Year in Review: Top 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.

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90Y Radioembolization Versus Drug-Eluting Bead Chemoembolization for Unresectable Hepatocellular Carcinoma: Results From the TRACE Phase II Randomized Controlled Trial

Dhondt E, Lambert B, Hermie L, et al. Radiology. 2022;303:699-710. doi: 10.1148/radiol.211806

SUMMARY

This single-center randomized controlled trial (RCT) compared drug-eluting bead transarterial chemoembolization (DEB-TACE) versus yttrium-90 (Y-90) transarterial radioembolization (TARE) with glass microspheres in patients with intermediate-stage hepatocellular carcinoma (HCC). DEB-TACE was performed with DC Beads (Boston Scientific Corporation; 100–300 µm and 300–500 µm) in a selective fashion, allowing a maximum of three TACE sessions per tumor and five sessions per patient. TARE was performed with glass microspheres with a target absorbed dose of 120 Gy, with a preference of segmental rather than lobar TARE. Eligibility criteria including Barcelona Clinic Liver Cancer stage B (BCLC B) patients primarily, but allowing BCLC A patients not eligible for ablation, transplant, or resection, up to a Child-Pugh grade 7, and an Eastern Cooperative Oncology Group (ECOG) performance status of 1 or less. The primary endpoint was time to progression (TTP). A total of 72 patients were randomized at a center in Belgium: 34 to DEB-TACE and 38 to TARE. On interim analysis, median TTP was 17.1 months for the TARE arm versus 9.5 months for the DEB-TACE arm (hazard ratio [HR], 0.36; 95% CI, 0.18-0.70; $P = .002$). Median progression-free survival (PFS) was 11.8 months for the TARE arm versus 9.1 months for DEB-TACE (HR, 0.40; 95% CI, 0.24-0.67; $P < .001$). Ten participants underwent transplant in the TARE arm versus four in the DEB-TACE arm. Median overall survival (OS) was 30.2 months in the TARE arm and 15.6 months in the DEB-TACE arm (HR, 0.48; 95% CI, 0.28-0.82; $P = .006$). Median OS after censoring for liver transplant was 27.6 months for TARE and 15.6 months for DEB-TACE (HR, 0.49; 95% CI, 0.28-0.87; $P = .01$).

WHY THIS STUDY MATTERS

Retrospective series from single centers and combined data from multiple centers have demonstrated a high tumor control rate of TARE for HCC, especially for tumors < 3 cm. The PREMIERE trial previously demonstrated a benefit in TTP for HCC patients treated with TARE compared to conventional Lipiodol (Guerbet) TACE. However, the majority of patients in the PREMIERE trial had single, unilobar tumors (BCLC A) and no benefit in OS was noted. In contrast, the TRACE trial had predominantly BCLC B patients with bilobar disease and larger tumor size than the PREMIERE trial. More importantly, this trial confirmed, even on interim intent-to-treat analysis (16% of patients in the TARE arm did not undergo TARE), a benefit in OS and TTP for this subgroup of HCC patients. With recent inclusion of TARE as a treatment option in the BCLC guidelines for patients who are not candidates for or fail ablation, transplant, resection, or TACE, this trial is an important milestone in recognized TARE as a primary treatment option for intermediate-stage HCC.

Lenvatinib Combined With Transarterial Chemoembolization as First-Line Treatment for Advanced Hepatocellular Carcinoma: A Phase III, Randomized Clinical Trial (LAUNCH)

Peng Z, Fan W, Zhu B, et al. J Clin Oncol. 2023;41:117-127. doi: 10.1200/JCO.22.00392

SUMMARY

This multicenter, randomized, open-label, phase 3 trial compared clinical outcomes of lenvatinib (LEN) combined with TACE (LEN-TACE) versus LEN alone in patients with advanced HCC. Patients with primary treatment-naive or initial recurrent advanced HCC after surgery were randomly assigned (1:1) to receive LEN plus on-demand TACE (LEN-TACE) or LEN monotherapy. LEN was initiated within 3 days after randomization. Eligibility criteria included a Child-Pugh A grade; an ECOG performance status of 1 or less; and adequate blood, liver, and kidney function. TACE was initiated 1 day after LEN initiation. The primary endpoint was OS. A total of 338 patients were randomized at 12 centers in China: 170 to LEN-TACE and 168 to LEN. Patients in the LEN-TACE arm underwent treatment with TACE 560 times, with a median of three sessions per patient. After a median follow-up of 17.0 months, median OS was significantly longer in the LEN-TACE group (17.8 vs 11.5 months; $P < .001$). The median PFS was 10.6 months in the LEN-TACE group and 6.4 months in the LEN group ($P < .001$). Patients in the LEN-TACE group had a higher objective response rate according to modified RECIST (54.1% vs 25.0%; $P < .001$). Multivariable analysis revealed that portal vein tumor thrombus and allocation to the LEN-TACE group were independent risk factors for OS.

