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THERASPHERE™ Y-90 Glass Microspheres | LEGACY STUDY

A robust study confirming TheraSphere as a neoadjuvant or standalone therapy in treating HCC.

Salem R, Johnson GE, Kim E, Riaz A, Bishay V, Boucher E, Fowers K, Lewandowski R, Padia SA. Yttrium-90 Radioembolization for the Treatment of Solitary, Unresectable Hepatocellular Carcinoma: The LEGACY Study. Hepatology. 2021 Mar 19. doi: 10.1002/hep.31819.

STUDY OBJECTIVE

To assess local tumor control and duration of response following treatment with Y-90 glass microspheres in patients with unresectable solitary HCC lesions.

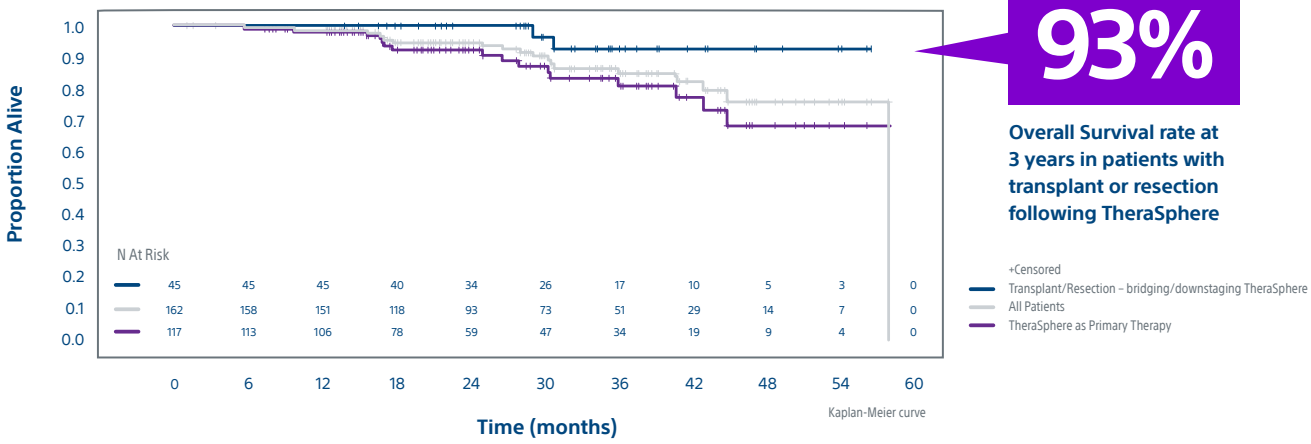
KEY RESULTS

100%

Patients in the LEGACY study responded to TheraSphere treatment(s)

- 96.8% with one TheraSphere treatment
- 100% with two TheraSphere treatments

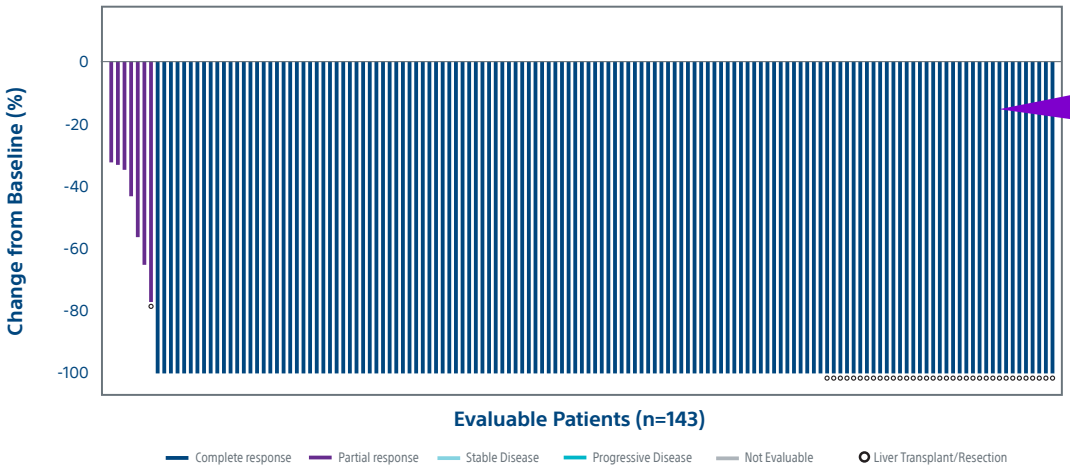
Overall Survival
(Treated Population)



93%

Overall Survival rate at 3 years in patients with transplant or resection following TheraSphere

Tumor Response
(Best Response in evaluable population, localized mRECIST)



88%

(95% CI: 82.4-92.4 N =162)

Demonstrated rate of best response by TheraSphere
(i.e. CR, PR) by localized mRECIST

- CR: 136 (84%)
- PR: 7 (4.3%)
- Transplanted or Resected n=36

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STUDY DESIGN

Multi-center, single-arm, retrospective study conducted at 3 U.S. sites.* Consecutive patients meeting the eligibility criteria were treated with TheraSphere Y-90 glass microspheres at each site between January 2014 and December 2017.

FIRST AND ONLY

- Used highly clinically relevant criteria for localized tumor control (mRECIST)
- Reported a median dose to perfused liver volume of 410 Gy
- Demonstrated 100% of patients achieved CR or PR (localized mRECIST)

KEY ELIGIBILITY CRITERIA

Unresectable solitary lesions (≤ 8 cm); Selective, lobar, or mixed administration of Y-90 glass microspheres (TheraSphere); Treatment purpose (neoadjuvant to transplantation or resection or stand-alone treatment); Child-Pugh score A; BCLC A or BCLC C (ECOG 1); No prior liver transplantation, resection, locoregional treatment or systemic therapy; No portal vein thrombosis or extrahepatic disease.

KEY BASELINE CHARACTERISTICS (N=162)

	% of patients		
Median Age: 66 years	≥ 75 years: **17.9**	BCLC A: **60.5**	BCLC C: **39.5**
Median Tumor Size: **2.6 cm (0.9-8.1 cm)**			

PRIMARY STUDY ENDPOINTS WERE MET

determined by Blinded Independent Central Review (BICR)

Objective Response Rate

72.2%[1]
(n=117/162)

Objective Response Rate (ORR) defined as CR or PR using localized mRECIST (defined as the response within the Y-90 glass microsphere treatment area) with confirmation of response (> 4weeks).

Duration of Response

76.1%[2]
(n=89/117)

(≥ 6 months)

Duration of Response[3] (DoR) using localized mRECIST

Safety: Majority of adverse events were mild and resolved without medical intervention

LEGACY STUDY CONCLUSION

LEGACY is the first multicenter study to report a high median perfused volume absorbed dose of 410 Gy with TheraSphere, which resulted in an 88% best response, excellent and durable tumor control and high overall survival rate in patients with early and advanced HCC.

HCC: hepatocellular carcinoma; BCLC: Barcelona Clinic Liver Cancer staging system; Y-90: Yttrium-90; Gy: Gray; IQR: Interquartile Range

*University of Washington, Seattle, WA; Northwestern University, Chicago, IL; Mount Sinai Health System, New York, NY
1. Complete Response (CR) and Partial Response (PR) within the treatment area according to localized mRECIST
2. Duration of Response (DoR) According to localized mRECIST
3. Median follow-up was 29.9 months [95% CI: 24.7, 34.6]

