What are Epithelial Alarmins and Why are they Important? New Understanding of Severe Asthma Pathophysiology and the Inflammatory Cascade

PLATFORMQ HEALTH EDUCATION

Final Outcomes Report

Live Date: June 9, 2021; On Demand: Through June 9, 2022

Presented by:

ResInsightsLive

National Jewish Health®

This educational activity is supported by an educational grant from AstraZeneca Pharmaceuticals LP.

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HCP Initiative - Executive Summary

Participation and Satisfaction

1,496 Total Learners

69 Live Learners

1,427 On Demand Learners

73% MD/DO/ NP/PA

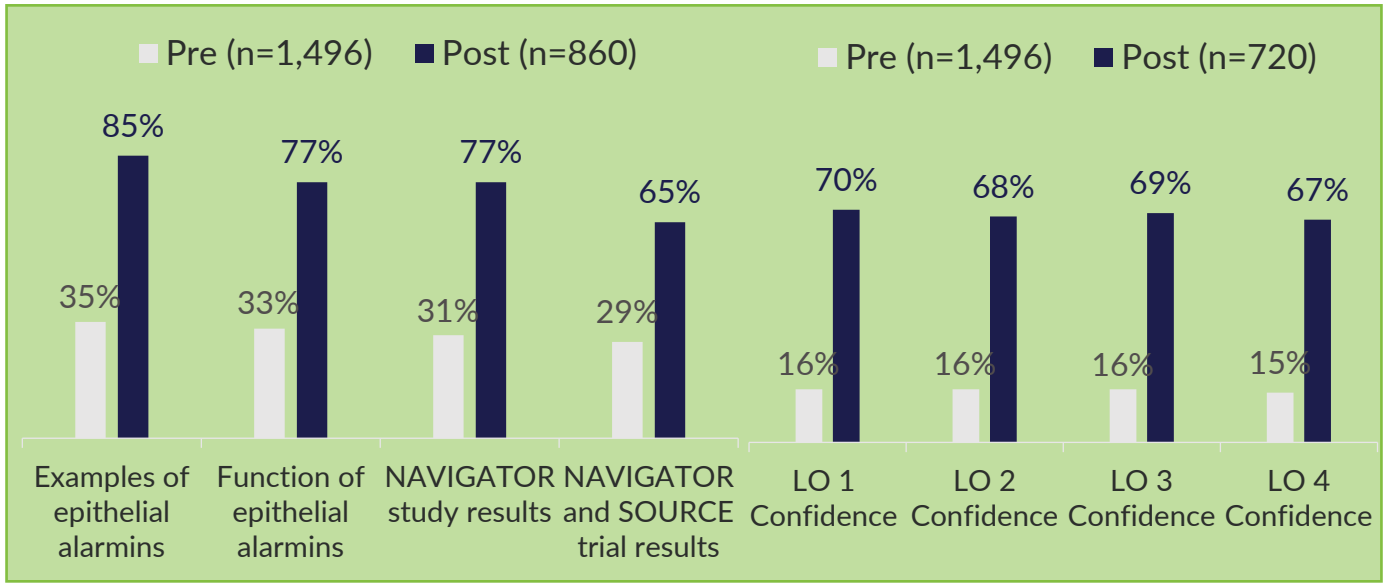
90% Reported LOs were achieved

Practice Change and Patient Impact

86% Reported Positive Impact on Practice

7,943 Patients impacted per week by learner participation in this education

Individual Question Performance & Confidence



Learner Feedback and Future Educational Needs

"Evaluating more patients for asthma subtypes and starting them on therapy when appropriate."

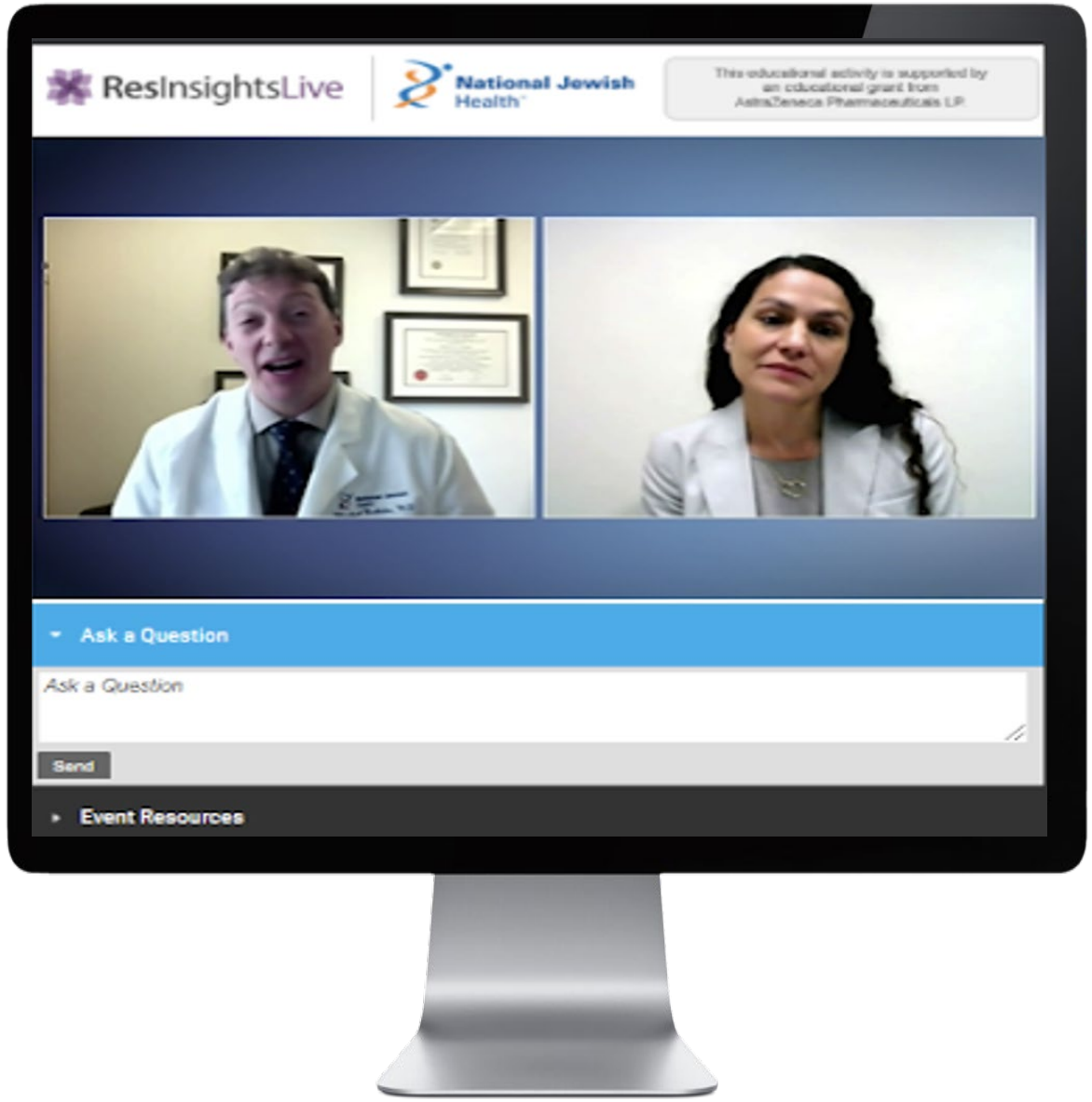
"Better understanding of biologics."

"Stimulated further discussions I have with patients about their asthma."

