



THERASPHERE™ Y-90 Glass Microspheres | **PROACTIF STUDY: HCC RESULTS**

PROACTIF: The largest prospective, real-world Y-90 study with TheraSphere for the treatment of liver malignancies

This study was sponsored by Boston Scientific Corporation. Lead investigators: Etienne Garin, MD and Boris Guiu, MD.

STUDY OBJECTIVES

Evaluate effectiveness, safety and patient quality of life (QoL) with TheraSphere treatment in real-world clinical practice, and to identify clinical and dosimetric factors associated with survival

Primary Endpoints

Overall survival (OS) and quality-of-life (QoL)

Key Secondary Endpoints

Safety, conversion to surgery and factors associated with OS



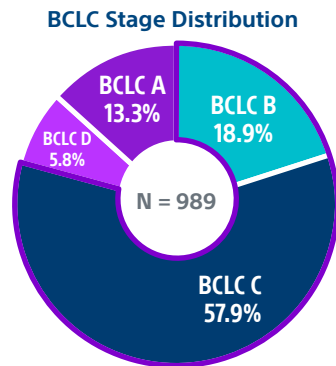
1,259 total patient population
(HCC, ICC, mCRC)



34 sites
All-comers over 5 years

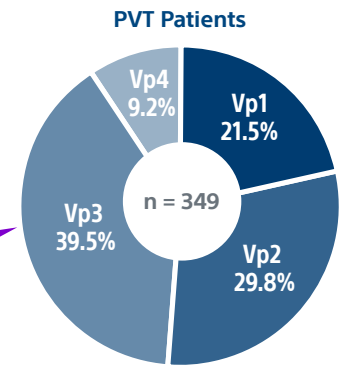
FULL HCC ANALYSIS - 989 PATIENTS ACROSS 34 SITES

REPRESENTATIVE OF REAL-WORLD CLINICAL COMPLEXITY



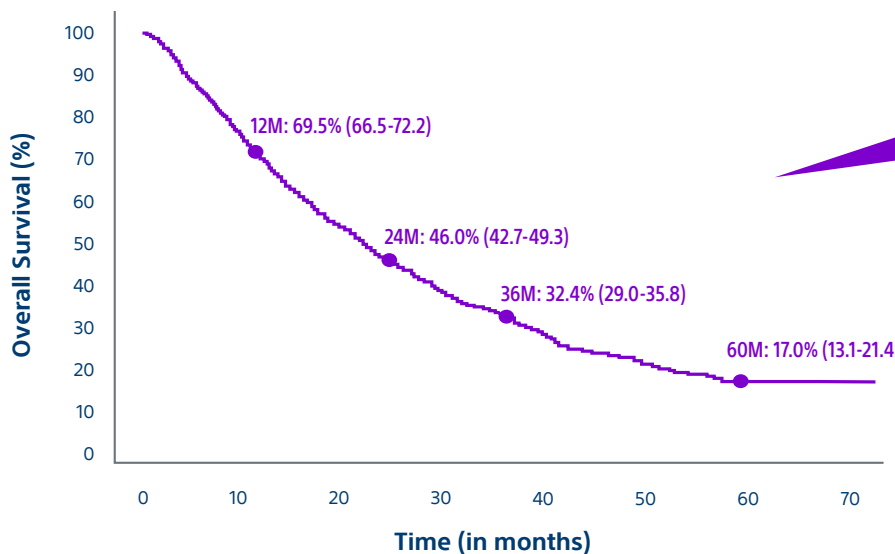
77% Intermediate or advanced stage patients

35% Patients with PVT*



MEANINGFUL SURVIVAL ACROSS BCLC STAGES

HIGH OVERALL SURVIVAL FOR INTERMEDIATE & ADVANCED STAGE HCC PATIENTS



MEDIAN OS
21.8 months
(95% CI: 20.1 – 23.3)

27.0 months INTERMEDIATE BCLC B
(95% CI: 20.7 – 31.4)

21.1 months ADVANCED BCLC C
(95% CI: 18.0 – 22.8)

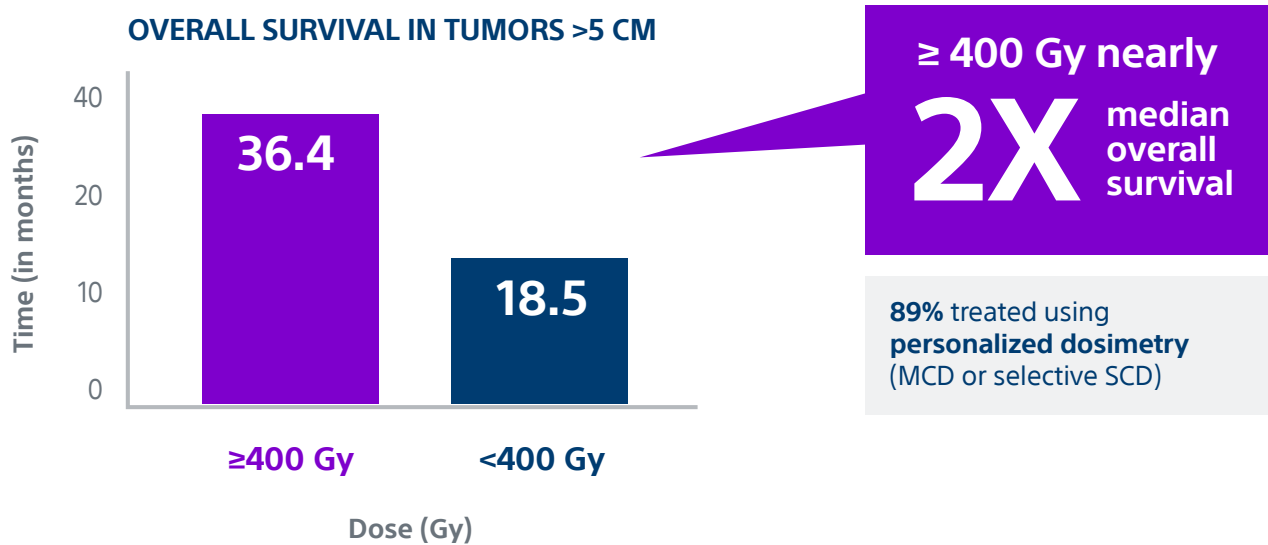
At Risk: 989, 732, 438, 226, 107, 44, 14, 1

*TheraSphere is not approved or intended for use outside of its current FDA-approved indication in the United States. Any discussion of off-label use is for scientific and educational purposes only.

DOSE MATTERS EVEN IN LARGE TUMORS

OPTIMIZING DOSE IMPROVES SURVIVAL IN LARGE TUMORS

A ≥ 400 Gy tumor absorbed dose significantly improved survival in lesions >5 cm (n = 631) (36.4 vs. 18.5 months; $p < 0.001$), consistent with prior TheraSphere studies¹



6.8 cm Median tumor size

68.2% Patients with solitary tumors >5 cm

SIGNIFICANT SURVIVAL IN LOCALIZED PVT

Vp1/Vp2 PATIENTS MATCHED NON-PVT PATIENTS' OVERALL SURVIVAL

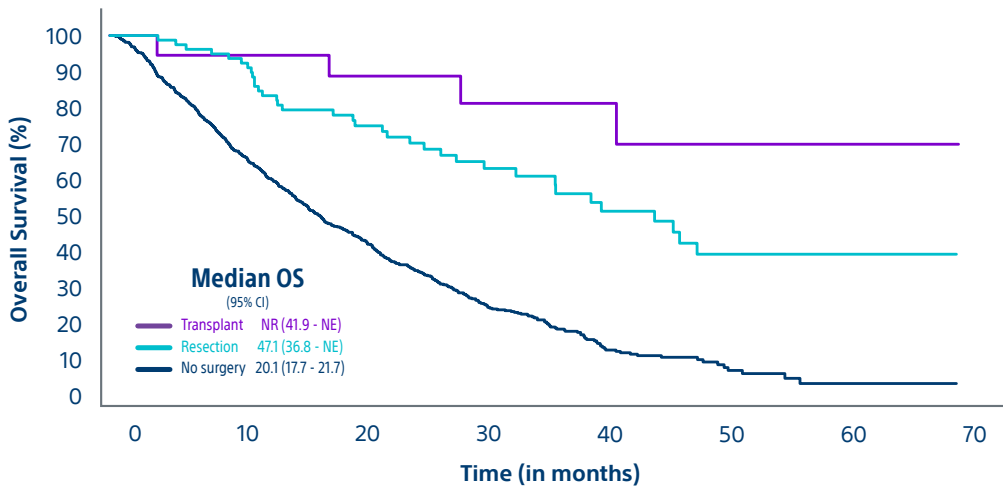


Median OS was 24.8 months in patients with localized PVT* (Vp1/Vp2; n=179) vs. 23.1 months in patients without PVT (n = 623) ($p < 0.001$)

