Clinical Presentation

Emerging Treatment Options for Food Allergy

Learning Objectives

Emerging Treatment Options for Food Allergy

After this presentation, participants will be able to:

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OBJECTIVE 01

Review the current therapeutic landscape for IgE-mediated food allergy.

OBJECTIVE 02

Compare emerging immunotherapy strategies.

Evaluate biologic and small-molecule therapies.

OBJECTIVE 04

Apply shared decision-making to patient selection.

OBJECTIVE 03

Why Treatment is Changing

From Avoidance to Disease Modification

鵲 Key Drivers

- Burden of food allergy on everyday life
- Psychosocial impact on patients and families
- Accidental exposures remain highly common
- Evolution from strict avoidance to active treatment

Treatment Evolution Timeline

01 Avoidance Traditional risk minimization

02 Immunotherapy Active desensitization (OIT/SLIT)

03**Biologics**Targeted monoclonal antibodies

04 Patient-specific molecular

profiling

BEFORE TREATMENT

Getting the Diagnosis Right

Clinical Pearl

髂Key Messages

- Confirm true IgE-mediated allergy
- Limitations of SPT and serum IgE
- OFC remains the gold standard
- Emerging biomarkers and component testing

THERAPEUTIC ENDPOINTS

Treatment Goals

鏝Progressive Protection

Therapeutic goals in allergy immunotherapy focus on progressively raising the patient's tolerance threshold.

The ultimate objective is to transition from basic allergen avoidance to active, long-term disease modification and sustained protection.

02Desensitization Protection relying on continuous exposure

03 Sustained unresponsiveness after therapy

昪Levels of Protection

01Reaction Threshold Increased safety margin against trace exposure

ORAL IMMUNOTHERAPY (OIT)

Key Discussion Points

鸡Clinical Focus Areas

•Palforzia & maintenance dose strategies

•Clinical trial evidence (IMPACT & POISED) •Key predictors of treatment success

•Safety considerations & EoE monitoring

•Addressing long-term maintenance questions

But greatest treatment burden.

OIT delivers unmatched protective desensitization progress, but demands consistent compliance and presents a higher profile of adverse events and maintenance challenges.

CLINICAL TRIAL EVIDENCE

IMPACT & POISED Trials

IMPACT Trial (Ages 1–3) (NCT01867671)

DESENSITIZATION (5g Peanut Protein)

71% with OIT vs 2% with Placebo

SU after 26 weeks avoidance:

- **50%** of 1 year olds
- **27%** of 2 year olds
- **13%** of 3 year olds

SLIT (Sublingual)

- Low allergen dose
- Excellent safety profile
- Promising remission data in preschool children

POISED Trial (Ages 7–55) (NCT02103270)

DESENSITIZATION (4g Peanut Protein) 33% with OIT vs 4% with Placebo

SU after avoidance:

- After **12 weeks** avoidance: **35%**
- After **50 weeks** avoidance: **13%**

Side-by-Side Comparison

SLIT and EPIT

EPIT (Epicutaneous)

- Skin patch delivery
- Minimal systemic adverse reactions
- Supported by positive Phase 3 trials

Benefit–Risk Matrix: A balanced comparison of therapeutic efficacy against treatment safety boundaries.

SUBLINGUAL IMMUNOTHERAPY (SLIT)

Clinical Trial Evidence

Overview & Safety

- 2-8mg of food protein daily dose
- Generally safe with mild local symptoms
- Lacks large placebo-controlled trials

- Most clinical study data is in children

Ages 1–11

4mg - 4 Years (NCT01373242)

70% tolerated >800mg peanut protein

36% passed 5000mg challenge

2723 mg mean threshold

reached (~10 peanuts)

4mg - 3 Years (NCT02304991)

tolerated 4443mg peanut protein vs 0% placebo

sustained tolerance 3 mos post-therapy

epinephrine use; oral itch was most common AE

EPICUTANEOUS IMMUNOTHERAPY (EPIT)

Phase 3 Clinical

Evidence

Minimize Systemic

Exposure

Increase reaction threshold while minimizing systemic allergen exposure.

