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THERASPHERE™ Y-90 Glass Microspheres | Y-90 & LIVER TRANSPLANT

TheraSphere™ Y-90 Glass Microspheres: Revolutionizing Liver Transplant Eligibility

TheraSphere™ Y-90 Glass Microspheres is a leading treatment for patients with unresectable hepatocellular carcinoma (HCC), helping achieve surgical candidacy and preserving liver transplant eligibility through prolonged local tumor control.[1-4]

Key advantages of utilizing TheraSphere™ Y-90 Glass Microspheres to maintain or achieve transplant eligibility:

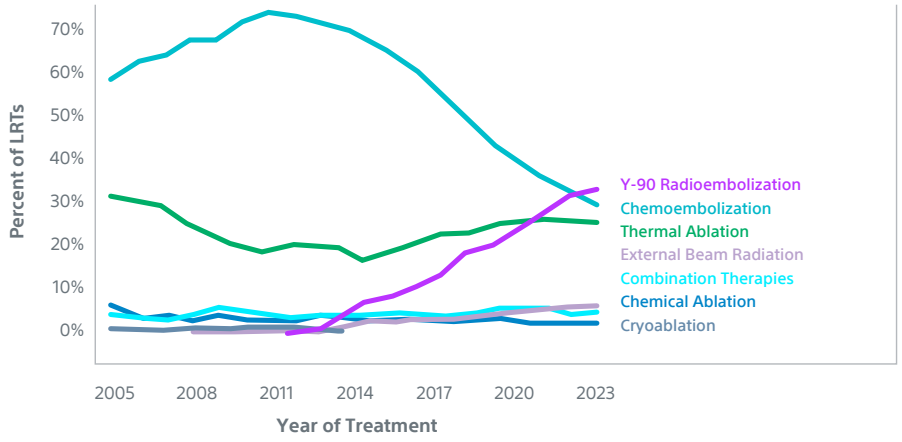
- **Tumor Biology Insight:** Enhances patient selection for optimal post-transplant outcomes.
- **UNOS Priority Upgrade:** For patients meeting MILAN criteria of T2 or less.
- **Complete Pathological Necrosis:** High rates optimize outcomes for HCC patients.

Locoregional Therapy (LRT) of Choice for Preserving Transplant Eligibility

A consistently high percentage of patients were bridged to liver transplant in contemporary clinical trials utilizing TheraSphere as the locoregional therapy of choice for bridging.

Y-90: the #1 bridging strategy for liver transplant candidates with HCC in the US[5]

Recent analysis of data from the Organ Procurement and Transplant Network (OPTN) reflects the increasing adoption by many transplant centers of TARE as the primary LRT option surpassing both chemoembolization and thermal ablation.[5]



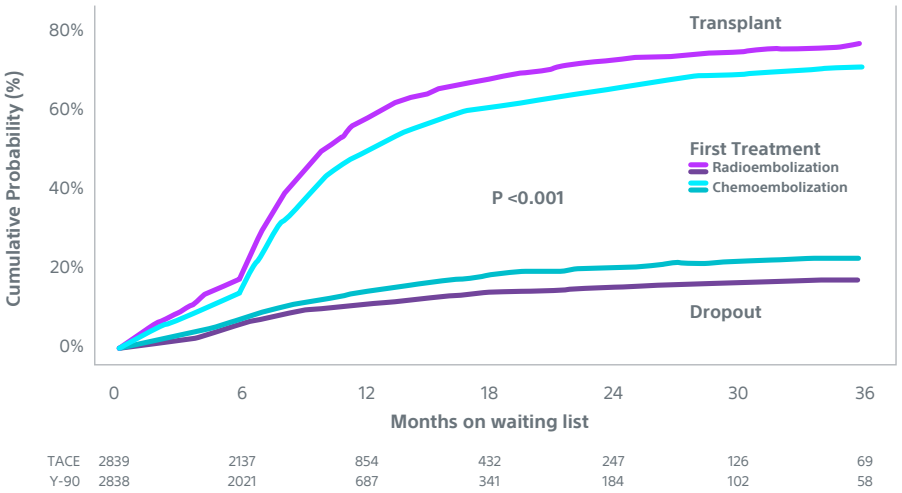
Adapted from Riad, et. al. 2024, JVIR.

