ReachMD
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Nucala
(mepolizumab)
Injection 100 mg/mL

ReachMD
Treating Severe Eosinophilic Asthma Patients Who Are OCS-Dependent

Nucala
(mepolizumab)
Injection 100 mg/mL

The Autoinjector is for patients aged ≥12 years.

INDICATION

- NUCALA is indicated for the add-on maintenance treatment of adult and pediatric patients aged 6 years and older with severe asthma and with an eosinophilic phenotype. NUCALA is not indicated for the relief of acute bronchospasm or status asthmaticus

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

- NUCALA should not be administered to patients with a history of hypersensitivity to mepolizumab or excipients in the formulation.

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

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.

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.

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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.

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

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.

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

Dr. Goldman:
Hello, I'm Dr. Yaron Goldman, and I'm a practicing Pulmonologist.

Thank you for joining me for this talk on treating severe eosinophilic asthma patients who are oral corticosteroid dependent.

As a pulmonologist, I can tell you that this is a significant problem that we encounter quite a bit in our practice. And now that we have additional medication options for the patients, we're excited to share this with you.

We'll start by introducing a typical severe eosinophilic asthma patient who is also OCS dependent.

Sarah L.
OCS dependent severe eosinophilic asthma

47 years old
5 ft 4 in, 194 lb
Diagnosed with asthma at age 29

Medical History and Report

Current Medications
High-dose ICS/LABA + LTRA, OCS 12.5 mg (daily, 9 months), albuterol as needed

Exacerbation History
2 exacerbations treated with OCS in past year; 1 outpatient, 1 ED visit

Patient Report
Daily cough and wheeze with mucus production
Symptoms often restrict daily activities and interfere with work
Weight gain of 15 lbs in last 9 months
Asthma triggers: URIs and sinusitis, smoke (nonsmoker), and exertion
(Atopic status: negative)

Spirometry

FEV_1: 62% predicted

FEV_1/FVC ratio: 0.70

Laboratory Assessment

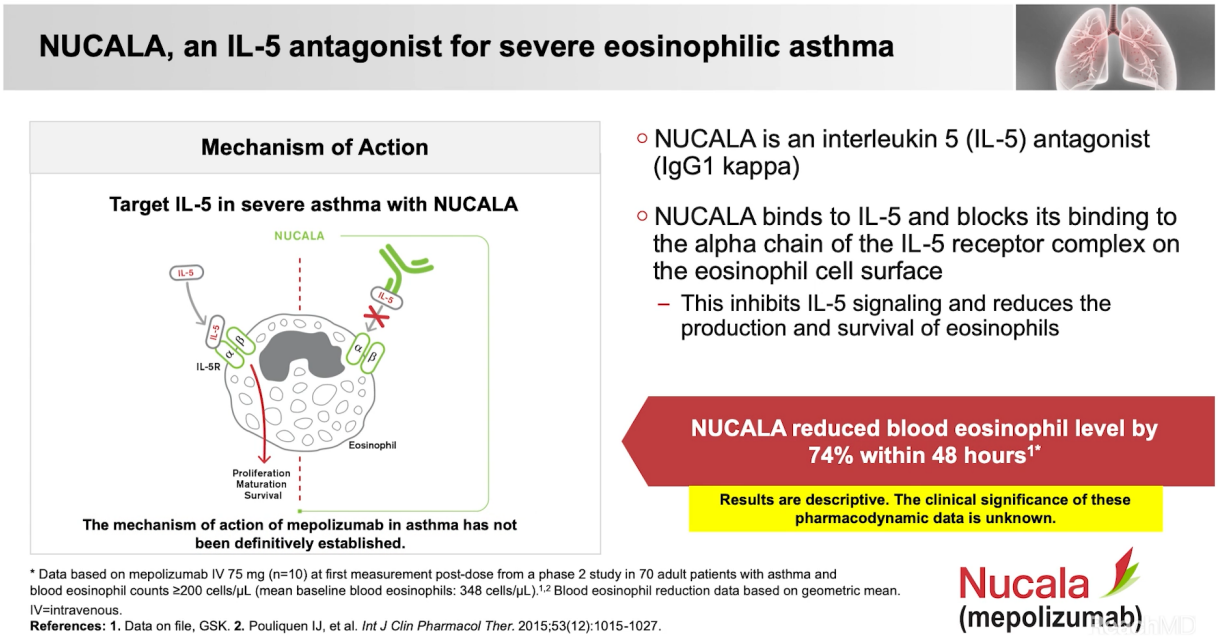
CBC with differential
Eosinophil count: 190 cells/μL
Historical eosinophil count (1 year ago): 390 cells/μL
Total IgE 102 kU/L

URI=upper respiratory infection.

Sarah is maximized on traditional combination therapy, all the way to the higher steps of the GINA report and a significant dose of oral steroids. She already had two exacerbations treated in the past year, one outpatient and one emergency department visit, which is usually a marker of a more severe exacerbation. This tells us that her asthma is not well controlled. She has daily cough and wheezing, and her asthma is restricting her activities. She is also experiencing significant weight gain, which many of our asthmatic patients struggle with.

As you can see, she has multiple triggers, significant obstruction on her spirometry, and elevated eosinophils of 190 cells/μL. But keep in mind this is while on daily oral steroids, which can lower the eosinophil count. Note that one year ago, her eosinophil count was even higher at 390 cells/μL.

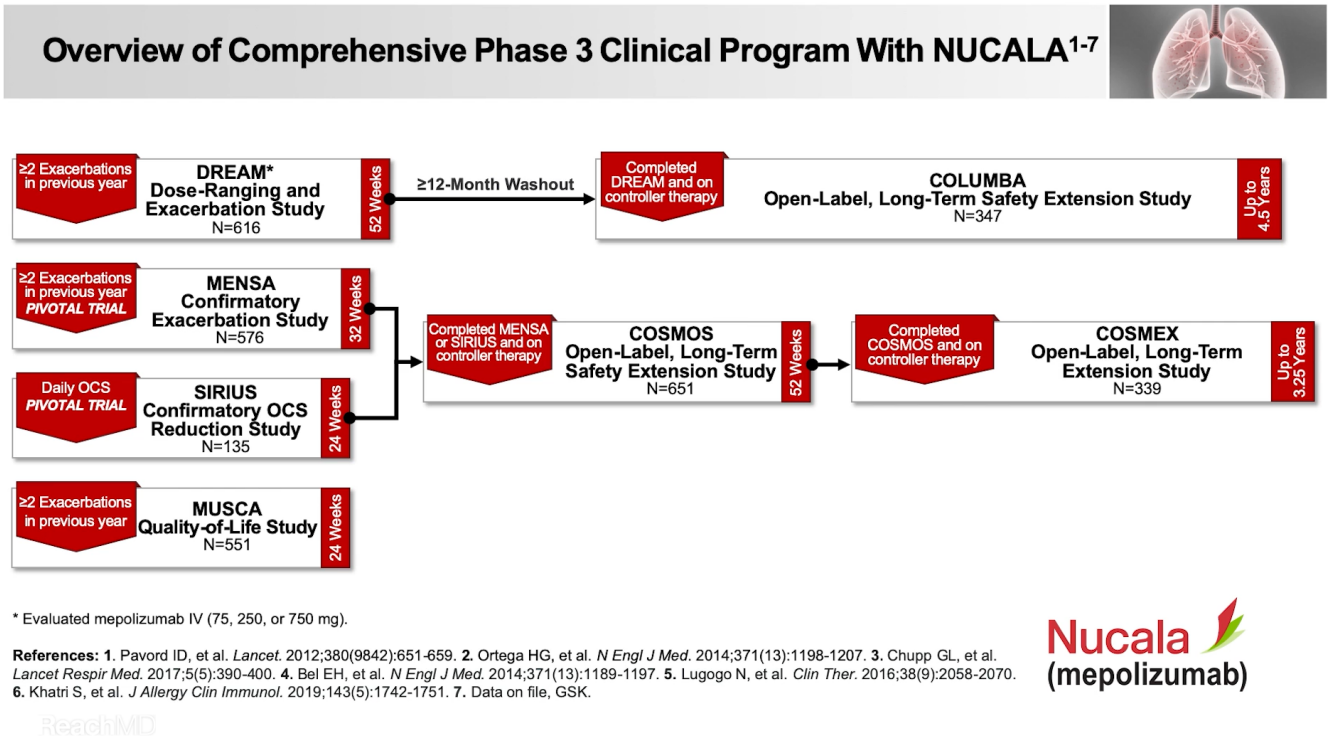
This severe eosinophilic asthma patient is clearly uncontrolled. We need to think about additional treatment options for her. And I'd like to share with you an option called NUCALA.



So how does NUCALA work?

