

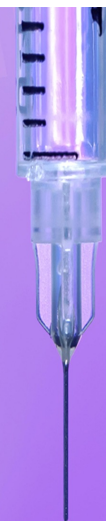


Autoimmune
Learning Network

HMP Education

Preparing for the Biosimilar Era in Allergy and Immunology:

Scientific Principles, Clinical Evidence,
and Implications for Patient Care



Faculty

Mario Castro, MD, MPH

L. E. Phillips and Lenora Carr Phillips Professor

Chief, Pulmonary, Critical Care and Sleep Medicine

Vice Chair for Clinical and Translational Research Director, Frontiers Clinical and Translational Science

Institute at the University of Kansas University of Kansas School of Medicine

Kansas City, Kansas

Faculty Disclosures

- **Mario Castro, MD, MPH:** Grant/research support—American Lung Association, Apogee Therapeutics, Apreo Health, AstraZeneca, Celldex, Connect BioPharma, Enveda, Expedition Therapeutics, Gala Therapeutics, Genentech, GlaxoSmithKline, Kinaset, Kymera, NIH, Nacion, Patient-Centered Outcomes Research Institute (PCORI), Pfizer, Regeneron, Sanofi-Aventis, Shionogi, Teva; consultant—Admin Physicians World, Amgen, Apogee, Apreo Health, AstraZeneca, Blueprint Medicines, Citrus Health, Connect BioPharma, Enveda, Evommune, Genentech, Generate:Biomedicines, Genzyme, GlaxoSmithKline, Iqvia, ITA Group, Johnson & Johnson, Kymera, Lilly, Meetings by Design, Novartis, Pfizer, Pioneering Medicines, Polarean, Regeneron, Sanofi-Aventis, Syneos, Teva, Uniquity Bio, Upstream Bio, VIDA; speaker's bureau—Amgen, AstraZeneca, Med Learning Group, Peerview, Regeneron, Sanofi-Aventis; major stockholder—Aer Therapeutics

Disclosures

- The faculty have been informed of their responsibility to disclose to the audience if they will be discussing off-label or investigational use(s) of drugs, products, and/or devices (any use not approved by the US Food and Drug Administration)
- Applicable CME staff have no relationships to disclose relating to the subject matter of this activity
- This activity has been independently reviewed for balance
- This CME activity includes brand names for participant clarity purposes only. No product promotion or recommendation should be inferred

Learning Objectives

- Assess disease severity, patient profile, and access barriers for the optimal implementation of IgE-targeted biologic therapy in appropriate candidates with moderate-to-severe allergic or immunologic disease
- Evaluate available and emerging biosimilars for IgE-mediated conditions to inform evidence-based biologic selection and treatment decision-making
- Examine FDA biosimilar and interchangeability principles to guide evidence-based strategies for biosimilar initiation, substitution, switching, and patient counseling

Program Information

- This program is provided by HMP Education, an HMP Global Company
- Supported by an educational grant from Celltrion, Inc