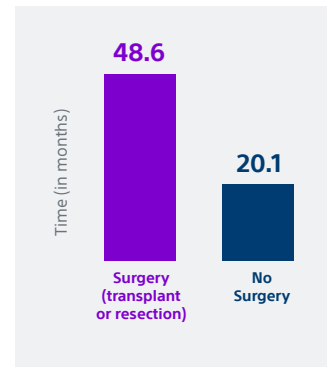
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UNLOCKING CURATIVE POTENTIAL AND PRESERVING SURGICAL ELIGIBILITY

THERASPHERE PATIENTS SUCCESSFULLY DOWNSTAGED TO CURATIVE-INTENT SURGERY, WITH MEANINGFUL SURVIVAL BENEFIT

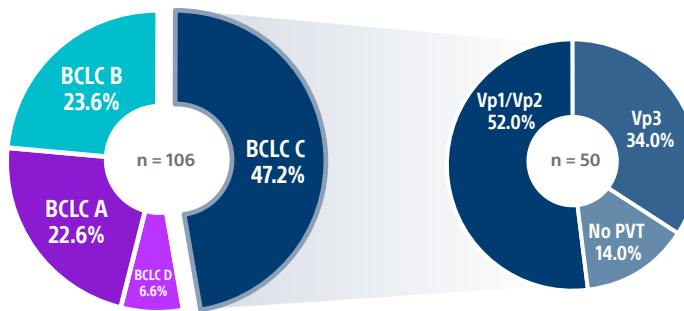


MEDIAN OVERALL SURVIVAL MORE THAN 2X with subsequent surgery



At Risk	0	10	20	30	40	50	60	70
Transplant	877	626	358	172	71	25	5	0
Resection	20	19	17	12	9	5	1	1
No surgery	86	81	59	39	26	13	8	0

BREAKDOWN OF PATIENTS WITH SUBSEQUENT SURGERY

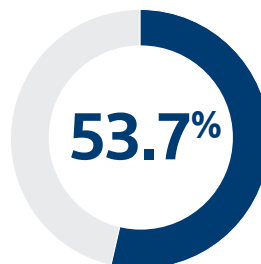


FAVORABLE SAFETY PROFILE

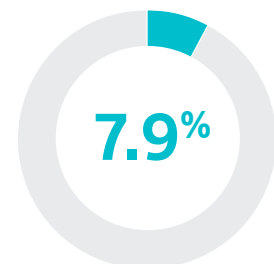
Therasphere Y-90 preserved liver function, supporting eligibility for future treatments



Preserved Hepatic Function
>95% of patients had no liver decompensation at 12 months (n = 243)



Subsequent Treatments
53.7% of patients received surgery, locoregional, or systemic therapy



Low Adverse Event Rate
7.9% of patients had related grade ≥ 3 AEs

PATIENT DEMOGRAPHICS & DISEASE CHARACTERISTICS

Variable	N (%)
Age, median (years)	71.0
≥ 18 to < 65	260 (26.3)
≥ 65 to < 75	401 (40.5)
≥ 75	328 (33.2)
Gender¹	
Male	889 (89.9)
Female	100 (10.1)
Child-Pugh¹	
A5/A6	618 (62.5) / 190 (19.2)
B7	47 (4.8)
>B7	21 (2.1)
Unknown/Missing	113 (11.4)
ALBI Grade¹	
1	380 (38.4)
2 / 3	440 (44.5) / 15 (1.5)
Unknown/Missing	154 (15.6)
ECOG¹	
0	568 (57.4)
>0	349 (35.3)
Unknown/Missing	72 (7.3)