Y-90: Reducing Repeat Procedures, Improving Waitlist Outcomes

A recent study of 5,677 liver transplant patients (UNOS OPTN data, May 2019 - October 2024) reveals a major advantage for those treated with Y-90. With **80% of Y-90 patients needing only one LRT**, compared to 56% of TACE patients requiring multiple treatments, Y-90 offers a more streamlined path to transplant.[6]

Y-90 patients are more likely to maintain transplant eligibility

Patients treated with Y-90 experienced a **22% lower risk of waitlist dropout** than TACE, making it a critical factor in successful outcomes.[6]



Adapted from Kim, et. al. 2026, JHEP.

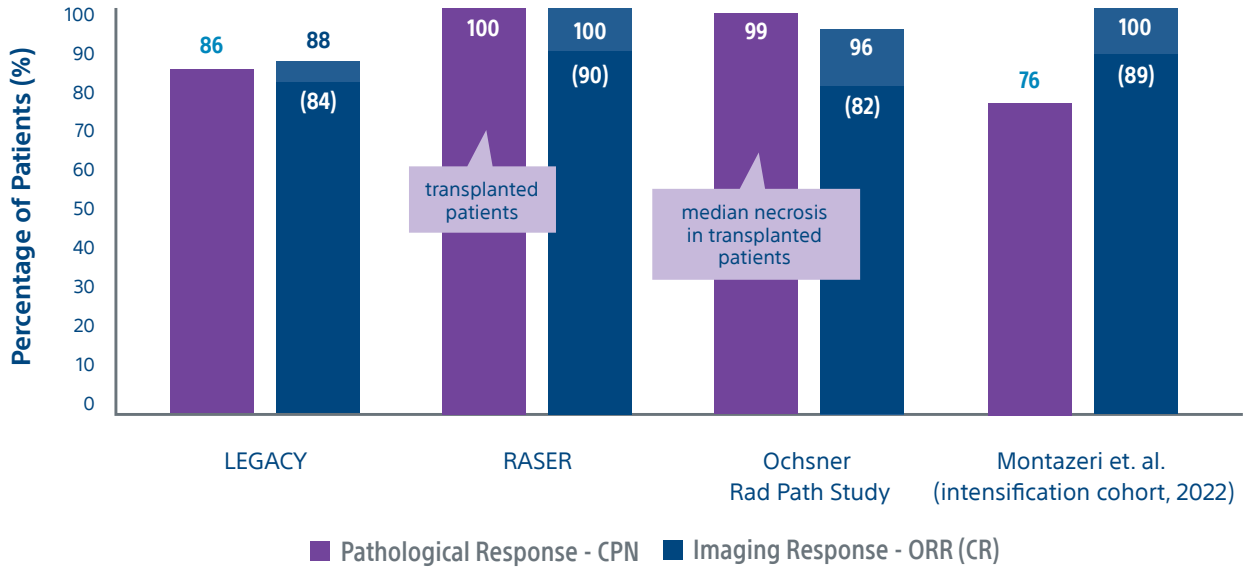
Superior and Durable Outcomes

The uniquely engineered high radiation per microsphere (RPM) of TheraSphere is purpose-built to drive complete pathologic necrosis (CPN), the hallmark of ablative radiation segmentectomy. [7,8,9]

Studies have shown that more patients can access liver transplantation and have better outcomes following TheraSphere treatment.[2,3,4,10]

1 Increased Probability of Complete Pathological Necrosis (CPN) and Objective Response (ORR)

- Contemporary dosimetry planning has enhanced the precision of tumor targeting, enabling a higher tumor-absorbed dose and correlating with increased rates of CPN.
- Targeted delivery with unmatched RPM helps achieve CPN.[2]
- CPN has been associated with lower rates of tumor recurrence and improved survival after transplant.



