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Targeting IL-5 in Severe Asthma: The Role of Biologic Therapies

Announcer:
You're listening to *Deep Breaths: Updates from CHEST* on ReachMD. This series is produced in partnership with the American College of Chest Physicians, and this episode is a non-promotional, non-CME educational program brought to you by CHEST in collaboration with and sponsored by GSK. And now, here's your host, Dr. Diego Maselli.

Dr. Maselli:
Welcome to *Deep Breaths: Updates from CHEST* on ReachMD. I'm Dr. Diego Maselli, a Professor of Medicine from the Long School of Medicine at UT Health in San Antonio. Joining me to share essential information on the role of interleukin 5 in severe asthma, and the impact of anti-IL-5 biologic therapies are Dr. Anju Peters and Dr. Monica Kraft. Dr. Peters works in the Division of Allergy and Immunology at Northwestern in Chicago, where she is currently a Professor of Medicine and Associate Chief of Clinical Research and Practice Innovation. Anju, it's really great to have you with us today.

Dr. Peters:
Thank you, Diego. Thank you for including me. I'm delighted to be here.

Dr. Maselli:
And Dr. Monica Kraft is a Assistant Chair of the Samuel Bronfman Department of Medicine and a Professor of Medicine at Icahn School of Medicine at Mount Sinai Health Systems in New York. Monica, thank you so much for joining us today.

Dr. Kraft:
Thank you, Diego. It's a pleasure to be here.

Dr. Maselli:
Okay, let's dive right in. Today, we're focusing on IL-5, a driver of type 2 inflammation, and its significant impact on severe asthma. Monica, can you begin by explaining the role of IL-5 in the context of Type 2 inflammation?

Dr. Kraft:
Absolutely. IL-5 is a key cytokine in the pathobiology of Type 2 inflammation. It influences the differentiation, proliferation and survival of eosinophils, which are central to the inflammatory response we see in severe asthma, especially Type 2 asthma. But we have learned a lot about IL-5 biology over the last several years, and really, the impact goes well beyond eosinophils. It affects mast cells, basophils, epithelial cells and fiberglass as examples, so it has very broad-ranging effects in the lung.

Dr. Maselli:
Okay, I'm going to turn to you, Anju. Could you elaborate a little bit more on how IL-5 influences inflammation in our patients with severe asthma?

Dr. Peters:
Absolutely. And just like Monica said, IL-5 plays a role in many different cells. IL-5 facilitates crosstalk between these immune cells, especially between eosinophils and mast cells. We've always known its role in eosinophil activation, but it also promotes basophil activation and even plays a role in smooth muscle activity. What is really interesting is that IL-5 also modulates T-regulatory cells and activates Type 2 innate lymphoid cells, or ILC2s. All of this contributes to the persistent inflammation and airway remodeling that we see in severe asthma.

Dr. Maselli:
It seems like IL-5 can orchestrate a wide range of immune responses and it really affects multiple cellular lines. Very interesting.

Monica, what can you tell us about how IL-5 can have some downstream effects on mucus plugging? I know that's a very hot topic in airway diseases nowadays.

Dr. Kraft:
It absolutely is, and it's one of the really serious consequences of severe asthma. So we know that the epithelial cell produces mucus, but in asthma, it tends to be very sticky and becomes difficult to clear from the airways. And how IL-5 changes or influences the situation is it promotes eosinophil activation, and these eosinophils release a product called eosinophil peroxidase that increases the stickiness or the viscosity of this mucus through cross-linking. And so, what can happen is, that actually adds to air flow obstruction because this mucus really isn't cleared well, even with oral corticosteroids.

Dr. Maselli:
That's very, very interesting. Let's change gears a little bit towards the airway epithelium. Anju, what is the latest evidence of how IL-5 may promote epithelial barrier dysfunction in the airways?

Dr. Peters:
So, Diego, it's important that we don't forget epithelial barrier dysfunction. We know IL-5 contributes to the increased epithelial permeability and immune balance, both of which further exacerbate asthma severity. And that's why targeting IL-5 is very important because it gets to the root of several compounding problems and where the inflammation starts—at the epithelium.

