Top Recent Papers in Interventional Oncology

An overview of significant interventional oncology articles published in the recent literature and summaries of the potential impact each may have on the field.

By Eric Wehrenberg-Klee, MD, and Suvranu Ganguli, MD, FSIR

Radioembolization With Chemotherapy for Colorectal Liver Metastases: A Randomized, Open-Label, International, Multicenter, Phase III Trial (EPOCH)

Mulcahy MF, Mahvash A, Pracht M, et al; EPOCH Investigators. J Clin Oncol. 2021;39:3897-3907. doi: 10.1200/JCO.21.01839

SUMMARY

In this randomized, open-label, international, multicenter, phase 3 study, patients with unresectable colorectal liver metastases (CLM) planned for standard second-line chemotherapy (either oxaliplatin or irinotecan based) were additionally randomized to receive either radioembolization with yttrium-90 (Y-90) glass microspheres or the control (chemotherapy alone). Of the 428 patients randomized, 87% in the radioembolization arm received radioembolization plus chemotherapy and 90% in the control arm received chemotherapy alone. Both groups received the same chemotherapy intensity. The overall response rate (ORR) was 34% in the radioembolization arm versus 21% in the control arm. Median progression-free survival (PFS) was 8 versus 7.2 months, and hepatic PFS (hPFS) was 9.1 versus 7.2 months (all comparisons were statistically significant). However, there was no difference in the median overall survival (OS) between the two treatment arms (14 vs 14.4 months). The radioembolization arm was associated with increased toxicity, with a 68.4% rate of grade 3 adverse events compared with 49.3% and an increased incidence of neutropenia and anemia relative to chemotherapy alone.

WHY THIS ARTICLE IS IMPORTANT

This large randomized study demonstrated improvement in hPFS and PFS in the second-line setting with the addition of radioembolization compared with standard second-line chemotherapy, but it unfortunately did not show improvement in OS. Although, as the authors note, the study was not powered to do so. Clinically, the improvement in overall PFS would translate to a slight overall delay in the initiation of subsequent lines of therapy for patients, at the risk of some increased toxicity. However, the perspective of the treating oncologist community, as reflected in a concurrently published editorial by Lentz and Messersmith,[1] does not favor the addition of radioembolization in the second-line setting based on these data. They argue that although the study was not powered to evaluate OS, the modest improvement in PFS suggests that OS would not significantly improve and that improvement in OS is the standard in the field.

The study authors note a variety of caveats in interpretation of the data that also represent future avenues of investigation. For example, certain subpopulations were identified that may respond better to the addition of radioembolization, including *KRAS* mutation tumors. Additionally, the protocol administrations were either lobar or whole liver, whereas radioembolization is increasingly applied in segmental or even more selective administrations, with delivery of much higher dose to tumor.

Survival and Toxicities After 90Y Transarterial Radioembolization of Metastatic Colorectal Cancer in the RESIN Registry

Emmons EC, Bishay S, Du L, et al. Radiology. Published online June 28, 2022. doi: 10.1148/radiol.220387

SUMMARY

The RESIN registry is a prospective, multicenter, observational registry study of resin Y-90 microspheres. A total of 498 patients were enrolled for the treatment of CLM. Radioembolization was used for first-line therapy in 74 (17%) patients, second-line therapy in 180 (41%) patients, and third-line or later therapy in 188 (43%) patients. Median PFS by line of therapy was 7.9, 10, and 5.9 months in the first line, second line, and salvage setting, respectively. Median OS was 15 months overall and 13.9, 17.4, and 12.5 months in the first line, second line, and salvage setting, respectively; however, it should also be noted that the 95% CIs overlapped for all three lines of therapy.

WHY THIS ARTICLE IS IMPORTANT

The RESIN registry provides valuable information on real-world use of resin Y-90 microspheres and helps better define which subpopulations will derive the most benefit. Important findings include that OS was 16.2 months in patients without extrahepatic disease, whereas it was 12.6 months with disease outside the liver. There were statistically more grade 3 bilirubin elevations among patients receiving radioembolization in the salvage setting. With the release of two studies that include data on Y-90 devices in second-line CLM, it may be tempting to directly compare the results of glass and resin microspheres. However, we caution against making any such evaluation due to the differences in study methodologies and patient populations.