2 Rapid and Durable Tumor Control, Optimizing Patients for Curative Transplant

Two recent studies noted the superior and sustained tumor response for long-term control when treated with TheraSphere.

Durable response at 2 years

97% **of treated tumors**[11]

Median duration of response (mDOR)

20.9 **months**[8]

Durability matters when patients may wait months to years for transplant. TheraSphere has the ability to **deliver high radiation doses through the Radiation Segmentectomy technique** which provides sustained local control, reduces waitlist dropout, and supports curative transplant outcomes.

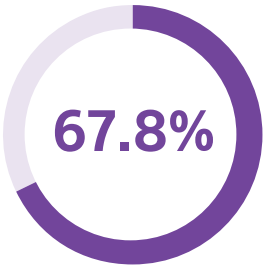
3 Reducing AFP

Clinical data demonstrate that Y-90 radioembolization (TARE) can effectively reduce alpha-fetoprotein (AFP) levels in patients with HCC, and this reduction is associated with improved outcomes and eligibility for liver transplantation.[12]

After Y-90 TARE in HCC: Biochemical Response & Transplant Eligibility Signals

AFP biochemical response

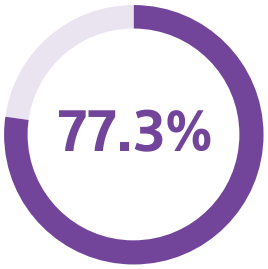
1 Month



AFP-producing tumors with CR/PR at 1 month

Transplant eligibility signal

6 Months



Downstaged to or maintained within Milan at 6 months

Sustained for 74.4% and 70% of patients 1 year and 2 years after treatment

Retrospective single-center study (n=88 HCC). AFP response defined as complete or partial biochemical response at 1 month; 77.3% downstaged to or maintained within Milan criteria at 6 months.[12]

4 Longer Time to Tumor Progression vs TACE

TheraSphere extends time to tumor progression, as shown in the PREMIERE and TRACE trials, which demonstrated significant improvements over cTACE and DEB-TACE.

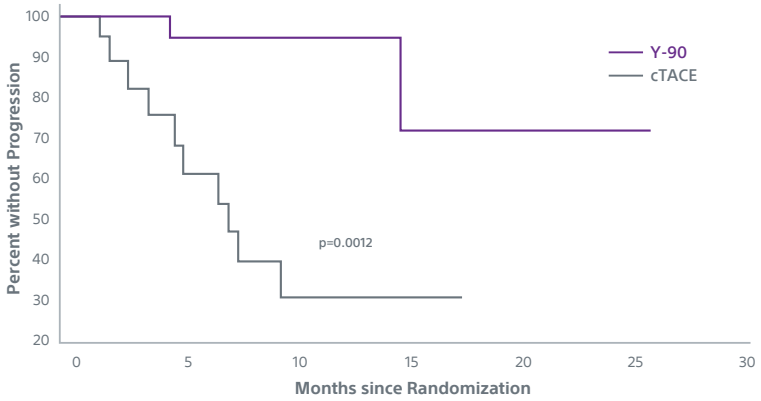
PREMIERE TRIAL[3]

Prospective, randomized, open label, single-center study of 45 patients from 2009-2015 cTACE vs. Glass Y-90 TARE for treatment of unresectable, unablatable HCC

