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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

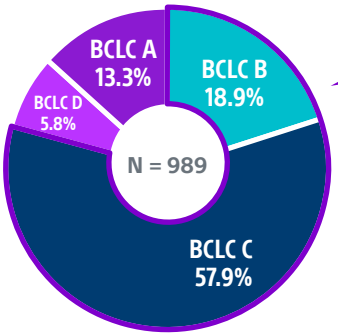
1,259 total patient population
(HCC, ICC, mCRC)

34 sites
All-comers over 5 years

FULL HCC ANALYSIS - 989 PATIENTS ACROSS 34 SITES

REPRESENTATIVE OF REAL-WORLD CLINICAL COMPLEXITY

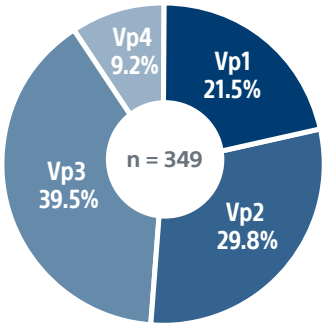
BCLC Stage Distribution



77% Intermediate or advanced stage patients

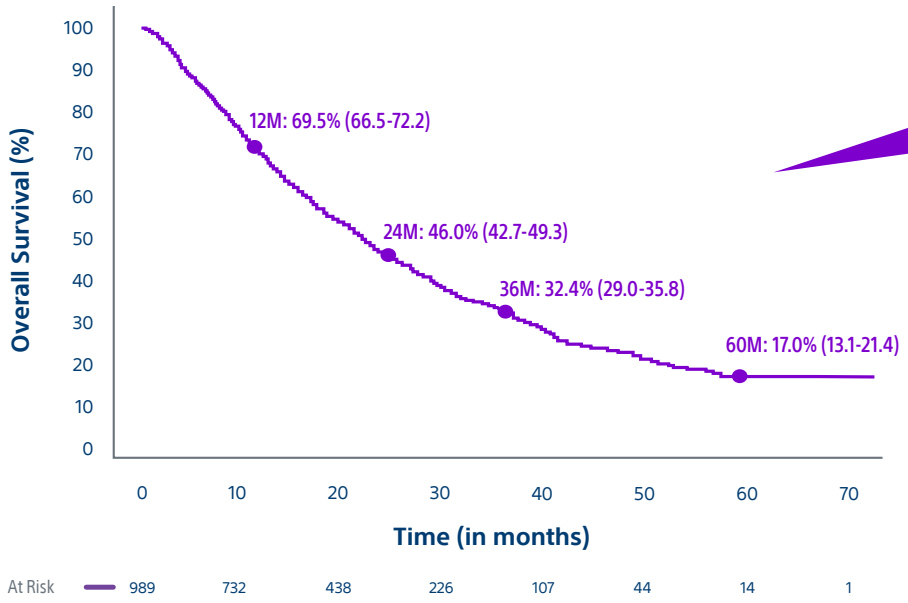
35% Patients with PVT*

PVT Patients



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)

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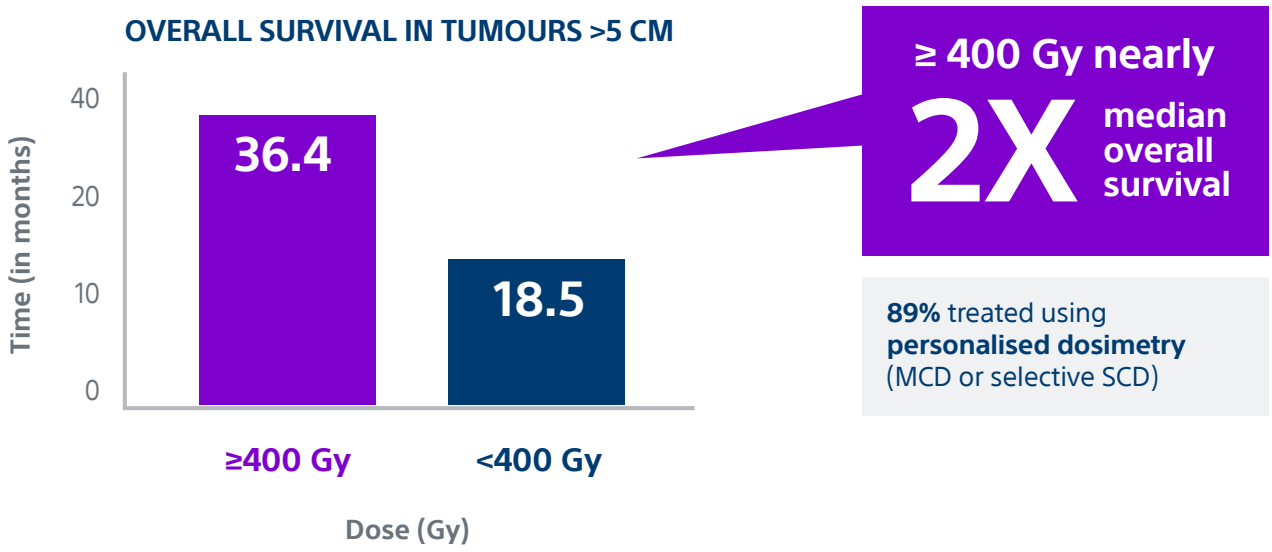
DOSE MATTERS EVEN IN LARGE TUMOURS

OPTIMISING DOSE IMPROVES SURVIVAL IN LARGE TUMOURS

A ≥400 Gy tumour absorbed dose significantly improved survival in lesions >5 cm (n = 631) (36.4 vs. 18.5 months; p<0.001), consistent with prior TheraSphere studies[1]



≥ 400 Gy nearly 2X median overall survival

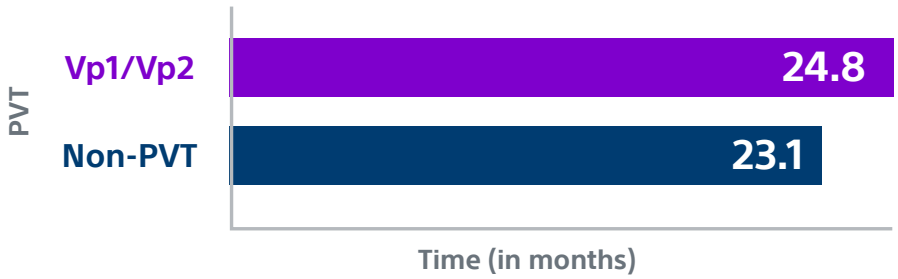
89% treated using **personalised dosimetry** (MCD or selective SCD)

6.8 cm Median tumour size

68.2% Patients with solitary tumours >5 cm

SIGNIFICANT SURVIVAL IN LOCALISED PVT

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



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

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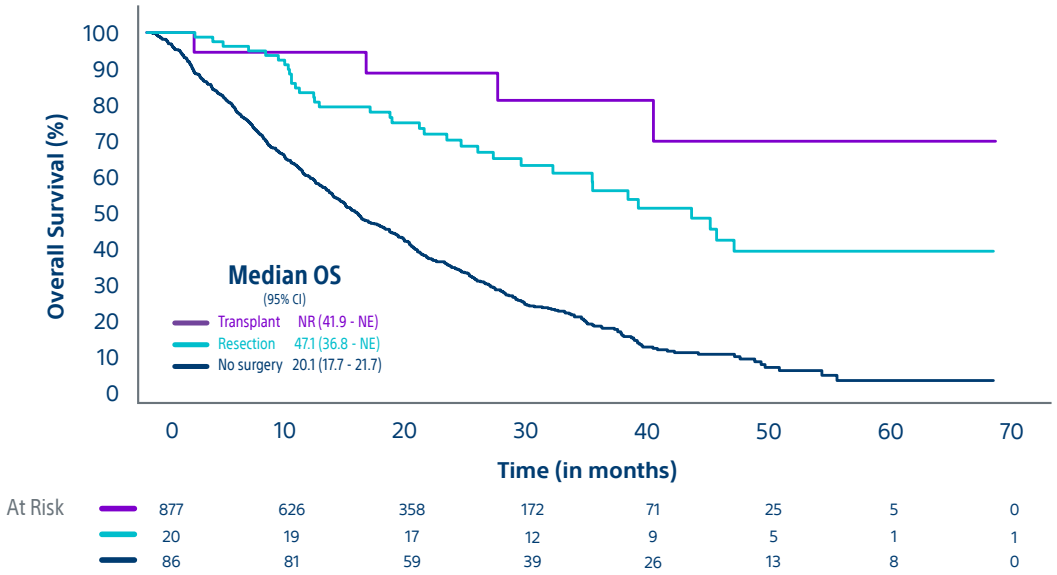
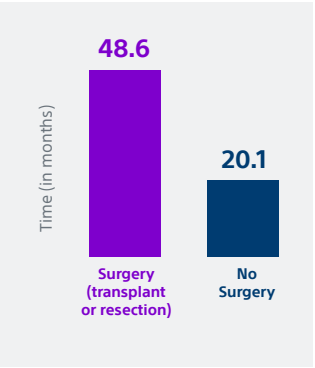
UNLOCKING CURATIVE POTENTIAL AND PRESERVING SURGICAL ELIGIBILITY