Mechanism of Action

- Daily application of a peanut protein-containing skin patch
- Allergen delivery through intact skin to cutaneous antigen-presenting cells

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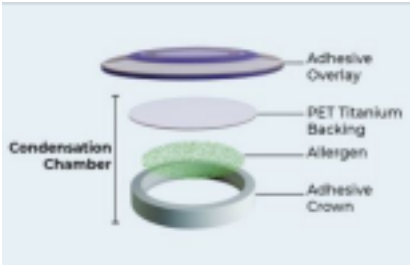
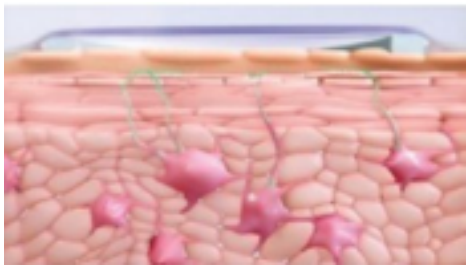
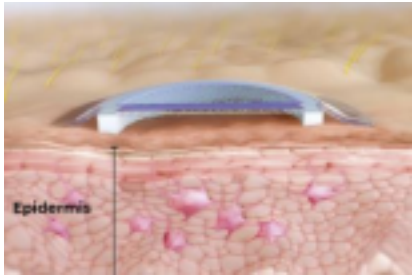
EPICUTANEOUS IMMUNOTHERAPY (EPIT)

Viaskin Patch Technology







Structure

Featuring an adhesive overlay, PET backing, allergen chamber, and adhesive crown.

Application

The condensation chamber creates a humid environment to solubilize the dried allergen on the skin.

Delivery

Allergens penetrate the epidermis to interact directly with Langerhans cells without entering the bloodstream.

PHASE 3 CLINICAL TRIAL

EPITOPE Trial (NCT03211247)

- Daily EPIT skin patch delivery
- Primary endpoint: increased tolerated peanut protein during oral food challenge after 12 months

Study Highlights

- Children aged **1–3 years** with peanut allergy

desensitization in active arm

in placebo arm reached primary endpoint (Δ of only 33%)

of treated children achieved clinically meaningful

Demonstrated increased protection from accidental exposures

Baseline <10mg **300mg**

Baseline >10mg **1000mg**

PHASE 3 CLINICAL TRIAL

VITESSE Trial (NCT05741476)

Study Highlights

- Children aged **4–7 years** with peanut allergy
- Daily EPIT patch treated over **12 months** (N=654)
- Avg. eliciting dose (ED) at baseline: **30mg**

met responder criteria in Viaskin arm vs 14.8% placebo (Δ = 31.8%)

Most common TEAEs were mild-to-moderate local skin reactions

Baseline ED ≤30mg

300mg Target

Baseline ED = 100mg **600mg Target**

Discontinuation: 3.2% in active arm vs 0.5% in placebo arm

Anaphylaxis 0.5%

EPICUTANEOUS IMMUNOTHERAPY (EPIT)

Current Limitations

FDA Approval

Not FDA approved at the time of presentation preparation.

