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Released: 12/30/2024
Valid until: 12/30/2025
Time needed to complete: 1h 14m

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Expert Opinion: Key Insights on GI Malignancies—Integrating NCCN Clinical Practice Guidelines Into Practice

Announcer:
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Dr. Venook:
This is CME on ReachMD. I'm Dr. Alan Venook, and with me today are Dr. Aparna Parikh and Dr. Sara Lonardi.

Our discussion today will focus on practical considerations when applying treatment guidelines when tailoring treatment for patients with gastrointestinal cancer.

We'll start with colorectal cancer. Aparna, can you tell us about how you optimize therapy for colorectal cancer patients based on the current NCCN Guidelines?

Dr. Parikh:
Hi, good to see you, Alan and Sara. Thanks for hosting this discussion today.

So for stage IV colorectal cancer patients, when we're first meeting them, we're also thinking around their whole treatment journey. I'm always thinking about, for a patient that's metastatic, is there a path towards cure? We know that, unlike other GI cancers, colorectal cancer is certainly a cancer type where, for patients that have limited metastatic disease, there could be potentially a curative path. So assuming a patient may not be on a curative path, at the outset of meeting a patient, I do biomarker testing, both tissue and blood for all patients. And those biomarkers include several biomarkers. So testing for microsatellite instability status, testing for RAS, RAF, HER2, and then understanding what patients might benefit from targeted therapies, depending on not only the RAS status, but the sidedness of the tumor. So those are the key biomarkers I test for up front, biomarker testing in parallel with tumor sidedness and disease burden often guiding our first-line treatment management.

Dr. Venook:
And as you deal with that, some of the issues you might worry about, for example, do the guidelines help you with the challenge of translating treatment into reality?

Dr. Parikh:
I think one great example of this is HER2-directed therapy. So for the HER2-directed therapies that have been conducted in clinical trials, the majority of clinical trials have been done after patients receive first-line chemotherapy. However, in the NCCN Guidelines, noting the fact that some patients may not be eligible for cytotoxic chemotherapy allows patients potentially access to a targeted therapy for whom cytotoxic chemotherapy may not be the best option.

I think the guidelines also help insofar as when you have several options for patients, allowing the provider, along with shared decision-making with the patient, to pick the best option for that patient based on tumor location, tumor burden, comorbidities, kind of personal

preferences, and not feeling that you're prescribed to only a subset of options.

So I find that the guidelines are really helpful to empower patients and providers to have some choice, noting the fact that all the guidelines obviously are kind of vetted very carefully before treatment recommendations are put into the guidelines. But can be quite helpful, not only for coverage, but to have conversations with patients around why we think certain practices may be in their best interest, even if there isn't a phase 3 trial, for example, to support that.

Dr. Venook:
And so more or less the guidelines provide the whole range of treatments.

Dr. Parikh:
Exactly.

Dr. Venook:
And so, of course, you'll defer to patients. How do you involve patients in the decision?

Dr. Parikh:
Yeah. I mean, I think, as I'm sure you both are kind of well aware of, I think there's a spectrum of patients who are very knowledgeable to deferent in terms of looking to the provider to provide guidance. And so particularly when there's gray areas around management, I find the guidelines being a helpful reference to kind of support the decision-making with the patient. So I think can help anchor discussions, especially in areas where there's not a 100% right answer. Thinking, for example, first-line doublet data for immunotherapy soon. But over the past couple years, when you had a chance of giving doublet immunotherapy or monotherapy for the MSI-high patients, you can have that shared decision-making with the patient, and the guidelines allow you to have both options for the patients, even, again, to date not having that randomized data.

Alan, so the same question that you asked to me in terms of translating the guidelines into clinical practice. What are your thoughts on this?

