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Revisiting Anti-TNFs: Role, Risks, and Real-World Considerations

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Dr. Rubin:
Hi, I'm Dr. David Rubin from the University of Chicago, and here with me today is Dr. Michael Dolinger from the NYU School of Medicine.

We're going to talk today a little bit about anti-TNF therapies, which continue to play a central role in managing Crohn's disease with high-risk features, as well as patients with ulcerative colitis. Having said that, their use still requires some thoughtful positioning, and although we have many other new therapies, there are some patients in whom an anti-TNF strategy is still the right choice as a first-line therapy.

So Mike, why don't you share with us some of your thoughts and perspective and wisdom about when you consider using anti-TNF as a first-line therapy in this modern age?

Dr. Dolinger:
Thank you. When I think about anti-TNF therapy, when someone comes into the clinic, the first question I ask myself and when going through their records is, do they need anti-TNF therapy? What I mean by that is, are they someone who there's data that clearly indicates that first-line anti-TNF therapy is the most likely option that's going to treat their specific inflammatory bowel disease?

But I also think it's often never the wrong choice unless there's certain comorbidities or risk factors malignancy. We can talk about those things when you have moderate to severe disease. We often focus on positioning therapies and choosing, but if you're in the community, it's often not the wrong choice to choose infliximab, and it's a safe bet when someone has moderate to severe either Crohn's disease or ulcerative colitis.

Who do I really focus in who needs this is I think about perianal Crohn's disease. First-line treatment for perianal Crohn's disease involvement with abscesses, fistula, and plain skin tags, to me, should always be infliximab as the first line.

And then I think about proximal small bowel disease. I'm thinking about extensive small bowel moderate to severe disease, and that leads to, in pediatrics, growth abnormalities. First-line therapy should be infliximab.

Now in adults, we have other therapies that we'll talk about in other episodes, but I do think it's never the wrong choice to choose infliximab.

And then when we think about outside of the GI tract or extraintestinal manifestations, using therapies that targets the joint, such as adalimumab when we go after our spondyloarthropathies or our arthritis that goes along with IBD, then we think about inflammatory skin

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conditions, anti-TNF therapies, anti-tumor necrosis factors indicated in those treatments.

So that's how I kind of think about some of the positioning of who absolutely needs anti-TNF therapy. And if they don't, then we can go on to the gamut of treatment options that exist in IBD.

Dr. Rubin:
I think that's a really good overview. And I would just add that TNF is what I call an upstream cytokine, so it really covers a lot of downstream inflammatory problems. And certainly many of our colleagues, especially our older or more wise colleagues have grown up using anti-TNF and may be most comfortable starting there, but it's still an absolutely appropriate therapy.

In fact, some of our newer therapies don't seem to work quite as well in the small bowel. They work, but what we still see is that anti-TNF may do better in that setting as well. And then of course the patient who has hidradenitis or who has more inflammatory arthropathies, as you've mentioned, an anti-TNF strategy is terrific. And now we have, of course, subcutaneous infliximab in maintenance as another formulary option for some patients.

How do you distinguish, Mike, between IV infliximab and the subq adalimumab or certolizumab or golimumab options?

Dr. Dolinger:
When I think about IV infliximab and its benefit over adalimumab, let's say, I really think about it acting in both the colon and the small intestine, whereas I think as adalimumab as an excellent therapy when you have limited small bowel disease. Some of the most common places that Crohn's disease causes inflammation, that last foot of the terminal ileum, adalimumab is an excellent option. But when you have moderate to severe ileocolonic disease or perianal disease or proximal small bowel disease, that's where I think infliximab is a superior choice to our other anti-TNF therapies.

I don’t know how you feel about that?

Dr. Rubin:
I still think that's right. And even when you look at the more modern attempts to compare therapies in network meta-analyses and other ways, but frankly even in clinical practice, it still seems to be one of the most effective strategies we have. And among my patients who've cycled to other drugs over time, many of them will reflect back to that first dose of infliximab, where they really felt amazingly well, and so I think that there's relevance there.

Of course, we've also learned the most about anti-TNF when it comes to understanding measurements of serum concentrations. And in fact, to this day and despite other monoclonal antibody strategies, it's really only with anti-TNF that we know how to interpret and use drug levels.

So our final point today would be, how are you using serum concentrations, Mike, in your practice? In everybody, proactive, reactive, what are you doing?

Dr. Dolinger:
My practice is to use it in everybody in a proactive manner during induction because I think it's critical to get the dosing right of anti-TNF therapies during induction, either for infliximab at that third or fourth dose trough is critical, and for adalimumab at that week-4 level.

However, I think the biggest use that you can do for checking serum concentrations is if your patient's not responding in a reactive manner, to make sure that they have a detectable drug level, to make sure they don't have antibodies. That's really where you can have a key decision point for the use of serum concentrations that I think most gastroenterologists could probably agree on.

Dr. Rubin:
I do the same thing you mentioned. And just for our colleagues, the pre week-6 drug level, so prior to the third loading dose, I want it to be higher than 17. That's the statistical analysis cutoff. And if it's not, then I give the next dose at week 10. I don't wait 8 weeks after week 6, and I may adjust the amount of drug as well.

And in fact, in our colleagues in Belgium who really taught us about serum concentration assessments, have started just routinely giving a week-10 dose, so they essentially give four loading doses. So I think that that's a really important point, so you capture people who are clearing drug too fast early rather than waiting for them to lose response later.

So this has been a very short discussion, but on a really important topic with the drug that was revolutionary when it arrived, infliximab, and all the subsequent anti-TNF analogs.

I really want to thank you, Mike, for giving us those pearls and for joining me today in this conversation.

Dr. Dolinger:

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Thank you.

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