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THERASPHERE™ Y-90 Glass Microspheres | DOSISPHERE-01 Trial

Level I randomised trial showed that unresectable HCC patients who receive a personalised TheraSphere dose using multicompartment dosimetry had a median OS of 26.6 months– a 16-month improvement compared to the control arm.

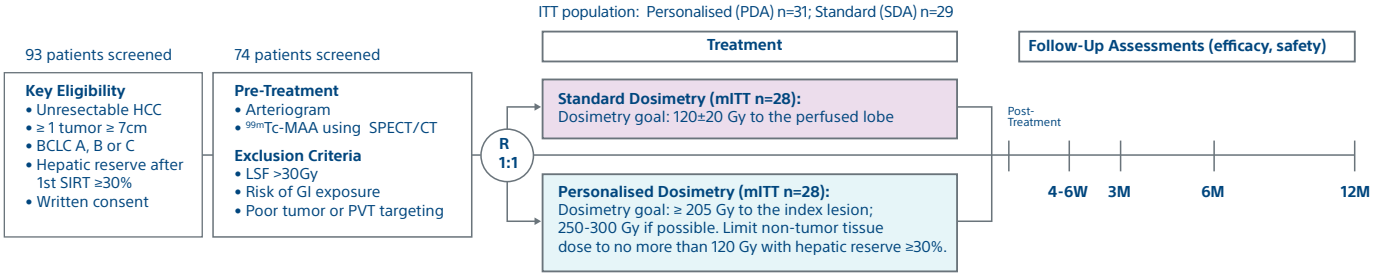
Garin E, Tselikas L, Guiu B et al. Personalized versus standard dosimetry approach of selective internal radiation therapy in patients with locally advanced hepatocellular carcinoma (DOSISPHERE-01): a randomised, multicentre, open-label phase 2 trial. Lancet Gastroenterol Hepatol. 2021, 6: 17-29

"Personalised dosimetry is safe and leads to a meaningful improvement in the objective response rate and overall survival of patients with locally intermediate/advanced hepatocellular carcinoma [...] when compared with standard dosimetry."

STUDY OBJECTIVE

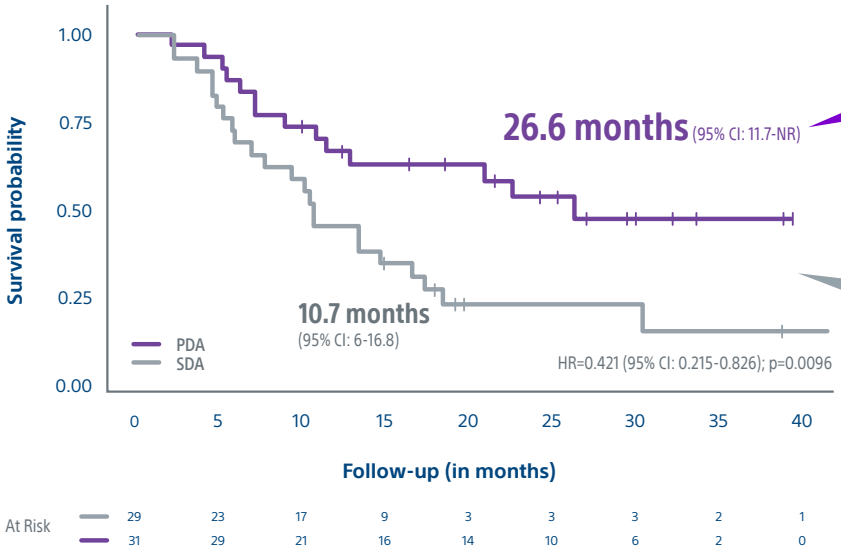
A **randomised, multicenter,** investigator sponsored phase II trial comparing the clinical outcomes of SIRT with TheraSphere in patients with intermediate/advanced HCC using two pre-treatment dosimetry determination methods: (1) Standard, single-compartment dosimetry (SDA); defined as a uniform distribution of absorbed dose within the perfused volume – both tumor and normal liver or (2) Personalised (PDA); defined as multi-compartment Y-90 distribution of absorbed dose within the perfused volume that accounts for preferential blood flow into the tumor compared with normal parenchyma.

STUDY DESIGN



KEY RESULTS: PERSONALISED DOSIMETRY IMPROVED SURVIVAL

MEDIAN OVERALL SURVIVAL (ITT POPULATION)



16 Month

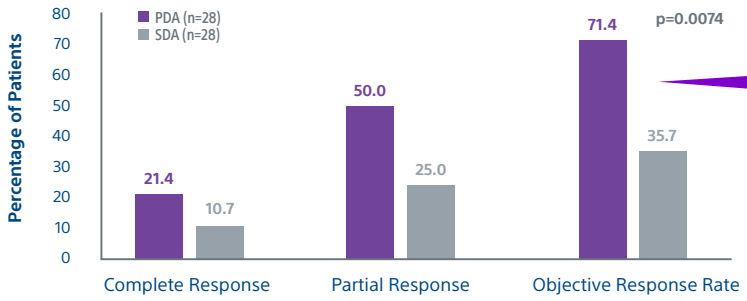
Survival Improvement
(personalised vs. standard dosimetry)

22.9 Month

Median Overall Survival for PVT patients in personalised arm vs. 9.5 months in standard arm