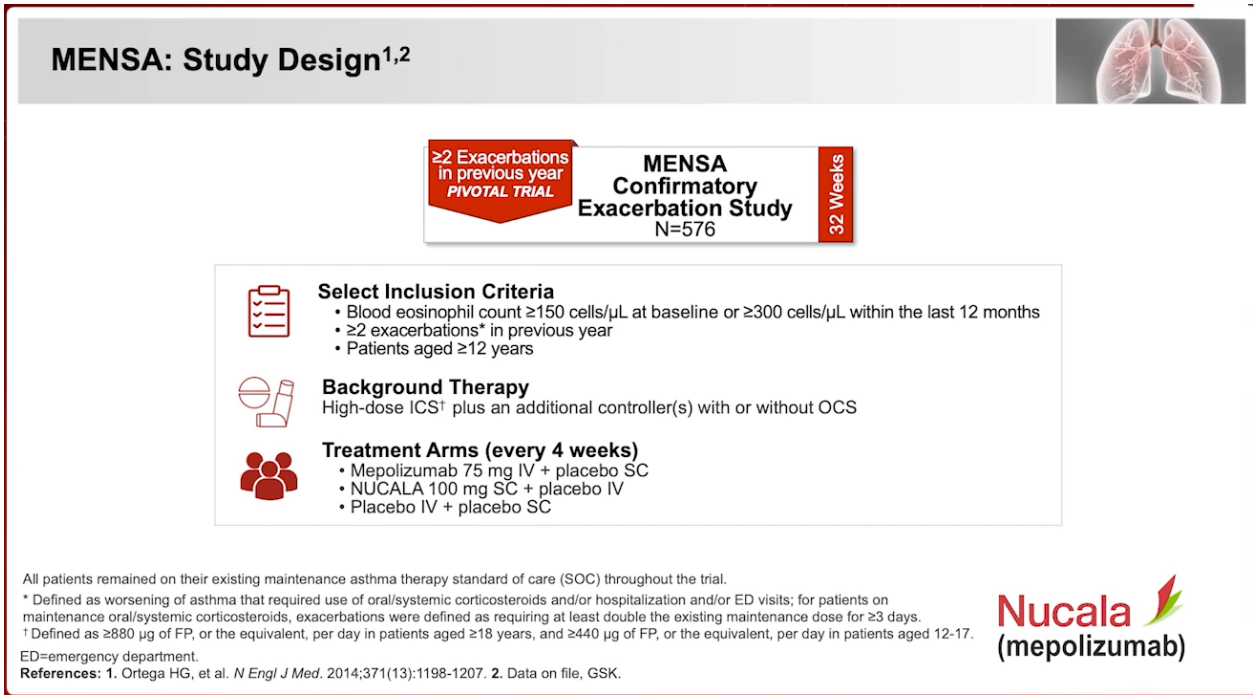
NUCALA binds to the IL-5 and prevents it from binding to the alpha chain of the IL-5 receptor complex on the eosinophil. This inhibits IL-5 signals and eosinophil production and survival, which is what was seen in a phase 2 study with the first injection of NUCALA: a 74% reduction of eosinophils within 48 hours.

Now let's look at the clinical trial data.



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

Today we're going to look at three of these — MENSA, SIRIUS, and COSMOS — that focus on exacerbations and steroid reduction and safety, and, therefore, are very relevant to our patient, Sarah.

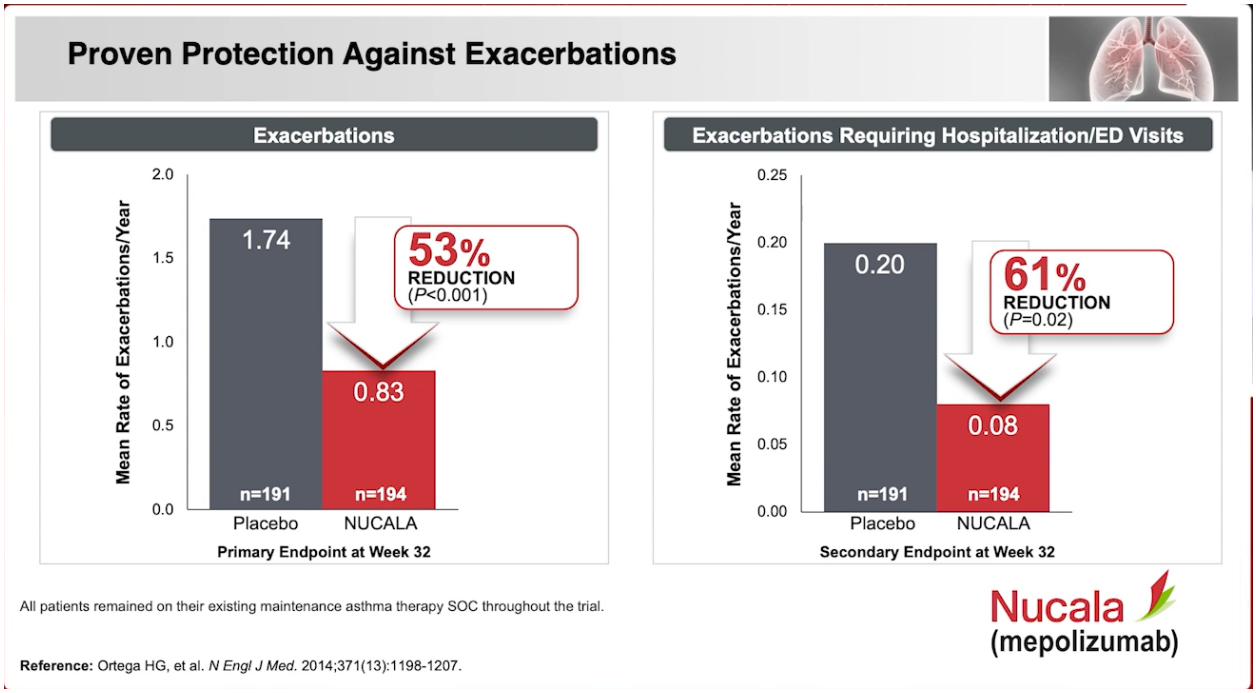


With MENSA, the question we are looking at is: can NUCALA reduce the amount of exacerbations in patients with severe eosinophilic asthma who had two or more exacerbations in the last year, despite high-dose traditional inhaled therapy and an eosinophil count equal to or greater than 150 cells/µL?

Recall that our patient Sarah had a blood eosinophil count of 190 cells/µL and a historical count of 390 cells/µL one year ago.

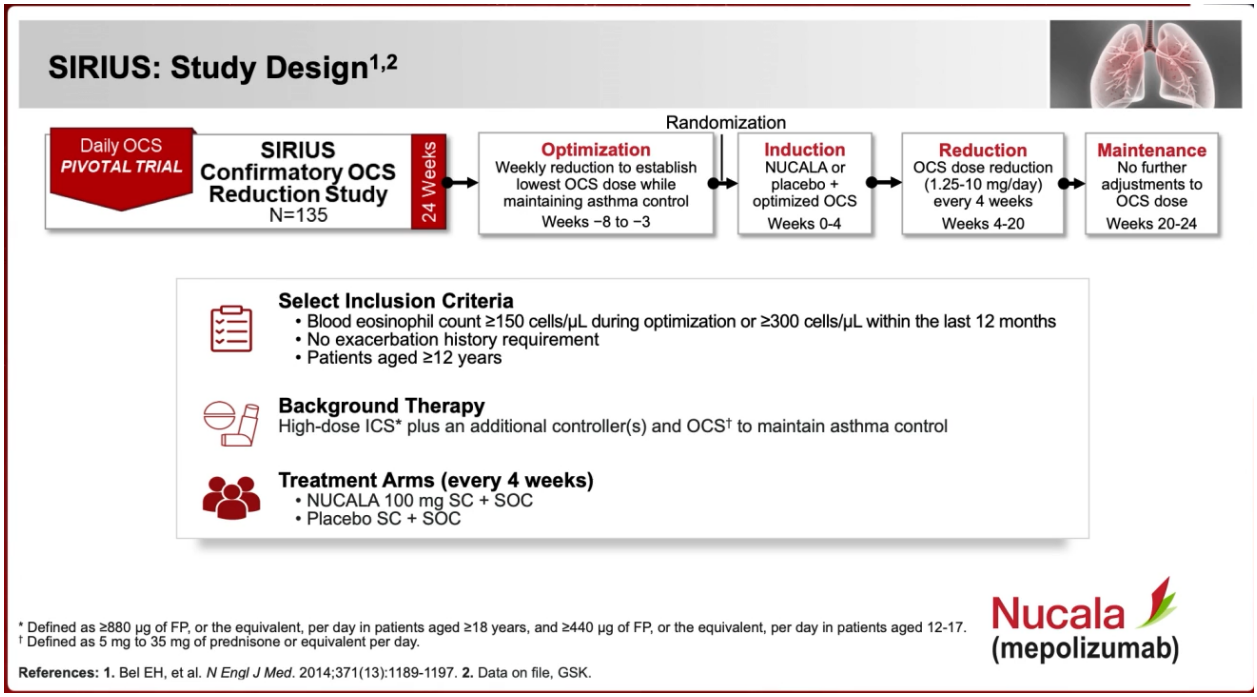
Patients in this study were randomized to receive the currently approved dose of NUCALA, 100 mg subcutaneous, or mepolizumab 75 mg IV, or placebo. All therapies were added to the standard of care.

So, let's look at the results.



As you can see, with NUCALA there was a 53% reduction in exacerbations as well as a 61% reduction in exacerbations requiring hospitalizations vs. placebo. A significant reduction for these patients with frequent exacerbations

Next, the SIRIUS study looked at reduction in oral corticosteroids.



This was the same type of patient population with elevated eosinophils. But notice, there was no requirement for exacerbation history. They were on a high-dose maintenance traditional therapy along with oral corticosteroid to maintain control of their asthma.

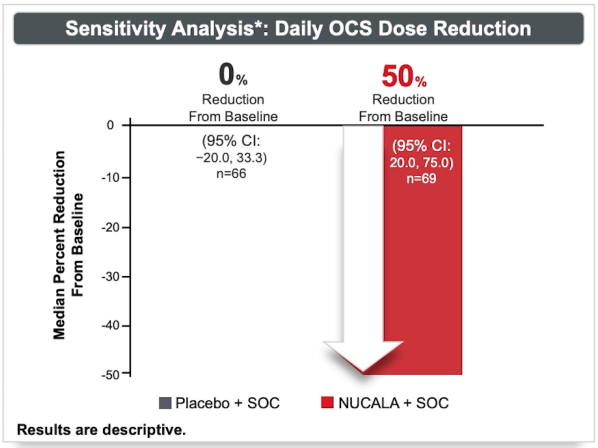
The nice thing about this study is that investigators went through an optimization period. Patients were brought down to the lowest possible level of oral corticosteroids to keep their asthma well controlled, to truly reflect the benefit of
NUCALA in reducing their oral corticosteroid dose.

Patients were then randomized to receive NUCALA or placebo as add-on therapy, then oral corticosteroids was reduced according to a reduction protocol and maintained at that dose.

Again, potentially good news for our patients such as Sarah.

Proven Reduction in OCS Dose

Patients treated with NUCALA achieved significantly greater reductions in daily OCS dose, while maintaining asthma control, compared with placebo (primary endpoint, *P*=0.008).



* Sensitivity analysis to the primary endpoint.

Reference: Bel EH, et al. *N Engl J Med*. 2014;371(13):1189-1197.

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We see a powerful reduction in the OCS dose while maintaining asthma control.

More specifically, in a sensitivity analysis to this endpoint, there was a 50% median reduction from baseline compared to a 0% reduction for placebo.

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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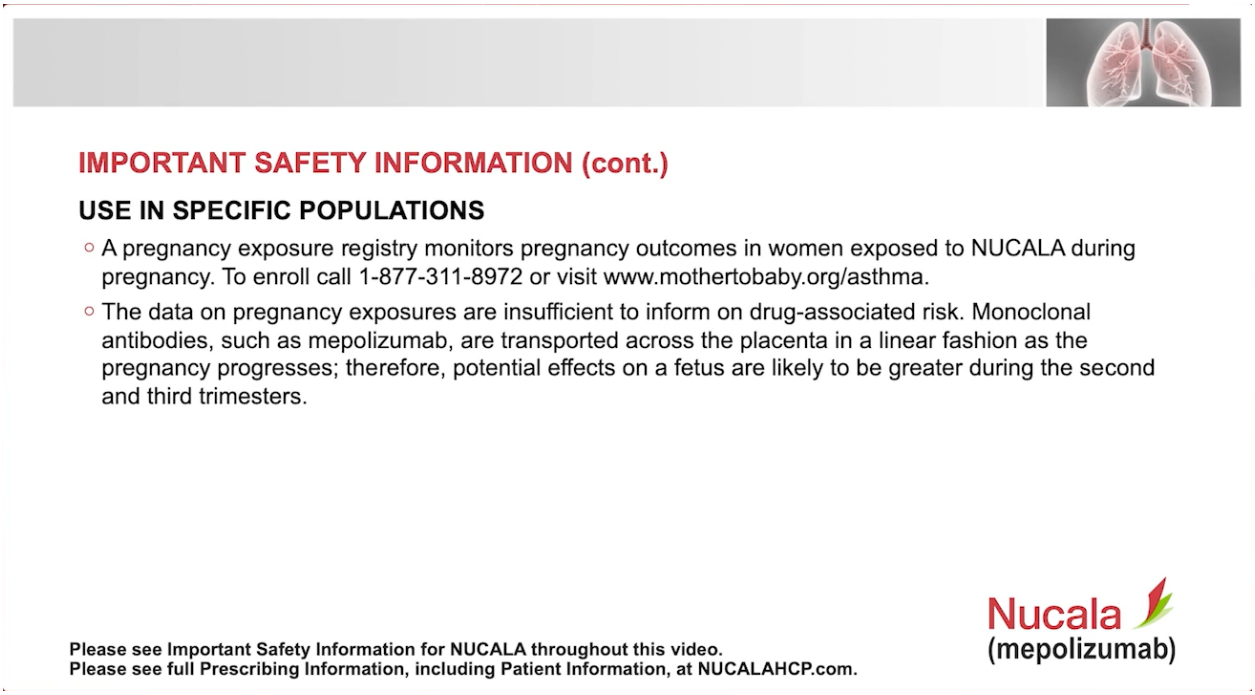
The most common adverse reactions with NUCALA with incidence of 3% or more and more common than placebo reported in the first 24 weeks of MENSA and SIRIUS are shown in this table and included: headache, injection site reaction, back pain, fatigue, influenza, urinary tract infection, upper abdominal pain, 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. Note that this includes patients experiencing systemic reactions, including injection site reactions. Other manifestations included rash, flushing, pruritus, headache, and myalgia, and a majority of these were experienced on the day of dosing.

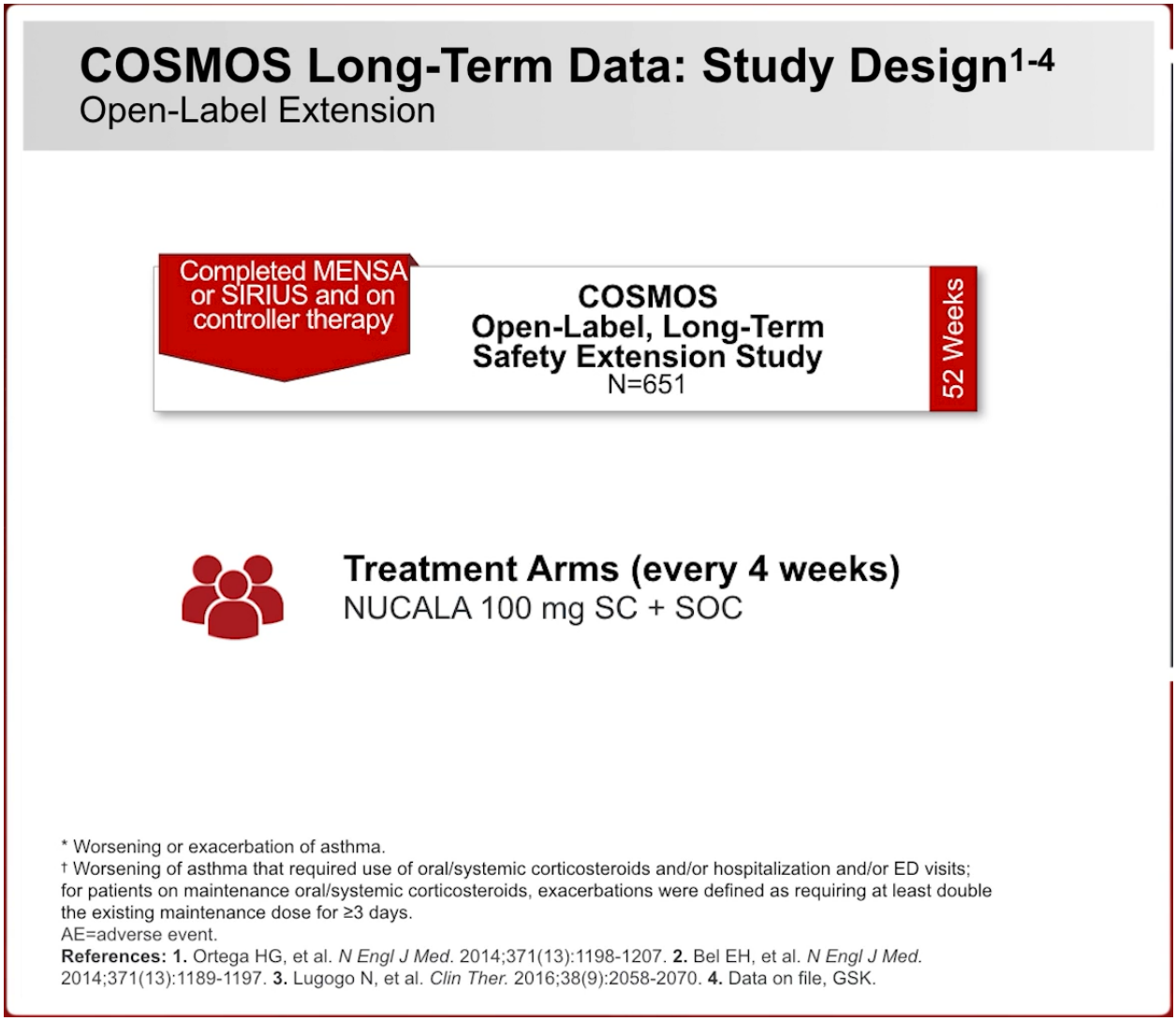
Let's look at Use in Specific Populations.



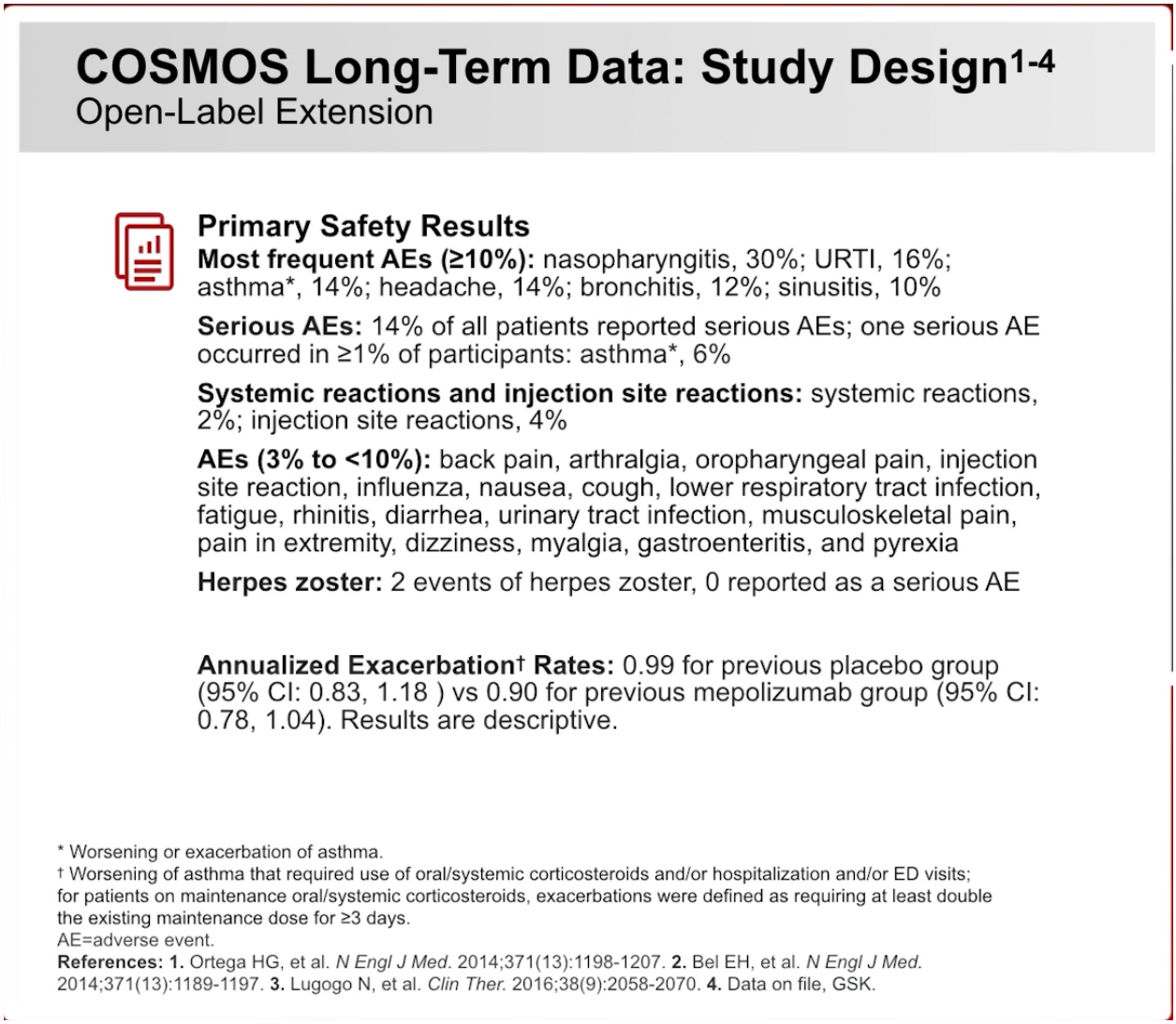
Pregnant women were excluded from the studies, and women of childbearing age were required to use effective birth control.

Keep in mind that monoclonal antibodies do cross the placenta, particularly in the second and third trimester.

If you have patients who become pregnant while taking NUCALA or after she stops taking NUCALA, please consider enrolling her into this mothertobaby.org website so that the third party administrating this observational study can gather safety information that may be useful to future patients receiving NUCALA.



Next, let's look at COSMOS, an open-label, extension study to MENSA and SIRIUS about long-term safety.



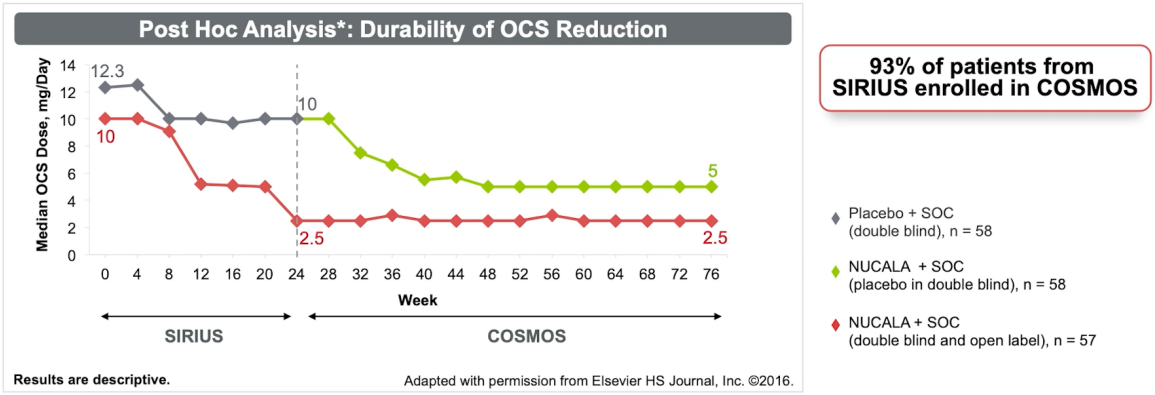
The most common adverse events reported included nasopharyngitis, headache, and some sinus issues.

Note that worsening asthma was among the reported serious adverse events.

The study showed that the side effect profile in the long-term is similar to that seen in controlled studies.

What about long-term durability of reduction in steroids?

Lasting Reduced OCS Dose Observed for an Additional 52 Weeks



93% of patients from SIRIUS enrolled in COSMOS

- Placebo + SOC (double blind), n = 58
- NUCALA + SOC (placebo in double blind), n = 58
- NUCALA + SOC (double blind and open label), n = 57

Durability of response was defined as OCS dose reduction when combined with SIRIUS data.

* Graph only includes patients who completed COSMOS.

Reference: Lugogo N, et al. *Clin Ther.* 2016;38(9):2058-2070.

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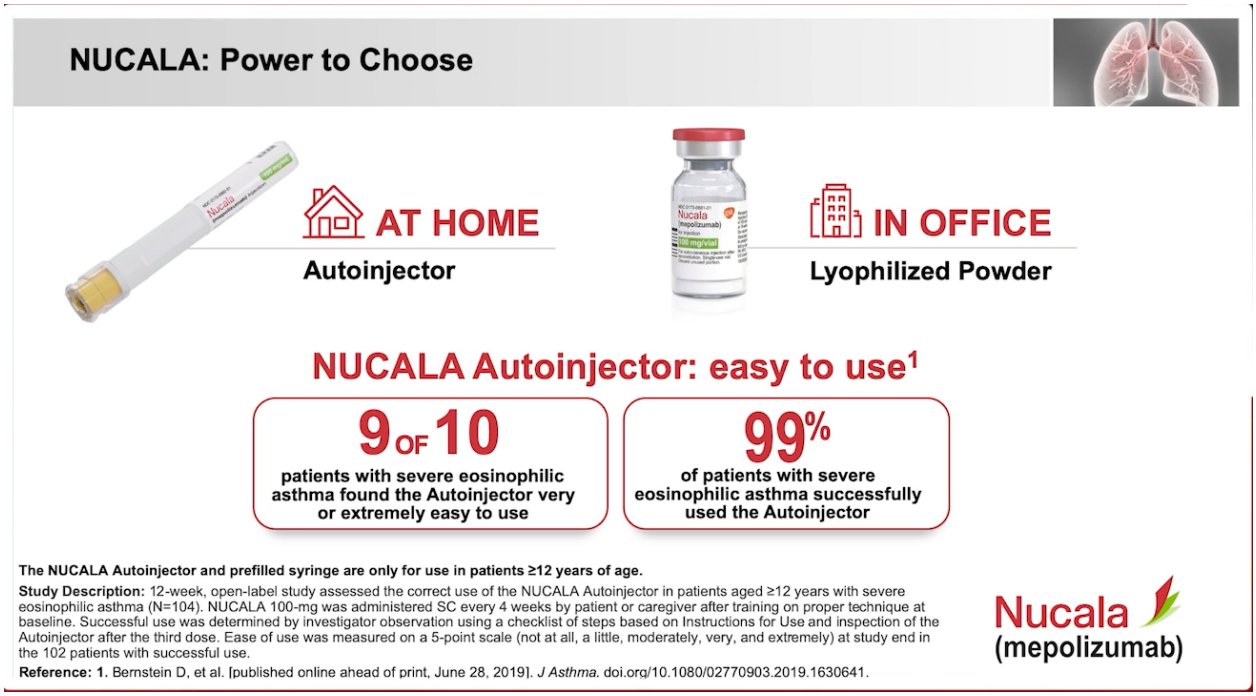
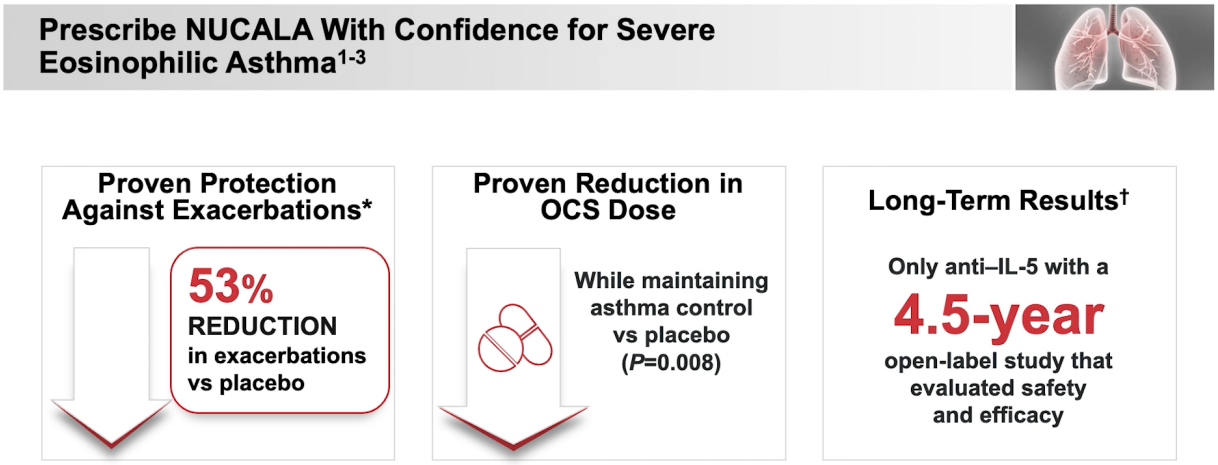
If we look at the original study, SIRIUS and then COSMOS, this post hoc analysis showed sustained durability of the reduction in oral corticosteroids for an additional 52 weeks for patients previously on NUCALA. You can also see that those previously on placebo were then able to reduce their steroid dose once switched to NUCALA.



The availability of NUCALA Autoinjector for at-home administration gives us and our appropriate patients the choice of which route of administration is best for them.

In the clinical study, almost all of the patients found the Autoinjector very or extremely easy to use and demonstrated successful administration. Of course, keep in mind the need for close follow up for those patients who use home injections — they have severe asthma after all.

How many of our patients would love the option of fewer injection visits and at-home administration? Well, NUCALA Autoinjector may offer that.



So, in summary, good news for our appropriate patients. Now, we have long-term data and experience with NUCALA, a medication that works on the IL-5 eosinophil pathway, that offers protection against exacerbations and significantly reduces the use of chronic oral steroids.

It allows patients improved exacerbation control, affords more flexibility in administration and hope for long-term efficacy and stability.

Thank you.

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