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THERASPHERE™ Y-90 Glass Microspheres | **PUBLICATION SUMMARY**

Y-90 Radioembolization Significantly Prolongs Time to Progression Compared with Chemoembolization in Patients with Hepatocellular Carcinoma

Gastroenterology. 2016 Dec;151(6):1155-1163.e2. doi: 10.1053/j.gastro.2016.08.029. Epub 2016 Aug 27.
Salem R, Gordon AC, Mouli S, Hickey R, Kallini J, Gabr A, Mulcahy MF, Baker T, Abecassis M, Miller F, Yaghmai V, Sato K, Desai K, Thornburg B, Benson AB, Rademaker A, Ganger D, Kulik L and Lewandowski RJ

OVERVIEW

Upon initial diagnosis, patients with HCC are frequently ineligible for curative options – transplant or surgical resection

- Locoregional therapies (ablation, cTACE, Y-90 radioembolization) can be applied to HCC patients deemed ineligible for curative options per the published guidelines[1,2]
- Ablation is commonly recommended for early-stage HCC, however, when contraindications to ablation exist, cTACE is typically determined to be the next best therapy and is considered standard-of-care for intermediate-stage HCC
- In this study, Y-90 radioembolization increased time to progression (TTP)[3], improved quality of life[4], served a neoadjuvant role prior to resection[5-7] and offered high tumor control in select patients with portal vein invasion[8]

OBJECTIVES

- Experts have strongly advocated for randomized trials that study cTACE versus Y-90 therapy
- The objective of this study was to compare cTACE versus Y-90 radioembolization in a prospective, randomized, phase II setting for the treatment of unresectable, unablatable HCC
- The primary endpoint of this study was TTP and the secondary endpoints included safety, response rate and overall survival
- The investigators hypothesized Y-90 would prolong TTP when compared to cTACE

METHODS

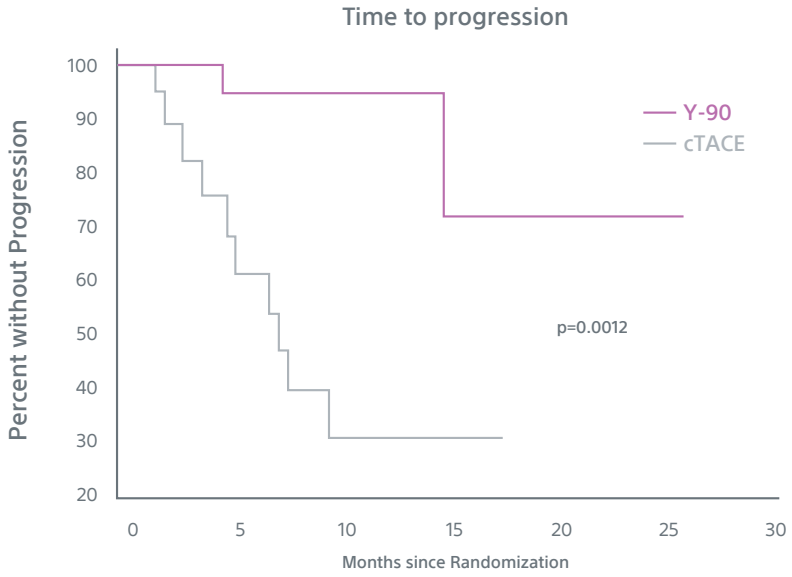
- Open label, single-center study that lasted from 2009-2015 [n= 45 randomized 1:1 to cTACE (n = 21) or Y-90 (n = 24)]
  - Inclusion criteria: image/biopsy confirmed HCC, unablatable/unresectable disease with no vascular invasion, Child Pugh A/B and bilirubin ≤ 2.0 mg/dl and AST/ALT ≤ 5x upper limit of normal
  - BCLC A patients not eligible for ablation or resection due to lesion size/location, liver function, multifocal disease, or presence of portal hypertension
  - BCLC B patients were considered eligible for cTACE or Y-90 with post-treatment intent of liver transplantation

TREATMENT ARMS	
cTACE	**Y-90 Radioembolization**
• 75 mg/m2 dose of drug/lipiodol combination followed by embolic microspheres • Patients admitted for 24-48 hour observation	• Glass microspheres • Dose = 120 Gy • Outpatient treatment

RESULTS

- > 50% of all patients exhibited solitary lesions; selective treatment delivery was performed in 16 cTACE patients and 17 patients Y-90 patients
- Three cTACE patients experienced grade 3+ toxicities (hyperbilirubinemia, abdominal pain from progress and sepsis) and four Y-90 patients experienced delayed grade 3+ toxicities (ascites and bacterial peritonitis)

TTP	Imaging Response
Median TTP was significantly longer for the Y-90 group: 6.8 months for cTACE vs. not reached for Y-90 (>26 months), p=0.0012	Response rates were similar for both groups: – WHO Criteria: 63% (n=12) and 52% (n=12) for cTACE and Y-90, respectively – EASL Criteria: 74% (n=14) and 87% (n=20) for cTACE and Y-90, respectively
Overall Survival	**Bridge to Transplant**
OS was similar for both groups: – Median OS (censored to liver transplantation) was 17.7 months and 18.6 months for cTACE and Y-90, respectively	More patients in the Y-90 group (87%, n=13) were bridged to transplant as compared to the cTACE group (70%, n=7)



CONCLUSION

- This study showed Y-90 significantly increased time to progression compared with cTACE for early to intermediate stage HCC patients
- While longer TTP did not translate to increased overall survival, improved tumor control could potentially reduce dropout from transplant waitlists and increase bridging to transplantation
- Study Strengths: Randomized design, comprehensive imaging review, real-world clinically relevant patient flow of unablatable BCLC A/B patients
- Study Limitations: Required censoring of imaging/survival to transplant, difficulty in enrollment, patient compliance with follow-up and imaging

cTACE= conventional transarterial chemoembolization ; TTP= time to progression ; BCLC= Barcelona Clinic Liver Classification ; WHO= World Health Organization ; EASL= European Association for the Study of the Liver ; OS= overall survival

1. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines). Hepatobiliary Cancers. 2016 **2.** EASL-EORTC clinical practice guidelines: management of hepatocellular carcinoma. J Hepatol. 2012; 56:908–43. **3.** Salem R, Lewandowski RJ, Kulik L, et al. Radioembolization results in longer time-to-progression and reduced toxicity compared with chemoembolization in patients with hepatocellular carcinoma. Gastroenterology. 2011; 140:497-507.e2. **4.** Salem R, Miller FH, Yaghmai V, et al. Response assessment methodologies in hepatocellular carcinoma: complexities in the era of local and systemic treatments. J Hepatol. 2013; 58:1260-2. **5.** Gaba RC, Lewandowski RJ, Kulik LM, et al. Radiation lobectomy: preliminary findings of hepatic volumetric response to lobar yttrium-90 radioembolization. Ann Surg Oncol. 2009; 16:1587-96. **6.** Vouche M, Lewandowski RJ, Atassi R, et al. Radiation lobectomy: time-dependent analysis of future liver remnant volume in unresectable liver cancer as a bridge to resection. J Hepatol. 2013; 59:1029-36. **7.** Gabr A, Kallini JR, Gates VL, et al. Same-day 90Y radioembolization: implementing a new treatment paradigm. Eur J Nucl Med Mol Imaging. 2016. 8. Kulik LM, Carr BI, Mulcahy MF, et al. Safety and efficacy of 90Y radiotherapy for hepatocellular carcinoma with and without portal vein thrombosis. Hepatology. 2008; 47:71-81.

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