PERSONALISED DOSIMETRY IMPROVED RESPONSE

INDEX LESION RESPONSE RATE AT 3 MONTHS USING EASL IN THE MITT POPULATION



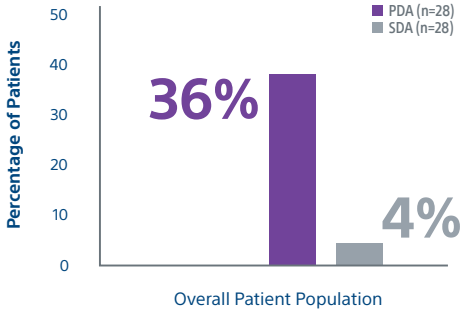
PRIMARY STUDY ENDPOINT

71.4%

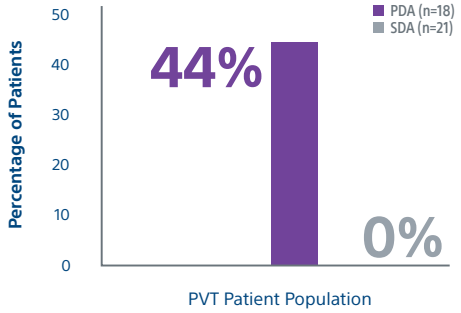
Objective Response Rate (personalised vs. 35.7% in standard dosimetry)

PERSONALISED DOSIMETRY DOWNSTAGED MORE PATIENTS TO SURGERY

PATIENTS SUCCESSFULLY DOWNSTAGED TO SURGERY



36% of patients in the personalised arm were downstaged vs. 4% in the standardised arm



44% of PVT patients in the personalised arm were downstaged vs. 0% in the standardised arm

DOSISPHERE-01 EDITORIAL:

"The DOSISPHERE-01 Study challenges the evolving narrative that patients with advanced hepatocellular carcinoma should have systemic therapy at the expense of locoregional therapy. [...] Personalised dosimetry (ie, reaching specific threshold radiation doses) is a natural evolution of selective internal radiation therapy with ^{90}Y-labelled microspheres."[3]

– Robert J Lewandowski, MD, Riad Salem, MD, DOSISPHERE Editorial, Lancet Gastroenterology & Hepatology

1. Reasons for censoring: received another anti-cancer treatment before M3 evaluation (n=2), no evaluation at M3 evaluation (n=1) (10.7%)
2. Reasons for censoring: early deaths (before M3) (n=2), no evaluation at M3 (n=1), start another anti-cancer treatment before M3 evaluation (n=1) (14.3%)
3. Lewandowski, Robert J, Salem, Riad. Radioembolisation with personalised dosimetry: improving outcomes for patients with advanced hepatocellular carcinoma. Lancet Gastroenterol Hepatol 2020; Published Online: November 06, 2020 https://doi.org/10.1016/S2468-1253(20)30306-X

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PATIENT DEMOGRAPHICS (mITT population)

Parameter	PDA (n=28)	SDA (n=28)
Male (%)	92.9	92.9
Child-Pugh Status (%)	CP A5: 78.6 CP A6/B7: 21.4	CP A5: 78.6 CP A6/B7: 21.4
BCLC (%)	BCLC B = 11 BCLC C = 89	BCLC B = 7 BCLC C = 93
Bilobar (%)	43	57
Mean Total Bilirubin (µM/L±SD)	14.0±6.4	14.3±6.4
PVT present (%)	64.3	75.0
PVT Location (%)	Segmental 29.6 Main/Lobar 30/33	Segmental 32.1 Main/Lobar 32/43
Index lesion (mean, cm)	10.5±2.4	10.9±2.57

TREATMENT CHARACTERISTICS AND DOSIMETRY (mITT population)

Investigator Assessments	PDA (n=28)	SDA (n=28)	*P* value
Number of Y-90 glass microspheres treatment	One treatment, n=26 Two treatments, n=2	One treatment, n=23 Two treatments, n=5	ns (*not significant*)
Activity administered GBq (mean, min-max)	3.6 (2.4-4.8)	2.6 (2.2-3.0)	0.0049
AD* to perfused liver (Gy) Mean (±SD)	178.4±59.9	120.3±15.2	0.0001
% of patients with AD to perfused liver> 150 Gy	68	4	<0.0001
AD to index lesion (Gy) Mean (±SD)	331.1±131.5	221.3±139.4	0.0007
% of patients with AD to index lesion > 205 Gy	88	38	<0.0008
AD to perfused normal tissue (Gy) Mean (±SD)	92.8±30.1	64.5±36.6	0.007

*AD=absorbed dose

LIVER ADVERSE EVENTS (Grade ≥3) Related to Y-90*

	PDA (n=35)	SDA (n=21)
Patients with ≥ 1 AE	3 (8.6%)	3 (14.3%)
Death	1 (2.8%)	1 (4.7%)
Liver AEs	4 (11.4%)	5 (23.8%)
Ascites	1	1
Encephalopathy	0	0
GI hemorrhage	0	2
Bilirubin increase/jaundice	1	2
Hepatic failure	2	0

*patients allocated to either PDA or SDA based on treatment received (dose received) versus allocation by randomisation

Note: Dose to the liver does not exceed 150 Gy. The physician should always take the above-noted Pre-treatment High Risk Factors into consideration for each patient when making decisions regarding the use of TheraSphere for treatment.

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PI-931202-AB

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