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Evaluating Biologic Therapy Response in Severe Asthma Care

Dr. Turck:
This is *Clinician's Roundtable* on ReachMD, and I'm Dr. Charles Turck. Joining me to share strategies for evaluating a patient's response to biologic therapy for severe asthma is Dr. Sara Assaf. She's a senior faculty member in the Division of Pulmonary and Critical Care at Baylor College of Medicine. Dr. Assaf, welcome to the program.

Dr. Assaf:
Thank you. Thanks for having me.

Dr. Turck:
Well, let's start with the big picture, Dr. Assaf. When you're assessing a patient after they've started biologic therapy, what outcomes matter most to you in determining whether the treatment is truly working?

Dr. Assaf:
You know, I think it's very patient dependent. There's definitely not one metric that we can use to measure response to biologics in severe asthmatic patients. So while we think about reduction of exacerbations, being able to wean patients off oral corticosteroids, and improvement in symptomatology, sometimes it differs depending on what matters most to the patient.

Some of them have been on steroids for a very long time, and they want to try to come off of them to minimize the side effects. Others may be more focused on symptom improvement; they want to try to get through the night sleeping, do their day-to-day functions, and avoid any absenteeism or not going to work or other activities.

So in general, it's not just one metric. It's more like a multidimensional assessment of those outcomes. And of course, keep it always centered on what the patient wants or prioritizes as an outcome rather than just focusing on one objective metric or other patient-reported metric.

Dr. Turck:
Well, taking a closer look at some of those key measures and starting with exacerbation reduction in real-world practice, how do you balance that objective outcome with day-to-day symptom measures like the Asthma Control Test or Asthma Control Questionnaire?

Dr. Assaf:
I think those two are mostly complementary but not necessarily interchangeable. At times, they also lag behind; one might lag behind the other one. So we might see reduction in exacerbations because in the immune cascade, we're doing a certain anti-inflammatory targeting. But patients can continue to have symptoms where we have to look into other comorbid conditions, like heart failure, overlap with COPD or other conditions, GERD, and any other uncontrolled comorbidities.

So they sometimes diverge, meaning that we can meet one of the targeted outcomes and not the other one. That does not necessarily mean treatment failure, but we need to dig further to make sure there are no other patient-related or treatment-related factors that we need to look into.

In general, the exacerbation outcome is a more longitudinal one that we have to watch over a longer period of time. And as I said, the symptom outcome also might vary depending on what other comorbid factors can be contributing to it.

Dr. Turck:
Now, lung function and oral corticosteroid reduction are two other key measures, as they sometimes tell a different story than symptom scores. So how do you interpret situations where symptom control improves, but these other domains don't change as much as

expected?

Dr. Assaf:
We see it a lot in our patients where they're having reductions in exacerbation and they're having improvement in symptoms, yet spirometry may or may not improve. It can lag behind, plateau, or just not really improve. And I think it also depends on the history of longstanding asthma, having any airway remodeling or structural changes, having any asthma-COPD overlap, or having improvement in small airway disease but not necessarily in FEV1 measurements. So things like asymmetry or air trapping can help better discern that rather than getting a single measurement with FEV1.

Now, regarding corticosteroids, depending on their ability to be weaned off or minimize bursts, that can also not go hand in hand at times with improvement in symptomatology. And sometimes, they get that energy effect from corticosteroids rather than being necessarily needed for any exacerbation or maintenance treatment.

Dr. Turck:
For those just joining us, you're listening to *Clinician's Roundtable* on ReachMD. I'm Dr. Charles Turck, and I'm speaking with Dr. Sara Assaf about applying evidence-based measures to assess treatment response, guide biologic therapy adjustment, and optimize outcomes when caring for patients with severe asthma.

Even with these measures, one of the practical challenges clinicians face is knowing when to formally reassess biologic therapy. So, Dr. Assaf, what's your typical timeline for evaluating response, and what are you looking for during that reassessment window?

Dr. Assaf:
I think in general, we try to follow the guidelines and what we have mostly in the literature in terms of a trial of at least four to six months to assess outcomes and responses like we talked about—exacerbation risk reduction, corticosteroid tapering or not needing corticosteroid bursts, and symptom improvement.

We use some questionnaires like ACT—the asthma control test—ACQ, or other metrics. We do follow-up spirometry, and then we decide sometimes if we even need to further extend that timeline from four to six months and be more lenient with six to 12 months depending on which outcomes we're reaching, which ones are still lingering behind, or if we're having some different or divergent responses in our outcomes. And we always assess the priorities in terms of what the patients are looking for as prioritized target outcomes for them.

But in general, four to six months is the timeline to assess. Of course, we also ask them about how much they're using their relieving medication, and we again go with inhaler and biologic adherence and review all of those factors.

Dr. Turck:
Now, another common challenge is that not every patient has a clear or complete response to biologic therapy. So how do you approach situations involving partial response, plateau, or possible non-response?

Dr. Assaf:
That's also clinically based on the factors that we talked about in terms of outcomes. We assess it at multiple levels. At the patient level, are we missing an opportunity to optimize a comorbidity's management? Sometimes we have GERD, obstructive sleep apnea, heart failure, overlap with COPD, and other comorbidities that need optimization to reach better outcomes.

We also look into other biologic-related factors. We look at the underlying inflammatory biomarkers because those can tell us a lot about response. So we remeasure a lot of our Th2 inflammatory pathway biomarkers and see if there's any residual Th2 markers or if we need to address one domain of the cascade more than the other.

And also, we talk to patients regarding any side effects to those biologics or any adherence issues. So it's a multilevel assessment to see where we're lacking optimization or if we need to switch gears and consider another biologic.

Dr. Turck:
Well, speaking of that, if we look at one more scenario before we close, Dr. Assaf, let's say a patient isn't achieving the outcomes you'd hoped for. How do you decide whether to optimize the current approach or switch to another biologic?

Dr. Assaf:
We always go back to the basics—making sure that we're really dealing with severe asthma that is uncontrolled or difficult to control despite our medications or targeted therapies, making sure that there are no other comorbidities as we spoke about, and doing more radiological examinations at times. We consider high-resolution CTs and other factors that could be contributing.

And if all this is done—we don't think we need to optimize any other comorbidities, and we look at our T2 inflammatory biomarkers and we have residual activity or non-Th2 activity—this is where switching biologic to better target any inflammatory domain might be something that we consider, depending on what is more predominant. So sometimes we see a more residual predominant eosinophilic response, allergic response, or FeNO. This helps us better target our sequencing of biologics down the line.

Dr. Turck:
Well, with those practical considerations in mind, I want to thank my guest, Dr. Sara Assaf, for joining me to discuss how we can evaluate biologic therapy response in patients with severe asthma. Dr. Assaf, it was great having you on the program.

Dr. Assaf:
Thank you so much for having me.

Dr. Turck:
For ReachMD, I'm Dr. Charles Turck. To access this and other episodes in our series, visit *Clinician's Roundtable* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening!