Putting It Into Practice: Medical Management of NETs

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Well, thank you very much for asking me to give my thoughts on the preceding webinar hosted by Dr. Goodwin and with the key panelist as Dr. Simron Singh. I think the webinar that was just given was very appropriate in terms of how we treat neuroendocrine tumours.

I'm a medical oncologist at the Stronach Regional Cancer Centre up in Newmarket. I treat lung, GI, including neuroendocrine tumours. I do melanoma and skin as well. I think the landscape on how to treat neuroendocrine tumours has changed quite dramatically, especially with NETTER-1 and NETTER-2 that was briefly touched on the previous webinar.

But I think more importantly that those of us in the community who see these tumours, they don't make up a bulk of our practise. So I think we get a bit rusty in terms of what to choose first, what to choose second, which is better, which is not, what is the preferred first-line option.

All of those questions, I think, always come to mind. And I think there has been paradigm shifts in terms of how we actually monitor these cancers, especially now no longer really using chromogranin A, using more urine 5-HIAA. And as Dr. Singh alluded to, I think their sender has moved on to using serum serotonin levels to monitor disease. We're still a ways away from that.

I think it's always good to remind ourselves that the primary, first-line treatment for patients who have grade 1, or low-risk, or low grade 2 neuroendocrine tumours is a somatostatin analogue. And I think we will touch on how I choose in my practise in the community as to which somatostatin analogue I use above another.

I think it's also important to know that the treatment landscape has changed in the sense that we now have evidence from NETTER-2, suggesting that patients who have higher grade 2 or well-differentiated grade 3 do very well with lutetium PRRT or radioligand therapy.

I think also from that data that was discussed with Dr. Goodwin and Dr. Singh is that even using a higher dose of a somatostatin analogue can afford some patients progression-free survival. I think it was also good to highlight how the evolution of clinical trials in this space has changed.

I think the first trial, the PROMID trial, followed by CLARINET, and now the NETTER-1, NETTER-2, and whole bunch of slew of studies in between has refined the protocol design to ensure that we're consistent throughout these studies, so we can actually somewhat compare them as it were.

I think overall discussion on how we escalate the somatostatin analogues looking out for the toxicities and the differential diagnosis of potentially diarrhea and perhaps new ways of potentially treating some of the side effects is really pertinent.

I think it was an excellent webinar on reminding us in the community as to what and how we can treat neuroendocrine tumours, at least in the first-line setting. It gets a lot more complex after that.

I think the next step is to determine-- and I think as part of this discussion was to allude to how I choose between the different somatostatin analogues. And I have to say that in my practise, I use predominantly lanreotide. And there's several issues that I use, or several characteristics that I use to make my decision.

I think the important thing to remember is that long-acting or octreotide LAR versus lanreotide-- their physiological effects are very similar in how they affect the same SSTR2 and to a lesser degree SSTR5. I think their half lives are roughly about the same. And they work because they engage with the receptors for a longer amount of time.

I think from an efficacy perspective, we saw from the webinar with Dr. Goodwin and Dr. Singh that there were definitely some trial differences between PROMID and CLARINET-- the size of the patients, the grades of the patients, as well as if they were progressing or not.

The PROMID trial probably had slightly more aggressive patient population, and CLARINET maybe not as much. But that being said, we saw great benefit in PFS of these patients getting long-acting somatostatin analogue.

I think the efficacy is-- most of us will consider them the same. I think we also have to take into account evidence and for the ability to escalate. I think, as was alluded to in the webinar, that CLARINET FORTE was a non-randomized trial, where they increased the dose of the lanreotide from q. 28 days to q. 14 days, and we saw that there was a good progression-free survival in those patients who did do that.

Equally NETTER-1 and NETTER-2, the control arm was a higher dose of octreotide LAR. And we can see that afforded patients between 9 and 10 months of PFS. So I think there's good evidence to escalate the two.

I think using some subtle differences in terms of the administration in Ontario where I practise as well as Dr. Singh and Dr. Goodwin, octreotide LAR is now generic, as such the patient support program for injections was stopped. I think they may still have that going on.

However, lanreotide still does have a patient support program, where they actually will go out to patients' houses and still inject the lanreotide. I think that one-to-one nursing support for a patient to get to know their injector is really, really important.

These nurses that do go around see a lot of patients who have neuroendocrine tumours. They know how to talk about the toxicities. And they can actually flag when patients are having issues.

Other patients, for example, for octreotide LAR, because when it went to generic, it actually had to go and find other areas to get injections. And so they would, maybe, go to an injection Centre, which was available. Some of my patients went to their family doctors.

And the problem with that is a, it might be a different nurse every time. The doctor is obviously the same. But I was finding that I wasn't actually getting injection or infusion reports from patients that were not on part of the patient support program.

So there was definitely some hiccups in getting those injection reports. But at least I know my patient is getting it. So every time I see them every two or three months, I can look back and see, OK, yes, the injection was given q. 28 Months, or it wasn't. So I think that's also very important in terms of getting a report.

So I think the patient support and patient home injection is very important, and also having a nurse come out and see the patient and lay eyes on them and call me if there's an issue is really important as well.

I think another issue to remember is that with the generic-- and I should note that I believe that lanreotide is also going generic. But when octreotide LAR went generic, there was a lot of stuttering start and go because of supply chain issues.

And so it got to the point where patients were actually having a hard time getting the generic, which was auto substituted. And then we had to also now figure out how they were going to go back to the brand name because the generic was not available.
Thankfully with lanreotide, it's been consistent. We've been able to get drug. And so that's why I do prefer the lanreotide for that reason. It's injectable where patients can actually get it injected by a nurse. I can get confirmation that they actually got the injection. And there's a steady supply.
The other thing is that we've all talked about the Sub-Q versus the deep IM. Lanreotide is a deep Sub-Q-- sorry-- and octreotide LAR is an IM injection. There is data to suggest that up to 50% of patients with the IM injection or maybe not getting delivery into the musculature. So it was not actually intramuscular.
And I believe that even with training of the administrators of the drug, that only increased to 75% of accurate injection into the musculature. As such, a deep Sub-Q is a little bit easier to give.
And I have to say that I've had patients who have actually learned to administer it to themselves, which made it a lot easier for them to travel and not have to be getting injections or waiting at home for the nurse to come by. Especially if they're on the escalated dose, it makes it a lot easier. So I think those are two important things to look at as well as the method of delivery.
Now, there's also some suggestion that giving lanreotide is a little bit easier. It's easier to constitute. It might be a little bit faster to do. So that's another thing. And then also there was a concern that octreotide gets to its steady state after about three injections, whereas lanreotide becomes steady state after the first injection.
I think the other thing that we need to worry about is what's coming down the pipeline when we're talking about generics, and also the fact that SSAs may be going oral as well. So I think as it stands right now, I think there is no evidence from an efficacy perspective to choose one over the other. They have not been compared head to head.
But I think there's a couple of other nuances that makes me favour slightly lanreotide. That being said, if I had access to somatuline-- sorry, to sandostatin or octreotide LAR, I would be fine using that for a patient for tumour control and symptom control.
So I think all in all, there's no right answer as to which want to use. These are some of the characteristics that I look at when I'm choosing which SSA I would use in the first line.
I also want to thank Dr. Singh and Dr. Goodwin for doing this summary because I think that webinar is going to help those of us in the community that don't see neuroendocrine tumours on a daily basis to remind us as to what the treatment landscape looks like and how it is changing and to remind us that we now do have radioligand therapy as a first-line option for patients with neuroendocrine tumours. Thank you very much.
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