Biologic Therapy in Allergic and Immunologic Diseases



Type 2 Inflammation: A Shared Pathway across Conditions

Type 2 inflammation

IgE

TODAY'S FOCUS

Severe allergic asthma, CSU, CRSwNP, food allergy

IL-5 / IL-5R

Eosinophilic asthma

IL-4 / IL-13

Asthma, atopic dermatitis, CRSwNP

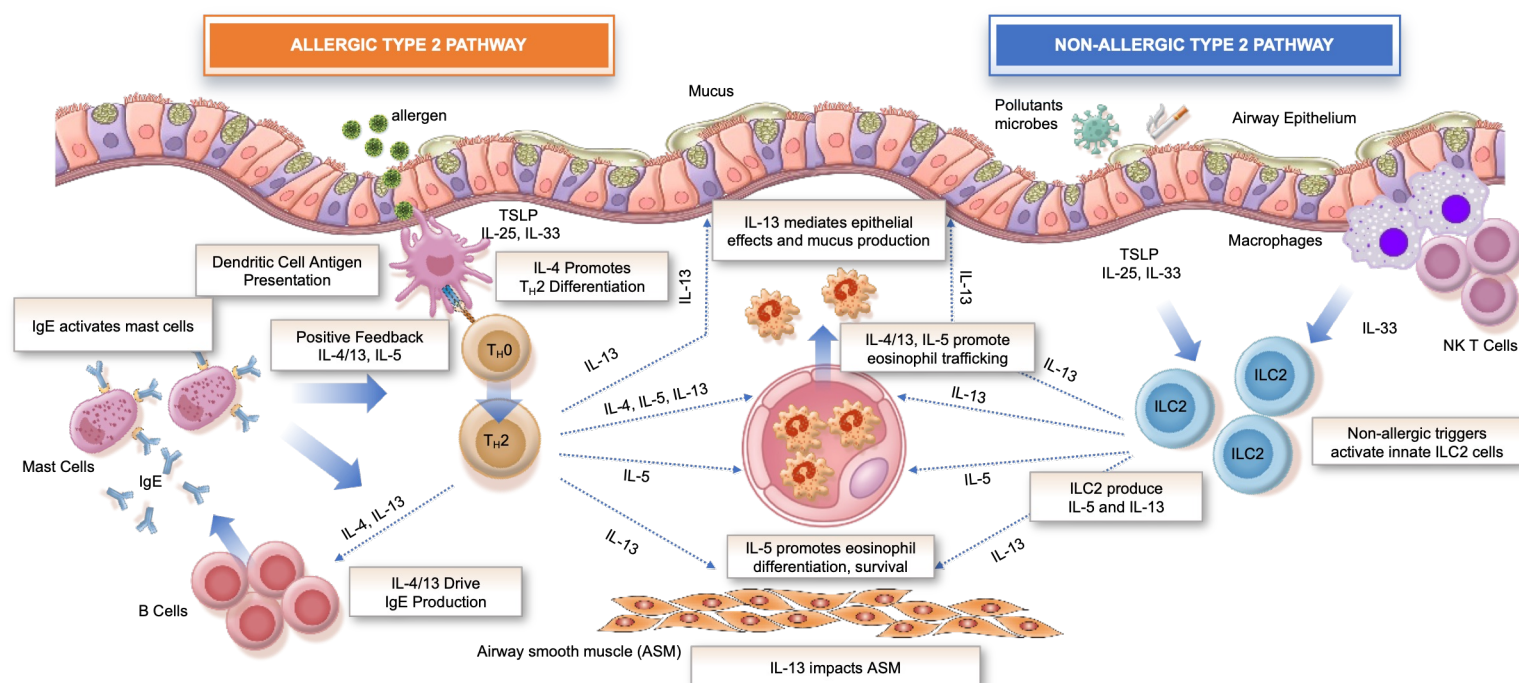
TSLP

Severe asthma

CSU = chronic spontaneous urticaria; CRSwNP = chronic rhinosinusitis with nasal polyps; IL = interleukin; IL-5R = interleukin-5 receptor; TSLP = thymic stromal lymphopoietin.

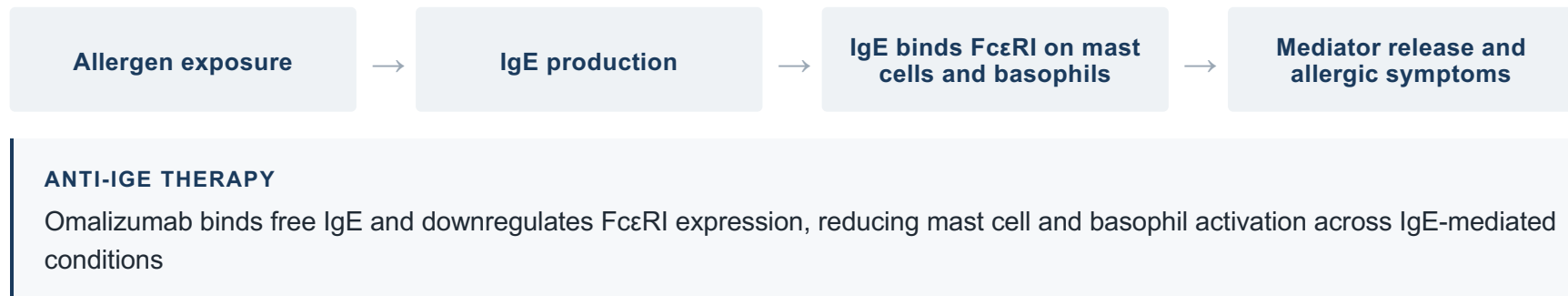
Fildan AP, et al. *Exp Ther Med.* 2021;22(5):1263. Alska E, et al. *J Clin Med.* 2025;14(4):1079.

Allergic and Non-Allergic Triggers Initiate Type 2 Inflammatory Pathways that Drive Airway Pathology in Asthma



Adapted from Brusselle GG, et al. *Nature Medicine*. 2013;19(8): 977-979. Gandhi NA, et al. *Nat Rev Drug Discov*. 2015;15(1):35-50. Burton OT et al. *Immunol Rev*. 2011;242(1):128-143. Vatrella A et al. *J Asthma Allergy*. 2014;7:123-130. Bossé Y et al. *Int Arch Allergy Immunol*. 2008;146(2):138-148. Grunstein MM et al. *Am J Physiol Lung Cell Mol Physiol*. 2002;282(3):L520-L528. Fulkerson PC, et al. *Nat Rev Drug Discov*. 2013;12(2):117-129. Steinke J, et al. *Respir Res*. 2001;2:66-70. Corren J. *Curr Allergy Asthma Rep*. 2013;13(5):415-420.

The IgE Pathway and Anti-IgE Mechanism of Action



FcεRI = high-affinity IgE receptor.
Kothari A, et al. *Front Immunol.* 2026;16:1746790.

- Omalizumab has anchored anti-IgE treatment for more than two decades

Severe allergic asthma

Inadequately controlled on inhaled corticosteroids

Anti-IgE approved

Severe allergic asthma

Inadequately controlled on inhaled corticosteroids

Anti-IgE approved

Severe allergic asthma

Inadequately controlled on inhaled corticosteroids

Anti-IgE approved

Chronic spontaneous urticaria

Antihistamine-refractory wheals
and angioedema

Anti-IgE approved

Chronic spontaneous urticaria

Antihistamine-refractory wheals and angioedema

Anti-IgE approved

Chronic spontaneous urticaria

Antihistamine-refractory wheals and angioedema

Anti-IgE approved

CRSwNP

Add-on therapy for inadequately controlled disease

Anti-IgE approved

CRSwNP

Add-on therapy for inadequately controlled disease

Anti-IgE approved

CRSwNP

Add-on therapy for inadequately controlled disease

Anti-IgE approved

IgE-mediated food allergy

Reduces reactions after accidental exposure

Approved 2024

IgE-mediated food allergy

Reduces reactions after accidental exposure

Approved 2024

IgE-mediated food allergy

Reduces reactions after accidental exposure

Approved 2024

Anagnostou A, et al. *J Allergy Clin Immunol*. 2025;155(1):62-69.e1. Drugs@Food and Drug Administration (FDA): FDA-Approved Drugs. Accessed June 30, 2026. www.accessdata.fda.gov/scripts/cder/daf/.