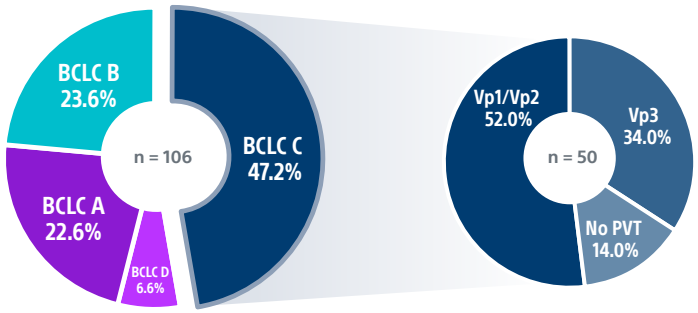
THERASPHERE PATIENTS SUCCESSFULLY DOWNSTAGED TO CURATIVE-INTENT SURGERY, WITH MEANINGFUL SURVIVAL BENEFIT



MEDIAN OVERALL SURVIVAL MORE THAN 2X with subsequent surgery

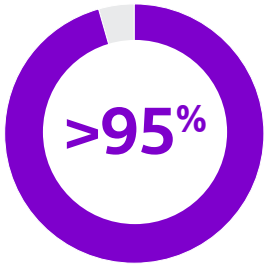


BREAKDOWN OF PATIENTS WITH SUBSEQUENT SURGERY

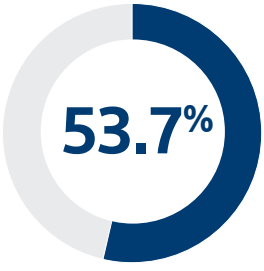


FAVORABLE SAFETY PROFILE

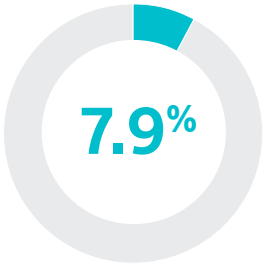
TheraSphere Y-90 preserved liver function, supporting eligibility for future treatments



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)
Gender[1]	
Male	**889 (89.9)**
Female	100 (10.1)
Child-Pugh[1]	
A5/A6	**618 (62.5) / 190 (19.2)**
B7	47 (4.8)
>B7	21 (2.1)
Unknown/Missing	113 (11.4)
ALBI Grade[1]	
1	380 (38.4)
2 / 3	440 (44.5) / 15 (1.5)
Unknown/Missing	154 (15.6)
ECOG[1]	
0	568 (57.4)
>0	349 (35.3)
Unknown/Missing	72 (7.3)

Variable	N (%)
Liver Status[1]	
No history of liver disease	138 (14.0)
Liver cirrhosis	**690 (69.8)**
Liver fibrosis	108 (10.9)
Unknown/Missing	53 (5.4)
Disease Extent[1]	
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 Disease[1]	
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 Lesions[3]	
1	485 (49.0)
>1	**484 (48.9)**
Unknown/Missing	20 (2.0)
Index Lesion Diameter[3] (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 personalised 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.

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PI-2474406-AA
CE 0123