1. **Recognizing the function of epithelial alarmins**
2. **Interpreting the results of the anti-TSLP trials NAVIGATOR and SOURCE as pertains to the reduction in exacerbation rates and the reduction in oral steroid usage**
3. **Identifying examples of epithelial alarmins**

Session 1 (6/9/2021) Learning Objectives

1. Define the epithelial alarmins and their pivotal role in inflammation in asthma
2. Describe how the epithelial alarmins impact both T2 and non-T2 downstream inflammation in asthma
3. Explain how therapies, such as anti-TSLP, would be expected to modulate airway inflammation in patients with either a T2-high or T2-low phenotype
4. Evaluate the results of clinical trials of novel therapies that target the epithelial alarmins



Program Agenda and Faculty

What Are Epithelial Alarmins and Why Are they Important? New Understanding of Severe Asthma Pathophysiology and the Inflammatory Cascade

- Severe Asthma overview, epidemiology
- Types of asthma Inflammation and clinical features of each phenotype/endotype
  - 2-High
  - T2-Low
- Types of Asthma inflammation
- Role of Epithelieum
- Epithelial alarmins
- Inflammatory Cascade: Pathways of Inflammation
- Targets for Current and Emerging Treatments

Faculty

Flavia Cecilia Lega Hoyte, MD
Fellowship Training Program Director
National Jewish Health

Michael Wechsler, MD, MMSc
Director of The Cohen Family Asthma Institute
National Jewish Health

Event Engagement

1,496

Total Learners

73%

Physician & Advanced Practitioner Learners

28%

Target Audience*

Live Engagement

69	63%
Learners	MD/DO NP/PA

On Demand Engagement

1,427	73%
Learners	MD/DO NP/PA

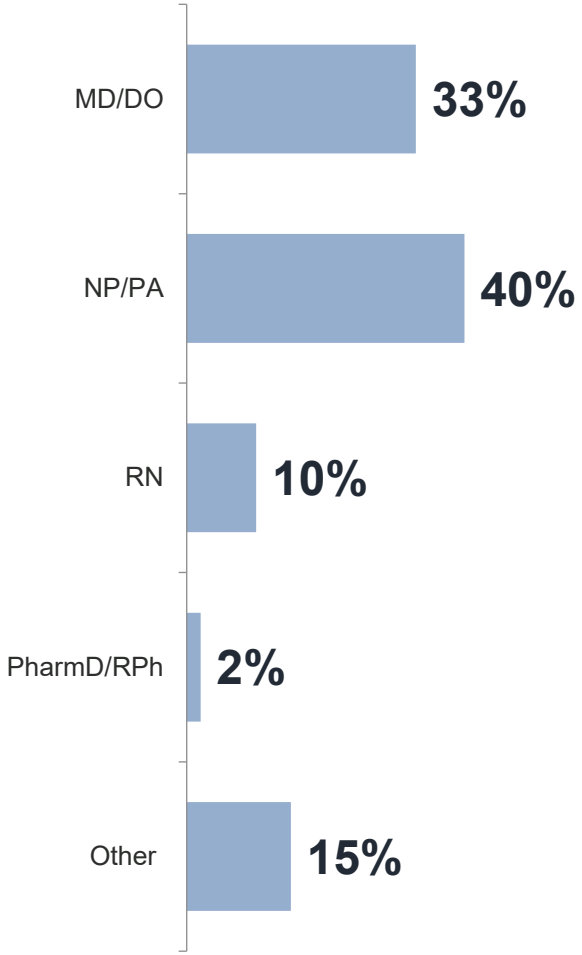
***Target Audience:** Pulmonologists, allergists, pediatricians, specialist nurse practitioners, and physician assistants

Definitions: Learner – An HCP who starts the educational content; term is designated only for individuals who have progressed beyond the CME front matter and pre-test, and have started to consume the educational content

Demographic Snapshot

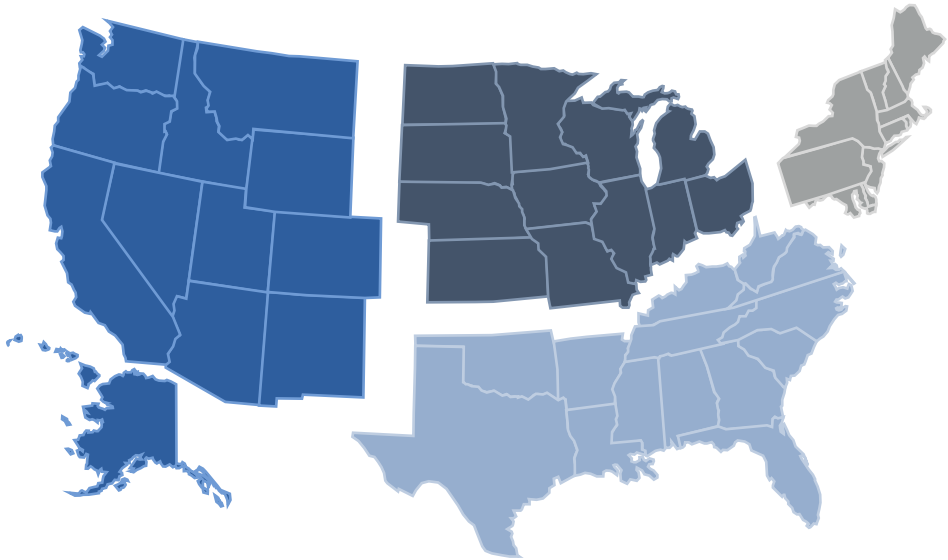
Degree Breakdown

n = 1,496



Breakdown of US Learners by Region

n = 113



27% west

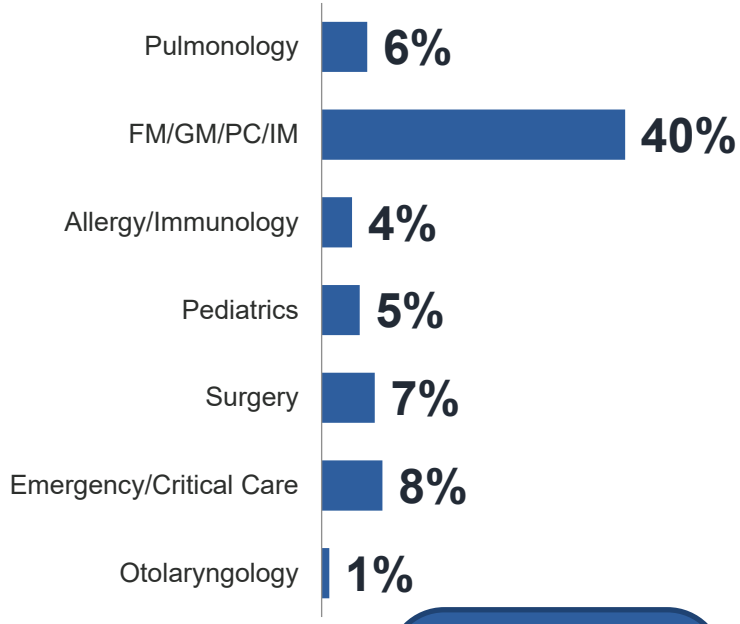
19% midwest

33% south

21% northeast

Specialty Breakdown

n = 1,496



***The majority of the remaining 29% of learners identify their specialty as cardiology, dermatology, education/research, endocrinology, nephrology, neurology, occupational medicine, oncology, pharmacology, physical medicine/rehabilitation, and psychiatry.**

414 Allergy, Immunology, Pulmonology, Pediatrics Physicians and Specialist NP/PAs

Key Statistics

721

Total CME credits awarded (Live-Online + OD)

90%

Learners reported that the objectives of the sessions were met (n = 720)

98%

Learners did NOT perceive any commercial bias in the content of the educational program (n = 720)

34:41

Avg minutes viewed of 60-minute session

175

Total responses to in-session polling

73

Slide Downloads

Satisfaction

Program Satisfaction		
(Respondents selecting "Excellent" or "Good")		
Please rate how well the activity:	**n**	**%**
Met your educational needs	720	89%
Reinforced and/or improved your current skills	720	88%
Gave you tools and strategies to apply in practice	720	86%
Improved your ability to treat or manage your patients	720	87%
(Respondents selecting "Yes")		
Did the activity address strategies for overcoming barriers to optimal patient care?	720	72%
Was the content presented evidence-based and clinically relevant?	720	98%

Faculty Satisfaction		
(Respondents selecting "Strongly Agree" or "Agree")		
Please indicate the extent to which you agree with the following statements about this activity:	**n**	**%**
Flavia Hoyte, MD - Demonstrated expertise in the content	720	87%
Flavia Hoyte, MD - Effectively communicated the key points of the presentation	720	86%
Flavia Hoyte, MD - Effectively engaged the audience	720	84%
Michael Wechsler, MD - Demonstrated expertise in the content area	720	87%
Michael Wechsler, MD - Effectively communicated the key points of the presentation	720	86%
Michael Wechsler, MD - Effectively engaged the audience	720	85%