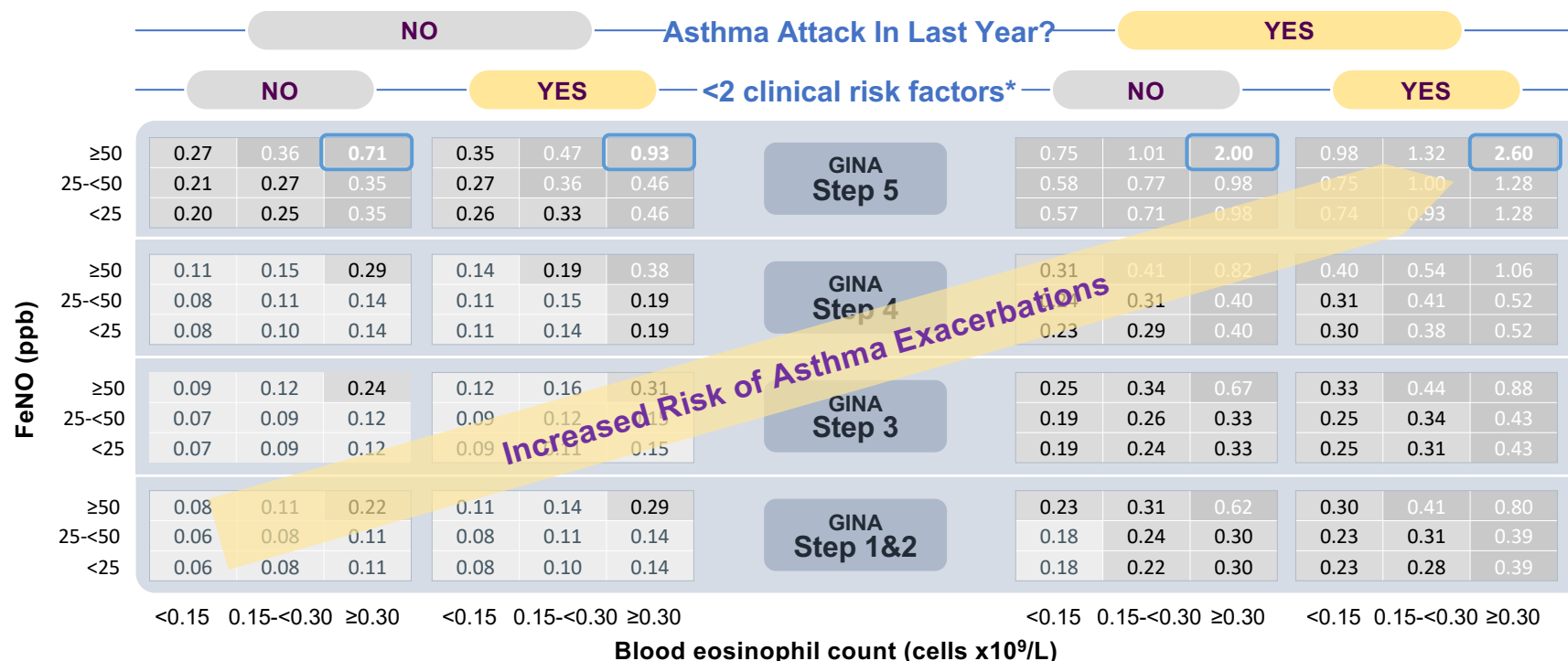
Comparison of Type 2 Inflammation Biomarkers in Asthma

Biomarker	T2 Levels			Limitations
	Low	Medium	High	
Total IgE (IU)	<30	31–149	>150	Affected by age; poor predictor of response rate to biologic therapy. Does not correlate well with asthma severity. Elevations are not specific to asthma (also elevated in atopic dermatitis, allergic bronchopulmonary aspergillosis, etc.)
Blood eosinophils (cells/ μ L)	<150	151–399	>400	Affected by weight, allergen exposure, steroids, and infection; optimal cutoff value varies by therapy. Elevations are not specific to asthma (also in allergic rhinitis, drug reactions, etc.)
Sputum eosinophils	—	—	$\geq 3\%$	Semi-invasive; confined to research settings
FeNO (ppb)	<25	26–49	>50	Affected by age, weight, sex, smoking, and respiratory infections

T2 = T-helper cell type 2; ppb = parts per billion.

Parulekar AD, et al. *Curr Opin Pulm Med*. 2016;22:59-68. Peters MC, et al. *Curr Allergy Asthma Rep*. 2016;16:71.

FeNO and Blood EOS Are Independently and Additively Associated with the Risk of Asthma Exacerbations

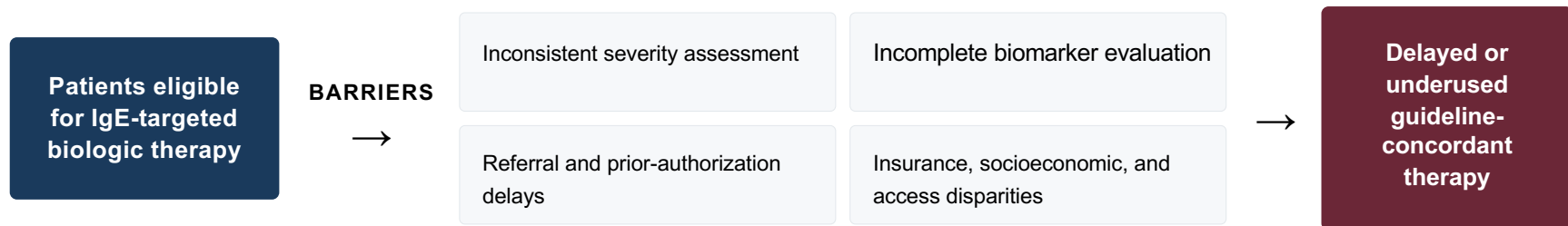


Systematic review of RCTs was used to create a prototype risk scale. Cell numbers represent the predicted annual asthma attack rate if treatment is not changed. *Risk factors as defined by GINA include poor symptom control, low lung function, intubation or intensive care unit admission for asthma previously, comorbidities, and environmental exposures.

EOS = eosinophil; FeNO = fractional exhaled nitric oxide; RCT = randomized controlled trial.

Couillard S, et al. *Thorax*. 2022;77(2):199-202.