Variable	N (%)
Liver Status¹	
No history of liver disease	138 (14.0)
Liver cirrhosis	690 (69.8)
Liver fibrosis	108 (10.9)
Unknown/Missing	53 (5.4)
Disease Extent¹	
Unilobar	763 (77.1)
Bilobar	184 (18.6)
Unknown/Missing	42 (4.2)
Disease Etiology^{1,4} (top 5)	
Alcohol	470 (47.5)
Hepatitis B / C	67 (6.8) / 178 (18.0)
No underlying disease	168 (17.0)
Metabolic / MASH	120 (12.1) / 108 (10.9)
Extrahepatic Disease¹	
Yes	45 (4.6)
No	907 (91.7)
Missing or not assessed	37 (3.7)

Variable	N (%)
BCLC Stage	
A	132 (13.3)
B	187 (18.9)
C	573 (57.9)
D	57 (5.8)
Unknown/Missing	40 (4.0)
Number of Lesions³	
1	485 (49.0)
>1	484 (48.9)
Unknown/Missing	20 (2.0)
Index Lesion Diameter³ (mRECIST)	
Median size, cm (IQR)	6.80 (4.6 – 9.0)
≤ 5 cm / > 5 cm	294 (31.8) / 631 (68.2)
≤ 7 cm / > 7 cm	517 (55.9) / 408 (44.1)
Unknown/Missing	64 (6.5)
PVT^{3*}	
Yes	349 (35.3)
Vp1	75 (21.5)
Vp2	104 (29.8)
Vp3	138 (39.5)
Vp4	32 (9.2)
No	623 (63.0)
Unknown/Missing	17 (1.7)

Abbreviations: ALBI, albumin-bilirubin; BCLC, Barcelona Clinic Liver Cancer; ECOG, Eastern Cooperative Oncology Group; IQR, interquartile range; MASH, metabolic dysfunction-associated steatohepatitis; mRECIST, modified Response Evaluation Criteria in Solid Tumors; PVT, portal vein thrombosis. 1. Assessment by investigator. 2. Programmatically derived using data entered by investigator. 3. Assessment by central review. 4. Patients may have had more than one.

CONCLUSION

PROACTIF, the largest, prospective, real-world Y-90 study, demonstrated favorable effectiveness and safety of TheraSphere Y-90 in HCC, with robust 5-year outcomes in an all-comers population. The study reflects clinical practice complexity, with 76.8% of patients presenting with intermediate or advanced disease, 35.3% with PVT, and a median tumor size of 6.8 cm.

Outcomes were strongest in patients achieving higher absorbed doses (≥400 Gy) and in those downstaged to surgery, including PVT. These findings underscore the importance of patient selection and personalized dosimetry, and establish TheraSphere as the first and only Y-90 technology supported by this level of prospective real-world evidence.

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Results from studies conducted using TheraSphere should not be assumed to apply to other products.

1. Lam, M., Garin, E., Maccauro, M. et al. A global evaluation of advanced dosimetry in transarterial radioembolization of hepatocellular carcinoma with Yttrium-90: the TARGET study. *Eur J Nucl Med Mol Imaging* 49, 3340–3352 (2022). <https://doi.org/10.1007/s00259-022-05774-0>; Garin E, Tselikas L, Guiu B, et al. Personalised versus standard dosimetry approach of selective internal radiation therapy in patients with locally advanced hepatocellular carcinoma (DOSISPHERE-01): a randomized, multicentre, open-label phase 2 trial. *Lancet Gastroenterol Hepatol* 2021; Choi JW, Suh M, Choi Y, Lee M, Paeng JC, Kim HC. Yttrium-90 glass microsphere radioembolization as frontline treatment for hepatocellular carcinoma with localized portal vein invasion. *Eur Radiol* 2025

Guiu B, Bailly C, Vibert E et al. Effectiveness and safety of selective internal radiation therapy using yttrium-90 glass microspheres for hepatocellular carcinoma: real-world results from the multi-center prospective PROACTIF cohort of 989 patients. *eClinicalMedicine*, 2026; 95.



TheraSphere™ Y-90 Glass Microspheres Indications, Safety, and Warnings

<https://www.bostonscientific.com/therasphere-indications>



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