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## Insights to Pharmaceutical Approaches in COPD

### Announcer:

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### Dr. Han:

Hello. My name is Dr. Meilan Han, and this is CME on ReachMD. Here with me today is Dr. Surya Bhatt. So let's get to it. Let's discuss the current landscape of biologics in the management of patients with COPD. Surya, what's the evidence for biologics in COPD?

### Dr. Bhatt:

Thank you, Dr. Han. So I think we are living in really exciting times where there are lots of new therapies being explored, investigated, and we are seeing results of phase 3 clinical trials. So these are really exciting times for the investigation of inflammatory pathways in COPD.

There are several biologics that have either completed phase 3 trials and are waiting to be read out or have already reported their results. And perhaps the one that is most prominent right now in everybody's mind is dupilumab, which had two phase 3 trials that read out and were positive in terms of exacerbation reduction and improvement in several secondary outcomes such as lung function and quality of life. Dupilumab targets IL-4 receptor alpha, and this has been approved in the European Union, and an application to the FDA has been submitted and is awaiting decision. This has also been approved for other indications, such as asthma and atopic dermatitis.

There are other biologics that have looked at IL-5. Benralizumab is an IL-5 receptor antagonist, and the two phase 3 trials did not work initially, so there are now ongoing phase 3 trials that are looking at benralizumab with a higher eosinophil target of 300 and above. Mepolizumab is a monoclonal antibody against IL-5. And here also the two phase 2 trials that were METREX and METREO, did not meet their primary endpoints, and the FDA did not approve this medication for COPD. But the MATINEE trial has just finished reading out, and there was an announcement that it was successful in decreasing exacerbation frequency with a higher eosinophil target of 300 and above.

And there are also several ongoing trials for blocking the alarmins such as IL-33 in the form of itepekimab for which two phase 3 trials are ongoing. ST2 blocker in the form of astegolimab, for which two phase 3 trials are ongoing.— Tozorakimab, which is an IL-33 antibody, for which also phase 3 trials are ongoing. And then there is tezepelumab, which is approved for asthma, but in COPD, a phase 2a trial was read out, and a phase 3 trial is planned.

### Dr. Han:

So it's certainly a really exciting time, Surya, with lots of active clinical investigation and certainly a suggestion that there may be patients who benefit from treatment with biologics. How do you envision using biomarkers to help identify and optimize patients for the right treatments?

### Dr. Bhatt:

I think the most exciting biomarker right now is eosinophils, because we can use that to detect type 2 inflammation for which most of the biologics are being developed and tested. The one that recently read out was BOREAS and NOTUS for dupilumab. And here, there is evidence that if you use blood eosinophils and fractional exhaled nitric oxide, perhaps you can target the right patients. For instance, there is evidence that the higher the blood eosinophil counts, the greater the exacerbation reduction with dupilumab, and the higher the baseline FeNO level, the greater the reduction in exacerbation frequency. Also, there is data to suggest that if you use dupilumab, the FeNO levels decrease substantially from baseline over 52 weeks of treatment, but the blood eosinophils remain stable, and they don't really increase or decrease to significant levels.

**Dr. Han:**

Well, it sounds like we really do have some emerging targeted therapies with both good efficacy and safety profiles in symptomatic patients with COPD and evidence of type 2 inflammation who are at risk for exacerbations, despite use of triple therapy, which is really, I think, an unmet need. And in particular with dupilumab, as you just outlined, patients had fewer exacerbations, improved lung function, and improved quality of life. So I would anticipate, pending FDA approval, that we'll start to have targeted biologics as standard of care for COPD, hopefully in the near future.

Well, that's all the time we have for this clip. Thank you so much for listening.

**Announcer:**

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