TheraSphere™ Yttrium-90 Glass Microspheres

INDICATION FOR USE: TheraSphere is indicated for use as selective internal radiation therapy (SIRT) for local tumor control of solitary tumors (1-8 cm in diameter), in patients with unresectable hepatocellular carcinoma (HCC), Child- Pugh Score A cirrhosis, well-compensated liver function, no macrovascular invasion, and good performance status. **CONTRAINDICATIONS:** TheraSphere is contraindicated in patients: whose Tc-99m macroaggregated albumin (MAA) hepatic arterial perfusion scintigraphy shows any deposition to the gastrointestinal tract that may not be corrected by angiographic techniques • who show shunting of blood to the lungs that could result in delivery of greater than 16.5 mCi (0.61 GBq) of Y-90 to the lungs. Radiation pneumonitis has been seen rarely in patients receiving doses to the lungs greater than 30 Gy in a single treatment. • in whom hepatic artery catheterization is contraindicated, such as patients with vascular abnormalities or bleeding diathesis • who have pulmonary insufficiency (conventionally defined by an arterial oxygen pressure (Pa,O2) of < 60 mmHg, or oxygen saturation (Sa,O2) of < 90%) or severe liver dysfunction, including hepatic encephalopathy, clinically evident ascites or treatment with diuretics for ascites • with portal vein thrombosis (PVT) Type 4 involvement and lack of Tc-99m MAA deposition on the PVT seen on the Tc-99m MAA imaging with >70% tumor replacement in the liver • with comorbidities or poor overall health (e.g., ECOG performance status rating > 2) which may make the patient a poor candidate for locoregional radiation treatment. • who are pregnant. **WARNINGS:** The following pre-treatment, high-risk factors (disease characteristics) have been associated with serious adverse events deemed possibly related to use of the device: infiltrative tumor type • tumor nodules too numerous to count • AST or ALT > 5 times ULN • bilirubin > 2 mg/dL • tumor volume > 50% combined with albumin < 3 g/dL. Keep the TheraSphere dose vial upright and stored in its lead pot before and during patient treatment, except as required for radiation measurement. Do not open the dose vial acrylic shield prior to patient treatment. Post-treatment, waste materials require caution to prevent contamination and beta shielding due to residual glass microspheres. **PRECAUTIONS:** GENERAL PRECAUTIONS: As in any intra-arterial procedure, aseptic technique should be practiced, and care should be taken to ensure minimum patient anesthesia exposure extraneous to therapeutic objective. • Consideration of patient comorbidities should be used when determining the type and volume of fluid to infuse via catheter to avoid electrolyte imbalance, fluid shift, and hyperglycemia. • It is important to avoid any aggressive arterial procedure that may lead to arterial spasm that impairs TheraSphere distribution into the perfused liver target volume which may lead to underdosing or non- target deposition of TheraSphere. PRECAUTION IN PATIENTS WITH IMPAIRED LIVER FUNCTION: No efficacy or safety data from the LEGACY study are available to support the use of the device in patients with Child-Pugh score B or C cirrhosis. PRECAUTION IN VULNERABLE PATIENTS: No effectiveness or safety data are available to support the use of the device in children or breast- feeding women. ENDOCRINE DISRUPTION, CARCINOGENICITY, MUTAGENICITY, TOXICITY TO REPRODUCTION: Ideally the use of this radioactive device in women of childbearing capability should be performed during the first few (approximately 10) days following the onset of menses. RADIATION SAFETY: Radioactive products should be used only by healthcare professionals who are qualified by specific training in the safe use and handling of radionuclides and whose experience and training have been approved by the appropriate government agency authorized to license the use of radionuclides. • As in the use of any radioactive material, ensure minimum radiation exposure to the patient extraneous to the therapeutic objective, and to minimize radiation exposure to workers and others in contact with the patient. RELEASE AND POST-TREATMENT PRECAUTIONS: Post treatment patient care: use universal precautions for body fluid contact. Trace Y-90 may be detectible in blood and urine; handle with gloves and dispose as normal body fluids. The radiation field is expected to be less than 1 mrem/h (10 μSv/h) at 3 ft (1 m) from the patient's abdomen. Supplemental shielding and segregation of the patient are not required to maintain exposure to others below regulated limits. • Release instructions: The patient should follow good hygiene (e.g., proper hand washing). Caregivers, family, and others do not require restrictions on patient contact; however, they can minimize their radiation exposure by avoiding prolonged time (>12 hours per day) within 1 ft (0.3 m) of the patient's abdomen for the first week post therapy. Patients should be advised that radiation emitted from the patient may be detectible at security screening (e.g., international travel). • Special precautions post-administration: If the patient requires hospitalization, surgery, medical assessment or treatment regarding any part of their thorax or abdomen within first 2 weeks of treatment, the patient should advise the hospital and treating physician of the Y-90 TheraSphere implant. The physician should consult their radiation safety staff for handling and disposal of liver tissue. • Special liver tissue handling: Special liver tissue handling may be required for post-treatment surgery, explant, or transplant since the glass microspheres remain permanently implanted in the liver tissue. Disclosure of the treatment will be required if cremation is considered. **POTENTIAL ADVERSE EVENTS:** The use of this product leads to irradiation of both tumorous and normal liver tissue. As a result, patients with compromised liver function may be at greater risk of liver function impairment and hence could experience complications. Clinical side effects usually occur within the first 4 to 6 weeks after treatment. Based on clinical trial data, literature reviews and post market surveillance, adverse events potentially associated with treatment using Y-90 microspheres, including TheraSphere, may include the following: Allergic reaction • Altered liver function, acute or chronic • Anorexia • Anxiety • Ascites • Bile Duct injury • Bleeding/hemorrhage • Chills / rigors • Cholecystitis (inflammatory or infectious) • Colitis • Death • Dehydration • Diarrhea • Dizziness • Dyspnea • Edema (any location) • Electrolyte abnormalities • Elevated BUN/creatinine • Fall • Fatigue • Fever • Gastrointestinal bleeding / hemorrhage • Gastrointestinal ulcer or ulceration • Hepatic encephalopathy • Hepatorenal failure • Hiccups • Hypertension • Hypotension • Infection (any location) • Liver failure, acute or chronic • Lymphopenia • Malaise • Mood alteration • Muscle weakness • Nausea • Neutropenia • Pain (any location) • Pancreatitis • Platelet count abnormalities • Pleural effusion • Portal hypertension • Pre-existing chronic liver disease decompensation • Pulmonary edema • Pulmonary fibrosis • Radiation hepatitis • Radiation induced disease, acute • Radio Embolization Induced Liver Disease (REILD) • Sepsis • Supraventricular arrhythmia • Thrombosis (arterial or venous) • Tumor inflammation (including tumor edema) • Tumor-lysis syndrome • Vomiting • Weight loss. Complications related to the administration procedure itself may include: Allergic reaction: Arterial injury including vessel dissection • Aspiration pneumonia • Bruising/ bleeding/hematoma at site • Constipation/abdominal distension • Fatigue • Flushing • Infection • Nausea • Nerve damage. **CAUTION:** Federal (USA) law restricts this device to sale by or on order of a physician. PI-992004-AA. **Note:** Dose to the liver does not exceed 150 Gy.

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To order product or for more information contact customer service at 1.888.272.1001.

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