Transcript Details

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Voices of COPD: How The Right Option Can Help Make a Difference

Announcer:
Welcome to ReachMD. This medical industry feature, titled “Voices of COPD: How Triple Therapy Could Help Make a Difference,” is sponsored by AstraZeneca.

Here’s your host, Dr Jennifer Caudle.

Dr Caudle:
This is ReachMD, and I’m your host, Dr Jennifer Caudle. And in this program, we’ll explore how the treatment option BREZTRI AEROSPHERE® (budesonide 160 mcg, glycopyrrolate 9 mcg and formoterol fumarate 4.8 mcg) can help reduce the risk of exacerbations in patients with chronic obstructive pulmonary disease, or COPD for short. BREZTRI combines three medicines: budesonide, glycopyrrolate, and formoterol fumarate.

Joining me today are Dr Henry Naddaf and Ms Meredith Cooper. Dr Naddaf is a distinguished family medicine specialist and the President of the Toledo Clinic in Toledo, Ohio.

Dr Naddaf, welcome to the program.

Dr Naddaf:
Thank you for having me, Dr Caudle.

Dr Caudle:
Of course. And Ms Meredith Cooper is a patient advocate for COPD. Meredith, thank you for joining us today.

Meredith:
Of course, I’m happy to be a part of the conversation.

Dr Caudle:
Before we begin, let’s take a moment to review the indications and limitations of use for BREZTRI AEROSPHERE®.

Announcer:

- BREZTRI AEROSPHERE is indicated for the maintenance treatment of patients with chronic obstructive pulmonary disease (COPD)
- BREZTRI is not indicated for the relief of acute bronchospasm or for the treatment of asthma
- BREZTRI is contraindicated in patients who have a hypersensitivity to budesonide, glycopyrrolate, formoterol fumarate, or product excipients
- BREZTRI is not indicated for treatment of asthma. Long-acting beta$_2$-adrenergic agonist (LABA) monotherapy for asthma is associated with an increased risk of asthma-related death. These findings are considered a class effect of LABA monotherapy. When a LABA is used in fixed-dose combination with ICS, data from large clinical trials do not show a significant increase in the risk of serious asthma-related events (hospitalizations, intubations, death) compared with ICS alone. Available data do not suggest an increased risk of death with use of LABA in patients with COPD

Additional Important Safety Information will be provided at the end of this video. The full Prescribing Information, including Patient

Information are found in the links provided, and can also be found on BREZTRIHCP.com.

Dr Caudle:
Meredith, let's start with your personal story, which is at the heart of this discussion. Could you share some details about your experience with COPD and how exacerbations have impacted your life?

Meredith:
Of course. I was previously diagnosed with asthma. So, leading up to my COPD diagnosis, I was having a great deal of shortness of breath, which was assumed to be a part of my asthma-related condition. In 2017, I had a major health attack involving four systems, that was heart failure, respiratory failure, kidney failure, and hypovolemia. I was hypoxic and placed on supplemental oxygen and breathing treatments. With hard work, my medical team, caretakers, and I got my symptoms under control.

But two years later, I was able to come off the supplemental oxygen, although I still required a rescue inhaler, and I had to use the maintenance inhaler along with the corticosteroid. Despite all of the progress that had been made, I was hospitalized twice after that, and I had to be placed back on oxygen therapy for several months. Then, later that year, I went on a cruise with my daughter where I began to experience extreme difficulty in breathing. Just a few steps would take my breath away. I had to seek medical attention while on board, and it was suggested that I would stay in my cabin and rest for the remainder of the cruise because I wanted to prevent an emergency situation and maybe having to be flown home or something like that. But, you know, this was definitely a new experience for me. I was extremely terrified, and my daughter was also very scared. And I hated that, you know, that kind of messed it up for her as well.

