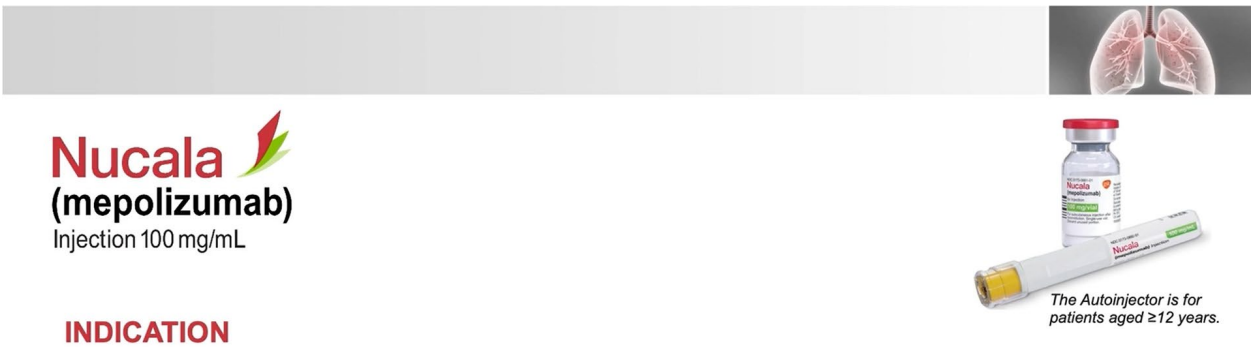
ReachMD
Treating Severe Eosinophilic Asthma Patients with Comorbid Nasal Polyps



Announcer:
NUCALA is indicated for the add-on maintenance treatment of patients 6 years and older with severe eosinophilic asthma.

NUCALA is not for relief of acute bronchospasm or status asthmaticus.

NUCALA should not be used in patients with a history of hypersensitivity to mepolizumab or its formulations.

Please see Important Safety Information throughout this transcript.

Please see full Prescribing Information and Patient Information for NUCALA in the related material section on the website, or visit NucalaHCP.com.

IMPORTANT SAFETY INFORMATION (cont.)

WARNINGS AND PRECAUTIONS

Hypersensitivity Reactions

- Hypersensitivity reactions (eg, anaphylaxis, angioedema, bronchospasm, hypotension, urticaria, rash) have occurred with NUCALA (mepolizumab). These reactions generally occur within hours of administration but can have a delayed onset (ie, days). If a hypersensitivity reaction occurs, discontinue NUCALA.

Acute Asthma Symptoms or Deteriorating Disease

- NUCALA should not be used to treat acute asthma symptoms, acute exacerbations, or acute bronchospasm.

Opportunistic Infections: Herpes Zoster

- In controlled clinical trials, 2 serious adverse reactions of herpes zoster occurred with NUCALA compared to none with placebo. Consider vaccination if medically appropriate.

Please see Important Safety Information for NUCALA throughout this video.
Please see full Prescribing Information, including Patient Information, at NUCALAHCP.com.

Nucala
(mepolizumab)

Hypersensitivity reactions including anaphylaxis, angioedema, bronchospasm, hypotension, urticaria, and rash have occurred. These generally occur within hours of administration but can have a delayed onset. If a hypersensitivity reaction occurs, discontinue NUCALA.

NUCALA should not be used to treat acute asthma symptoms, acute exacerbations, or acute bronchospasm.

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IMPORTANT SAFETY INFORMATION (cont.)

WARNINGS AND PRECAUTIONS (cont.)

Reduction of Corticosteroid Dosage

- Do not discontinue systemic or inhaled corticosteroids abruptly upon initiation of therapy with NUCALA. Decreases in corticosteroid doses, if appropriate, should be gradual and 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 (Helminth) Infection

- Treat patients with pre-existing helminth infections before initiating therapy with NUCALA. If patients become infected while receiving NUCALA and do not respond to anti-helminth treatment, discontinue NUCALA until infection resolves.

Additional important safety information, including adverse reactions, is presented later in this presentation.

Nucala
(mepolizumab)

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Do not discontinue systemic or inhaled corticosteroids abruptly when initiating NUCALA. Appropriate decreases in corticosteroid doses should be gradual and healthcare-provider supervised. Reduction in corticosteroid dose may be associated with withdrawal symptoms and/or unmask conditions previously suppressed by corticosteroid therapy.

Treat patients with pre-existing parasitic infections before initiating NUCALA. If patients become infected while receiving NUCALA and do not respond to anti-parasitic treatment, discontinue NUCALA until infection resolves.

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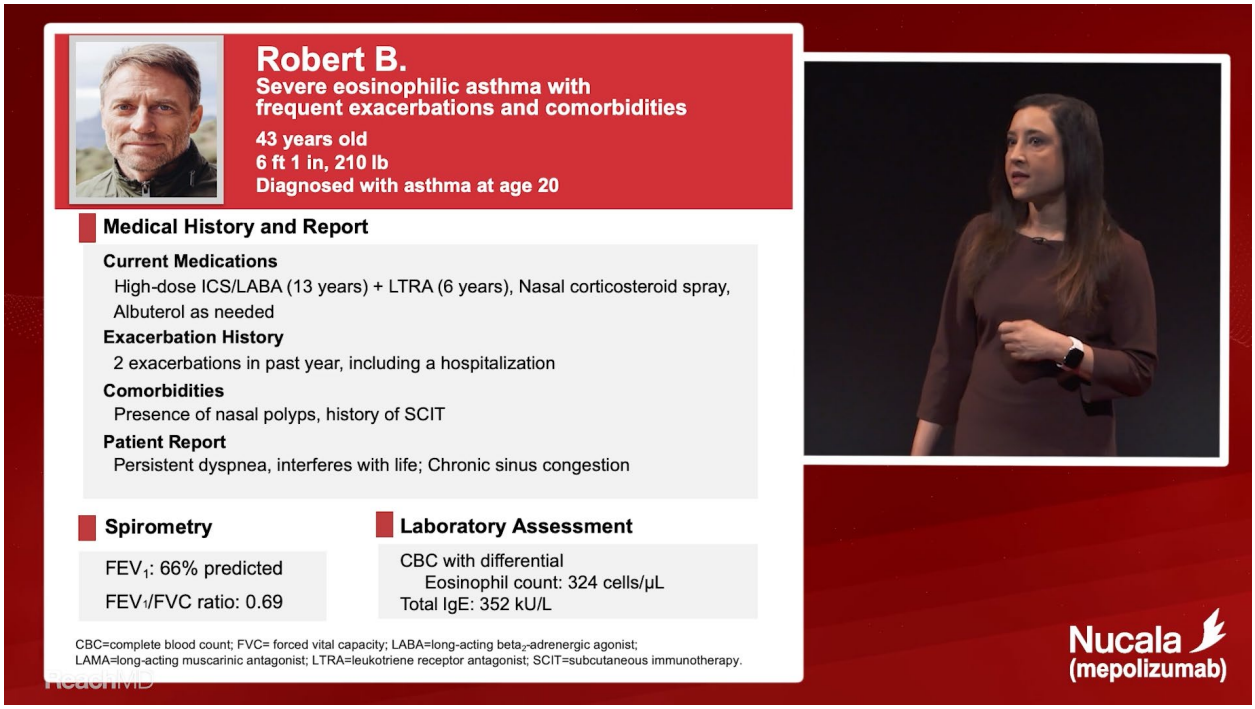
Dr. Fatteh:
Welcome. My name is Dr. Shahnaz Fatteh, and I'm a practicing Allergist in South Florida. Today we'll be talking about the Treatment of Severe Eosinophilic Asthma in Patients with Frequent Exacerbations and Comorbid Nasal Polyps.



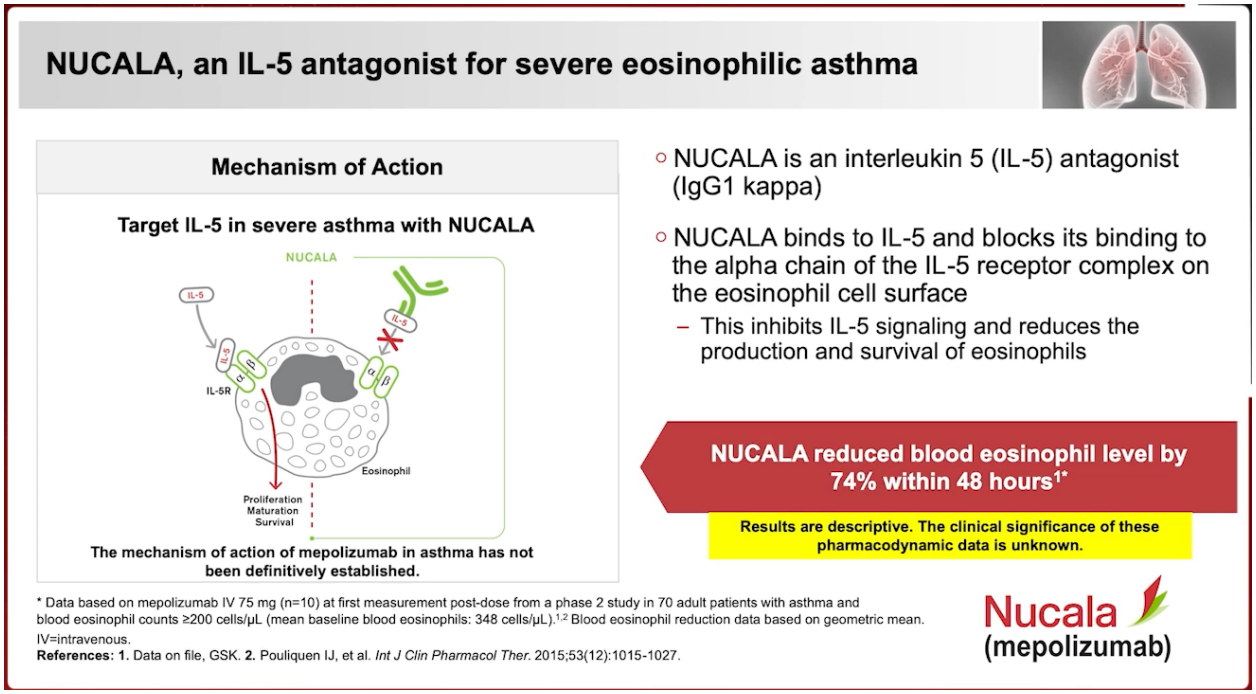
So here's a patient that I might see in my office. This is Robert B., who has severe eosinophilic asthma with frequent exacerbations and comorbidities.

Robert is 43-years-old, and was diagnosed with asthma at age 20. He's on medications for severe asthma, which include: high-dose inhaled corticosteroids/a long-acting beta agonist, and has been on this combination for 13 years, as well as a leukotriene inhibitor for the past 6 years. He uses a nasal steroid spray and albuterol as needed.

In this past year, he's had two exacerbations, including a hospitalization. On physical exam, he has nasal polyps. Although he's taking his medications, his quality of life and day-to-day function is affected by severe dyspnea. He has interference with his daily activities, and chronic sinus congestion.

As we evaluate Robert, his spirometry reveals decreased lung function, with an FEV1 of 66%; an FEV1/FVC ratio obstructed at 69%. On laboratory assessment, his CBC differential has an eosinophil count of 324. So, he also has an IgE that's elevated at 352. So Robert is also atopic.

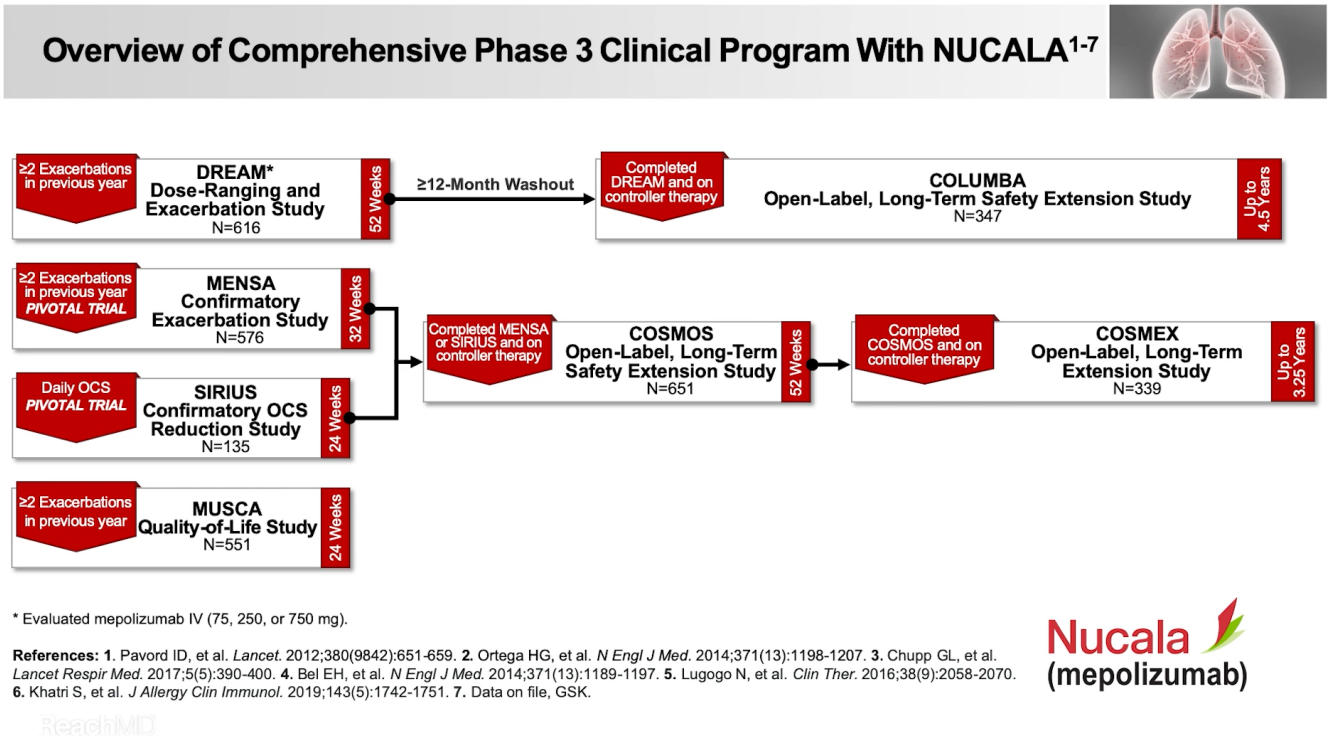
So, what can we do for Robert? He's already taking all these medications and still has symptoms. However, we can think about an add-on therapy: in this case, NUCALA.



So, why NUCALA? One reason is how it works. NUCALA binds to IL-5 and prevents it from binding to the alpha chain of the IL-5 receptor complex on the eosinophil cell surface.

So, eosinophils need IL-5 for survival, for differentiation, maturation, and proliferation.

So by inhibiting IL-5 signaling, eosinophil counts can be reduced. In fact, in a Phase 2 study, NUCALA reduced blood eosinophil levels by 74% in 48 hours.



As you can see, there's a comprehensive Phase 3 program for NUCALA: Confirmatory Exacerbations, OCS Reduction studies, a quality-of-life study, and multiple open-label long-term studies.

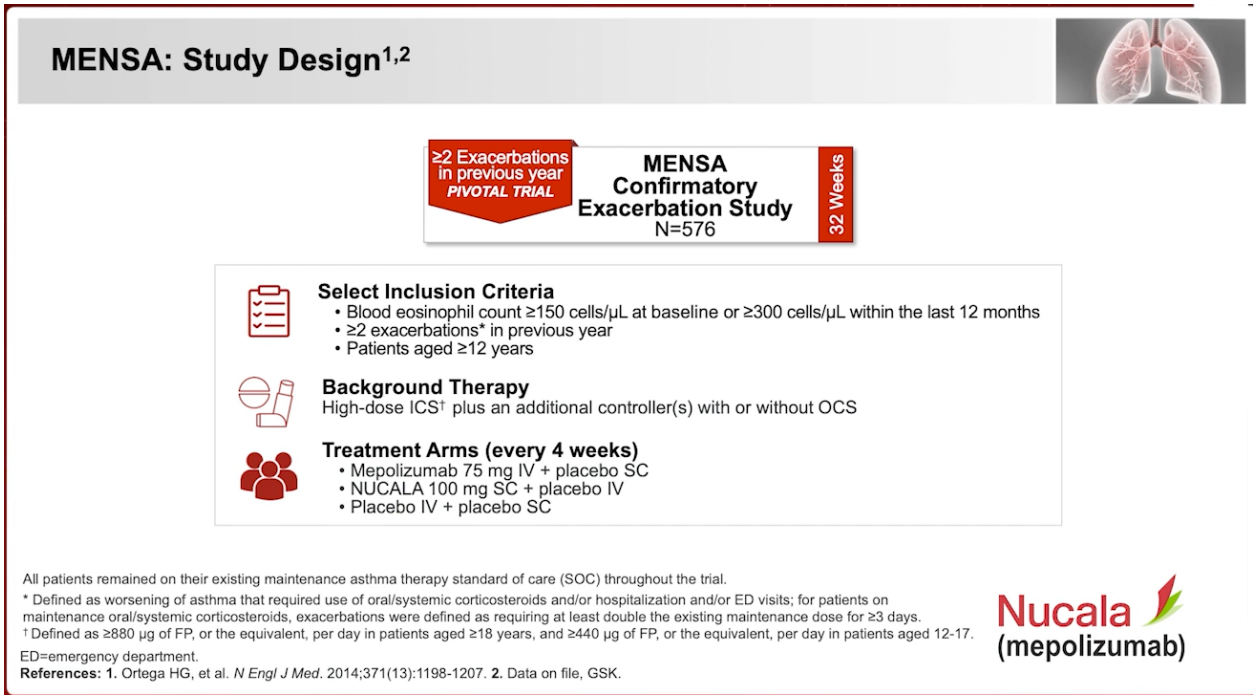
For Robert, we're looking for a reduction in his exacerbation rate.

The DREAM study was a dose-ranging and exacerbation study for 52 weeks.

MENSA was a pivotal confirmatory exacerbation study carried out for 32 weeks.

After at least a 12-month washout, patients from DREAM were enrolled into an open-label study, COLUMBA, which looked at the long-term safety and efficacy of NUCALA.

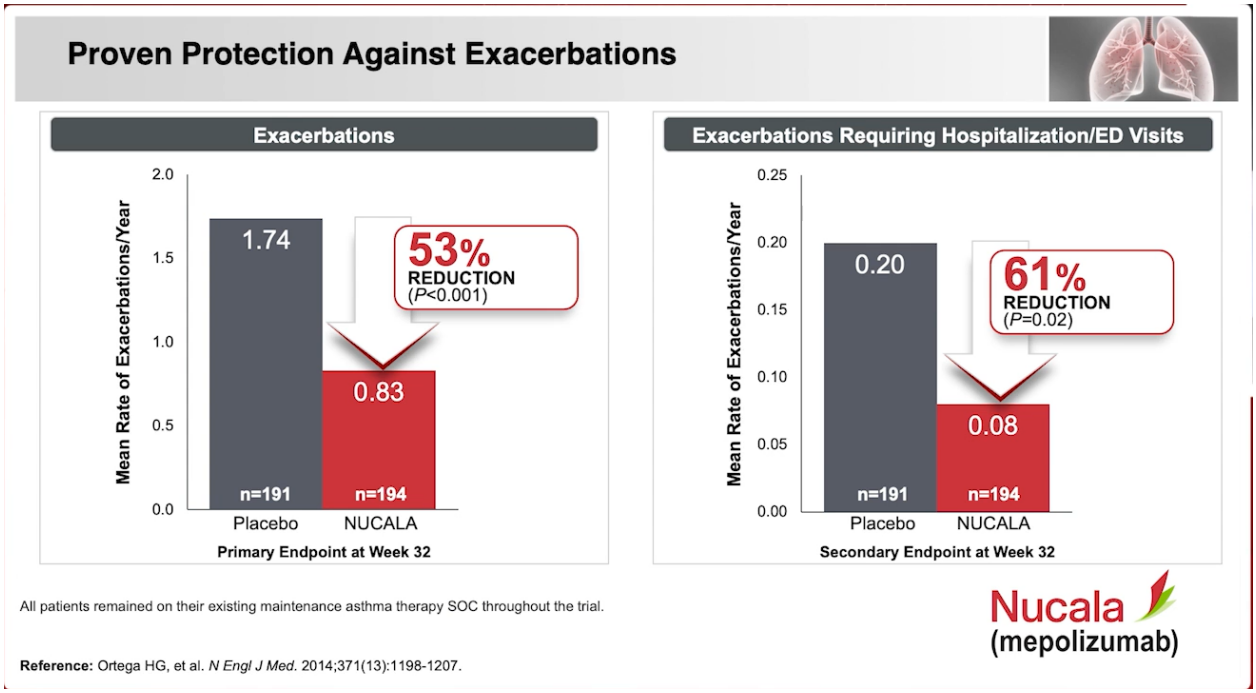
So, we're going to today, focus on MENSA: exacerbations — which is what Robert has had — and COLUMBA: long-term safety extension studies, to look at the safety and efficacy of NUCALA in reducing exacerbations.



In MENSA, a 32-week pivotal trial, patients were enrolled who had a blood eosinophil count of at least 150 cells at baseline, or at least 300 cells in the past 12 months.

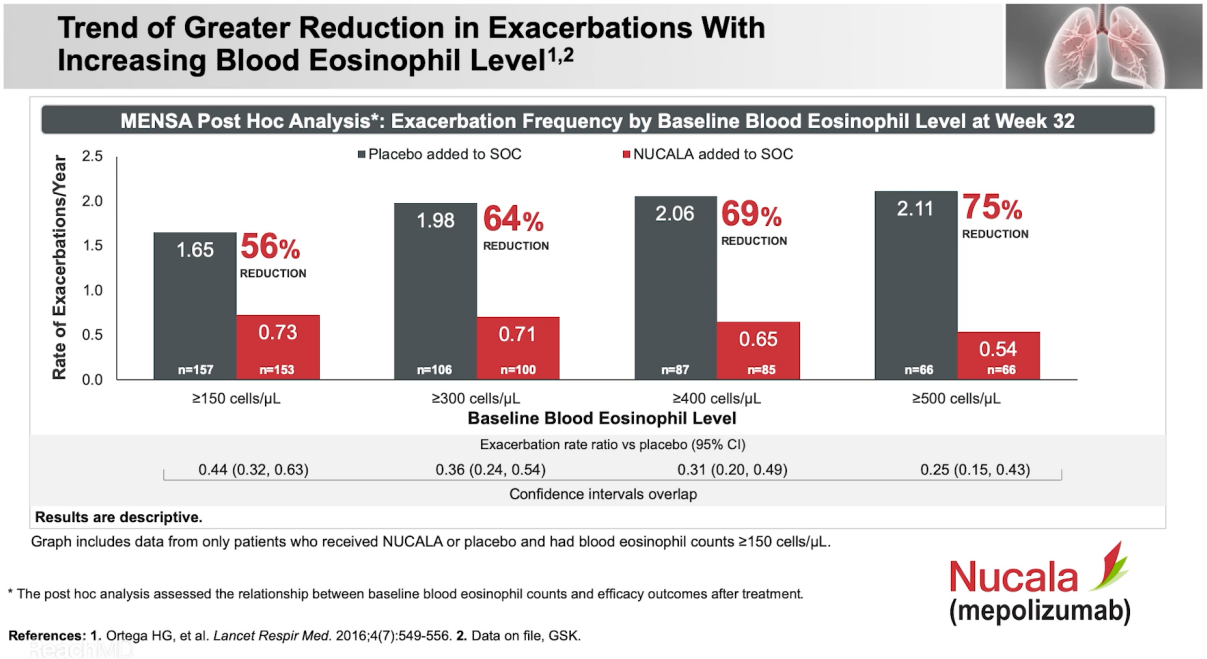
All patients were required to have two or more exacerbations, and they were on standard of care medications, including — like Robert — high-dose inhaled corticosteroids and additional controllers. They may have also been on oral corticosteroids.

Recall that Robert had a blood eosinophil count of 324, and a history of two exacerbations and one hospitalization.



The exacerbation rate was reduced by 53% compared to placebo at Week 32.
And on a secondary endpoint, exacerbations requiring hospitalizations and emergency visits were reduced by 61%.

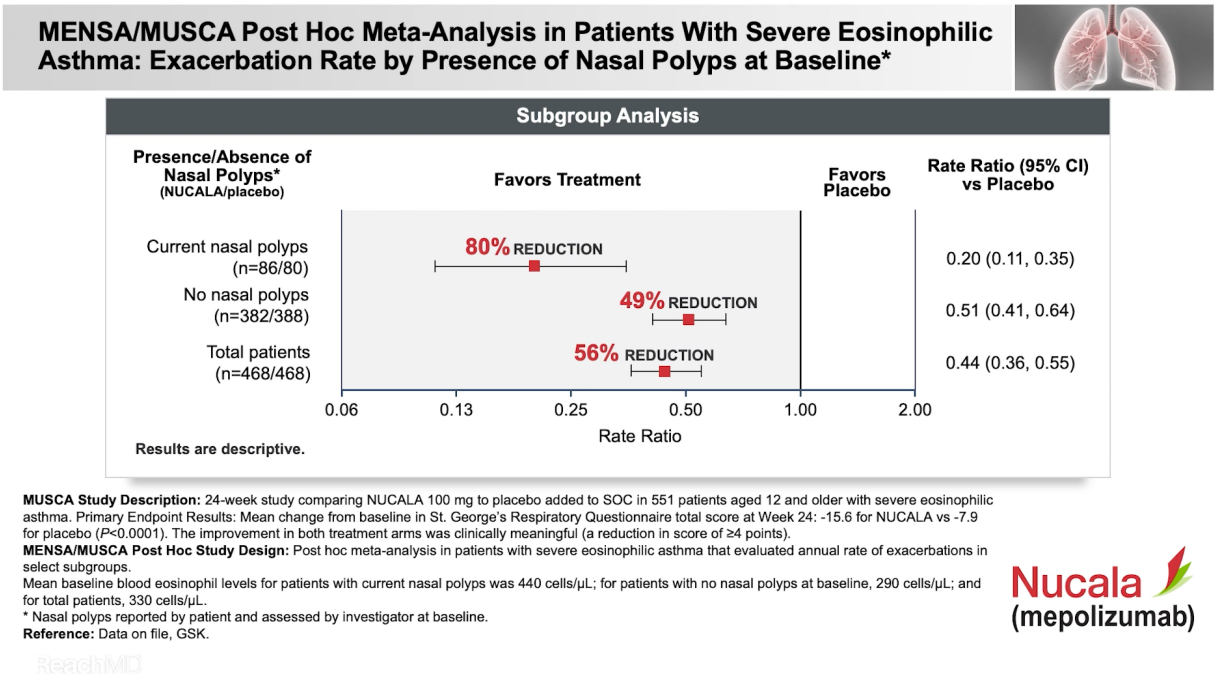
So, the important goals of reducing exacerbations and keeping patients like Robert out of the hospital and out of the emergency room were achieved.



In the post hoc analysis, the higher the patient's blood eosinophil level, the greater the reduction in exacerbation rates. In fact, this trend continues all the way through to the highest eosinophil counts in the study — up to 75% reduction in patients with blood eosinophil counts of 500 or more.

Note that the confidence intervals overlap, so the results are considered similar across the thresholds.

The MENSA and MUSCA post hoc meta-analysis in patients with severe eosinophilic asthma and nasal polyps is important.



The data for all patients that were enrolled in these trials and grouped by the presence or absence of nasal polyps at baseline is studied.

You can see the reduction in exacerbations.

In the total patient population, there was a 56% reduction in exacerbations versus placebo. So, reductions were seen regardless of the presence of nasal polyps.

In addition, important to note is that the mean baseline eosinophil count for patients with nasal polyps was higher at 440 cells/μL — higher than the mean baseline of 290 cells/μL for patients without nasal polyps.

IMPORTANT SAFETY INFORMATION (Cont.)

ADVERSE REACTIONS

MOST COMMON ADVERSE REACTIONS WITH NUCALA WITH ≥3% INCIDENCE AND MORE COMMON THAN PLACEBO REPORTED IN THE FIRST 24 WEEKS OF TRIAL 2 (MENSA) AND TRIAL 3 (SIRIUS)

Adverse Reaction	NUCALA (n=263), %	Placebo (n=257), %
Headache	19	18
Injection site reaction	8	3
Back pain	5	4
Fatigue	5	4
Influenza	3	2
Urinary tract infection	3	2
Abdominal pain upper	3	2
Pruritus	3	2
Eczema	3	<1
Muscle spasms	3	<1

Systemic Reactions, including Hypersensitivity Reactions: In 3 clinical trials, the percentages of subjects who experienced systemic (allergic and nonallergic) reactions were 3% for NUCALA and 5% for placebo. Manifestations included rash, flushing, pruritus, headache, and myalgia. A majority of the systemic reactions were experienced on the day of dosing.

Injection site reactions (eg, pain, erythema, swelling, itching, burning sensation) occurred in subjects treated with NUCALA.

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Nucala
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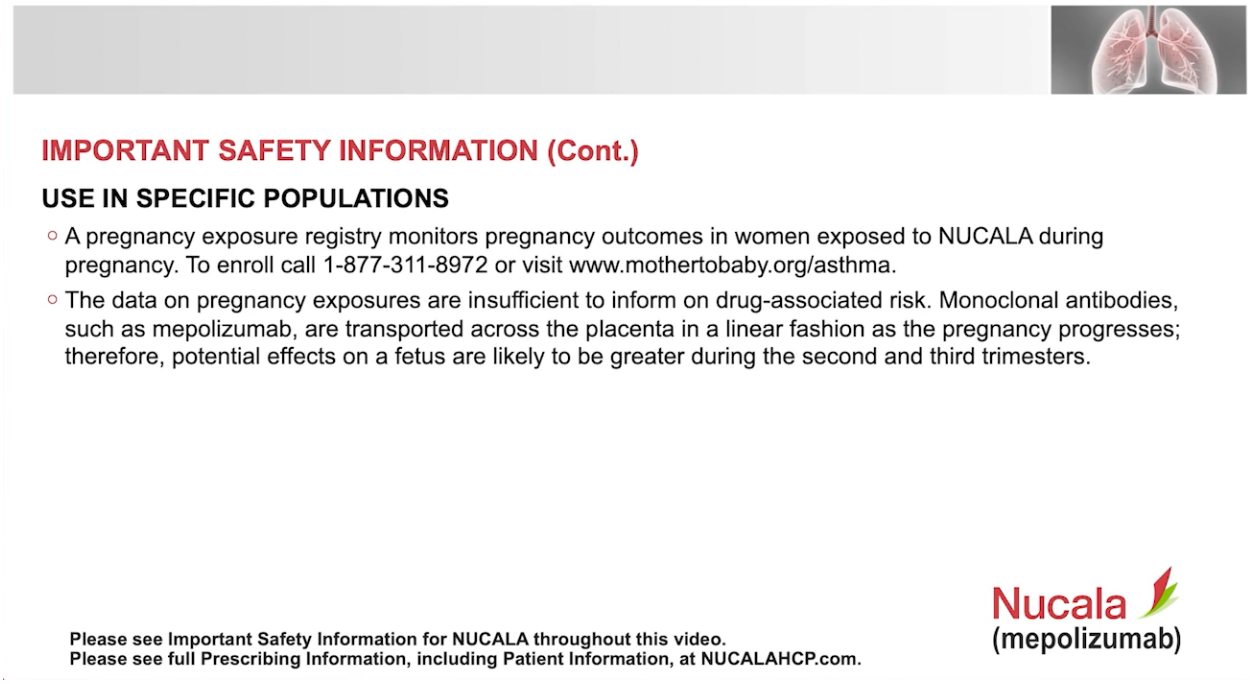
The most common adverse reactions with NUCALA with incidence 3% or greater, and more common than placebo reported in the first 24 weeks of MENSA and SIRIUS are shown in this table and include: headache, injection site reaction, back pain, fatigue, influenza, urinary tract infection, upper abdominal pain, pruritus, eczema, and muscle spasms.

In 3 clinical trials, 3% of subjects who received NUCALA experienced systemic (allergic and nonallergic) reactions, compared to 5% in the placebo group. Manifestations included rash, flushing, pruritus, headache, and myalgia, and a majority of these were experienced on the first day of dosing. Also note that patients receiving NUCALA experienced more injection site reactions than the placebo group.

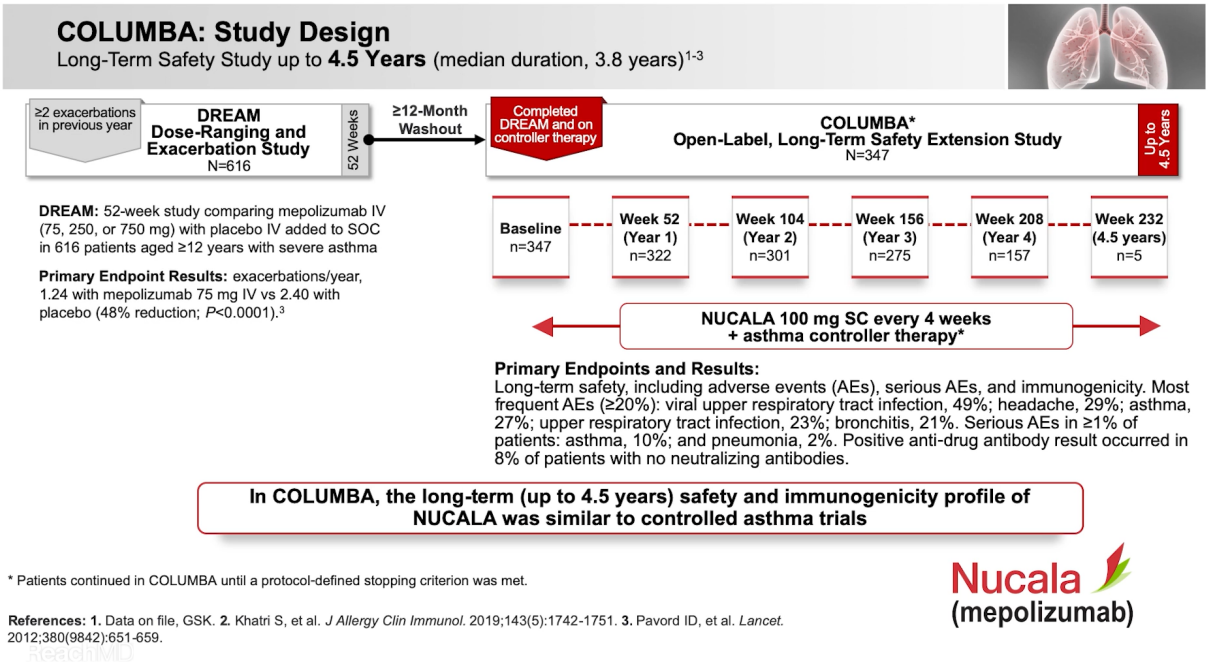
Let's look at the Use in Specific Populations.



Pregnant women were excluded from the studies, and women of childbearing age were required to use effective birth control. Keep in mind that monoclonal antibodies do cross the placenta, particularly in the second and third trimester.

If you have a patient who becomes pregnant while taking NUCALA or after she stops using NUCALA, please consider enrolling her in the mothertobaby.org website so that the third party administering the observational study can gather safety information that may be useful to future patients receiving NUCALA.

So when we have a patient like Robert that we are thinking about putting on an add-on biologic, what are some of the things patients are concerned about in the long term? Is it safe? Is it going to continue to work? These are the types of questions that the COLUMBA study looked at. COLUMBA was a long-term safety study that looked at patients for up to 4 and 1/2 years.

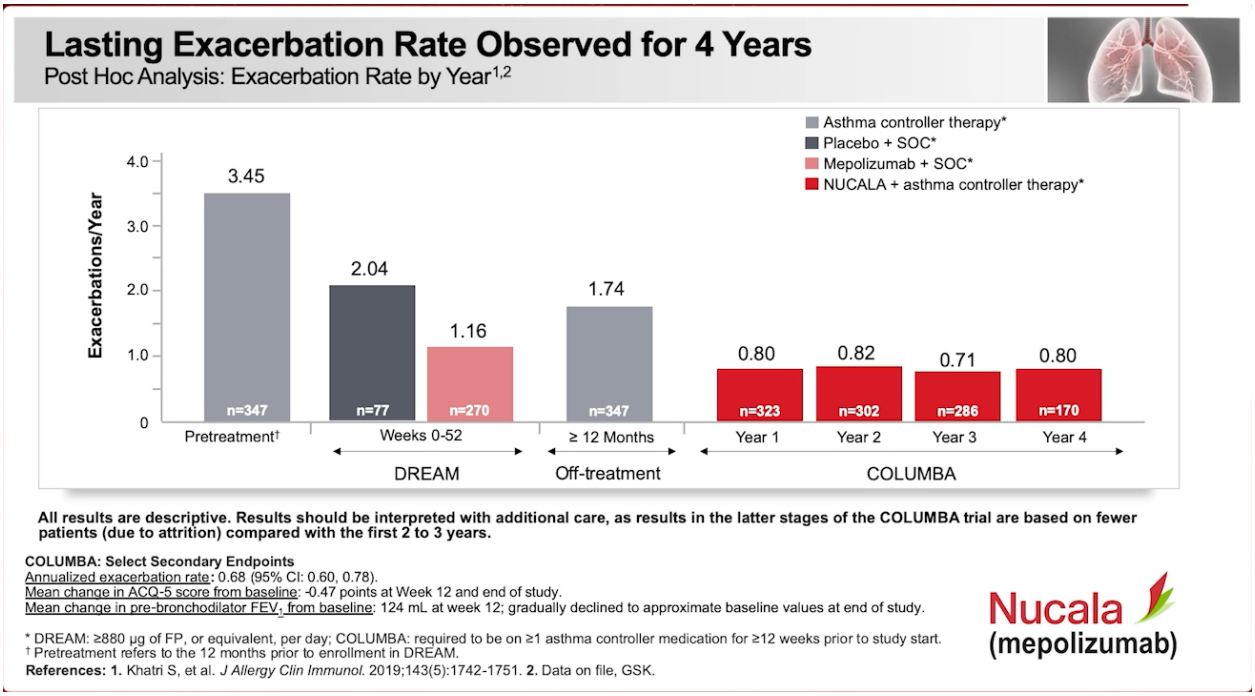


Let's first look at how patients got into COLUMBA. They started with an exacerbation study called DREAM, in which 616 patients with severe asthma were enrolled. They were treated with an add-on mepolizumab IV or placebo for 52 weeks. After at least a 12-month washout, they didn't receive any medications, eligible patients then were enrolled into COLUMBA and received NUCALA added to their asthma controller therapy. Three hundred forty-seven patients were followed over this 4 and 1/2 years.

The long-term safety and immunogenicity profile of NUCALA over the 4.5 years was similar to controlled asthma trials.

So the most frequent AEs were: viral upper respiratory tract infection, headaches, asthma, upper respiratory tract infection, and bronchitis.

The most frequent serious AEs were worsening of asthma and pneumonia. Note that positive anti-drug antibodies occurred in 8% of patients, but with no neutralizing antibodies.



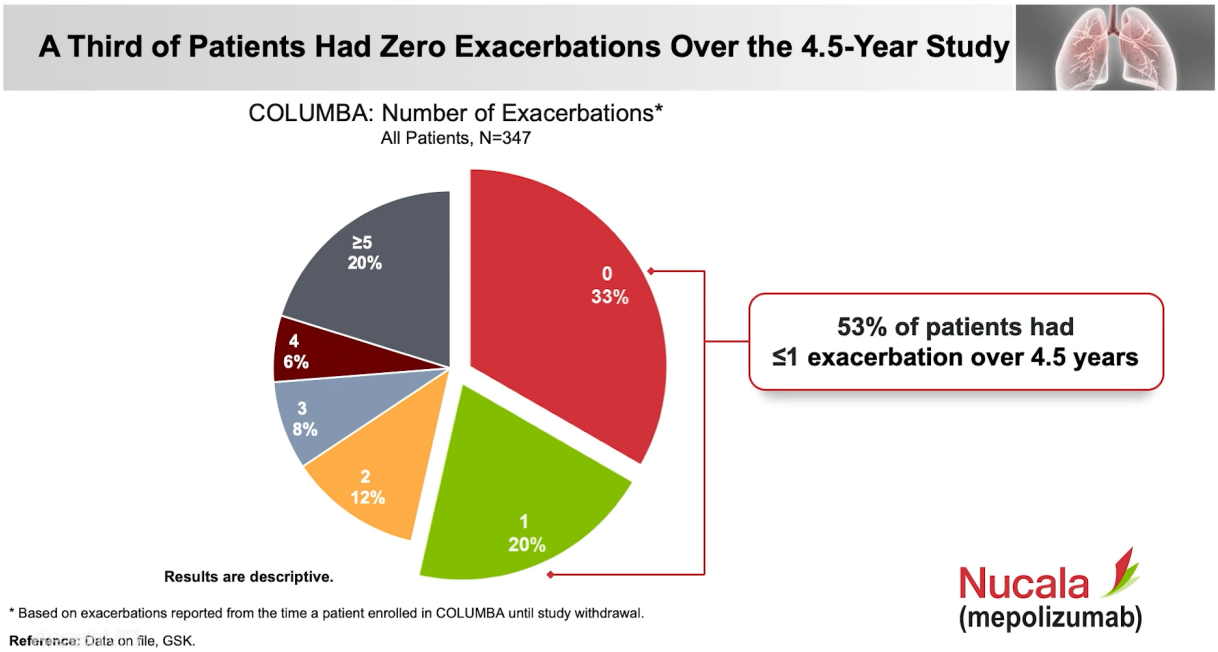
This post hoc analysis looked at exacerbation rates over four years.

Patients began the DREAM study with an average of 3.45 exacerbations. In the DREAM study, the patients that were on mepolizumab went down to 1.16 exacerbations per year, compared to 2.04 in patients taking placebo.

After the washout period, patients began COLUMBA with an average of 1.74 exacerbations. So off of mepolizumab, what happened? The rate of exacerbations increased.

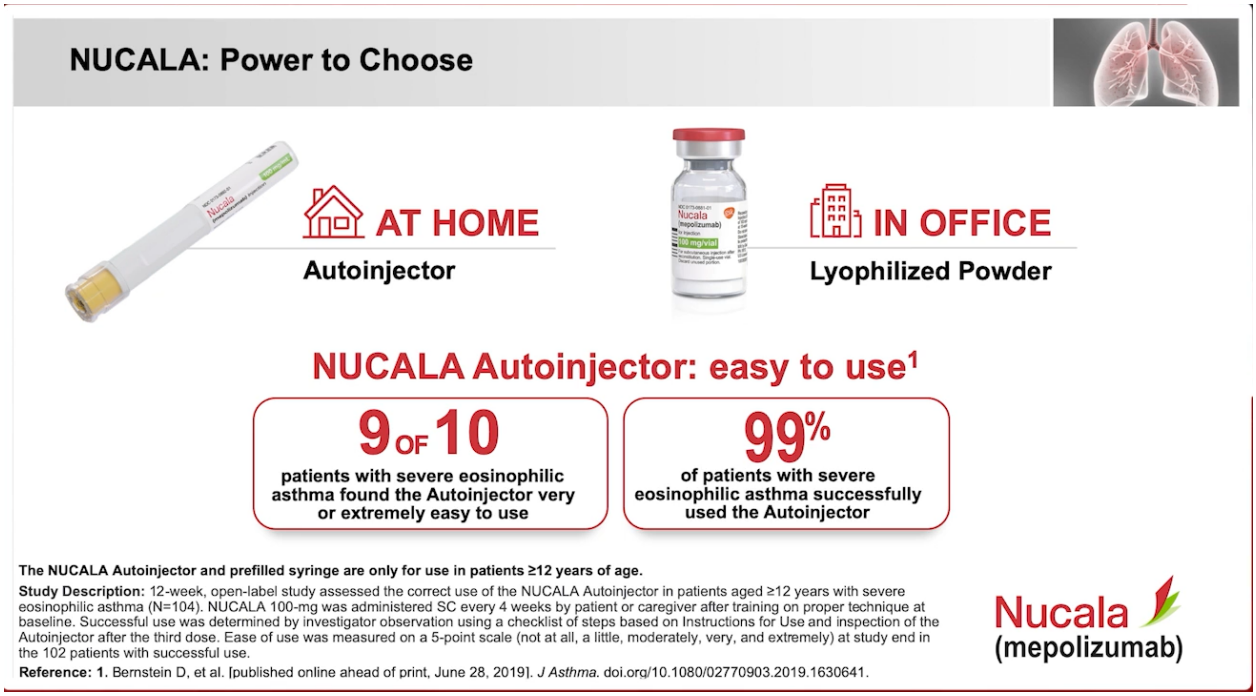
Again, remember that our patient Robert had two exacerbations including a hospitalization this past year. That 1.74 exacerbation rate dropped down to about half, 0.8 at year 1, and stayed that low over 4 years.

So keep in mind that over the course of this long-term study, fewer patients remained in the study, so results should be viewed in that way.



So, looking at the data from a different perspective, we can see that 33% of patients had zero exacerbations. And 20% had one. So, over the 4 and 1/2 years, 53% of patients had one or less exacerbation while on NUCALA.

Earlier I asked about what we could do to help our patient, Robert. I think NUCALA gives us a good option as an add-on therapy. We can share decision-making with our patients to help them determine how they would like to have NUCALA provided for them, particularly someone like Robert who lives far away from the office.

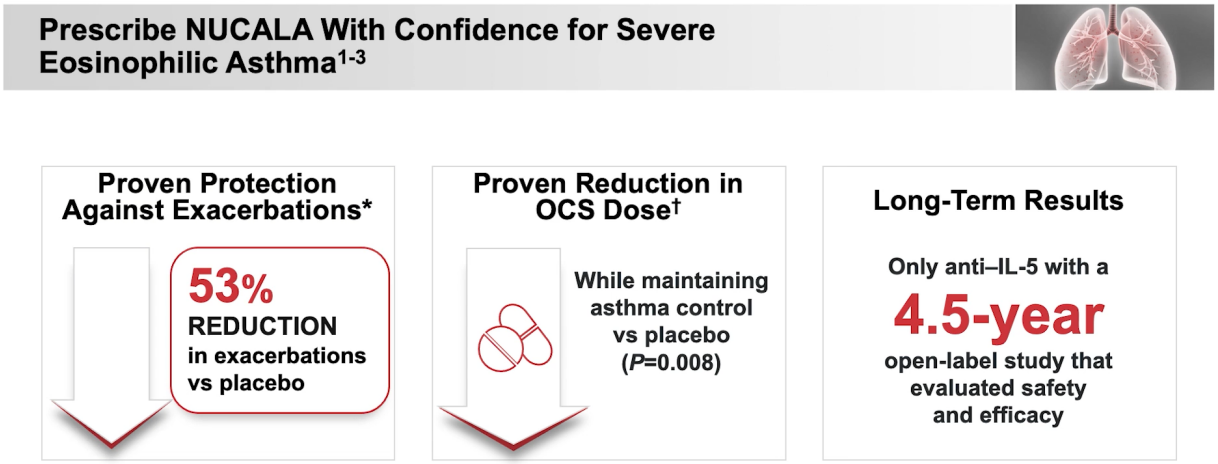


NUCALA has an Autoinjector for at-home use. Looking at the data, almost all patients could successfully self-administer the Autoinjector, and found it very or extremely easy to use.

The Autoinjector and pre-filled syringe are indicated for patients 12 and older.

We can also give NUCALA in the office using a lyophilized powder formulation.

Now we can talk to the patient about both options and see which is more appropriate and preferred by the patient.



One of the goals that we wanted to achieve with our patient, Robert, was reduction in exacerbations. The MENSA study demonstrated a 53% reduction in exacerbation.

The reduction in oral corticosteroid dosing is very important so that we can reduce OCS use while maintaining asthma control.

And the COLUMBA trial evaluated safety and efficacy, including exacerbation rates, out to 4 and 1/2 years.

I believe we can prescribe NUCALA with confidence for our patients like Robert, with severe eosinophilic asthma.

Thank you.

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