Dr. Maselli:
For those just joining us, this is *Deep Breaths: Updates from CHEST* on ReachMD. I'm Dr. Diego Maselli, and I'm speaking with Dr. Anju Peters and Dr. Monica Kraft about how anti-IL-5 biologic therapies can help manage our patients with severe asthma.

So, given the impact of IL-5 on severe asthma, let's discuss how we can identify patients who might benefit from IL-5 targeted therapy. Monica, what should clinicians be looking for when considering anti-IL-5 biologics?

Dr. Kraft:
Great question. I think the key is to recognize severe uncontrolled asthma, especially in those patients not responding to standard treatments like high-dose inhaled corticosteroids and long-acting bronchodilators, and also addressing comorbidities like rhinitis, GERD, heartburn, and obstructive sleep apnea, as examples. But also, it's important to check biomarkers and a CBC with diff to check blood eosinophil count. It should be a standard part of asthma care. Because we know that the elevated eosinophils, one, suggest responsiveness to anti-IL-5 biologics, and also, there's a positive correlation between blood eosinophils and exacerbation frequency. So, it gives you multifaceted information. The higher the blood eosinophils, the higher the annual exacerbation rate. And that would again, give you information that that particular patient would be a candidate for biologic therapy such as an anti-IL-5.

Dr. Maselli:
We have to really look out for these specific characteristics of the patients. Now, even when patients are eligible for these types of biologics, some patients and providers may still have some hesitation about initiating them. Anju, what are some of the barriers that have you have seen in your practice about initiating these types of therapies?

Dr. Peters:
That's actually a really good question too, Diego, because we see barriers both on the patient's side and the provider's side. Some barriers on the patient's side that may lead to hesitancy in initiating biologic therapy include patients who are fearful of injections. They worry about potential side effects from these biologics. Additionally, many patients don't perceive their asthma as being severe, despite them frequently using their rescue inhalers, and they live down their disease through avoiding activities to manage their symptoms. Costs are a big issue. Loss of hope on patient's side may be a barrier to starting these biologics.

And unfortunately, lack of urgency from healthcare professionals also may play a role in this hesitancy. This is where shared decision making comes in. We need to take the time to explain how biologics work, reassure the patients about the benefits, and talk to them about the safety profile. These biologics in general are very safe. And we have to emphasize our goals for these patients with asthma: fewer exacerbations, better symptom control, and improved quality of life. These can all help the patients feel more empowered in their treatment plan.

Dr. Maselli:
That shared decision making, it's so important when we're making these decisions for our patients and their families. I think it's so critical. Thank you so much for that.

So, as we wrap up, I would like each of you to share a key takeaway that you'd like to share with our providers that treat our patients with severe asthma. I'll start with you, Monica.

Dr. Kraft:
Absolutely. I think the key is, you want to start by identifying these patients early. Even one exacerbation per year that requires prednisone is something to be aware of. And I think providers don't always appreciate the seriousness of that. And many of these patients are, in primary care practices, followed by our colleagues, so as specialists, I feel like it's really important to work with our primary care colleagues to not only educate on how to identify these patients and how to check biomarkers like eosinophils, but to also realize that there are options, so that patients don't need to have prednisone even once a year. There may be options to stop the exacerbation, which is our goal, and allow these patients to receive optimal care.

Dr. Maselli:
Yes, education is so important. Anju, I'll give you the last word.

Dr. Peters:
Thank you, Diego. And I really would like to end by saying, never underestimate the power of education and communication. Shared decision-making can help promote trust between patients and clinicians, which can then help overcome biologic hesitancy and improve outcomes. It's important to note that patients might be waiting for you to bring up the next option or biologic, so don't assume potential receptivity to a biologic either. Instead, actively engage in discussions about all available options to ensure they feel informed and involved in their treatment plan.

Dr. Maselli:
Thank you both for those valuable insights. This was incredibly informative. I really appreciate the discussion. I would like to thank my guests, Dr. Anju Peters and Dr. Monica Kraft, for joining me to discuss how targeting IL-5 can help manage our patients with severe asthma. Anju and Monica, it was really great having you today.

Dr. Peters:
Thank you very much, Diego, for including me. It's been a pleasure.

Dr. Kraft:
Thanks very much, Diego. I really enjoyed it.

Announcer:
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