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Hepatocellular Carcinoma: Evaluating the Evolving Treatment Landscape

Dr. Sands:

The treatment landscape for hepatocellular carcinoma is constantly evolving. Most patients diagnosed with this disease have either unresectable, or we're going to discuss, intermediate-stage hepatocellular carcinoma and have liver-limited disease but aren't eligible for surgery. These patients are typically treated with local regional therapies. But what is the best management for them?

Welcome to *Project Oncology* on ReachMD. I'm Dr. Jacob Sands. And joining me to talk about current and emerging strategies for unresectable liver-limited hepatocellular carcinoma is Dr. Manish Shah, Bartlett Family Professor of Gastrointestinal Oncology and Chief of the Solid Tumor Service at Weill Cornell Medicine. Dr. Shah, thank you for joining me today.

Dr. Shah:

Oh, thank you for having me. This is a terrific opportunity.

Dr. Sands:

So let's begin with a look at the treatment landscape for unresectable hepatocellular carcinoma. Dr. Shah, you've previously described intermediate-stage hepatocellular carcinoma, but can you outline for us what exactly that means and what treatment options are currently available in unresectable hepatocellular carcinoma and how intermediate stage may impact those decisions?

Dr. Shah:

Yeah, absolutely. So most patients with hepatocellular cancer, you know, if they're being surveilled, will be identified with having a local lesion in the liver, and most of the time, that lesion can be addressed with either surgery or local regional treatment, either trans arterial chemoembolization or radioembolization or ablation, some method to try to get rid of that lesion, and that's very successful for lesions that are three centimeters or smaller. And sometimes, patients will have multiple lesions in the liver, but they can all be addressed by one of those local regional treatment options. Another option for local regional treatment is SBRT, or stereotactic brachyradiotherapy.

So the other extreme is where patients with hepatocellular cancer are diagnosed but with more advanced disease where it spread beyond the liver, sometimes to the bone or lungs or even the abdomen, and in that population, if someone has maintained their liver function, meaning that their Child-Pugh status is A or a high B, then patients would be eligible for systemic therapy, and that would be the best option. But there are a large number of patients where they have many liver lesions not really amenable to local regional treatments, and it hasn't spread outside the liver, and we're defining this as this intermediate-stage category.

Hepatocellular cancer is currently managed in a very much multidisciplinary approach. Typically, there are hepatobiliary surgeons, and then there's also interventional radiology as well as medical oncology all, you know, in a room or looking at radiographs to sort of see what's the best option for patients, and conceptually, the medical oncologist gets involved when the cancer spreads beyond the liver. However, what we're trying to sort of talk about here is that maybe the medical oncologist should get involved when the cancer is still in the liver but there isn't a really curative option for the patient. The patient will have too much extensive disease or too much surgery, so we can only try to manage the cancer locally, and at that point, we should also think about adding some systemic therapies. And so that's the intermediate stage we're talking about.

Dr. Sands:

So, if we focus on local regional therapies in particular, you've discussed some of the treatment, but what are some of the drawbacks that we need to be aware of?

Dr. Shah:

Yeah, so local regional treatment, another option for local regional treatment is SBRT, or stereotactic brachyradiotherapy. These are all treatments where they are able to direct some high energy, whether it's radiation or heat or radioactive beads or whatever directly to the area of interest within the liver, and the dangers of that is the spillover effect. For example, if we're doing ablation, we typically want to kind of do microwave to the lesion itself and then try to treat the margin as well, but if it's close to a venous structure or an arterial structure in the liver, it could cause damage, or if it's close to the capsule, it could cause pain or perforation. So the real concern about local regional treatment is the location of the lesion relative to other structures in the liver, particularly blood vessels and the capsule of the liver. And then the other part of the concern is that, you know, as we all know, HCC really exists in the context of an underlying damaged liver. So, if there is underlying cirrhosis already and you damage more of the liver with your local regional treatment, you could tip the patient into a more severe, cirrhotic picture, so that's the other concern that we have.

