Transcript Details

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Severe, Uncontrolled Eosinophilic Asthma: Helping Protect Your Patients from OCS Overexposure

Announcer:
Welcome to ReachMD. This medical industry feature, titled “Severe, uncontrolled eosinophilic asthma: Helping protect your patients from OCS overexposure,” is sponsored by AstraZeneca. Here's Dr Shyam Subramanian now.

Dr Subramanian:
This is ReachMD, and I’m Dr Shyam Subramanian—a pulmonologist working in Tracy, California—and I would like to talk to you today about the overuse of oral corticosteroids, or OCS for short, in patients with severe asthma.

You may know that approximately 25 million people in the United States suffer from asthma.[1] But did you know that as many as 10% of these patients have severe asthma, which may remain uncontrolled despite ICS/LABA with or without OCS?[2,3] This is, of course, a major issue as severe, uncontrolled asthma can be not just debilitating but, in a small percentage, fatal.[2]

It’s time to protect patients with asthma from overexposure to OCS and recognize that overuse of OCS can be a treatment plan failure.[4] Patients with severe asthma are often put on an OCS to treat asthma exacerbations and help control symptoms.[4,5]

OCS medications have been a long-standing option of acute asthma treatment for more than 60 years.[5] And there’s no doubt that such medications can improve symptoms and that they have their appropriate place in treatment.[2,6] For example, OCS are used routinely in the emergency setting. But as you know all too well, those benefits can come with unwanted consequences and can reduce patients’ health-related quality of life.[2] What’s more, OCS use can lead to OCS reliance.[7] This is why it’s important to protect your patients with severe, uncontrolled asthma from OCS overexposure.[2,8]

But what exactly constitutes OCS overexposure? Well, it may be much less than you think. In fact, even short courses of OCS are associated with a range of side effects.[2,9] OCS side effects can include fluid retention, weight gain, mood alteration, insomnia, hypertension, and peptic ulcers.[2,9] In fact, as few as four short courses of OCS can amount to one gram of exposure.[9]

The risk of side effects can increase as cumulative OCS doses increases.[9] For example, with increased risk of exposure to OCS, there is increased risk of cataracts, heart failure, cardio- or cerebrovascular disease, type 2 diabetes, osteoporosis, pneumonia, depression, anxiety, and even renal impairment.[9] Long-term OCS use can also bring the additional risk of potentially suppressing the hypothalamic-pituitary-adrenal axis, which can lead to adrenal insufficiency.[10]

Bearing these risks in mind, it’s easy to see why it may be prudent to avoid maintenance OCS use as much as possible in a patient with severe, uncontrolled asthma.[7] But is that easier said than done? Patients with uncontrolled severe asthma present with poor symptom control, frequent severe or potentially life-threatening exacerbations, or fixed airflow obstruction.[2,11] So could there be another way to help such patients keep their severe asthma under control over the long term while also helping them reduce OCS exposure?

Well, there are data to suggest this is possible, and that there are treatments that can offer benefits for more patients than you might imagine. For instance, certain treatments might be able to help patients with severe uncontrolled asthma become less dependent on oral corticosteroids and can be used to reduce exacerbations requiring steroids.[2,12]

For many patients, the path to potentially finding a treatment alternative to OCS can begin with appropriate diagnosis. After all, when it comes to severe, uncontrolled asthma, a number of different phenotypes exist. If, for example, you have a patient on high-dose

ICS/LABA also on maintenance OCS, that patient may have severe eosinophilic asthma.[2,13-15] Why? Because according to a US study, more than 2 out of every 3 adults with severe asthma have the eosinophilic phenotype.*[16,17]

If you have a patient with severe, uncontrolled asthma, getting a complete blood count with differential can help identify the presence of eosinophilic asthma.[2,16] Clinical guidelines don't currently define the cutoff for eosinophilic asthma, but a generally accepted characterization of eosinophilic asthma is a blood eosinophil count of greater than or equal to 150 cells/µL.[2,16] And keep in mind that eosinophil counts may be reduced in patients receiving OCS.[2,18]