Glass Y-90 Treatment showed longer time to tumor progression than cTACE

>26 mo Y-90 vs
6.8 mo cTACE, p=0.0012

TIME TO PROGRESSION



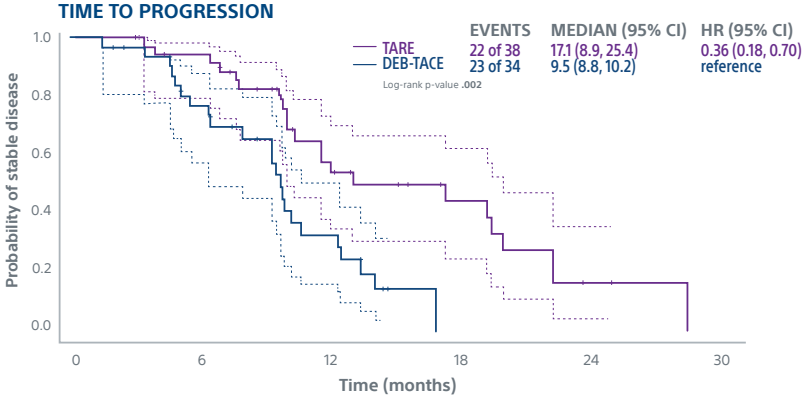
TRACE TRIAL[4]

Prospective, randomized, open label, single-center superiority study of 72 patients from 2011-2018 DEB-TACE vs. Glass Y-90 TARE for treatment of unresectable HCC

Glass Y-90 Treatment showed longer time to tumor progression than DEB-TACE. This study also reported 2x patients accessed liver transplant following TheraSphere vs Deb-TACE.