Pilot Study of Tremelimumab With and Without Cryoablation in Patients With Metastatic Renal Cell Carcinoma

Campbell MT, Matin SF, Tam AL, et al. Nat Commun. 2021;12:6375. doi: 10.1038/s41467-021-26415-4

SUMMARY

Authors investigated the treatment of metastatic renal cell carcinoma (mRCC) with tremelimumab (a cytotoxic T-lymphocyte–associated protein 4 [CTLA-4] inhibitor), with (n = 15) or without (n = 14) cryoablation. Metastatic lesions contributing to cancer-related symptoms (ie, pain) were selected, and metastatic lesions in the soft tissues, visceral organs, or bone were considered eligible for ablation. Immune monitoring analysis at baseline and posttreatment was performed. Patients with clear-cell histology only demonstrated increased immune cell infiltration and tertiary lymphoid structures within nonablated tumors posttreatment biopsy. There was no difference in response rate or survival between groups, although the study was not powered to show these differences. The rate of adverse events was not increased with cryoablation relative to tremelimumab alone.

WHY THIS ARTICLE IS IMPORTANT

The clinical outcomes of this study will not generate immediate impacts on clinical care. Cryoablation did not improve clinical outcomes relative to CTLA-4 inhibition with tremelimumab, and it should be noted that tremelimumab is not an approved therapy for the treatment of mRCC, and ipilimumab is only used in combination with nivolumab for the treatment of mRCC.

However, the correlative immune analyses do have significance for guiding future clinical evaluation of the role of cryoablation in stimulating an antitumoral immune response. Evaluating nonablated metastatic sites posttreatment, the authors found that within patients with clear-cell histology, there was a significant increase in density of CD8+ T cell infiltrate and CD20+ B cell infiltrate, as well as among markers of T cell activation. It is important clinical information that in the context of checkpoint inhibition, cryoablation can promote antitumoral systemic immunity. Inclusion of cryoablation with approved checkpoint inhibitor regimens for mRCC is of future clinical interest.

1. Lentz RW, Messersmith WA. Transarterial radioembolization in patients with unresectable colorectal cancer liver metastases. J Clin Oncol. 2021;39:3887-3889. doi: 10.1200/JCO.21.01993

Radioembolisation With Y90-Resin Microspheres Followed by Nivolumab for Advanced Hepatocellular Carcinoma (CA 209-678): A Single Arm, Single Centre, Phase 2 Trial

Tai D, Loke K, Gogna A, et al. Lancet Gastroenterol Hepatol. 2021;6:1025-1035. doi: 10.1016/S2468-1253(21)00305-8

SUMMARY

This single-center, open-label, single-arm clinical trial evaluated the combination of a checkpoint inhibitor with transarterial Y-90 radioembolization in advanced hepatocellular carcinoma (HCC). Eligible patients had Child-Pugh A liver disease, HCC not suitable for curative surgery, and a treatment plan in place for radioembolization. Radioembolization was performed with resin microspheres as a single administration using a variable-dose schema, followed by 240 mg of intravenous nivolumab at 21 days and then every 2 weeks thereafter. The primary endpoint was ORR, defined as the composite overall response observed for lesions both within and outside the radioembolization field per RECIST 1.1 (Response Evaluation Criteria in Solid Tumors, version 1.1), with a positive study defined as a 41% ORR. Among the 36 patients treated, 58% had chronic hepatitis B, 67% had Barcelona Clinic Liver Cancer stage C disease, 36% had extrahepatic spread, 44% had disease outside the radioembolization fields, and 42% had prior liver-directed therapy. The study did not meet its primary endpoint with an ORR of 30.6%. Of note, in the subset of patients with liver-confined disease, the ORR was 43.5%. The rate of grade 3/4 adverse events was 13.8%.

WHY THIS ARTICLE IS IMPORTANT

This is the first prospective study to report on the combination of radioembolization and checkpoint inhibition. Although the trial did not meet its primary endpoint, the ORR improved relative to that of either single-agent nivolumab or radioembolization alone with resin microspheres using similar dosimetry methods, and it argues for further clinical evaluation of radioembolization with checkpoint inhibition. In the setting of concurrent checkpoint inhibition, the issues of appropriate tumor dose selection will become further complicated as we weigh the direct tumoricidal effects with their relative immunogenicity. ■

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