

PANEL DISCUSSION

Liver-Directed Therapy in 2026: Redefining the Roles of Y90, cTACE, and Ablation in HCC

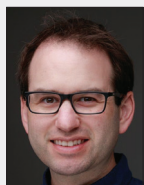
Perspectives on patient selection, treatment sequencing, combination strategies, and the growing influence of systemic therapy.

With Nadine Abi-Jaoudeh, MD; Zachary T. Berman, MD; and Ammar Sarwar, MD, FSIR



Nadine Abi-Jaoudeh, MD

Chief of Interventional Radiology
Director of Clinical Research
University of California Irvine Health
Orange, California
nadine@hs.uci.edu



Zachary T. Berman, MD

Interventional Radiologist
Associate Professor of Radiology
University of California San Diego Health
San Diego, California
zberman@health.ucsd.edu



Ammar Sarwar, MD, FSIR

Professor of Radiology, University of Pittsburgh
Chief of Interventional Radiology
Associate Chair for Radiology
University of Pittsburgh Medical Center
Pittsburgh, Pennsylvania
sarwara@upmc.edu

The treatment landscape for hepatocellular carcinoma (HCC) has become increasingly complex with advances in locoregional and systemic therapies. How have the roles of yttrium-90 (Y90), conventional transarterial chemoembolization (cTACE), and ablation changed over the past 5 years, and what do you see as the biggest drivers of that change?

Dr. Abi-Jaoudeh: In the past 5 years, the role of transarterial radioembolization (TARE) has significantly

increased in HCC, largely driven by the changes in dosimetry. When I trained, Y90 was a “Hail Mary,” associated with low response rates and toxicities. With the advent of radiation segmentectomy, the overall response rate in limited disease has consistently exceeded 90% regardless of product, with the majority being complete responses. The duration of responses is measured in years rather than months. With the advent of systemic therapies, there has been a dip in referrals to interventional radiology for HCC as more community oncologists are prescribing dual immunotherapy for disease treated with locoregional therapies. This is an issue of its own; I see patients who were started on systemic therapies with disease that could have easily been downstaged to transplantation. In the past year, there has been a resurgence of TACE in multifocal disease combined with systemic therapy secondary in combination trials, especially EMERALD-3 and LEAP-012.

Dr. Berman: Over the past 15 years, radioembolization has gone from a palliative treatment targeting just lobar infusions to now being more selective with ablative intent. This has driven a significant increase in the depth and durability of responses, which has become on par with other ablative therapies (eg, percutaneous ablation). Additionally, our understanding of pathologic necrosis has increased during this time, allowing us to better predict and plan to ensure that patients are having every single tumor cell destroyed as part of a locoregional therapy intent. At that point, we are on par with a surgeon removing the tumor, with a much less invasive approach. This has been accelerated with improved understanding in dosimetry as well as better understanding of minimum ablation margins for percutaneous ablation.

Dr. Sarwar: The biggest change in locoregional therapies in the last 5 years has been an increase in the volume of Y90 at the expense of cTACE. This is best seen in the United Network for Organ Sharing database where Y90 has become the most used locoregional therapy for patients with HCC on the waitlist. Ablation has more or less remained steady, which reflects its curative status in the Barcelona Clinic Liver Cancer (BCLC) algorithm.

When evaluating a patient with early or intermediate-stage HCC, what factors most strongly influence your decision among Y90, cTACE, and ablation? How has your approach to patient selection evolved over the past several years?

Dr. Sarwar: Over the past several years, I have substantially reduced my use of cTACE for early or intermediate-stage HCC. While the data supporting cTACE in early stage HCC is clearly demonstrated in the 99% local control rate seen in the DOORwaY90 study (NCT04736121), I have found that careful evaluation of the angiosome in intermediate-stage HCC can allow radiation segmentectomy approaches for multifocal disease while sparing the normal hepatocytes. These decisions have been driven by recent pivotal and randomized controlled trial (RCT) data (eg, TRACE trial) as well as the improved quality of cone-beam CT software that allows precise tumor targeting and post-Y90 dosimetry; this has allowed me to continuously refine my approach to maximize tumor dose and minimize normal liver dose.