Eligible Patients Often Wait Too Long for Therapy



- In a review of 21 studies, disparities in biologics access was determined by insurance type, race, affordability, and need for prior authorization by insurance
- Affordability, not clinical indication alone, increasingly determines who actually receives biologic therapy
 - Drug price is a primary determinant of biologic cost-effectiveness
 - Biosimilars offer a meaningful opportunity to improve affordability and equitable access

Key Learning Points

- Type 2 inflammation is the shared driver across IgE-mediated allergic and immunologic disease
- Systematic severity and biomarker assessment identifies appropriate biologic candidates
- Clinical, system, equity, and cost barriers drive delayed or underused therapy
- Biosimilars create an opportunity to expand affordable, equitable access

Biosimilar Basics: What HCPs Need to Know



Key Definitions

Biologic

A large, complex molecule produced in living systems

Reference product

The already-approved biologic against which a biosimilar is compared

Biosimilar

Highly similar to the reference product, with no clinically meaningful differences in safety, purity, or potency

Interchangeable

A biosimilar meeting additional requirements that may permit pharmacy-level substitution

How Biosimilars Differ from Generic Medications

	Generic	Biosimilar
Molecule	Small, chemically synthesized	Large protein from living cells
Copy fidelity	Identical	Highly similar, not identical
Approval basis	Bioequivalence	Totality of evidence
Variability	Minimal	Minor, tightly controlled

THE PATIENT GAP

Most patients cannot distinguish biologics from generics, and the majority are unfamiliar with biosimilars

Jacobs I, et al. *Patient Prefer Adherence*. 2016;10:937-948. American Autoimmune Related Diseases Association (AARDA). Accessed September 8, 2026. <https://autoimmune.org/wp-content/uploads/2017/02/InFocus-03-2015-3.pdf>

How Biosimilarity Is Established



No single study demonstrates biosimilarity. Each layer builds on the last, and the extensive **analytical foundation** carries the greatest weight.

PK/PD = pharmacokinetics/pharmacodynamics.

McClellan JE, et al. *Ther Adv Chronic Dis.* 2024;15:20406223231223286.

Biosimilarity vs Interchangeable Biosimilarity



- Biosimilar
 - Highly similar, with no clinically meaningful differences
 - Prescribed like the reference product
- Interchangeable biosimilarity
 - Meets additional FDA requirements
 - May be substituted at the pharmacy without prescriber intervention, subject to state law

Interchangeability is a regulatory and pharmacy-substitution designation, not a measure of clinical superiority

Switching, Substitution, and Treatment-Naive Use

Treatment-naive use

Starting a biosimilar in a patient new to the molecule

Switching

A prescriber-directed change between reference and biosimilar

Substitution

A pharmacy-level change permitted for interchangeable products under state law

Accumulated evidence shows switching generally maintains efficacy and safety

CMS and Payer Policy Affecting Access

2025 POLICY CHANGE

Medicare Part D plans may make midyear biosimilar substitutions without prior CMS approval

Formulary placement and rebates strongly influence biosimilar uptake

PBM practices and payer-driven transitions shape real-world access

CMS = Centers for Medicare & Medicaid Services; PBM = pharmacy benefit manager.

CMS. Contract Year 2025 Medicare Advantage and Part D Final Rule (CMS-4205-F). April 4, 2024. Accessed September 8, 2026. www.cms.gov.

Key Learning Points



- Biosimilars are highly similar biologics, not generics, evaluated by the totality of evidence
- The analytical foundation carries the greatest weight in demonstrating biosimilarity
- Interchangeability is a regulatory and pharmacy-substitution designation, not a quality ranking
- FDA and CMS policy are evolving to streamline interchangeability and expand access

Current Biosimilars in Allergy and Immunology: A Practical Approach



The Anti-IgE Landscape



REFERENCE PRODUCT

Omalizumab

Anti-IgE monoclonal antibody, four indications

FIRST BIOSIMILAR

Omalizumab-igec

First and only interchangeable omalizumab biosimilar

IN DEVELOPMENT

Additional candidates

Further omalizumab biosimilars advancing through review

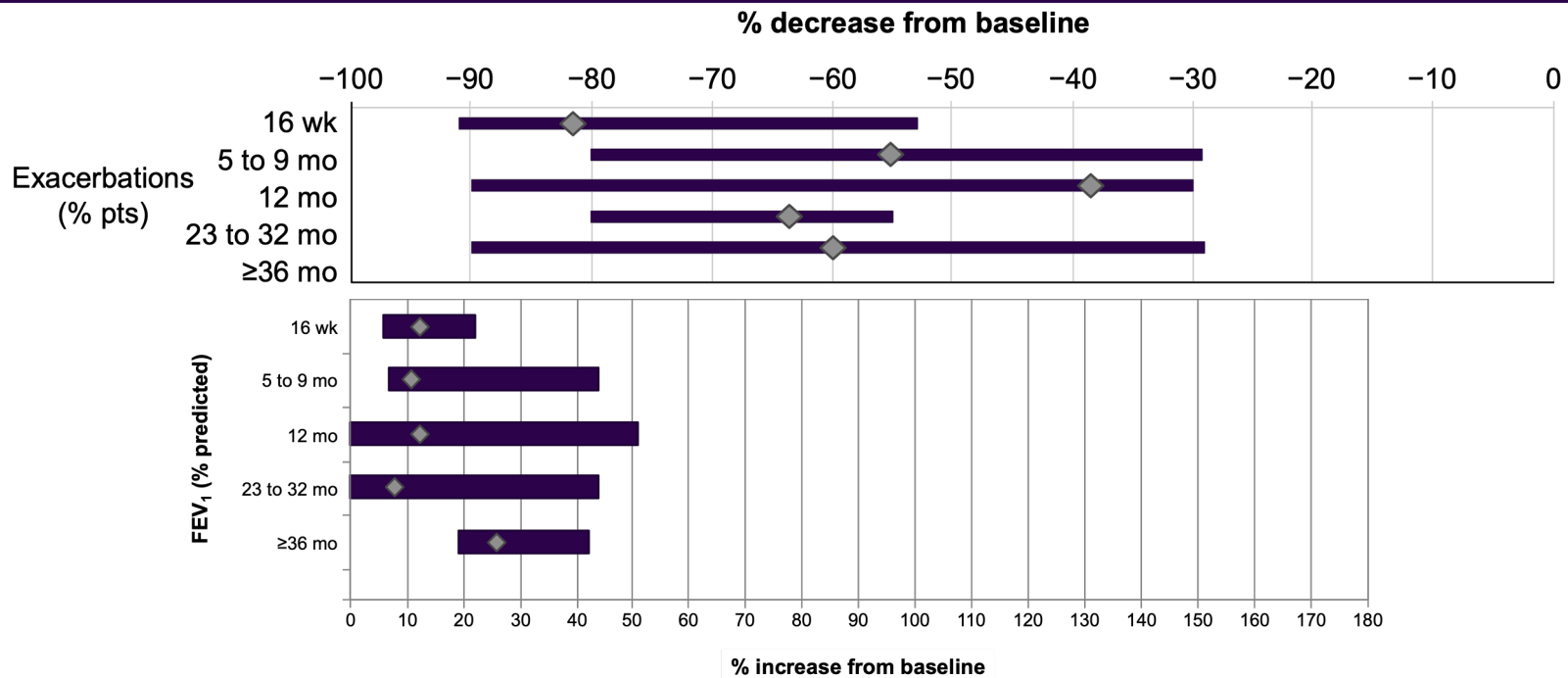
Mar 2025 FDA approval as first interchangeable

Sep 2026 Anticipated US market launch

Jeremias S. Center for Biosimilars. Accessed September 8, 2026. <https://www.centerforbiosimilars.com/view/fda-approves-first-omalizumab-biosimilar>. Myshko D. *Managed Healthcare Executive*. <https://www.managedhealthcareexecutive.com/view/biosimilars-in-2025-a-year-of-firsts>

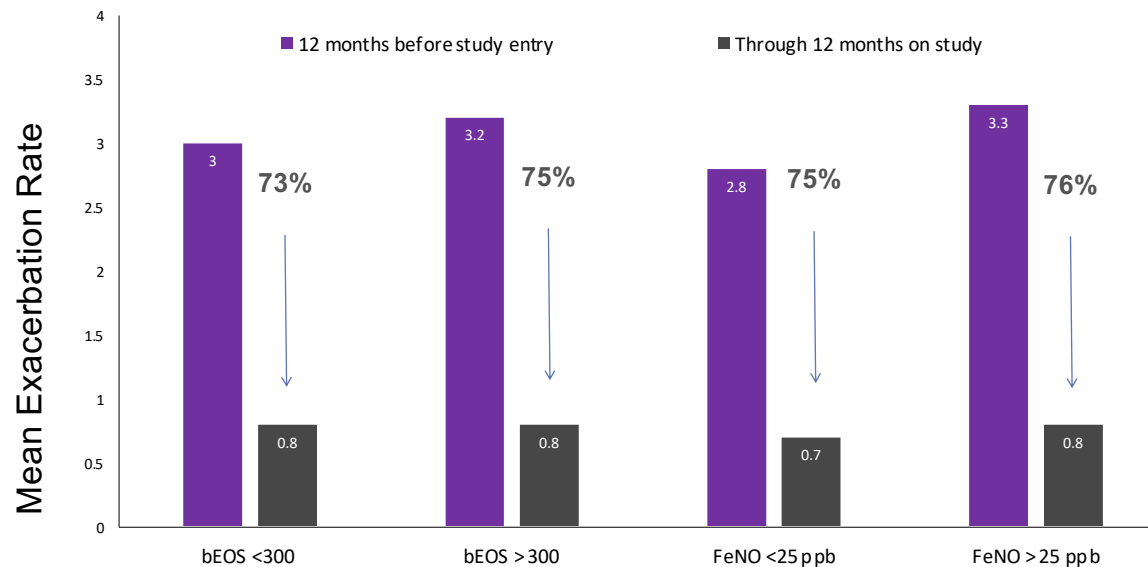
Omalizumab: Systematic Review of Real-World Studies

42 studies reporting data from up to 4 years of omalizumab treatment in patients with severe allergic asthma



Diamonds represent the point estimate of the pooled weighted mean change (%) over baseline. Bars denote the lowest and highest changes (%) reported by singular studies, and reflect the relative variation in rates reported across studies.
MacDonald KM, et al. *Exp Rev Clin Immunol*. 2019;15:553-569.

Omalizumab: Exacerbation Rate by Biomarker Status in a Real World Trial (PROSPERO)



Casale TB, et al. *J Allergy Clin Immunol Pract.* 2019;7(1):156-164.e1.

Omalizumab-igec: The First Interchangeable Biosimilar

First and only

The only omalizumab biosimilar with an interchangeability designation

All indications

Interchangeable with the reference product across all approved indications

Multiple strengths

Single-dose prefilled syringes supporting tailored dosing

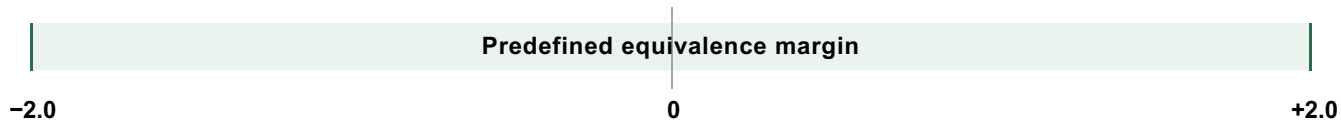
Pharmacy substitution

Interchangeability supports substitution, subject to state law



Phase 3 Evidence in Chronic Spontaneous Urticaria

- CT-P39 (omalizumab-igec) vs reference omalizumab; change from baseline in weekly itch severity score (ISS7) at week 12



Therapeutic equivalence met: The 95% CI of the treatment difference fell entirely within the -2.0 to +2.0 margin (schematic; values per primary publication)

Equivalent efficacy

Primary endpoint met

Comparable PK, safety, immunogenicity

Single switch

No impact on outcomes

Phase 3 Evidence in Chronic Spontaneous Urticaria

TABLE 2 | Primary efficacy results in TP1: Change from baseline in ISS7 at W12 (mITT set and PP set).

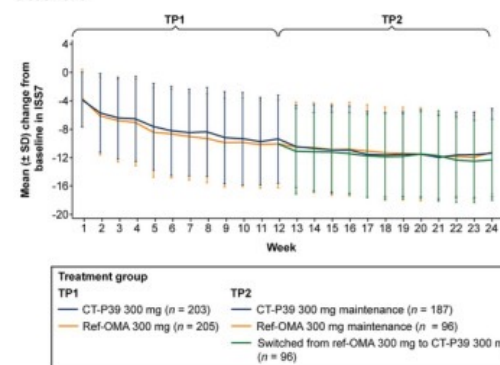
Global analysis ^a	<i>n</i>	LS mean (SE)	Estimate of treatment difference (95% CI) ^b
mITT set			
CT-P39 300 mg	186	−9.21 (0.796)	0.77 (−0.37 to 1.90)
Ref-OMA 300 mg	192	−9.98 (0.798)	
PP set			
CT-P39 300 mg	179	−9.48 (0.790)	0.69 (−0.45 to 1.84)
Ref-OMA 300 mg	183	−10.17 (0.792)	

US analysis ^b	<i>n</i>	LS mean (SE)	Estimate of treatment difference (90% CI) ^c
mITT set			
CT-P39 300 mg	203	−9.25 (0.787)	0.70 (−0.22 to 1.63)
Ref-OMA 300 mg	205	−9.96 (0.791)	
PP set			
CT-P39 300 mg	179	−9.48 (0.790)	0.69 (−0.27 to 1.66)
Ref-OMA 300 mg	183	−10.17 (0.792)	

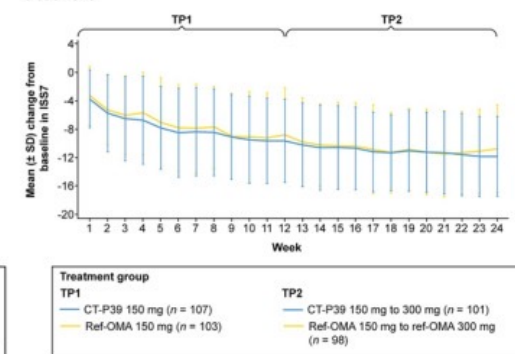
ITT = intention-to-treat.

Saini SS, et al. *Allergy*. 2025;80(8):2167-2177.

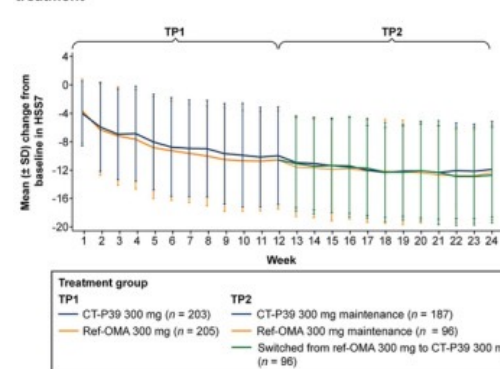
(A) Change in ISS7 with CT-P39 300 mg and ref-OMA 300 mg treatment



(B) Change in ISS7 with CT-P39 150 mg and ref-OMA 150 mg treatment



(C) Change in HSS7 with CT-P39 300 mg and ref-OMA 300 mg treatment



(D) Change in HSS7 with CT-P39 150 mg and ref-OMA 150 mg treatment

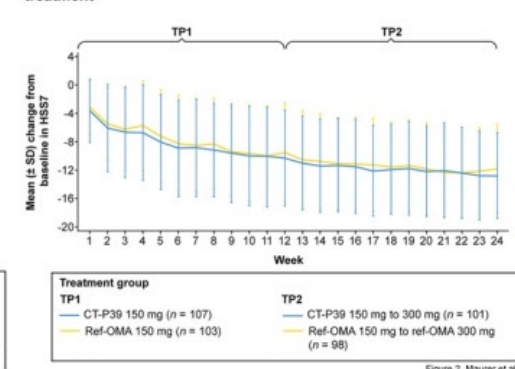


Figure 2, Maurer et al.

Patient Perceptions and the Nocebo Effect

LOW AWARENESS

Most patients cannot distinguish biologics from generics, and the majority are unfamiliar with biosimilars

THE NOCEBO EFFECT

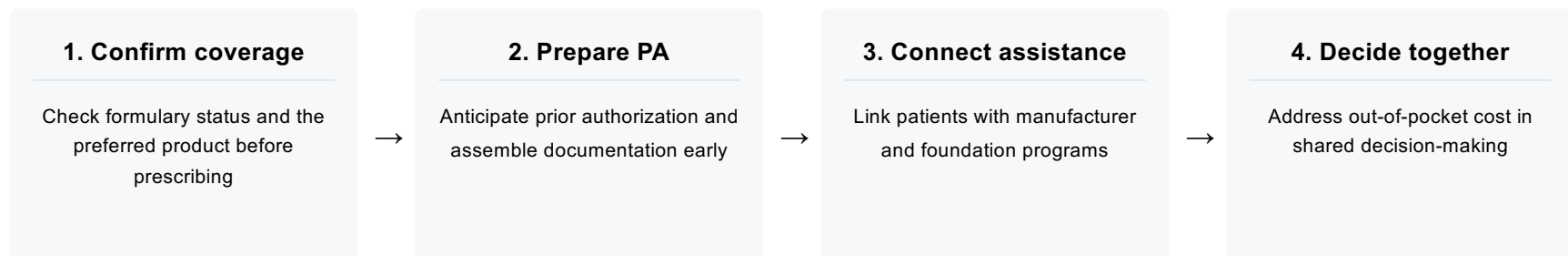
Negative expectations can produce perceived adverse effects and treatment discontinuation, directly affecting acceptance and adherence

Communicating Value and Minimizing the Nocebo Effect

- ✓ Frame biosimilars positively and proactively, not defensively
- ✓ Explain rigorous approval standards in plain language
- ✓ Provide written, plain-language resources patients can take home

- ✓ Use consistent, confident messaging across the entire care team
- ✓ Emphasize the same expected efficacy and safety as the reference product
- ✓ Reassure that response is monitored and therapy can be reassessed

Navigating Cost, Coverage, and Access



PA = prior authorization.

