Publication Summary

Institutional Decision to Adopt Y90 as A Primary Treatment for HCC Informed by a 1000-Patient 15-Year Experience

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OVERVIEW

- Locoregional (LRT) therapies such as ablation, TACE and TARE with Yttrium-90 (^{90}Y) are treatment options for HCC patients who are not eligible for curative resection or outside transplant criteria[1,2]
- TARE has become an increasingly accepted alternative to TACE. TARE with ^{90}Y glass microspheres has shown versatile treatment application and acceptable outcomes across all BCLC disease stages:
  - BCLC A (early stage): successful downstaging of tumors to liver transplant, hypertrophy of the future liver remnant for potential resection, treats recurrences following resection, significantly prolongs time to progression compared with TACE and represents an alternative to ablation for unablatable lesions[3-6]
  - BCLC B: comparable survival yet superior quality of life compared to TACE[7,8]
  - BCLC C: applicable in patients with portal vein thrombosis, minimizing the risk of ischemic hepatitis[9]

OBJECTIVES

- To report data from an institution's 15-year, 1000-patient experience that led to an institutional decision to adopt ^{90}Y TARE as the primary transarterial locoregional treatment for HCC

METHODS

- From 2003 to 2017, 1,000 HCC patients were treated with ^{90}Y glass microspheres as part of a prospective cohort study (the largest single-center cohort conducted) with 1,577 total treatments (median: 1, range: 1-8)
- Standard pre-treatment angiography and Tc-99m MAA were performed
- Target dose was 120 Gy for lobar infusions, however practice evolved with the application of radiation segmentectomy and lobectomy and target doses were modified to >190 Gy (potentially curative ablative dose) and 150 Gy, respectively
- Median dose per treatment was 119 Gy
- Follow-up included 4 to 6 week post-treatment scans and then subsequently at 2 to 3 month intervals
- Overall survival (OS) outcomes were reported using censoring and intention-to-treat (ITT) methodologies

Baseline characteristics	
ECOG	0 (56%); 1 (40%); 2 (4%)
Child-Pugh	A (51%); B (45%); C (4%)
BCLC	A (26%); B (15%); C (54%); D (4%)

RESULTS

- Survival for BCLC stages A–C patients treated with ^{90}Y (47, 25 and 15 months, respectively) compared favorably with survival expectations of BCLC A (36–50 months), BCLC B (18–26 months) and BCLC C (11 months) cited by EASL-EORTC guidelines
- Properly selected BCLC D patients may benefit from selective ^{90}Y glass therapy followed by liver transplantation
- Overall, 49 (5%) patients developed new grade 3/4 albumin toxicities and 110 (11%) showed grade 3/4 bilirubin toxicities for all Child-Pugh classes
- No patient developed radiation pneumonitis or gastritis

BCLC Stage	Child-Pugh (CP) score	Median OS [Censored] (months)	P-value	Median OS [ITT] (months)	P-value
A	CP A	47.3	<0.0001	102	0.005
	CP B	27		38	
B	CP A	25	0.037	30	0.2
	CP B	15		16	
C	CP A	15	<0.0001	16.6	<0.0001
	CP B	8		8.4	
D	C (non-transplanted)	4.6	–	–	–
	C (transplanted)	–		92% (n=14) alive at 5 years	

- Multivariate models confirmed baseline bilirubin, albumin, ascites, vascular invasion, metastases, distribution, performance status, alpha-fetoprotein (AFP) <100 and index tumor < 5 cm to be significant predictors of survival
- Survival was not affected by hepatitis C virus status
- Overall cohort mortality within 30 days of treatment was 1.6% (n=16)

CONCLUSION

- Northwestern University adopted ^{90}Y glass microsphere therapy as their first line transarterial locoregional therapy for liver-only HCC compared to TACE because it allows for fewer treatments, longer time to progression and has demonstrated versatile application as a neoadjuvant to surgical intervention or definitive treatment in all BCLC and Child-Pugh stages
- Their decision was informed by prospectively collected and incrementally reported outcomes over 15 years
- Moving ^{90}Y earlier in the disease care continuum may improve overall HCC outcomes
- *Study Strengths*: Largest single-center prospective cohort of HCC patients treated with ^{90}Y glass microspheres, sample size and follow-up permitted meaningful analyses that compensate for heterogeneity of lesion size and liver function
- *Study Limitations*: Single-center study, overestimation of survival in advanced HCC attributed by ECOG 1

TACE= transarterial chemoembolization ; TARE= transarterial radioembolization ; HCC= hepatocellular carcinoma ; BCLC= Barcelona Clinic Liver Classification ;
ECOG= Eastern Cooperative Oncology Group ; EASL= European Association for the Study of the Liver ; EORTC= European Organization for Research and Treatment of Cancer

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