Dr. Abi-Jaoudeh: There are many factors that influence my decision on which therapy to use, including my assessment of the patient; their liver function; the tumor size, number, and location; tumor board discussion; and transplant potential. For an easily accessible, small (< 3 cm) tumor, I will usually go for ablation unless the transplant surgeon prefers Y90. Ablation is well tolerated as a single outpatient procedure. Numerous RCTs and their meta-analyses have proven the equivalence of ablation to surgery. No other locoregional therapy has level 1 evidence demonstrating equivalence to surgery. If the tumor is larger or is central, I would pivot to Y90. I treat multifocal bilobar disease with superselective cTACE combined with systemic doublet immunotherapy.

Many HCC patients could reasonably receive more than one liver-directed therapy. Where do you believe one modality clearly offers advantages, and where is there still genuine equipoise?

Dr. Berman: Most patients these days do receive multiple different types of therapy, and no one therapy is definitively better than the other. They all depend on the tumor location as well as the patient's underlying liver status and therapy goals. There should be no dogma that patients should only receive one type of therapy; they need to receive what is best for them at different points in their care. The beauty of interventional oncology is that a provider is able to offer many different styles of therapy tailored specifically to the patient's presentation and goals and can choose what they think is best, not what is immediately available because it is all they do.

Dr. Sarwar: I think Y90 clearly offers advantages in one to three tumors that are > 3 cm. I think in tumors < 3 cm located in ablatable regions (an operator-dependent term), there is likely equipoise between an experienced Y90 user and experienced ablationist, but the guidelines favor ablation for these patients. I also believe that HCC patients with Vp1 or Vp2 portal vein tumor thrombus can be treated with curative intent using radiation segmentectomy.

Dr. Abi-Jaoudeh: I do not think that there is genuine equipoise in most cases. If a lesion is > 3 cm or centrally located, ablative TARE is better than ablation. A single 2-cm, segment 3 lesion should be ablated. If there are numerous bilobar lesions, cTACE with doublet immunotherapy is recommended. If there is major portal vein thrombus, I would pivot toward Y90 in combination with systemic therapies. There might be equipoise in cases where there are two or three small lesions in two or three segments. For these, I would go with radiation segmentectomy, but ablation is equivalent. I would discuss both options with the patient and have them choose.

At many high-volume United States centers, Y90 has assumed an increasingly prominent role in the treatment of HCC. In your own practices, which patients with HCC are still better served by cTACE, and what specific advantage does chemoembolization offer in those cases?

Dr. Berman: cTACE has the largest and longest amount of randomized data, and it will always have role in treating patients with HCC. Currently, cTACE has the largest body of safety and efficacy data in combination with immunotherapy. Additionally, it serves as a great imaging biomarker to be used in conjunction with ablation to allow for adequate margins to be achieved. It is important that we strive to make cTACE more reliable, repeatable, and predictable with future research as has been done with TARE and percutaneous ablation.

Dr. Sarwar: I reserve cTACE for HCC patients with a bilirubin > 2 mg/dL or Child-Pugh B cirrhosis at high risk for decompensation with further degradation of liver function. Otherwise, in my practice, pretty much any presentation of multifocal disease can be treated with targeted, hepatocyte-sparing radioembolization with curative intent.

Dr. Abi-Jaoudeh: Bilobar disease with numerous lesions is better served with superselective cTACE compared to Y90. Treating both lobes of the liver with radioembolization has low response rates, especially if tumor/normal liver ratio is not high as the deposited liver dose will be higher and result in toxicities. Superselective cTACE is more time consuming in those cases but safer and better when combined with immunotherapy. Additionally, because of the ability to piecemeal the treatments, I use superselective cTACE on patients who have performance status of 2 or who have borderline liver function. RCTs and prospective studies combining cTACE and doublet immunotherapy have demonstrated improved response rates and progression-free survival in intermediate and advanced disease. Chemoembolization's immunomodulation of the tumor microenvironment interplays with systemic therapies. That information is not available for Y90.

Radiation segmentectomy and advances in ablation have expanded the number of patients who may be candidates for potentially curative liver-directed therapy. How have these developments changed your approach to early stage disease?

Dr. Berman: Complete pathologic necrosis has become the gold standard for all locoregional therapies. The ability to accurately predict with high probability that a patient is going to achieve this result has become a lot more possible with recent developments in our understanding of radiation segmentectomy dosimetry as well as stereotactic/robotic guidance with ablation. Randomized trials have shown that these ablative techniques are on par with surgical resection, with significantly reduced morbidity. Further improvements will help refine this and perhaps, in the future, make it preferable over more invasive approaches.

How are contemporary systemic therapies, including immunotherapy, changing the way you sequence or combine Y90, cTACE, and ablation? Are there clinical scenarios in which you intentionally incorporate liver-directed therapy before, during, or after systemic treatment?

Dr. Abi-Jaoudeh: The trials exploring adjuvant or neo-adjuvant systemic therapy after ablation/surgery in early stage HCC were negative. I would not combine ablation nor radiation segmentectomy with systemic therapy; I would stage it. For curative treatment such as ablation or radiation segmentectomy, you can treat and the patient remains disease free for a prolonged period of time, giving them a break. If the patient experiences a quick relapse, then I would retreat and add immunotherapy. cTACE is usually combined with doublet therapy. Patients whom I treat with cTACE tend to have more advanced disease, and I usually like to have the immune system primed with an immunotherapy combination before TACE. I tend to favor durvalumab/tremelimumab or ipilimumab/nivolumab as regimens. If the oncologist wants to add a tyrosine kinase inhibitor, that is usually done after we have completed all the TACE procedures.

Dr. Berman: This is the largest open question in the literature today. A lot of people are considering this, and there are a lot of different reasons why you would want to combine. Right now, HCC is one of the few malignancies where combination, local, and systemic approaches are not combined up front. This is bread and butter for all other classes of malignancies. Additionally, our understanding of what is happening at a tumor microenvironment has also improved over time, and the different clinical scenarios where you might want to incorporate combination therapy may change depending on your objective. This is a rapidly evolving landscape, and many trials are going to actively change how we think about this in the coming few years.

Beyond sequencing with systemic therapy, are we entering an era in which combinations of liver-directed therapies will become increasingly common? Which approaches appear most promising, and what evidence is still needed to support broader adoption?

Dr. Abi-Jaoudeh: Yes, combination therapies will increase in early disease to downstage patients to curative therapies as well as in intermediate and advanced disease. Patients who present with curative disease may not need combination therapies.

There are a couple of prospective trials still preliminary but demonstrating very exciting results. For example, at the American Society of Clinical Oncology Gastrointestinal Cancers Symposium 2026, we presented the results of our trial that combines transarterial tirapazamine embolization and immunotherapy for advanced (including metastatic disease) HCC patients who have failed at least one line of doublet

immunotherapy.¹ There is no actual standard of care for these patients. Our response rate was twice as high in the second-line setting compared to first-line setting. Moreover, the duration of response was sustained. University of California San Diego has a first-line combination trial where patients with advanced/metastatic HCC undergo partial cryoablation, local delivery of nelitolimod, and immunotherapy with excellent results. These are a few examples, but larger prospective trials need to confirm these preliminary results.

Treatment burden is also an important consideration with combination therapy. Literature has demonstrated that when patients are prescribed four or more medications, their compliance drops significantly.²⁻⁴ These studies were examining hypertension and hypercholesterolemia medications with tinnitus as a side effect, not the toxicities seen with oncologic drugs. Single-agent systemic therapies were not effective against HCC; doublet therapy was promising and the field is now moving toward triplet, but this is difficult for patients. The adverse events are cumulative and may be unbearable. If we can deliver some of those medications locally, we can have a significant impact. I am most excited about combination therapies in advanced and even metastatic disease.

Dr. Sarwar: I think we are well into that era. Despite the lack of positive trials, combination approaches are being increasingly used, especially as systemic therapy becomes more effective and better tolerated. However, given the relative high rates of side effects to immunotherapy, the results of already initiated combination trials are eagerly awaited.

As treatment options continue to expand, how has multidisciplinary collaboration changed the way patients with HCC are evaluated and treated? What are the characteristics of a successful liver tumor board, and where do you still see opportunities to improve coordination among specialties?

Dr. Sarwar: In general, there is an expansion of multidisciplinary collaboration. I view multidisciplinary collaboration occurring in three stages. The early stage is multiple specialists who frequently discuss challenging HCC presentations to determine an optimum treatment strategy. The intermediate stage is multiple specialists who meet at regular intervals in an in-person multidisciplinary conference setting (teleconference or hybrid) to discuss challenging HCC presentations. The

advanced stage is multiple specialists who are present at regular intervals in a co-located clinic so that the patient benefits from having all experts under one roof at the same time. Of course, no multidisciplinary discussion of HCC is complete without a transplant expert present.

Dr. Abi-Jaoudeh: Tumor boards are essential, and in fact, there are RCT data showing that they improve overall survival and patient outcomes. The most successful tumor boards are comprised of every specialty involved in the disease treatment and allow everyone to have a voice. Unfortunately, many centers do not have tumor boards, nor do they have access to one. When you are a hammer, everything is a nail. In order not to fall into that trap, a multidisciplinary discussion is paramount to ensure patients receive the best recommendation. There should be mechanisms set up for stand-alone oncology groups or smaller practices to refer patients for tumor board recommendation to a larger regional center and then have the recommendation sent back to the referring physician. This is available in some areas but is not ubiquitous across the country.

