, TARE was a valuable component of the broader multimodal treatment strategy for HCC. No meaningful differences in survival emerged between the bridging without transplant and palliative groups. Future advances in HCC care will likely center on rational combinations of locoregional and systemic therapies, although the most effective integration strategies remain to be clarified. Upcoming research on TARE should prioritize refined, tumor-specific dosimetry optimization, appropriate microsphere selection according to tumor biology, and identification of synergistic pairings with targeted molecular agents.

Acknowledgments: None

Conflict of Interest: None

Financial Support: None

Ethics Statement: None

References

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2021;71(3):209-49.
2. Samuel D, Coilly A. Management of patients with liver diseases on the waiting list for transplantation: a major impact to the success of liver transplantation. BMC Med. 2018;16(1):113.
3. Rand A, Koch T, Ragaller M. Organ donation – not only a responsibility of intensive care medicine. Anaesthesist. 2022;71(4):311-7.
4. European Association for the Study of the Liver. EASL Clinical Practice Guidelines: liver transplantation. J Hepatol. 2016;64(2):433-85.
5. Kollmann D, Selzner N, Selzner M. Bridging to liver transplantation in HCC patients. Langenbecks Arch Surg. 2017;402(6):863-71.
6. Gabr A, Abouchaleh N, Ali R, Vouche M, Atassi R, Memon K, et al. Comparative study of post-transplant outcomes in hepatocellular carcinoma patients treated with chemoembolization or radioembolization. Eur J Radiol. 2017;93:100-6.
7. Oligane HC, Xing M, Kim HS. Effect of bridging local-regional therapy on recurrence of hepatocellular carcinoma and survival after orthotopic liver transplantation. Radiology. 2017;282(3):869-79.
8. Finkenstedt A, Vikoler A, Portenkirchner M, Mulleder K, Maglione M, Margreiter C, et al. Excellent post-transplant survival in patients with intermediate stage hepatocellular carcinoma responding to neoadjuvant therapy. Liver Int. 2016;36(5):688-95.
9. Bester L, Meteling B, Boshell D, Chua TC, Morris DL. Transarterial chemoembolisation and radioembolisation for the treatment of primary liver cancer and secondary liver cancer: a review of the literature. J Med Imaging Radiat Oncol. 2014;58(3):341-52.
10. Riemenschneider T, Ruf C, Kratzsch HC, Ziegler M, Spath G. Arterial, portal or combined arterio-portal regional chemotherapy in experimental liver tumours? J Cancer Res Clin Oncol. 1992;118(8):597-600.
11. Aliseda D, Marti-Cruchaga P, Zozaya G, Rodriguez-Fraile M, Bilbao JI, Benito-Boillos A, et al. Liver resection and transplantation following yttrium-90 radioembolization for primary malignant liver tumors: a 15-year single-center experience. Cancers (Basel). 2023;15(3):733.
12. Lopez-Lopez V, Miura K, Kuemmerli C, Capel A, Eshmuminov D, Ferreras D, et al. Selecting the appropriate downstaging and bridging therapies for

hepatocellular carcinoma: what is the role of transarterial radioembolization? A pooled analysis. Cancers (Basel). 2023;15(7):2122.
13. Lencioni R, Llovet JM. Modified RECIST (mRECIST) assessment for hepatocellular carcinoma. Semin Liver Dis. 2010;30(1):52-60.
14. BTG International. TheraSphere reference manual Europe, version US-USTHSP-2013-0569(2)a(1). London: BTG International; 2017.
15. Quirem Medical B.V. Instructions for use Ho-166-PLLA microspheres, version LS-1101-10. Deventer: Quirem Medical B.V.; 2017.
16. Sirtex Medical Limited. SIR-Spheres microspheres training manual, version TRN-RW-05. Woburn, MA: Sirtex Medical Limited; 2014.
17. Bauschke A, Altendorf-Hofmann A, Ardelt M, Kissler H, Tautenhahn HM, Settmacher U. Impact of successful local ablative bridging therapy prior to liver transplantation on long-term survival in patients with hepatocellular carcinoma in cirrhosis. J Cancer Res Clin Oncol. 2020;146(7):1819-27.
18. Benko T, Konig J, Theysohn JM, Schotten C, Saner FH, Treckmann J, et al. Bridging treatment prior to liver transplantation for hepatocellular carcinoma: radioembolization or transarterial chemoembolization? Eur J Med Res. 2022;27(1):74.
19. Gabr A, Kulik L, Mouli S, Riaz A, Ali R, Desai K, et al. Liver transplantation following yttrium-90 radioembolization: 15-year experience in 207-patient cohort. Hepatology. 2021;73(3):998-1010.
20. Kim MA, Jang H, Choi NR, Nam JY, Lee YB, Cho EJ, et al. Yttrium-90 radioembolization is associated with better clinical outcomes in patients with hepatocellular carcinoma compared with conventional chemoembolization: a propensity score-matched study. J Hepatocell Carcinoma. 2021;8:1565-77.
21. Crocetti L, Bozzi E, Scalise P, Bargellini I, Lorenzoni G, Ghinolfi D, et al. Locoregional treatments for bridging and downstaging HCC to liver transplantation. Cancers (Basel). 2021;13(21):5558.
22. Goyal P, Salem R, Mouli SK. Role of interventional oncology in hepatocellular carcinoma: future best practice beyond current guidelines. Br J Radiol. 2022;95(1138):20220379.
23. Yim SY, Chun HS, Lee JS, Lim JH, Kim TH, Kim BK, et al. Transarterial radioembolization for unresectable hepatocellular carcinoma: real-life efficacy and safety analysis of Korean patients. Cancers (Basel). 2022;14(2):385.
24. Yu CY, Huang PH, Tsang LL, Hsu HW, Lim WX, Weng CC, et al. Yttrium-90 radioembolization as the major treatment of hepatocellular carcinoma. J Hepatocell Carcinoma. 2023;10:17-26.
25. Hui RW, Mak LY, Cheung TT, Lee VH, Seto WK, Yuen MF. Clinical practice guidelines and real-life practice on hepatocellular carcinoma: the Hong Kong perspective. Clin Mol Hepatol. 2023;29(2):217-29.
26. Mantry PS, Mehta A, Madani B, Mejia A, Shahin I. Selective internal radiation therapy using yttrium-90 resin microspheres in patients with unresectable hepatocellular carcinoma: a retrospective study. J Gastrointest Oncol. 2017;8(5):799-807.
27. Radunz S, Treckmann J, Baba HA, Best J, Muller S, Theysohn JM, et al. Long-term outcome after liver transplantation for hepatocellular carcinoma following yttrium-90 radioembolization bridging treatment. Ann Transplant. 2017;22:215-21.
28. Zori AG, Ismael MN, Limaye AR, Firpi R, Morelli G, Soldevila-Pico C, et al. Locoregional therapy protocols with and without radioembolization for hepatocellular carcinoma as bridge to liver transplantation. Am J Clin Oncol. 2020;43(5):325-33.
29. Drescher R, Kohler A, Seifert P, Aschenbach R, Ernst T, Rauchfuss F, et al. Clinical results of transarterial radioembolization (TARE) with holmium-166 microspheres in the multidisciplinary oncologic treatment of patients with primary and secondary liver cancer. Biomedicines. 2023;11(7):1831.
30. Newell PH, Wu Y, Hoen H, Uppal R, Thiesing JT, Sasadeusz K, et al. Multimodal treatment of unresectable hepatocellular carcinoma to achieve complete response results in improved survival. HPB (Oxford). 2015;17(5):454-60.
31. Kudo M, Ueshima K, Ikeda M, Torimura T, Tanabe N, Aikata H, et al. Final results of TACTICS: a randomized, prospective trial comparing transarterial chemoembolization plus sorafenib to transarterial chemoembolization alone in patients with unresectable hepatocellular carcinoma. Liver Cancer. 2022;11(4):354-67.
32. Kim KJ, Kim JH, Lee SJ, Lee EJ, Shin EC, Seong J. Radiation improves antitumor effect of immune checkpoint inhibitor in murine hepatocellular