WHY THIS STUDY MATTERS

Retrospective studies had suggested promising outcomes combining TACE with LEN; however, a large-scale clinical trial was required to confirm a survival benefit. In this randomized phase 3 study, the combination LEN-TACE group showed significant improvement in OS (17.8 vs 11.5 months), as well as improved PFS and objective response rate. Combination therapies are a hot topic in interventional oncology, with numerous ongoing trials combining different liver-directed therapies with multiple systemic therapies for HCC. Moreover, clinically, combination therapies are being used without solid data as of yet. This is the first phase 3 study to show increased OS with a combination of liver-directed plus systemic therapy, making this combination one of the first to have substantial data to support its utilization. There were increased adverse events in the LEN-TACE group, including abdominal pain (50.6% vs 10.7%), fever (38.8% vs 5.4%), nausea (35.9% vs 10.1%), aspartate aminotransferase increase (26.5% vs 6.5%), alanine aminotransferase increase (21.2% vs 5.4%), hyperbilirubinemia (17.9% vs 9.5%), vomiting (17.6% vs 5.4%), hypoalbuminemia (14.3% vs 4.2%), and ascites (12.9% vs 4.2%). However, the authors concluded that LEN-TACE had a manageable side effect profile. As LEN is a first-line therapy for patients with advanced HCC, this study indicates that LEN-TACE is a potential first-line treatment for patients with advanced HCC.

IMbrave050: Phase 3 Study of Adjuvant Atezolizumab + Bevacizumab Versus Active Surveillance in Patients With Hepatocellular Carcinoma (HCC) at High Risk of Disease Recurrence Following Resection or Ablation

Chow P, Chen M, Cheng A, et al. Cancer Res. 2023;83(8 suppl):CT003. https://doi.org/10.1158/1538-7445.AM2023-CT003

SUMMARY

This phase 3 study evaluated the efficacy of adjuvant atezolizumab (atezo) with bevacizumab (bev) in delaying or preventing recurrence in patients with high-risk HCC. Patients with high-risk criteria (tumor burden, vascular invasion, and tumor differentiation) were randomized after resection or ablation into atezo plus bev (arm A) versus active surveillance (arm B). Eligibility criteria included a Child-Pugh A grade; an ECOG performance status of 1 or less; and adequate blood, liver, and

kidney function. Patients in arm A received 1200 mg of atezo plus 15 mg/kg of bev intravenously every 3 weeks for a period of 1 year or 17 cycles. Patients in arm B underwent active surveillance for 1 year and were eligible to crossover to atezo plus bev following independent review facility confirmation of recurrence. The primary endpoint was recurrence-free survival (RFS). Secondary efficacy endpoints included OS; RFS and OS according to PD-L1 status; and time to extrahepatic spread and/or macrovascular invasion. There were 334 patients each in study arm, with well-balanced baseline demographics. With a median follow-up of 17.4 months, the primary endpoint was met with an RFS HR of 0.72 (95% CI, 0.56-0.93; *P* = .0120), and results were generally consistent across clinical subgroups. At 1 year, the recurrence rate was 34% in the surveillance arm and 20% in the atezo plus bev arm. The safety of atezo plus bev was generally manageable and consistent with the well-established safety profile of each therapeutic agent.

WHY THIS STUDY MATTERS

The risk of HCC recurrence after liver resection or ablation with curative intent ranges from 60% to 80% within 5 years, indicating an unmet need for effective adjuvant therapies. There is a bimodal recurrence of HCC after resection, with recurrence rates peaking around 1 year, then gradually decreasing over the next 2 years. The current consensus is that these recurrences are from micrometastases. A second, lower postoperative recurrence peak occurs at 4 to 5 years, which likely represents de novo tumors associated with underlying liver disease. Until now, there is no standard-of-care treatment in the adjuvant setting for HCC after resection or ablation with curative intent. Atezo plus bev is already a first-line therapy for unresectable HCC, and now the first adjuvant regimen to demonstrate a statistically significant and clinically meaningful improvement in RFS versus active surveillance in patients at high risk for disease recurrence. At 1 year, disease recurrence was 33% lower in the atezo plus bev group than the active surveillance group. This study makes the case for atezo plus bev as a standard adjuvant therapy for high-risk HCC after resection and/or ablation.

Radioembolization With Yttrium-90 Glass Microspheres as a First-Line Treatment for Unresectable Intrahepatic Cholangiocarcinoma: A Prospective Feasibility Study

Kis B, Shridhar R, Mhaskar R, et al. J Vasc Interv Radiol. 2023;34:1547-1555. doi: 10.1016/j.jvir.2023.05.026

SUMMARY

This phase 2 study evaluated the feasibility of TARE with glass microspheres as a first-line treatment for unresectable intrahepatic cholangiocarcinoma (ICC). Patients with newly diagnosed ICC who had not received any prior treatment, had an ECOG performance status of < 2, adequate hematopoietic function, liver-localized disease without vascular invasion, and total bilirubin of < 2 mg/dL were recruited. Twenty-five patients were recruited and treated with Y-90–labeled glass microspheres. The target absorbed dose was 120 Gy for lobar treatments and 200-400 Gy for segmental treatments. The median OS was 19.4 months (95% CI, 5.0-33.7 months). Patients with solitary ICC had longer median OS at 25.9 months (95% CI, 20.8-31 months) than patients with multifocal ICC at 10.7 months (95% CI, 8.00-13.4 months) (*P* = .02). Median OS of patients who received chemotherapy versus who didn't receive chemotherapy after radioembolization was similar (19.4 months [95% CI, 7.1-31.6] vs 11.7 months [95% CI, 0-65.7 months], *P* = .22).

WHY THIS STUDY MATTERS

Numerous retrospective studies have shown the benefit of TARE in treating mass-forming ICC. A recent phase 2 study (MISPHEC trial) demonstrated a median OS of 22 months and a 22% downstaging rate for patients treated with concomitant TARE and systemic therapy with gemcitabine and cisplatin; however, TARE is still used either concomitantly or subsequent to systemic therapy, often in the salvage setting. This phase 2 trial shows promising results for the first-line use of TARE for mass-forming cholangiocarcinoma and a potential benefit for patients with unilobar disease, opening the door for larger trials.

BestFLR Trial: Liver Regeneration at CT Before Major Hepatectomies for Liver Cancer–A Randomized Controlled Trial Comparing Portal Vein Embolization With N-Butyl-Cyanoacrylate Plus Iodized Oil Versus Polyvinyl Alcohol Particles Plus Coils

Luz JHM, Veloso Gomes F, Costa NV, et al. Radiology. 2021;299:715-724. doi: 10.1148/radiol.2021204055

SUMMARY

In this RCT of 60 patients with liver malignancies, portal vein embolization (PVE) performed using N-butyl-cyanoacrylate (NBCA) glue mixed with iodized oil resulted in greater hypertrophy of the contralateral liver compared to patients with portal vein embolization performed using polyvinyl alcohol (PVA) particles and coils (absolute hypertrophy of 46% vs 30% at 14 days [$P < .001$] and 57% vs 37% at 28 days [$P < .001$], respectively). Moreover 87% of PVE patients treated with NBCA glue mixed with iodized oil achieved sufficient hypertrophy to undergo surgery within 2 weeks of PVE compared to only 53% of patients treated with PVA and coils ($P = .008$).

WHY THIS STUDY MATTERS

PVE is a standard technique for allowing hepatic resection in patients at risk for liver failure after resection due to a small future liver remnant. This technique was originally described using a combination of small microspheres and coils to occlude the portal blood flow to the diseased lobe, inducing contralateral lobe hypertrophy. The BestFLR trial, an investigator-initiated, single-blind, single-center, superiority trial randomly assigned patients to PVE using PVA particles plus coils versus NBCA glue plus iodized oils. Technical success rate was high with both techniques, but fluoroscopy time, total PVE time, and intravenous contrast usage was higher in the PVE with PVA particles/coils group compared to the NBCA glue/iodized oil group. NBCA-Lipiodol resulted in a faster kinetic growth rate, more hypertrophy, and shorter time to hypertrophy compared to the PVA/coils group. Surgery was performed in 78% of the participants. There was no difference in surgical resection rate, major complication rate, or mortality rate between the two groups. ■

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