Biosimilars at the Pharmacy Level

Substitution

Interchangeable products may be substituted without contacting the prescriber

State law

Notification and documentation requirements vary by state

Specialty pharmacy

Often manages dispensing and administration logistics

Coordination

Communicate with the pharmacy to avoid gaps during transitions

Severe Asthma Case

- 53-year-old male referred by Dr. J, not responding to benralizumab
- Started in late 2020 hospitalized with COVID-pneumonia requiring oxygen therapy and treatment with remdesivir
- Currently: Persistent frequent cough, DOE 3 flights
- 3 prior exacerbations requiring steroids in past year

Prior Evaluation

- Diagnosed with asthma ~2 year ago
 - Blood eos 850, total IgE level 532 and *Aspergillus* IgG +37, IgE neg
 - PFTs: Moderate airflow obstruction: FEV1 2.4 L (61% of pred, FVC 3.0 L (62% pred, positive BD response 29%)
 - Initially diagnosed with lower left lobe pneumonia. Bronchoscopy spring 2022 demonstrated extensive mucous plugs in the left lower lobe and the BAL was predominantly neutrophilic and polymicrobial
 - Subsequent CT chest from fall 2022 revealed resolution of the left lower lobe infiltrate right basilar atelectasis and a right lower lobe 4 mm nodule

PFT = pulmonary function test; BAL = bronchoalveolar lavage.

Medical History and Medication

- **Medical history**

- Chronic rhinosinusitis w/o polyps
- GERD – EGD esophageal inflammation treated with PPI which controls symptoms
- OSA – treated with CPAP since 2021
- Morbid obesity / MASLD
- HTN

- **Prior asthma medications**

- Fluticasone propionate/ salmeterol 500 µg/50 µg twice daily
- Montelukast 10 mg daily
- Tiotropium 2.5 mcg daily
- Benralizumab 30 mg every 8 wks (started 9 mon ago)

OSA = obstructive sleep apnea; CPAP = continuous positive airway pressure; GERD = gastroesophageal reflux disease; MASLD = metabolic dysfunction-associated steatotic liver disease; HTN = hypertension; EGD = esophagogastroduodenoscopy.

Environmental History

- Has 2 dogs (a pug and a Labrador mix) and they go into his bedroom and his bed; notes that he occasionally has hives when petting them
- Evidence of mold in the basement. Planning to have it cleaned but concerned it will cause his asthma to worsen
- He does have carpeting in his bedroom
- Does have a central air furnace. Does have a HEPA filter in his office but not in his bedroom
- No down pillows or comforters

Examination

- Initial examination
 - Nasal polyp congestion, no polyps; lungs – bilateral rhonchi with cough

Examination	Result	
Spirometry	FEV ₁ 2.76 L (74% of predicted value); 14% change after BD	
	FVC 3.98 L (85% of predicted value)	
ACT	12	
Methacholine bronchoprovocation PC ₂₀ , mg/mL	4.8	
Biomarkers	IgE, kU/L	566
	Exhaled NO	23
Allergy skin test	Positive for Der P, F, <i>Aspergillus f.</i> , dog, cat	
Sinus CT	Mild mucosal thickening, small mucous retention cyst R maxillary antrum	

BD = bronchodilation; FVC = forced vital capacity; kUA = units for allergen-specific antibodies; PC₂₀ = provocation concentration causing a 20% reduction in FEV₁.

HR Chest CT



Case

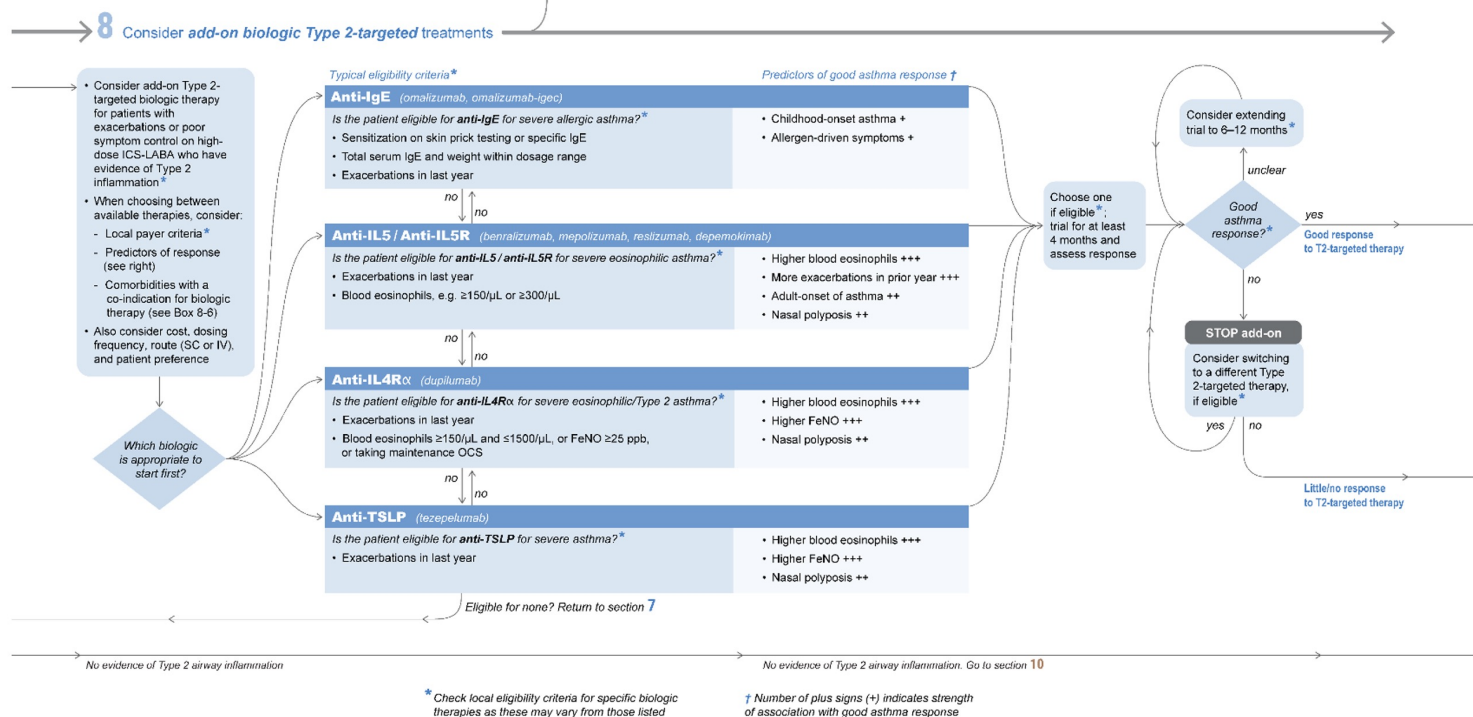
- What discussion about biologics response would you have with patient?
- Is patient a candidate for IgE-targeted therapy?
- How would you discuss an anti-IgE biosimilar with patient?
- How would you determine responsiveness to anti-IgE biosimilar?