carcinoma model. Oncotarget. 2017;8(25):41242-55.
33. D'Avola D, Granito A, Torre-Alaez M, Piscaglia F. The importance of liver functional reserve in the non-surgical treatment of hepatocellular carcinoma. J Hepatol. 2022;76(5):1185-98.
34. Fischer J, Wellhoner S, Ebel S, Lincke T, Bohlig A, Gerhardt F, et al. The liver maximum capacity test (LiMAx) is associated with short-term survival in patients with early stage HCC undergoing transarterial treatment. Cancers (Basel). 2022;14(21):5323.
35. Dinant S, de Graaf W, Verwer BJ, Bennink RJ, van Lienden KP, Gouma DJ, et al. Risk assessment of posthepatectomy liver failure using hepatobiliary scintigraphy and CT volumetry. J Nucl Med. 2007;48(5):685-92.
36. Aquina CT, Eskander MF, Pawlik TM. Liver-directed treatment options following liver tumor recurrence: a review of the literature. Front Oncol. 2022;12:832405.
37. Criss CR, Makary MS. Recent advances in image-guided locoregional therapies for primary liver tumors. Biology (Basel). 2023;12(7):999.
38. Stefanini B, Ielasi L, Chen R, Abbati C, Tonnini M, Tovoli F, et al. TKIs in combination with immunotherapy for hepatocellular carcinoma. Expert Rev Anticancer Ther. 2023;23(3):279-91.
39. Reig M, Forner A, Rimola J, Ferrer-Fabrega J, Burrel M, Garcia-Criado A, et al. BCLC strategy for prognosis prediction and treatment recommendation: the 2022 update. J Hepatol. 2022;76(3):681-93.
40. Sangro B, Inarrairaegui M, Bilbao JI. Radioembolization for hepatocellular carcinoma. J Hepatol. 2012;56(2):464-73.
41. Wang S, Zhou Z, Hu R, Dong M, Zhou X, Ren S, et al. Metabolic intervention liposome boosted lung cancer radio-immunotherapy via hypoxia amelioration and PD-L1 restraint. Adv Sci (Weinh). 2023;10(13):e2207608.
42. Zhou Z, Wang H, Li J, Jiang X, Li Z, Shen J. Recent progress, perspectives, and issues of engineered PD-L1 regulation nano-system to better cure tumor: a review. Int J Biol Macromol. 2024;254(Pt 2):127911.
43. Bastiaannet R, van Roekel C, Smits MLJ, Elias SG, van Amsterdam WAC, Doan D, et al. First evidence for a dose-response relationship in patients treated with 166Ho radioembolization: a prospective study. J Nucl Med. 2020;61(4):608-12.
44. Garin E, Tselikas L, Guiu B, Chalaye J, Edeline J, de Baere T, et al. Personalised versus standard dosimetry approach of selective internal radiation therapy in patients with locally advanced hepatocellular carcinoma (DOSISPHERE-01): a randomised, multicentre, open-label phase 2 trial. Lancet Gastroenterol Hepatol. 2021;6(1):17-29.
45. Hendriks P, Rietbergen DDD, van Erkel AR, Coenraad MJ, Arntz MJ, Bennink RJ, et al. Study protocol: adjuvant holmium-166 radioembolization after radiofrequency ablation in early-stage hepatocellular carcinoma patients—a dose-finding study (HORA EST HCC trial). Cardiovasc Interv Radiol. 2022;45(7):1057-63.
46. Weber M, Lam M, Chiesa C, Konijnenberg M, Cremonesi M, Flamen P, et al. EANM procedure guideline for the treatment of liver cancer and liver metastases with intra-arterial radioactive compounds. Eur J Nucl Med Mol Imaging. 2022;49(5):1682-99.
47. Stella M, Braat A, van Rooij R, de Jong H, Lam M. Holmium-166 radioembolization: current status and future prospective. Cardiovasc Interv Radiol. 2022;45(11):1634-45.
48. Levillain H, Bagni O, Deroose CM, Dieudonne A, Gnesin S, Grosser OS, et al. International recommendations for personalised selective internal radiation therapy of primary and metastatic liver diseases with yttrium-90 resin microspheres. Eur J Nucl Med Mol Imaging. 2021;48(5):1570-84.
49. Salem R, Johnson GE, Kim E, Riaz A, Bishay V, Boucher E, et al. Yttrium-90 radioembolization for the treatment of solitary, unresectable HCC: the LEGACY study. Hepatology. 2021;74(5):2342-52.
50. Heimbach JK, Kulik LM, Finn RS, Sirlin CB, Abecassis MM, Roberts LR, et al. AASLD guidelines for the treatment of hepatocellular carcinoma. Hepatology. 2018;67(1):358-80.
51. Granito A, Bolondi L. Non-transplant therapies for patients with hepatocellular carcinoma and Child-Pugh-Turcotte class B cirrhosis. Lancet Oncol. 2017;18(2):e101-12.