But it wasn't until I returned home that I was diagnosed with COPD. That was a shocker to me, even though it was still lung-related. I kind of had a hard time grasping that. And after that, I struggled for a while trying to find the perfect treatments. My doctor started me on a new maintenance inhaler, along with the continued use of the rescue inhaler and breathing treatments. Despite that, you know, every movement was difficult, and I could not keep my oxygen levels up, and I'm using the oximeter, trying to read it and everything, and it was very distressing. I also dealt with a few respiratory infections, and those sent me to the Emergency Department, and I had another hospitalization during that time. Even with the supplemental oxygen treatments, I found myself being homebound.

Dr Caudle:
Well, thank you, Meredith. I sincerely appreciate you sharing your challenging journey with us.

Now, Dr Naddaf, considering the challenges faced by patients like Meredith, could you tell us about BREZTRI's role as a triple therapy for patients with COPD?

Dr Naddaf:
Absolutely. But first, hearing Meredith's experiences truly underscores the impact that exacerbations can have on our patients' lives. And so it's important that we continue to act swiftly and decisively when managing symptoms for our patients with COPD.

Now, returning to your question about BREZTRI's role as a treatment option for COPD, let me start by providing a bit of background. BREZTRI was studied in over 8,500 patients with moderate to very severe COPD for 52 weeks in a multicenter, phase 3 clinical trial called ETHOS. These patients were 40 to 80 years of age with a history of:

- smoking at least 10 pack-years,
- symptomatic COPD while receiving 2 or more inhaled maintenance therapies,
- at least 1 moderate or severe COPD exacerbation in the previous year.[1]

Moderate exacerbations were defined as those leading to treatment with systemic corticosteroids and/or antibiotics, and severe exacerbations were defined as those resulting in hospitalization or death. In this double-blind, parallel-group trial, patients were randomized in a 1:1:1:1 ratio to compare BREZTRI with three treatment regimens:

- triple therapy with budesonide, glycopyrrolate, and formoterol fumarate,
- and two dual therapies—a LAMA/LABA consisting of glycopyrrolate and formoterol fumarate,
- or an ICS/LABA with budesonide and formoterol fumarate.[1]

Lastly, all treatments were administered twice daily by a metered dose inhaler.[1]

The findings showed that BREZTRI significantly reduced the annual rate of moderate-to-severe COPD exacerbations by 24 percent over 52 weeks when compared to dual therapy with LAMA/LABA. The ratio was 0.76, and the P-value was less than 0.0001.[1,2]

Similarly, BREZTRI also demonstrated a 13 percent reduction in such exacerbations compared to treatment with ICS/LABA, with a rate ratio of 0.87 and a P-value of 0.0027. And finally, the annual rate estimate for BREZTRI was 1.08, compared to 1.42 for LAMA/LABA and 1.24 for ICS/LABA.[1,2]

Dr Caudle:
For those of you who are just tuning in, you're listening to ReachMD. I'm your host, Dr Jennifer Caudle, and today I'm speaking with Dr Henry Naddaf and Ms Meredith Cooper about the use of triple therapy against COPD exacerbations.

So, Dr Naddaf, continuing our conversation on BREZTRI, can you tell us how this treatment option might help protect against exacerbations in patients with COPD?

Dr Naddaf:
Of course. I can share some additional analysis from the ETHOS study that I mentioned earlier to help answer your question.

The data from ETHOS was used to calculate the event-based number needed to treat, or NNT for short. In other words, the NNT value represents the number of patients needed to be treated for one year to prevent one COPD exacerbation. It's calculated by taking the reciprocal of the absolute risk reduction.[1,3] So for every seven patients treated over a year, BREZTRI could prevent one additional moderate or severe exacerbation compared with ICS/LABA. A 95 percent confidence interval here was between 4 and 18 patients. And when compared to LAMA/LABA, BREZTRI could prevent one additional moderate or severe exacerbation for every three patients treated over a year, with a 95 percent confidence interval between three to five patients.[1,3]

That said, it's important to discuss the safety profile of BREZTRI. It had a safety profile comparable with LAMA/LABA and ICS/LABA. All adverse reactions for BREZTRI occurring at an incidence of two percent or greater in patients, and more common in BREZTRI compared with LAMA/LABA and ICS/LABA, were:

- upper respiratory tract infection, 5.7 percent;
- pneumonia, 4.6 percent;
- back pain, 3.1 percent;
- oral candidiasis, 3 percent;
- influenza, 2.9 percent;
- muscle spasm, 2.8 percent;
- urinary tract infection, 2.7 percent;
- cough, 2.7 percent;
- sinusitis, 2.6 percent; and
- diarrhea, 2.1 percent.[2]

In my clinical experience, a triple therapy, like BREZTRI, can be a key approach to maintenance therapy as we create a care plan with our patients to actively manage their COPD.

Dr Caudle:
Excellent perspective, Dr Naddaf.

Now bringing the discussion back to your journey, Meredith, do you mind sharing the impact that BREZTRI has had on your care experience as some final thoughts?

Meredith:
Absolutely. My primary care provider introduced me to BREZTRI when I was having difficulty breathing and doing daily activities. Initially, I was reluctant because I had already tried other options, but I wanted to find a treatment that could help manage my symptoms better.

Since starting BREZTRI, I've noticed an improvement in my ability to breathe easier. I also haven't visited the emergency room or been hospitalized for my COPD.

And so I feel a little more confident pushing my boundaries now. I can finish house chores without frequent interruptions for rescue inhaler treatments or long breaks. With careful planning, I can also do more activities away from home. I can walk to my car with less trouble breathing, and I feel encouraged to go to the grocery store by myself. I use my rescue inhaler less often when leaving my home. Plus, being able to use my inhaler without a spacer has been a lot more convenient.

So overall, BREZTRI has really made a difference for me. I wish it had been available to me from the very beginning of my COPD

journey.

Dr Caudle:
Well, thank you for sharing your personal experience, Meredith.

Meredith:
You're welcome.

Dr Caudle:
As we wrap up today's program, I'd want to acknowledge Dr Henry Naddaf and Ms Meredith Cooper for their valuable viewpoints on the role of BREZTRI in managing future exacerbations for patients with COPD.

Dr Naddaf and Meredith, it was great speaking with you both today.

Dr Naddaf:
Thank you, Dr Caudle, for having me. And Meredith, it was truly inspiring hearing your story.

Meredith:
Thank you so very much. I'm so glad that I was able to be a part of the conversation.

Dr Caudle:
For ReachMD, I'm your host, Dr Jennifer Caudle. And before we close, let's take a moment to review some important safety information.

Announcer:

- BREZTRI should not be initiated in patients with acutely deteriorating COPD, which may be a life-threatening condition
- BREZTRI is NOT a rescue inhaler. Do NOT use to relieve acute symptoms; treat with an inhaled short-acting beta$_2$-agonist
- BREZTRI should not be used more often than recommended; at higher doses than recommended; or in combination with LABA-containing medicines, due to risk of overdose. Clinically significant cardiovascular effects and fatalities have been reported in association with excessive use of inhaled sympathomimetic drugs
- Oropharyngeal candidiasis has occurred in patients treated with orally inhaled drug products containing budesonide. Advise patients to rinse their mouths with water without swallowing after inhalation
- Lower respiratory tract infections, including pneumonia, have been reported following ICS. Physicians should remain vigilant for the possible development of pneumonia in patients with COPD as the clinical features of pneumonia and exacerbations frequently overlap
- Due to possible immunosuppression, potential worsening of infections could occur. Use with caution. A more serious or fatal course of chickenpox or measles can occur in susceptible patients
- Particular care is needed for patients transferred from systemic corticosteroids to ICS because deaths due to adrenal insufficiency have occurred in patients during and after transfer. Taper patients slowly from systemic corticosteroids if transferring to BREZTRI
- Hypercorticism and adrenal suppression may occur with regular or very high dosage in susceptible individuals. If such changes occur, consider appropriate therapy
- Caution should be exercised when considering the coadministration of BREZTRI with long-term ketoconazole and other known strong CYP3A4 Inhibitors. Adverse effects related to increased systemic exposure to budesonide may occur
- If paradoxical bronchospasm occurs, discontinue BREZTRI immediately and institute alternative therapy
- Anaphylaxis and other hypersensitivity reactions (eg, angioedema, urticaria or rash) have been reported. Discontinue and consider alternative therapy
- Use caution in patients with cardiovascular disorders, especially coronary insufficiency, as formoterol fumarate can produce a clinically significant cardiovascular effect in some patients as measured by increases in pulse rate, systolic or diastolic blood pressure, and also cardiac arrhythmias, such as supraventricular tachycardia and extrasystoles
- Decreases in bone mineral density have been observed with long-term administration of ICS. Assess initially and periodically thereafter in patients at high risk for decreased bone mineral content
- Glaucoma and cataracts may occur with long-term use of ICS. Worsening of narrow-angle glaucoma may occur, so use with caution. Consider referral to an ophthalmologist in patients who develop ocular symptoms or use BREZTRI long term. Instruct patients to contact a healthcare provider immediately if symptoms occur
- Worsening of urinary retention may occur. Use with caution in patients with prostatic hyperplasia or bladder-neck obstruction. Instruct patients to contact a healthcare provider immediately if symptoms occur
- Use caution in patients with convulsive disorders, thyrotoxicosis, diabetes mellitus, and ketoacidosis or unusually responsive to sympathomimetic amines