For appropriate patients with severe eosinophilic asthma, a targeted treatment option may provide the asthma control they need while also helping to protect against OCS exposure.[2,12] There are various treatments available, but today we'll focus on FASENRA®, or benralizumab, a targeted treatment option for severe asthma patients with an eosinophilic phenotype.[12]

FASENRA is an anti-eosinophil biologic medication indicated for the add-on maintenance treatment of patients with severe eosinophilic asthma aged 12 years or older.[12] It's important to note that FASENRA isn't indicated for the treatment of other eosinophilic conditions or for the relief of acute bronchospasm or status asthmaticus.[12] As for dosing, it's given subcutaneously at a recommended dose of 30 milligrams once every 4 weeks for the first 3 doses, and then once every 8 weeks as a maintenance dose. That makes FASENRA the only respiratory biologic to provide patients with the convenience of once every 8 weeks maintenance dosing.[12] It also offers the option of in-office and at-home administration.[12]

FASENRA has a unique mechanism of action by which it targets blood eosinophils. It binds directly to the IL-5 or interleukin-5 receptor alpha on eosinophils to attract natural killer cells, which then induce the apoptosis of eosinophils without the release of inflammatory markers.[12,19] As a result, FASENRA rapidly achieves the near-complete depletion of blood eosinophils.†[20] Please note that the mechanism of action of FASENRA in asthma has not been definitively established.[12]

Now let's take a look at some of the data on FASENRA. The FASENRA clinical program included three Phase 3 studies: SIROCCO, CALIMA, and ZONDA. In the 28-week, randomized, double-blind, placebo-controlled ZONDA study, FASENRA demonstrated power to protect patients from OCS exposure.[12,22]

The patients enrolled in ZONDA were OCS-dependent, which was defined as requiring the equivalent of between 7.5 and 40 mg per day of prednisone. They were on high-dose ICS/LABA with or without additional controller medications, with a history of at least one exacerbation in the prior year and a blood eosinophil count of 150 cells per microliter. The primary endpoint of the study was the median percent reduction from baseline in final OCS dose while maintaining asthma control.[12,22]

In ZONDA, OCS-dependent patients who received FASENRA plus standard of care achieved a statistically significant 75% reduction in median final OCS dose. That's compared to a 25% reduction in patients receiving placebo plus standard of care while maintaining asthma control.[12,22]

FASENRA also demonstrated OCS sparing in the single-arm, open-label PONENTE trial, which is currently the largest steroid-sparing study undertaken with asthma biologics.[11,23,24] Results from PONENTE were descriptive only; no formal hypotheses were tested. PONENTE enrolled 598 adults with asthma who required high-dose ICS/LABA for at least 6 months plus OCS, which was defined as 5 mg or more of prednisone or equivalent per day for at least 3 months. Of note, all patients had blood eosinophil counts greater than or equal to 150 cells/µL at baseline or greater than or equal to 300 cells/µL in the previous 12 months.[24]

At 4 weeks following FASENRA initiation, patients in PONENTE began an OCS-reduction algorithm with down-titration made possible by the lack of placebo.[24] For patients with daily prednisone dosages greater than or equal to 7.5 mg/day, this tapering schedule was more rapid than any used in previous studies.[11] What's more, tapering was personalized based on the presence of adrenal insufficiency.[11,24]

62.2% of patients receiving FASENRA in PONENTE achieved complete elimination of daily OCS use, while 80.6% either eliminated OCS use or reduced their daily dose to 5 mg or less if adrenal insufficiency prevented further reduction.[24]

A daily dose of 5 mg or lower was achieved by 91.3% of patients receiving FASENRA.[24] OCS reductions were seen irrespective of baseline eosinophil count.[24]

The occurrence of exacerbations was also evaluated in PONENTE. During the OCS-reduction phase of the study, 74.2% of patients experienced zero exacerbations.[24] Additionally, if patients had continued exacerbations, which was defined as 2 or more

exacerbations, tapering was halted or was modified.[11]

Lastly, 60% of patients had partial or complete adrenal insufficiency at baseline, which decreased to 37.5% 2 to 3 months later.[24] The analyses from PONENTE were descriptive only.