Box 8-4. Decision tree – consider add-on biologic Type 2-targeted treatments

SPECIALIST CARE; SEVERE ASTHMA CLINIC IF AVAILABLE

Assess and treat severe asthma phenotypes *cont'd*

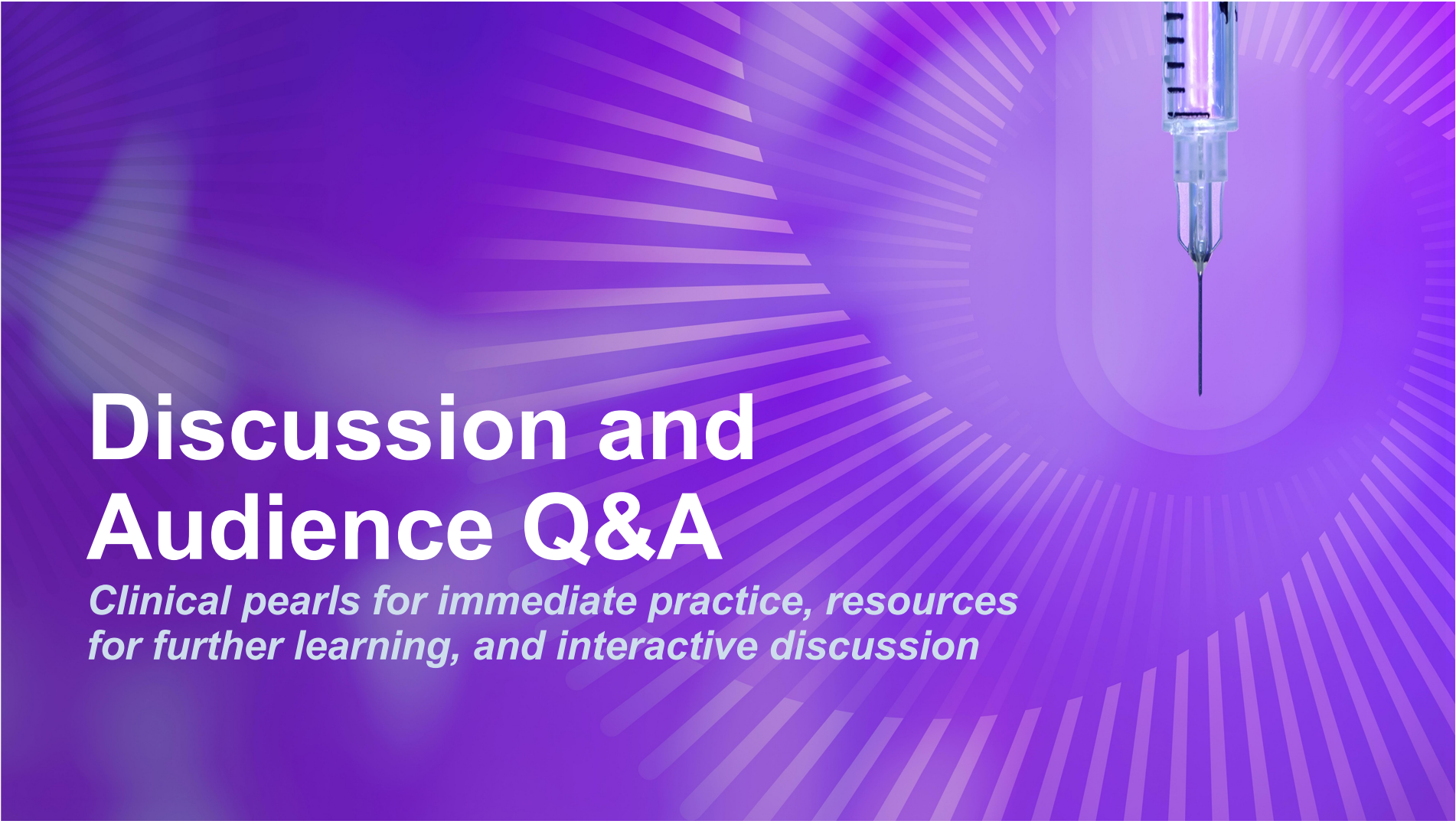
Continue to optimize management as in section 3 (including inhaler technique, adherence, comorbidities, non-pharmacologic strategies)



Key Learning Points



- Omalizumab-igec is the first interchangeable omalizumab biosimilar, with US launch anticipated in 2026
- Phase 3 evidence shows equivalent efficacy and comparable safety and immunogenicity
- Clear, confident communication minimizes the nocebo effect and supports adherence
- Proactive cost, coverage, and pharmacy planning enables timely access



Discussion and Audience Q&A

*Clinical pearls for immediate practice, resources
for further learning, and interactive discussion*

Clinical Pearls for Practice

- Use severity and biomarkers to systematically identify IgE-targeted therapy candidates
- Understand biosimilars as rigorously evaluated, highly similar biologics
- Apply interchangeability appropriately and communicate it clearly to patients
- Plan proactively for cost, coverage, and pharmacy logistics