Dr. Sands:

Now let's dive into some of your research. Can you share some of the key findings on systemic therapies, particularly related to intermediate-stage hepatocellular carcinoma?

Dr. Shah:

Absolutely. The systemic treatment for hepatocellular cancer has evolved a lot, and because we've become much more successful, we can begin to think of treating the cancer a little bit earlier in this intermediate stage. So, because we have more effective treatments in the metastatic setting, the consideration is that for intermediate-stage cancers where we don't have a curative intent option, you might consider doing some systemic therapy as well, and that really is even under consideration because of the advances that others have made with regard to systemic treatment.

Dr. Sands:

For those just tuning in, you're listening to *Project Oncology* on ReachMD. I'm Dr. Jacob Sands, and I'm speaking with Dr. Manish Shah about hepatocellular carcinoma treatment strategies.

Now, Dr. Shah, we've reviewed some of your key findings, but let's dive into one component of your research. Given the number of treatment options emerging for hepatocellular carcinoma, how should clinicians go about selecting the right one for their patient?

Dr. Shah:

Yeah, that's a great question. So there are several options available for patients with hepatocellular cancer. And as we talked about earlier, it's not one disease, but two diseases. It's the cancer itself but also the underlying liver damage. And I think, you know, with great options you can now tailor your treatment based on specifics of the patient. So immunotherapy is a great option and the standard of care, but there are some patients that may not be eligible for immunotherapy. I think for HCC specifically, if you get HCC after transplant—so this happens occasionally where someone was treated with a liver transplant and then maybe years later they develop a new HCC lesion for some reason or the other. In those patients that have a transplant, you can't use immunotherapy because immunotherapy can actually lead to rejection of the transplanted liver in about 30 to 50 percent of the time, so in that case, you would start with the tyrosine kinase inhibitor, either sorafenib or lenvatinib, and there are some data for that. But there are other reasons why you might not be able to use, the current standard first-line treatment. And so I think that what we're really saying is that we want to tailor the treatment to the side effects anticipated and the risks to the individual patient.

Dr. Sands:

And to that point, when talking about tailoring it to the patient, based off some of your key findings, do you think that patients need to be categorized as local regional therapy refractory before discussing systemic treatments, or can that be discussed even earlier?

Dr. Shah:

Yeah, it's a great question. I think that what we're trying to say is that for this intermediate stage where these are patients that have incurable but localized disease, we should begin to think of novel strategies, perhaps adding systemic therapy to local regional treatment or considering systemic therapy earlier. Those are the types of questions that we're trying to ask now. And, in fact, there was one recent study that looked at the combination of lenvatinib plus a TACE procedure, trans arterial chemotherapy, compared to TACE alone, and the combination was far superior, so we are getting some data now that this combination approach for this intermediate stage might be the best approach for our patients.

Dr. Sands:

And as we look to the future, what kind of role do you think emerging treatment options, such as combination therapy, will have on the treatment landscape of hepatocellular carcinoma?

Dr. Shah:

That's a great question. So, there's a lot of excitement about combination therapy. So in the next few years we're going to learn, the efficacy of some of these combinations and that they may actually be superior than these single agents that they are being compared to. And I think then the next step is how to select patients, you know, in the best way for each particular combination. I think that's going to be the next sort of evolution of treatment for hepatocellular cancer in the current era.

Dr. Sands:

And with those forward-looking thoughts in mind, I want to thank my guest, Dr. Manish Shah, for sharing his perspective on the treatment landscape for unresectable liver-limited hepatocellular carcinoma. Dr. Shah, it was wonderful having you on the program.

Dr. Shah:

Thanks so much for having me. This was a great discussion.

Dr. Sands:

I'm Dr. Jacob Sands. To access this and other episodes in our series, visit reachmd.com/projectoncology, where you can Be Part of the Knowledge. Thanks for listening.