So just to bring all this together, there may be additional options to help your patients with uncontrolled, severe asthma reduce the risk of cumulative OCS exposure while maintaining asthma control. It's time to find out whether your patient with uncontrolled, severe asthma may have elevated eosinophils because as we touched on earlier, there's a 2 out of 3 chance your patient does. If so, then your patient may be appropriate for add-on maintenance treatment with FASENRA—an asthma biologic that may help reduce the rate of exacerbations and their exposure to OCS.[12] So how will you incorporate this knowledge in your practice to help patients reduce the risk of cumulative OCS exposure with FASENRA? I'm Dr Shyam Subramanian. Thanks for joining me today, and please stay tuned for some Important Safety Information on FASENRA.

Announcer:
IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS
Known hypersensitivity to benralizumab or excipients.

WARNINGS AND PRECAUTIONS
Hypersensitivity Reactions
Hypersensitivity reactions (for example, anaphylaxis, angioedema, urticaria, rash) have occurred after administration of FASENRA. These reactions generally occur within hours of administration, but in some instances have a delayed onset (ie, days). Discontinue in the event of a hypersensitivity reaction.

Acute Asthma Symptoms or Deteriorating Disease
FASENRA should not be used to treat acute asthma symptoms, acute exacerbations, or acute bronchospasm.

Reduction of Corticosteroid Dosage
Do not discontinue systemic or inhaled corticosteroids abruptly upon initiation of therapy with FASENRA. Reductions in corticosteroid dose, if appropriate, should be gradual and performed under the direct supervision of a physician. Reduction in corticosteroid dose may be associated with systemic withdrawal symptoms and/or unmask conditions previously suppressed by systemic corticosteroid therapy.

Parasitic (or Helminth) Infection
It is unknown if FASENRA will influence a patient's response against helminth infections. Treat patients with pre-existing helminth infections before initiating therapy with FASENRA. If patients become infected while receiving FASENRA and do not respond to anti-helminth treatment, discontinue FASENRA until infection resolves.

ADVERSE REACTIONS
The most common adverse reactions (incidence greater than or equal to 5%) include headache and pharyngitis.

Injection site reactions (for example, pain, erythema, pruritus, papule) occurred at a rate of 2.2% in patients treated with FASENRA compared with 1.9% in patients treated with placebo.

USE IN SPECIFIC POPULATIONS
A pregnancy exposure registry monitors pregnancy outcomes in women exposed to FASENRA during pregnancy. To enroll call 1-877-311-8972 or visit www.mothertobaby.org/fasenra.

The data on pregnancy exposure from the clinical trials are insufficient to inform on drug-associated risk. Monoclonal antibodies such as benralizumab are transported across the placenta during the third trimester of pregnancy; therefore, potential effects on a fetus are likely to be greater during the third trimester of pregnancy.

INDICATION
FASENRA is indicated for the add-on maintenance treatment of patients with severe asthma aged 12 years and older, and with an eosinophilic phenotype.

- FASENRA is not indicated for treatment of other eosinophilic conditions
- FASENRA is not indicated for the relief of acute bronchospasm or status asthmaticus

Please see full Prescribing Information, including Patient Information, at FASENRAHCP.com.

You've been listening to ReachMD. This medical industry feature has been sponsored by AstraZeneca. To view the full US prescribing information for FASENRA, visit www.FASENRAHCP.com, and to revisit any part of this program, please visit ReachMD.com/industry-feature. This is ReachMD. Be Part of the Knowledge.

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