Dr. Berman: As our treatment paradigms become more complex, with many different options available to the patient, it is becoming increasingly important that a variety of treatment options are considered for each individual patient. The multidisciplinary clinic is the best way of providing this care. It is critical that local experts at each institution are in active communication to ensure that all possible opportunities are explored and that care is streamlined between the many different services that assist patients throughout their journey. It is not uncommon these days for a patient to initially see interventional oncology, followed by medical oncology and hepatology, and then ultimately, after rounds of therapy, be downstaged to a curative-intent therapy such as surgical resection. There are a lot of hands helping out throughout the patient's journey.

Over the next 5 years, which advance is most likely to meaningfully alter HCC practice (eg, more precise Y90 dosimetry, new microsphere technologies, nonthermal ablation, improved image guidance, combinations with systemic therapy, better biologic patient selection)? What evidence would be needed for that advance to change your current algorithm?

Dr. Berman: A better understanding of dosimetry including not only dose but also what type of microparticles, how many, and the microsphere activity is going to continue the dramatic increase in response

seen over the past decade. We are going to see more advancement in where we apply different dosimetry techniques and when. Radioembolization has had a swing from initial use in BCLC C to now being primarily used in BCLC A, but emerging evidence is showing improved efficacy in BCLC B, with encouraging prospective data in limited tumor vascular involvement cases and in combination with immunotherapy in BCLC C. In 5 years, I suspect there will be significant increases in TARE use throughout all HCC indications, with dosimetry and treatment intent personalized to every patient and every goal of therapy.

Dr. Sarwar: Can I say all of the above? As Yogi Berra said, "It's hard to make predictions, especially about the future." Within locoregional therapies, increased use of personalized dosimetry, new microsphere technologies, and improvements in imaging guidance will make Y90 more likely to be performed with curative intent. I think ablation is already considered curative, which is the highest level for HCC therapies, but imaging guidance improvements such as margin confirmation software will ensure each patient is treated adequately. Nonthermal ablation will have a high bar to cross since the only way to allow widespread clinical use will be a well-performed RCT against thermal ablation. The main X factor is systemic therapies and novel biomarkers for better biologic patient selection. Those fields are developing rapidly, and each new advance will need to be carefully observed and vetted for incorporation into treatment algorithms. ■

1. Abi-Jaoudeh N. A phase 2, open-label single-arm, multi-center study of trans-arterial tirapazamine embolization (TATE) combined with nivolumab (nivo) in patients with advanced immunotherapy-refractory hepatocellular carcinoma (HCC). Presented at: ASCO Gastrointestinal Cancers Symposium; January 8–10, 2026; San Francisco, California.
2. Kim SJ, Kwon OD, Han EB, et al. Impact of number of medications and age on adherence to antihypertensive medications: a nationwide population-based study. *Medicine (Baltimore)*. 2019;98:e17825. doi: 10.1097/MD.00000000000017825
3. Srivastava K, Arora A, Kataria A, et al. Impact of reducing dosing frequency on adherence to oral therapies: a literature review and meta-analysis. *Patient Prefer Adherence*. 2013;7:419–434. doi: 10.2147/PPA.S44646
4. Religioni U, Barrios-Rodríguez R, Requena P, et al. Enhancing therapy adherence: impact on clinical outcomes, healthcare costs, and patient quality of life. *Medicina (Kaunas)*. 2025;61:153. doi: 10.3390/medicina61010153

Disclosures

Dr. Abi-Jaoudeh: Receives research funding from Innova Vascular, Medtronic, Penumbra, Teclison Limited, RenovoRx, Impact Biotech, Sirtex Medical, Guerbet SA, Varian, Instylla HES, and ABK Biomedical; consulting advisory relationship with and speaker's bureau member for Replimune, IVQIA, Instylla, Sirtex Medical, ABK Biomedical, Boston Scientific Corporation, AstraZeneca, Guerbet SA, Eisai, Varian, and Terumo.

Dr. Berman: Consultant to Boston Scientific, Sirtex Medical, AstraZeneca, TriSalus Life Science, and Guerbet.

Dr. Sarwar: Consultant to Sirtex Medical, Boston Scientific, and ABK Biomedical.