- Be alert to hypokalemia or hyperglycemia
- Most common adverse reactions in a 52-week trial (incidence ≥ 2 percent) were upper respiratory tract infection (5.7 percent), pneumonia (4.6 percent), back pain (3.1 percent), oral candidiasis (3.0 percent), influenza (2.9 percent), muscle spasms (2.8 percent), urinary tract infection (2.7 percent), cough (2.7 percent), sinusitis (2.6 percent), and diarrhea (2.1 percent). In a 24-week trial, adverse reactions (incidence ≥ 2 percent) were dysphonia (3.1 percent) and muscle spasms (3.3 percent)
- BREZTRI should be administered with extreme caution to patients being treated with monoamine oxidase inhibitors and tricyclic antidepressants, as these may potentiate the effect of formoterol fumarate on the cardiovascular system
- BREZTRI should be administered with caution to patients being treated with:
    - Strong cytochrome P450 3A4 inhibitors (may cause systemic corticosteroid effects)
    - Adrenergic drugs (may potentiate effects of formoterol fumarate)
    - Xanthine derivatives, steroids, or non-potassium sparing diuretics (may potentiate hypokalemia and/or ECG changes)
    - Beta-blockers (may block bronchodilatory effects of beta-agonists and produce severe bronchospasm)
    - Anticholinergic-containing drugs (may interact additively). Avoid use with BREZTRI

Use BREZTRI with caution in patients with hepatic impairment, as budesonide and formoterol fumarate systemic exposure may increase. Patients with severe hepatic disease should be closely monitored.

You are encouraged to report side effects related to AstraZeneca products by calling 1-800-236-9933. If you prefer to report these to the FDA, please call 1-800-FDA-1088. You may report side effects related to AstraZeneca products.

This medical industry feature was sponsored by AstraZeneca. If you missed any part of this discussion, visit Industry Features on ReachMD.com, where you can Be Part of the Knowledge.

References:

1. Rabe KF, Martinez FJ, Ferguson GT, et al; ETHOS Investigators. Triple inhaled therapy at two glucocorticoid doses in moderate-to-very-severe COPD [article and supplementary appendix]. *N Engl J Med*. 2020;383(1):35-48.
2. BREZTRI AEROSPHERE® (budesonide, glycopyrrolate, and formoterol fumarate) [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2022.
3. Rabe KF, Martinez FJ, Ferguson GT, et al. COPD exacerbation benefits relative to pneumonia risk with budesonide/glycopyrronium/formoterol metered dose inhaler: analyses from ETHOS [abstract]. *Eur Respir J*. 2020;56(suppl 64):5230.