17.1 mo TARE vs
9.5 mo DEB-TACE, p=0.002

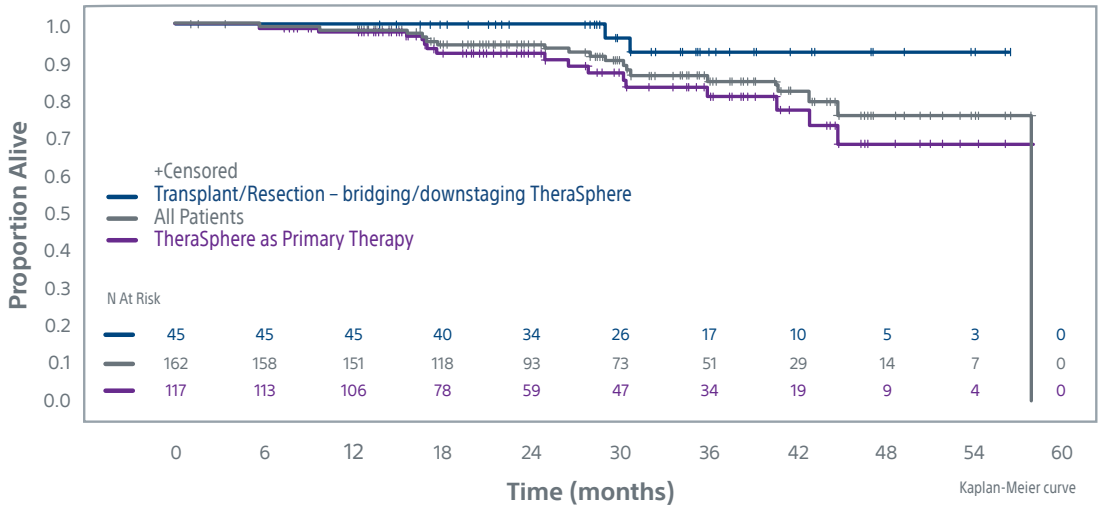
TIME TO PROGRESSION



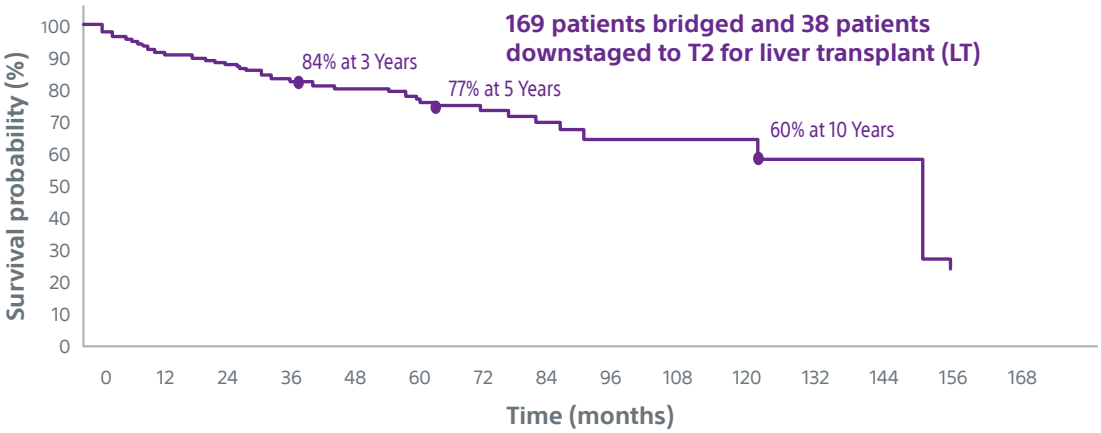
Neoadjuvant Use for Liver Transplant Showed Strong Overall Survival (OS) Outcomes

In the following trials, unresectable HCC patients receiving liver transplant following TheraSphere showed strong overall survival outcomes with an OS of 93% at 3 years and a median overall survival of 12.5 years after liver transplant.

LEGACY Study, 2021
Overall Survival
(Treated Population)



Gabr, et. al., 2020
Survival Probability Post Transplant
(N = 207 patients)



CONCLUSION

Y-90 is an effective local therapy for bridging patients within Milan Criteria, **expanding transplant eligibility** beyond Milan Criteria, and **delivering durable post-transplant outcomes with minimal tumor recurrence.**[13]

KEY TRIAL DESIGN AND BASELINE CHARACTERISTICS

	Local Tumor Control			Time to Tumor Progression	
	LEGACY Study 2021	**RASER, Kim et. al. 2022**	**Ochsner Rad Path Study 2024**	**PREMIERE Trial 2016**	**TRACE Trial 2022**
Trial Design	Multicenter, US	Single-center, US	Single-center, US	Prospective, randomized open label Single-Center, US	Open label, Single- Center, randomized Controlled Trial, EU
	Retrospective	Prospective	Retrospective	Prospective	Prospective
	N=162	N=29	N=56	N=45	N=66
Objective	To evaluate objective response rate (ORR) and duration of response (DoR) in patients with solitary unresectable HCC treated with Yttrium-90 glass microspheres.	To assess the safety and efficacy of radiation segmentectomy in patients with unresectable HCC deemed unfavourable for ablation.	To utilize voxel-based dosimetry following radiation segmentectomy to understand microsphere distribution and validate current literature regarding radiologic and pathologic outcomes.	To compare the effects of cTACE and Y-90 radioembolization in patients with HCC.	To compare the efficacy and safety of TARE with TACE for unresectable HCC.
Primary Endpoints	Objective Response Rate (ORR) Duration of Response (DoR)	Objective Response Rate (ORR) by mRECIST	Objective Response Rate (ORR) Complete Response (CR) by mRECIST	Time to progression (TTP)	Time to progression (TTP)
Baseline Patient Characteristics	BCLC A (60.5%) C (39.5%)	BCLC A (100%)	BCLC A (100%)	BCLC A (75%) B (25%)	BCLC A (12%) B (88%)
	Median Tumor Size: 2.7 cm (range: 1.0 – 8.1 cm)	**Median Tumor Size:** 2.1 cm	**Median Tumor Size:** 3.4 cm	**Median Tumor Size:** TACE = 2.6 cm TARE/Y-90 = 3.0 cm	**Median Tumor Size:** TARE/Y-90 = 4.2 cm DEB-TACE = 4.7 cm

†The safety and efficacy of TheraSphere in treatment of patients with PVT has not been established.

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TheraSphere™ Y-90 Glass Microspheres indications, safety, and warnings

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