Patients Impacted via HCP Learner Engagement

8.7

Average # of patient visits/week

×

913

Treaters

=

7,943

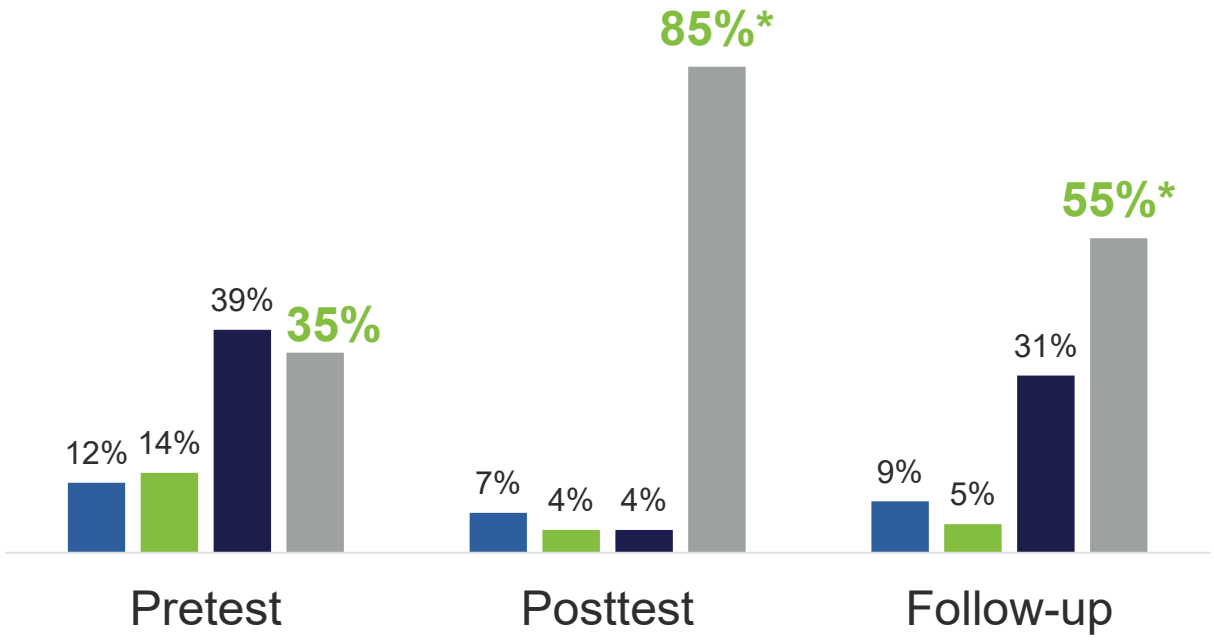
Patients impacted per week by this educational program

Extrapolation based on evaluation data (n = 720)

Pre/Post/2 mos. Knowledge/Competence

Aligned Pre/Post: What are Epithelial Alarmins and Why are They Important? New Understanding of Severe Asthma Pathophysiology and the Inflammatory Cascade

Which of the following groups of cytokines are examples of epithelial alarmins?

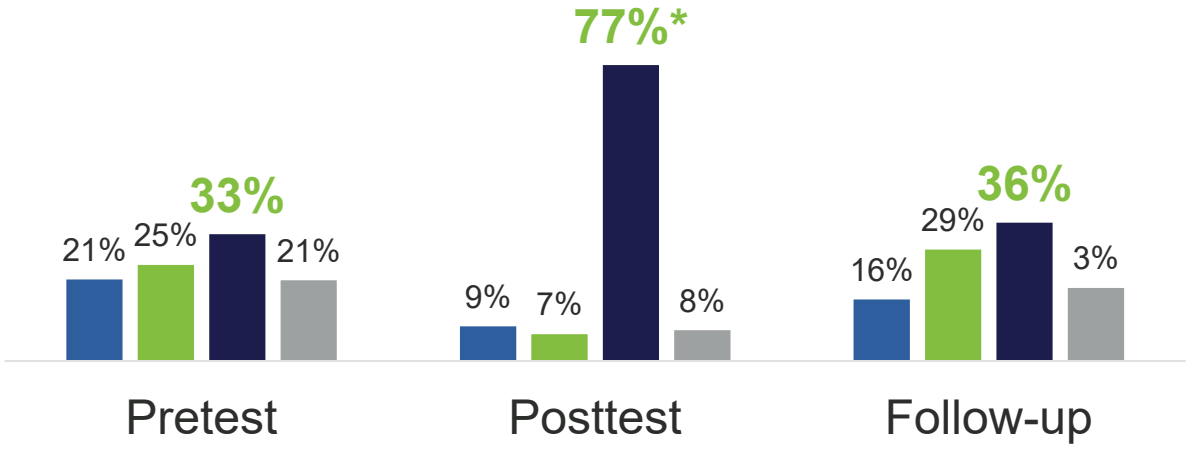


- GM-CSF, IL-5, and IL-3
- IL-12, IL-18, and IFN gamma
- IL-4, IL-5, and IL-13
- **TSLP, IL-25, and IL-33 (Correct)**

Question maps to Session 1 LO# 1, slide #4
n = 1,496 pretest, n = 860 posttest, n = 75 follow-up survey

* p < 0.05 (significant)

Which of the following is NOT a function of epithelial alarmins?



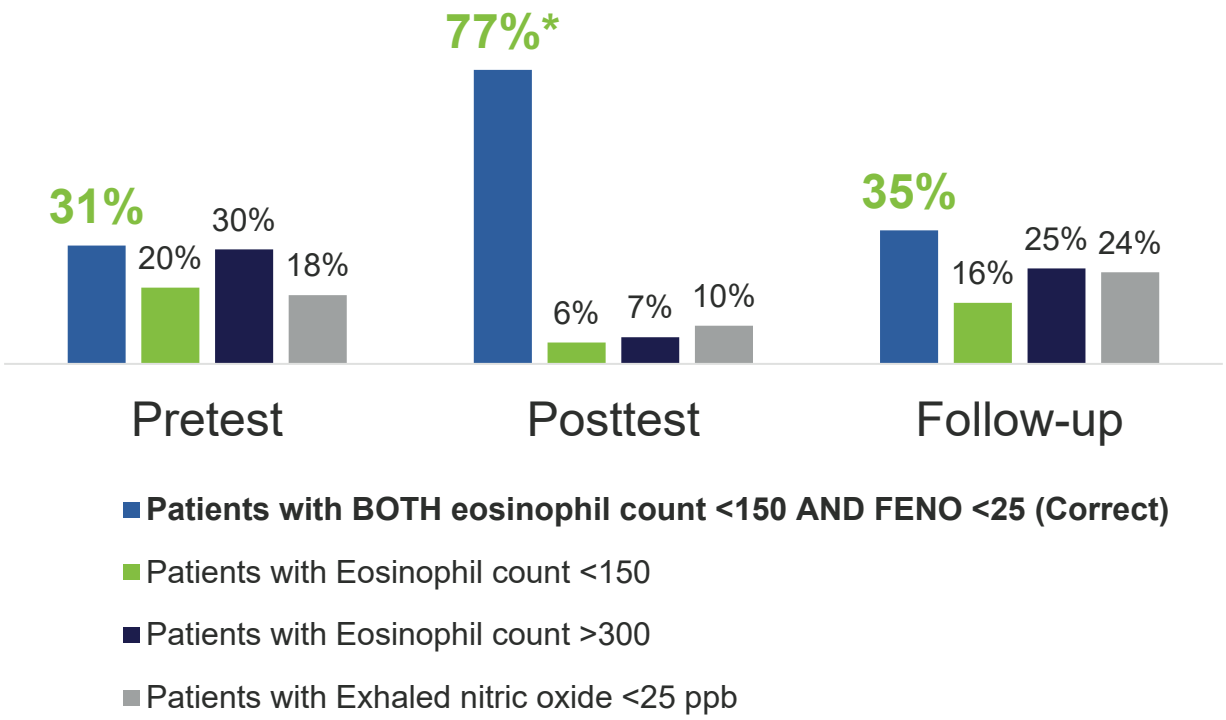
- Alarmins activate ILC2 cells, which can trigger eosinophilic inflammation even in individuals without allergies.
- Alarmins activate various different T cells, potentially impacting both Type 2 high and Type 2 low asthma.
- **Alarmins are triggered by cytokines like IL-4, IL-5, and IL-13 and act downstream of them to recruit effector inflammatory cells. (Correct)**
- Alarmins mediate structural cell effects that contribute to airway hyper-responsiveness and remodeling

Question maps to Session 1 LO# 1 & 2, slide #4
n = 1,496 pretest, n = 860 posttest, n = 75 follow-up survey

* p < 0.05 (significant)

Aligned Pre/Post: What are Epithelial Alarmins and Why are They Important? New Understanding of Severe Asthma Pathophysiology and the Inflammatory Cascade

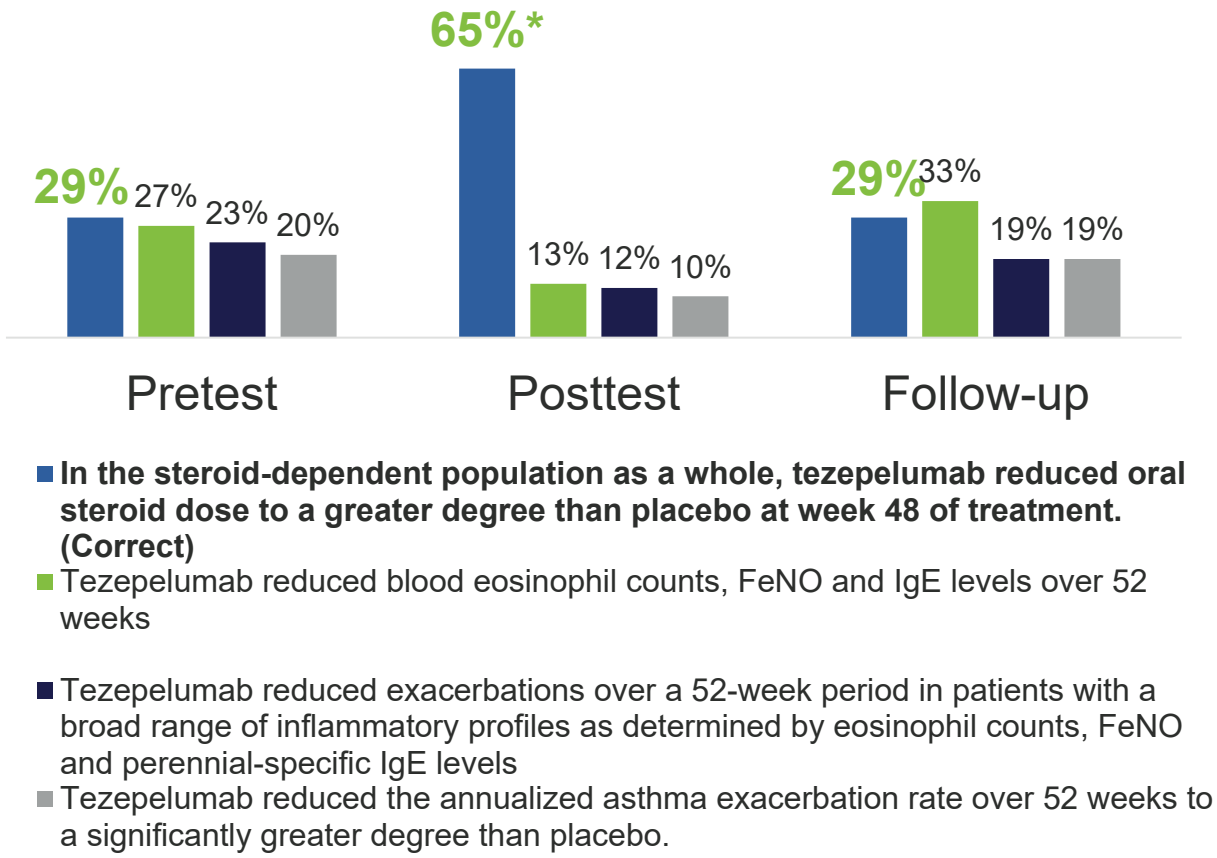
In the phase 3 NAVIGATOR study, Anti TSLP therapy with Tezepelumab showed a significant reduction in annualized exacerbation rate for patients with each of the following characteristics EXCEPT:



Question maps to Session 1 LO# 3 & 4, slide #4
n = 1,496 pretest, n = 860 posttest, n = 75 follow-up survey

* p < 0.05 (significant)

In the phase 3 tezepelumab (anti-TSLP) trials NAVIGATOR and SOURCE, which of the following was NOT demonstrated?

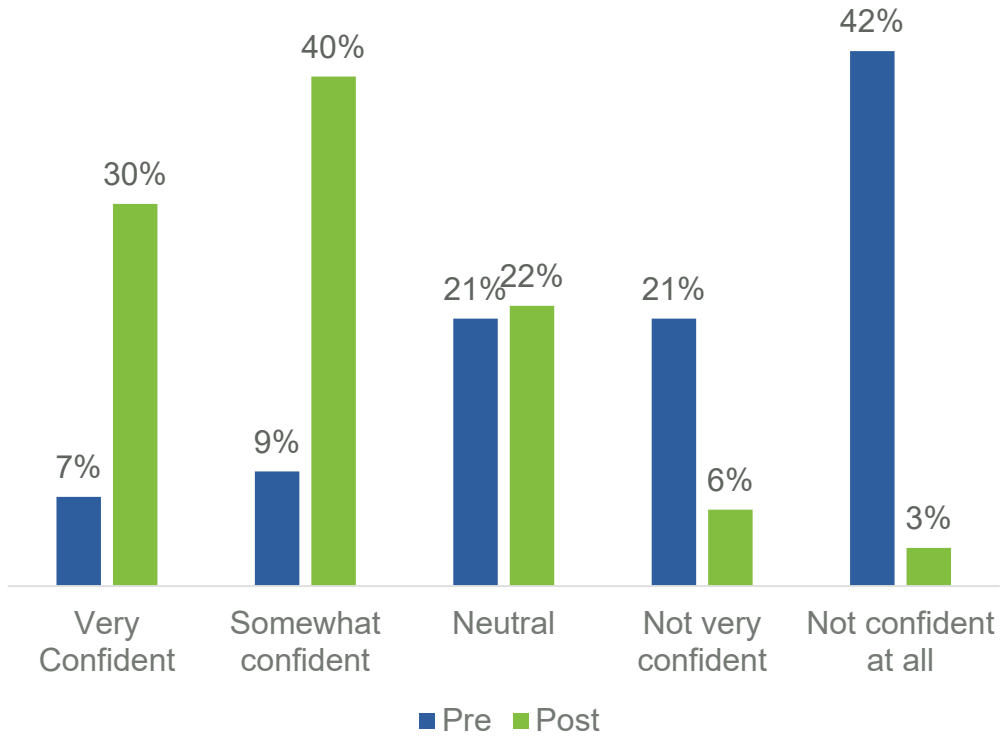


Question maps to Session 1 LO# 3 & 4, slide #4
n = 1,496 pretest, n = 860 posttest, n = 75 follow-up survey

* p < 0.05 (significant)

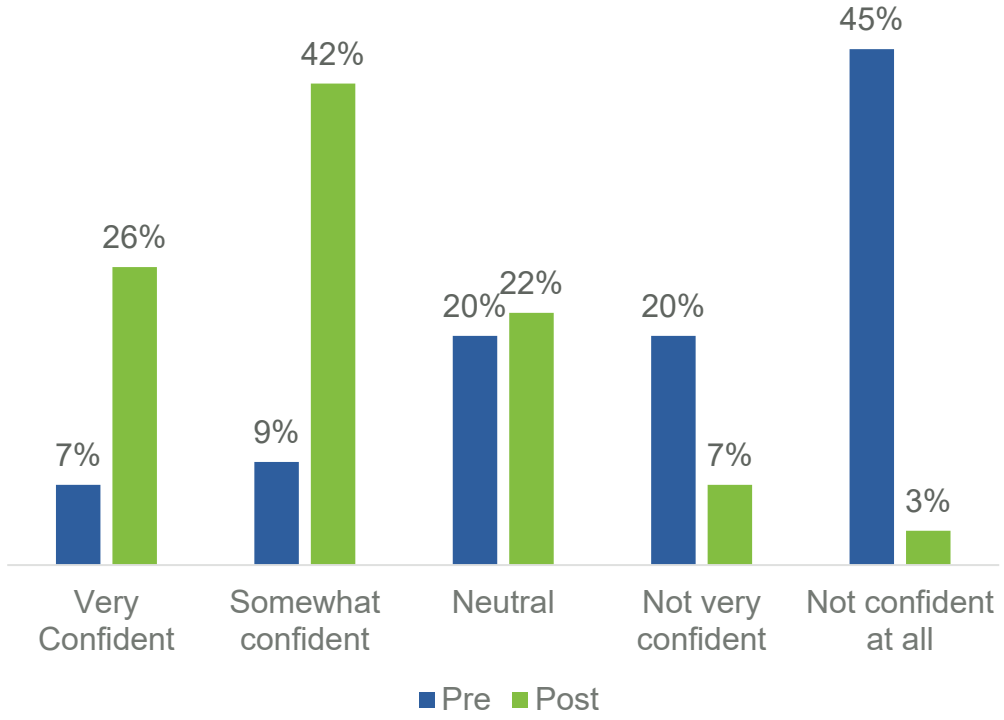
Provider Insights: Learning Objectives

How confident are you in your ability to define the epithelial alarmins and their pivotal role in inflammation in asthma



Pre n = 1,496, Evaluation n = 720

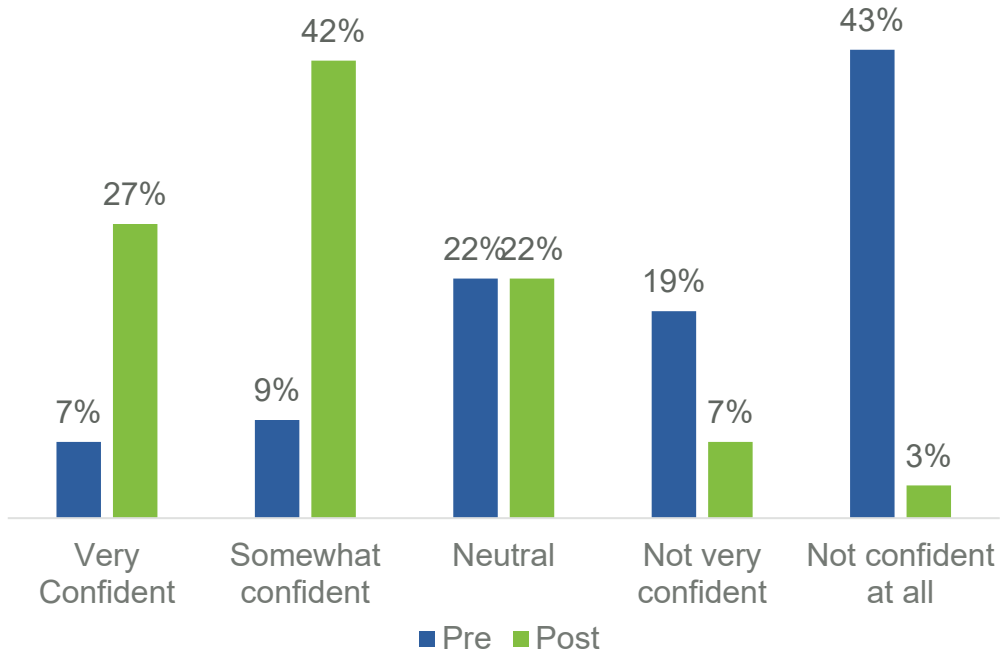
How confident are you in your ability to describe how the epithelial alarmins impact both T2 and non-T2 downstream inflammation in asthma



Pre n = 1,496, Evaluation n = 720

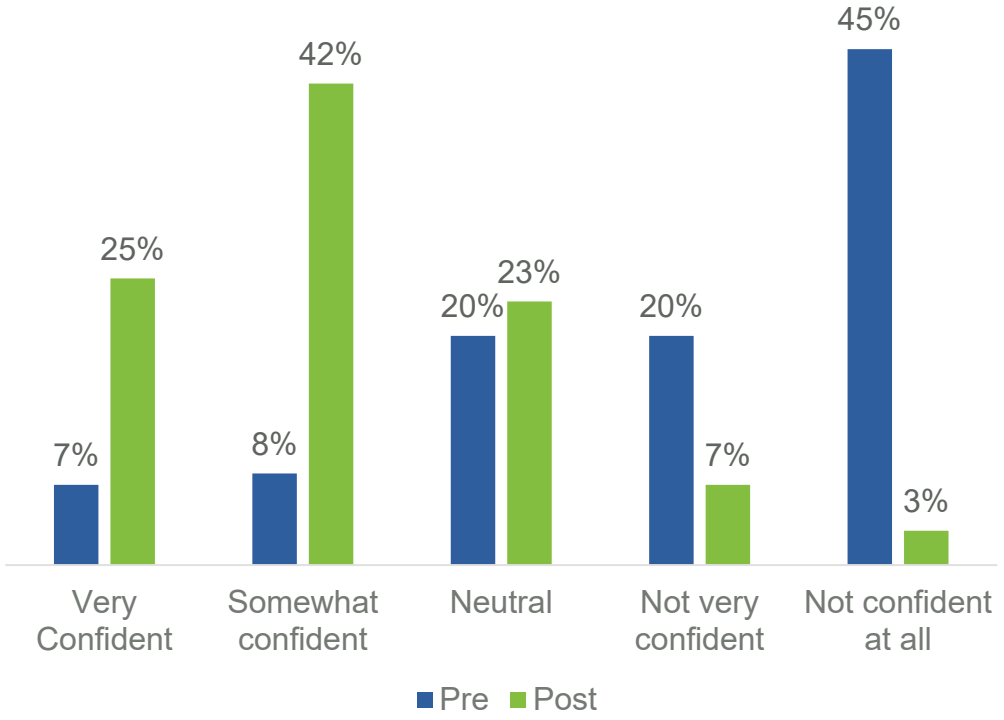
Provider Insights: Learning Objectives

How confident are you in your ability to explain how therapies, such as anti-TSLP, would be expected to modulate airway inflammation in patients with either a T2-high or T2-low phenotype



Pre n = 1,496, Evaluation n = 720

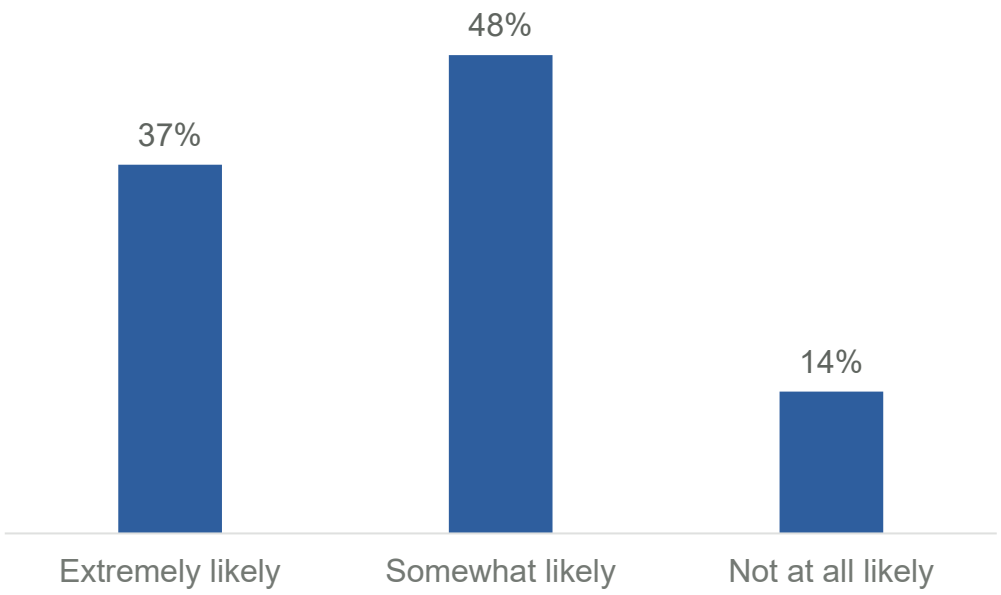
How confident are you in your ability to evaluate the results of clinical trials of novel therapies that target the epithelial alarmins



Pre n = 1,496, Evaluation n = 720

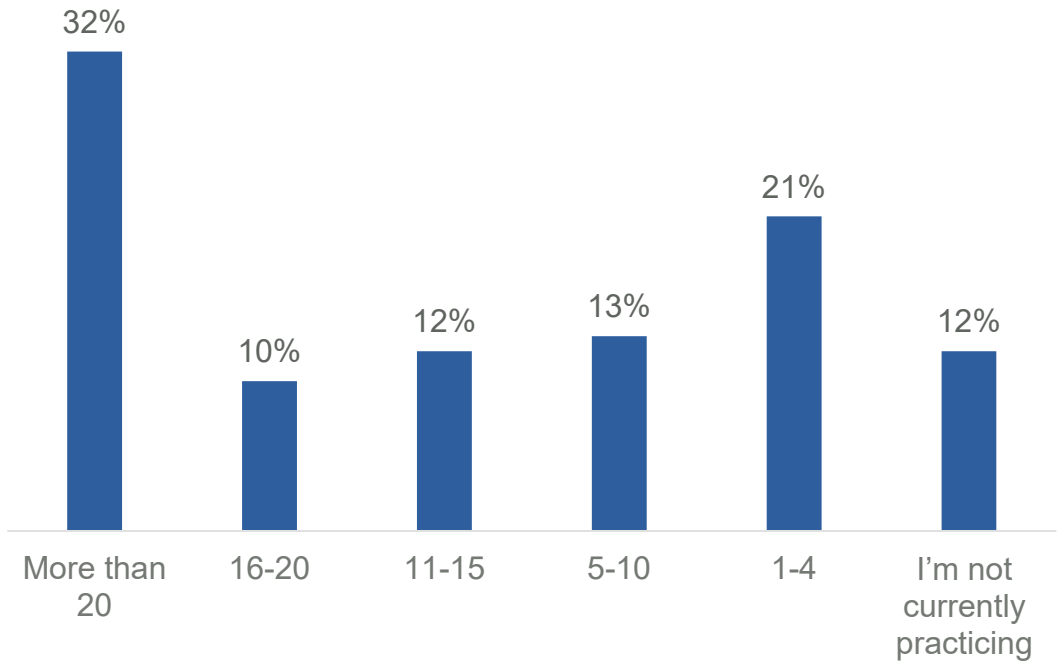
Provider Insights

As a result of what I learned, I intend to make changes in my practice:



n = 720

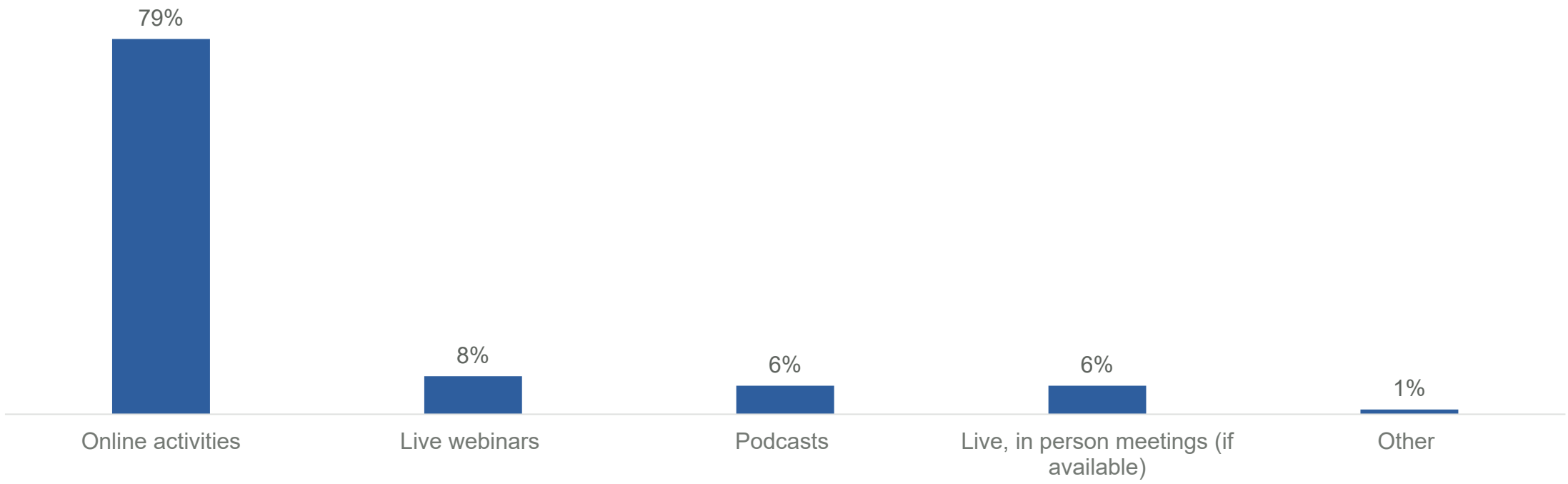
How many years have you been in practice?



n = 720

Provider Insights

During the current pandemic, how do you prefer to consume medical education?



n = 698

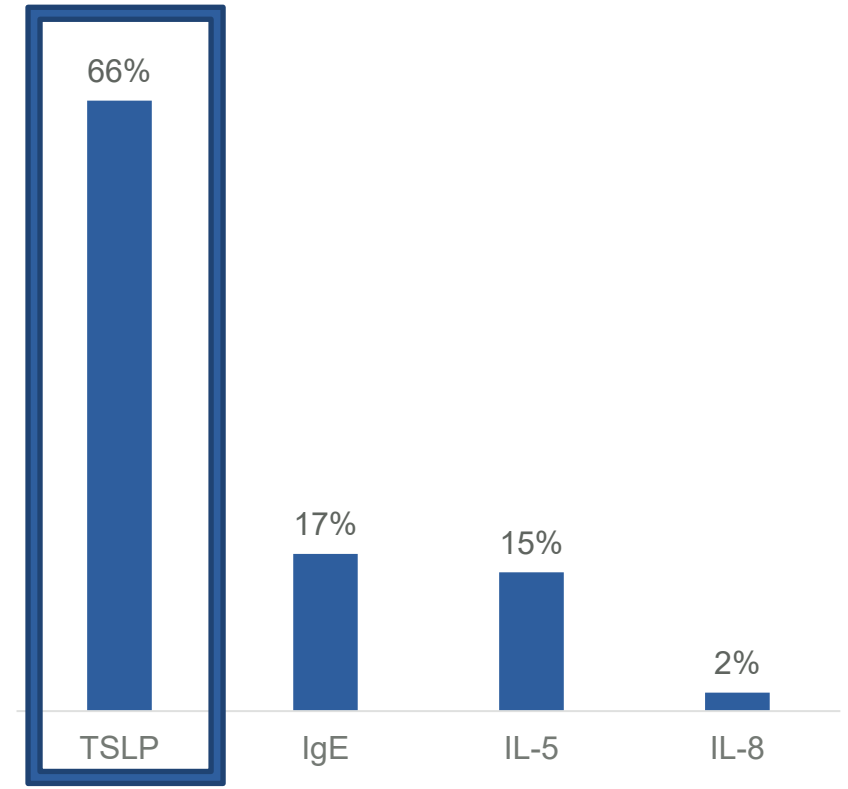
Polling Question

Case Study:
- 43-year-old male
- Allergies since childhood
- Mild intermittent asthma as a child (trigger: allergies)
- Now with severe persistent asthma, worsening over the past 10 years
- 4 hospitalizations as an adult, once in the ICU (triggers: allergies, wildfire smoke, poor air quality, viral infections)
- Having 2-3 OCS-requiring exacerbations per year

Medications:
- High dose ICS/LABA, LTRA, albuterol prn

Testing:
- Total IgE 153
- Absolute Eosinophil Count 600
- Exhaled Nitric Oxide 65
- ACT score 19
- Sputum cell count 10% eosinophils, 50% neutrophils

Targeting which of the following inflammatory molecules would be most likely to decrease exacerbations for this patient?



n = 65

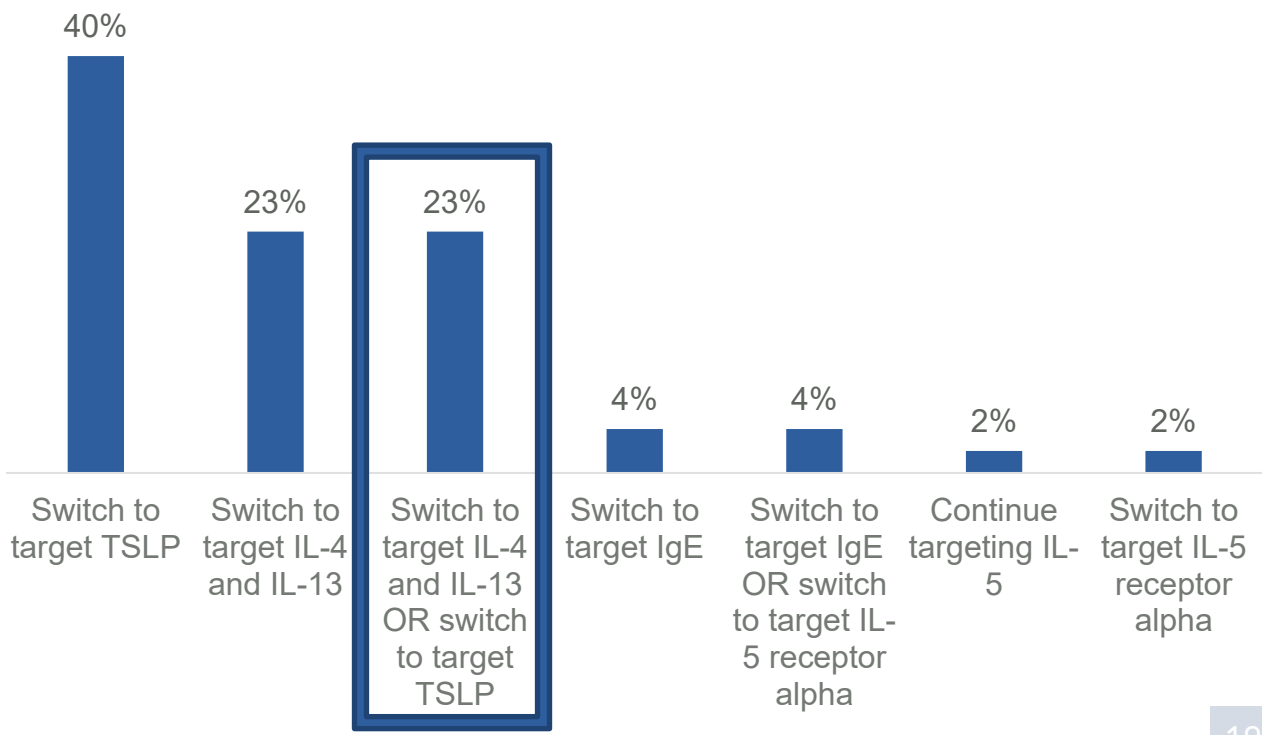
Polling Question

Case Study:
- 44-year-old male with daily asthma symptoms
- History of eosinophilic asthma
- No history of allergies
- 4 exacerbations/year
- FEV1 66% predicted

Medications:
- High dose ICS/LABA
- Started on Mepolizumab and improved but still with 2 exacerbations/year and symptoms 3-4 days/week

Testing:
- Total IgE 55
- Absolute Eosinophil Count 80
- Exhaled Nitric Oxide 36 ppb
- ACT score 16
- Sputum cell count not evaluated

Targeting which of the following is most likely to benefit this patient?



n = 47

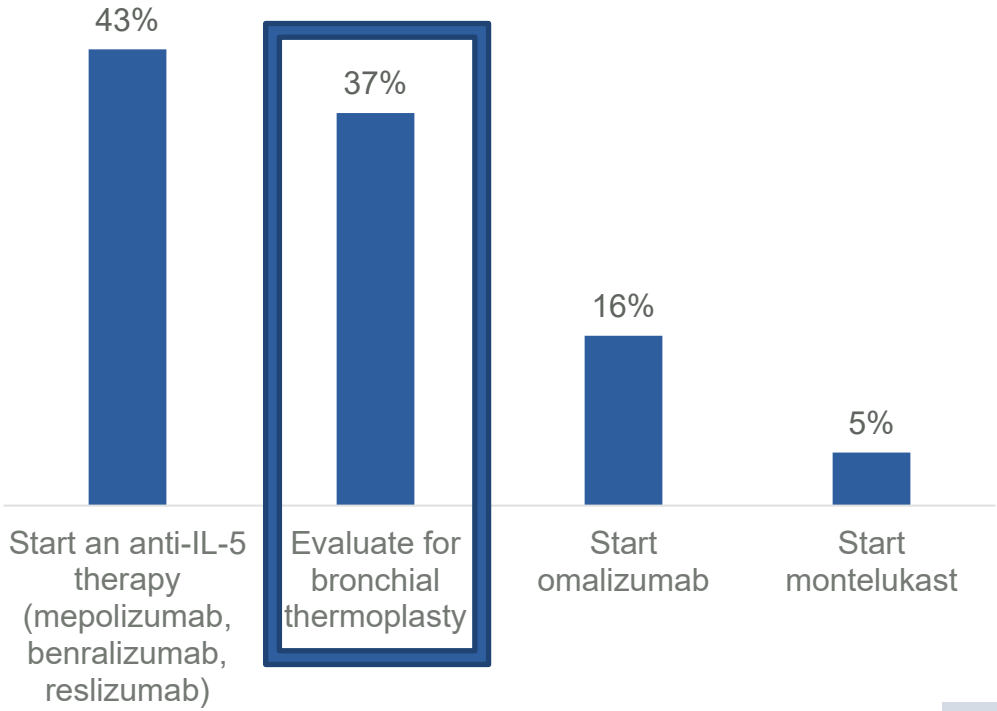
Polling Question

Case Study:
- 51-year-old obese female
- Diagnosed with asthma at age 34
- Was initially having 3-4 steroid-requiring exacerbations per year
- Started on daily OCS a year ago
- Still having daily symptoms and 2-3 exacerbations per year
- Dupilumab recently discontinued as it was not helpful

Medications:
- High dose ICS/LABA, LAMA, prednisone 10mg daily, albuterol prn

Testing:
- Total IgE 33
- Absolute Eosinophil Count 100
- Exhaled Nitric Oxide 15
- ACT score 14
- Sputum cell count showed few cells, no specific cell type predominance

Which of the following would be a possible next step in management?



n = 63

Q-Board: Pre-Activity Learner Submission of Questions with "upvoting" technology (8 questions, 16 upvotes)

Q Board | **Ask**

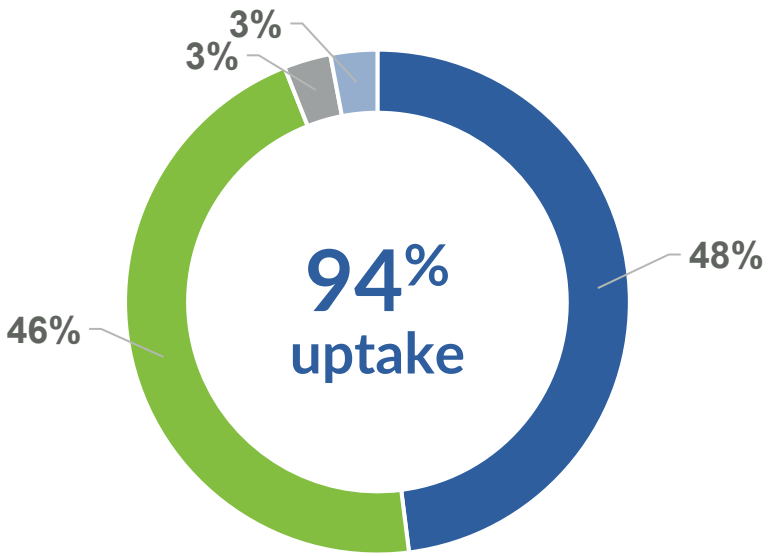
Vote by clicking / tapping the arrow

2	Can you discuss surrogate markers for efficacy in the treatment of severe asthma, such as circulating eosinophils and FeNO? Especially in the context of therapy with drugs targeting alarmins?
2	What the medicinal (1) and rehabilitation(2) key to threat severe asthma?
2	Assuming tezepelumab gets approved, how would you factor its use into your clinical practice? Who would you start on tezepelumab over some of the other biologics that are currently available? Would you switch any patients from their current biologic to tezepelumab?
2	Are you able to tell us more about the emerging therapies that target IL-33 or its receptor?
2	You mentioned that there is a subset of patients with eosinophilic inflammation who do not have a history of allergies. Can you give some examples of patients who might fit into this group?
2	What does blocking tslp do that other biologics don't do?
2	Can you discuss the tezepelumab OCS sparing study- why didn't it achieve its primary outcomes?
2	What are some other targets that should be considered beyond the ones discussed?

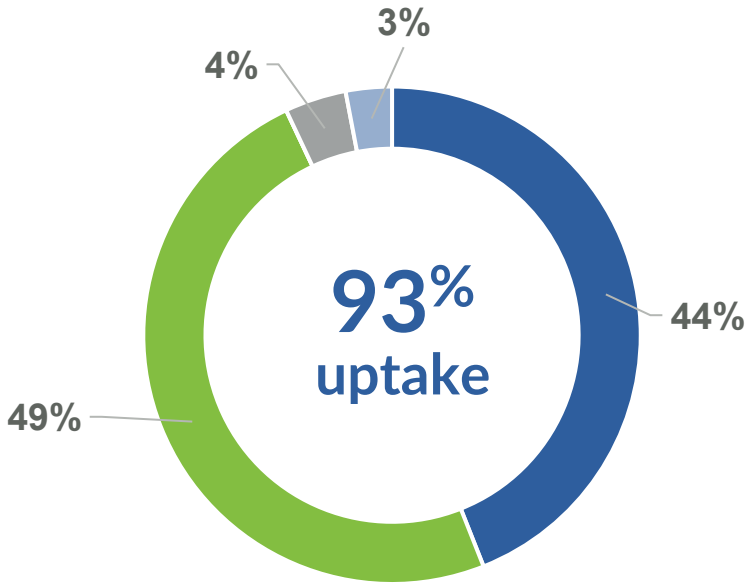
2 mos. Impact

Learning Objectives

LO 1: Define the epithelial alarmins and their pivotal role in inflammation in asthma



LO 2: Describe how the epithelial alarmins impact both T2 and non-T2 downstream inflammation in asthma

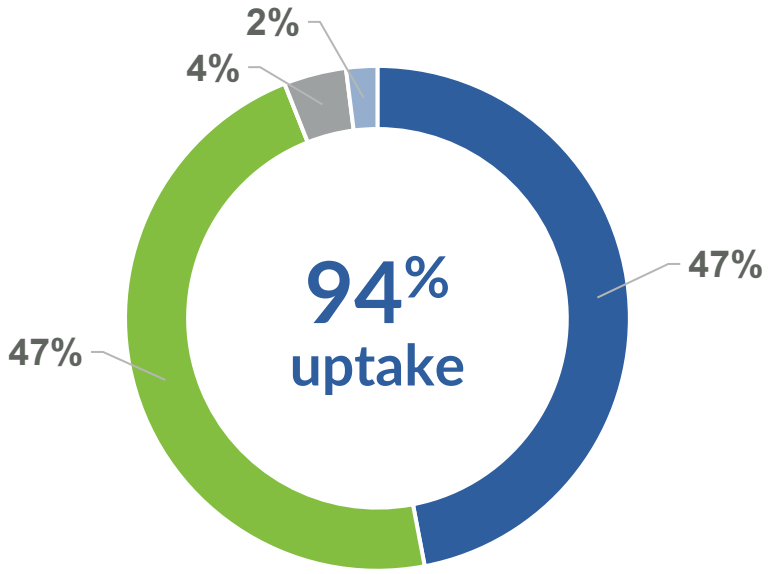


Source: follow-up survey, n = 75

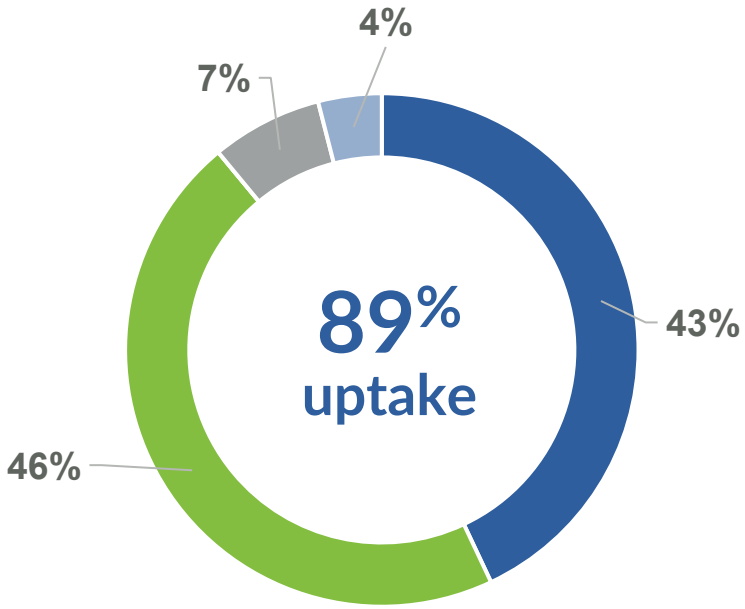
To a Great Extent Somewhat Not at all Not Applicable

Learning Objectives

LO 3: Explain how therapies, such as anti-TSLP, would be expected to modulate airway inflammation in patients with either a T2-high or T2-low phenotype



LO 4: Evaluate the results of clinical trials of novel therapies that target the epithelial alarmins



Source: follow-up survey, n = 50

To a Great Extent | Somewhat | Not at all | Not Applicable

81% reported positive impact on patient experience or outcome

Please specify the impact that the educational activity had on patient experience or outcome (self-reported, by theme/category):

Clinical Practice/Treatment

- Can present patient with options to help get them off steroids.
- Able to explain pathology better.
- Encourage patients to verbalize how asthma is affecting their QOL.
- Stimulated further discussions I have with patients about their asthma.
- I am better able to manage my patients.
- Improved care **(x4 responses)**
- Improved my plan therapy.
- Better disease management.
- Advocating for patients and requesting med consults for patients when I feel their symptoms are not being adequately managed.
- Decrease ER visits due to asthma attack.
- Discussing new option with patients.
- I am able to educate them about new clinical findings and treatment options.
- Use of anti-TSLP for patients.

Clinical Practice/Treatment (Cont.)

- I am able to risk stratify patients in a better way and optimize therapy to them to have better outcomes
- Provide me with options for my patients who need help

Knowledge/Confidence

- Improved understanding in the mechanism of action.
- Improve knowledge. **(x2 responses)**
- I feel myself more confident in asthma sub-type so the patient recognize my better understanding.
- Understanding what antigens to test for when assessing the cause for severe asthma symptoms
- I understand some of what triggers people's asthma more now.
- More knowledgeable about treating patients with severe asthma but the options are still limited for a FQHC.

Patient Management/Outcomes

- Better patient outcomes.
- Better control of asthma.
- Better control of symptoms.
- Better patient prognosis.
- Patients are aware of their options for treatment.

Source: follow-up survey, n = 48

86% reported positive impact on clinical practice change

Please provide an example of how you have changed your clinical practice as a result of having participated in this educational activity:

Clinical Practice

- Closer attention to clinical presentation. **(x2 responses)**
- Better utilization epithelial alarmins. **(x2 responses)**
- Using biologics for asthma control. **(x2 responses)**
- Evaluating more patients for asthma subtypes and starting them on therapy when appropriate.
- Use more Tezepelumab. **(x5 responses)**
- Evaluate eosinophil count more.
- Measuring more biomarkers.
- I am better able to manage my patients.
- I am better in treating asthma. **(x3 responses)**
- Educate my colleagues so that together we can change our practice.
- Implementation of treatment plan.
- Decrease episode of ER visit due to asthma.
- I am better able to risk stratify my patients and optimize therapy.
- Early referral to a specialist
- Starting to consider anti-TSLP as a treatment for patients.

Clinical Practice (Cont.)

- Routine screening of patients with asthma for eosiniphil count, feNO levels, and prescribing medicines for those who are not controlled on routine medications. **(x2 responses)**
- Understanding some of the triggers for severe asthma and how to manage these symptoms.
- Better phenotyping of the patient. **(x3 responses)**
- I ask more questions to quantify a person's asthma severity.
- Reading more articles to better understand different topics to help patients .

Knowledge/Confidence

- Improved knowledge. **(x4 responses)**
- I finally understand severe asthma!
- Better understanding of biologics. **(x3 responses)**
- Will know there is another treatment option for moderate to severe asthma in individuals refractory to other biologics or for those whose phenotype is unknown.
- Better understanding of severe asthma and the patient's impression that they just have asthma, without following the recommendations of their health care professional because "it's just asthma".
- I understand more about how each patient will respond to different treatments and management of their disease.

Source: follow-up survey, n = 51

What Changes Have You Made to Your Clinical Practice as a Result of Participating in This Activity?

I have greater knowledge of epithelial alarmins (eg, TLSP; IL-33; IL-25) and their pivotal role in downstream inflammation and their contribution to the inflammatory process in patients with asthma.	17%
I am more confident in my therapeutic management of patients with severe asthma.	17%
I have a greater understanding of how novel therapies, such as anti-TSLP, would be expected to modulate airway inflammation in patients with a T2-high or T2-low phenotype.	13%
I am better able to assess the therapeutic potential (eg, safety and efficacy) of novel therapies being investigated to target epithelial alarmins and improve outcomes in severe asthma.	12%
I have a better understanding of the inflammatory subtypes of severe asthma.	10%
I have a greater sensitivity to the burden of disease associated with severe asthma.	9%
I have a better understanding of the mechanisms of action of novel therapeutics (eg, tezepelumab) being investigated in clinical trials for the treatment of severe asthma.	9%
I am better able to utilize recommendations on severe asthma according to GINA 2021 clinical practice guidelines	6%
Not applicable	7%

Source: follow-up survey, n = 75

Educational Next Steps Suggested by Outcomes Results

Outcomes results and participant questions suggest the value of future education in the following areas:

- Recognizing the function of epithelial alarmins
- Interpreting the results of the anti-TSLP trials NAVIGATOR and SOURCE as pertains to the reduction in exacerbation rates and the reduction in oral steroid usage
- Identifying examples of epithelial alarmins

PLATFORM HEALTH

Thank You For Your Support

Appendix Follows

Our Methodology

- Program Evaluation
  - designed to measure learner satisfaction and commitment to change
- Pre- and post-activity challenge questions administered immediately prior to and following live and on-demand activity
  - designed to measure gain of specific knowledge and competence related to management skills reflected in program learning objectives
- Follow-up post-activity survey administered electronically two months post education
  - designed to measure knowledge and competence gain, as well as behavior change related to program learning objectives
- Statistical testing to assess strength of change over time was conducted using Chi-square test