Dr. Venook:
Well, taking hepatocellular carcinoma, for example, I mean, again, there are a variety of choices, and none of them is necessarily superior to the other. But having the guidelines gives us the flexibility of offering patients, if we think there's a niche or a nuance that might make sense for one treatment or another. Obviously, the guidelines can change rapidly, and hepatocellular carcinoma have gone from virtually nothing to just a panoply of options. But I think the guidelines give us the context, and when we know what the range of things are, we can offer patients. And that's huge. Again, the choice, the decision-making, is based largely on the preference of the patient.

And obviously, again, the problem with the hepatocellular carcinoma is these guidelines really only apply to a small subset of all the patients, those with preserved liver function. But within that range, I think the guidelines make us free to talk about the treatment and make nuanced decisions if they are warranted.

Sara, let me turn to you now. How do you use the guidelines for upper GI or gastric cancer?

Dr. Lonardi:
Yes, thank you, Alan, for asking me this question because I'm working in Italy at the Veneto Institute of Oncology, and clearly, even if we are on the other side of the ocean, the NCCN Guidelines are still a reference point for us. What we do really like of these guidelines is that they are very, very quickly incorporating the different options. When they are approved by a trial and they are considered by FDA, they are promptly included in the guidelines. And so we know that in the NCCN Guidelines, we can find all the options that are validated, that are evidence based, scientifically solid for the different settings of the disease and in this case of the gastric cancer.

On the other side, it's not easy for us to apply them because you know that the European and Italian system is completely different from the American one. And for us, we have two different levels of regulatory pathway. One is the level, and you know that EMA is less fast than FDA in approving the new drugs. And then also we have the reimbursement part that is obviously country based. And in a country like mine, where the healthcare is completely national, we need to wait for the reimbursement to prescribe. Even if we have the EMA approval and the FDA approval and the NCCN Guidelines inclusion, unfortunately, we are not always able to prescribe the new drug as soon as they are validated from a scientific point of view.

Dr. Venook:
So NCCN Guidelines notwithstanding, of course it's dependent on the state regulatory or the country, in the regulatory environment there. What do you do if patients don't fit into a niche in a guideline, can you use them to fashion a treatment that might not be

standard?

Dr. Lonardi:
Yes. Clearly, we have the NCCN that are really inclusive guidelines, including all the evidence based. Sometimes they specify the preferred option and we like it. Then we have the ESMO guidelines. And also we have the national guidelines. And so we have also the Italian Society of Oncology guidelines. Obviously, they cannot be different, but there are some shades. And as you said, that there are also some points that are not specified in the guidelines, because you can do one or other choice, and both are reasonable. Just to make an example on gastric cancer, we know that PD-L1 CPS-positive patients should receive chemotherapy plus immune therapy, checkpoint inhibitors. We know that the PD-L1-negative, if they are claudin 18.2 overexpressed, should receive chemotherapy plus zolbetuximab. But there is a part of patients with low PD-L1 where we can prescribe one or another, and we really don't know which one is better. And so, as you said just a couple of minutes before, it is very important in this gray area to discuss with the patient, to understand which is the main goal, if it is the response, if it is the long-term outcome, and also to discuss on the patient preference, and so the decision is sometimes very clinical, and it's not automatic always to see in the guidelines, okay, it's like this; you have to do this. Otherwise it would be easier to do our work.

Dr. Venook:
That's the reality of guidelines. When we think about guidelines, we really can only make them apply to the majority of patients. And if you think of the 5% rule, the rare patient, the 1 out of 20 patients, may not really have a place in the guideline, because not everybody exactly fits.

Dr. Lonardi:
Yeah. Exactly.

Dr. Venook:
That's actually where the art of medicine and clinical judgment comes in. Remember that. And I think that's one reason why we probably won't be replaced by AI anytime soon.

Well, thank you, Aparna and Sara, for providing these points and for talking with me today. I'd like to thank the audience for joining us. I hope you found this discussion useful for your practice.

Dr. Lonardi:
And thank you to all of you.

Dr. Parikh:
Thanks so much.

Announcer:
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