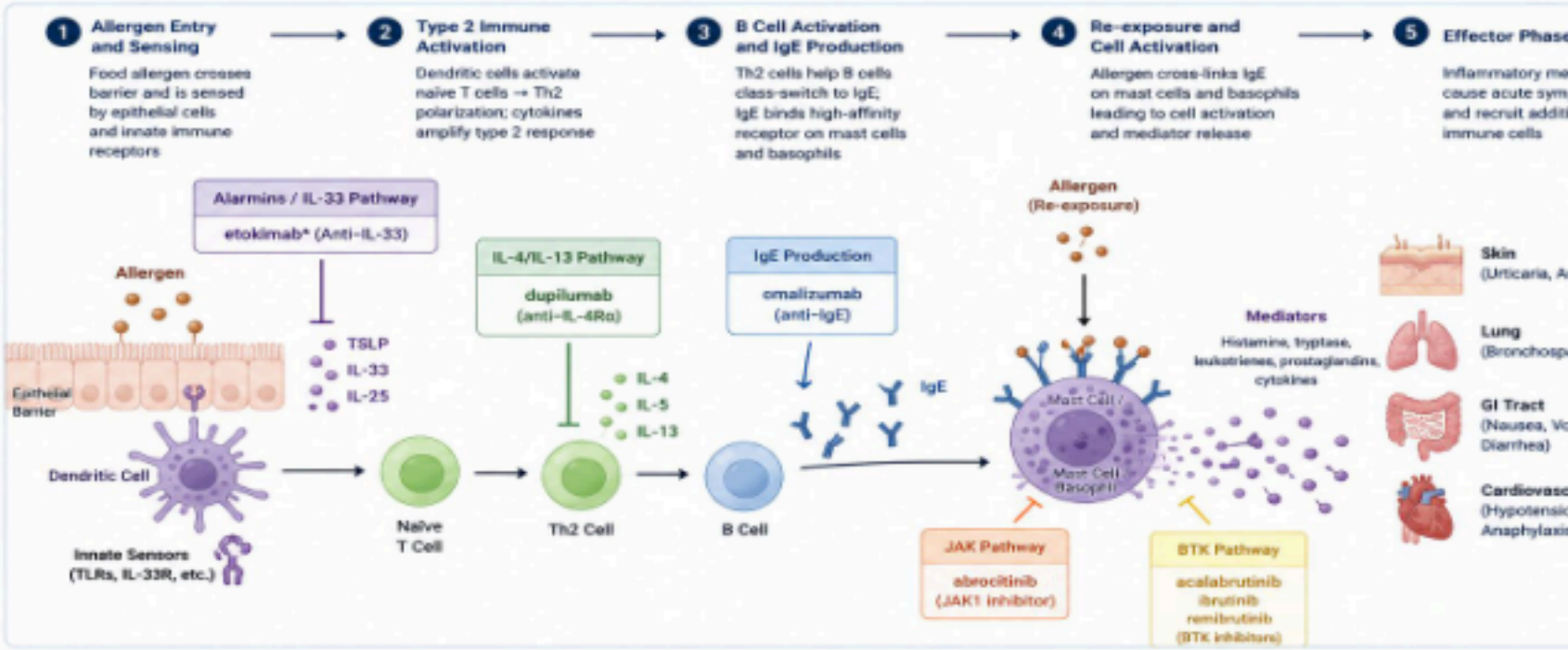
SU/Remission Data

Remission data remain limited at present.

Durability

Long-term durability of the therapy is currently unknown.

Where Emerging Biologics Work in IgE-Mediated Food Allergy



Alarmins / IL-33 Pathway

etokimab (Anti–IL-33)

- Blocks IL-33 signaling from epithelial cells
- Reduces type 2 inflammation initiation

IL-4/IL-13 Pathway

dupilumab (Anti–IL-4Rα)

- Blocks signaling of IL-4 and IL-13
- Decreases IgE production and type 2 inflammation

IgE Production / Function

omalizumab (Anti-IgE)

- Binds free IgE
- Prevents IgE from binding FcεRI on mast cells and basophils
- Reduces cell sensitivity and activation

JAK Pathway

abrocitinib (JAK1 inhibitor)

- Inhibits JAK1 signaling downstream of many cytokine receptors
- Reduces inflammatory cytokine signaling

BTK Pathway

acalabrutinib, ibrutinib, remibrutinib (BTK inhibitors)

- Inhibit BTK in mast cells, basophils and B cells
- Reduces cell activation and mediator release

Other / Emergi

- IgE disruptors (e.g., I – Prevent IgE binding
- UB-221 – Bispecific a targeting IgE and CD3
- Additional upstream a regulatory pathways i development

*Not FDA approved for food allergy.

Sites of action are simplified and may reflect multiple or overlapping mechanisms.

BIOLOGICS

The New Era

Clinical Trial Highlight

OUtMATCH Trial Findings

(NCT03881696)

67% vs **7%**

Of omalizumab-treated participants tolerated 600 mg peanut protein vs. placebo

Differentiating Factor: Unlike OIT, omalizumab is not allergen-specific and does not require post-dose precautions (e.g., avoiding exercise or hot water for 2 hours)

Clinical Implementation

Focus on Omalizumab

Mechanism of Action

Binds free IgE, prevents effector cell binding via high-affinity FcRI, leads to receptor down-regulation, and inhibits low-affinity CD23 binding

- **FDA approval indications**
- **Multi-food protection efficacy**
- **Adjunctive use alongside OIT**

EMERGING BIOLOGICS

Novel Anti-IgE & Clearance Mechanisms

higher affinity than omalizumab

瑛Also binds CD23 directly to downregulate IgE production

瑛Phase I (CSU) trial showed safe and durable relief

Ligelizumab

High-Affinity Anti-IgE

瑛44.7% tolerated >=600mg peanut vs 4.3% placebo

涿Lower response rate than omalizumab in OUtMATCH

Weaker inhibitor of IgE:CD23

UB-221

Next-Gen Anti-IgE Binder

瑛Binds free IgE with

IgE Disruptors

Receptor Dissociation Class

琢Actively strip IgE off receptors on mast cells & basophils

琢Offers potential for faster onset in acute situations

Preclinical: no human safety or PK data exist yet

Active Antibody Clearance

Physically removes IgE from bloodstream using LYTAC (lysozomal targeting chimera)

Engages receptors to internalize and degrade IgE in lysosomes

Designed for longer-lasting control of food allergies

PATHWAY TARGETS

Beyond Anti-IgE

瑛Abrocitinib

IL-4 / IL-13
Pathway

瑛Dupilumab

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IL-33
Pathway

瑛Etokimab

JAK
Inhibition

BTK
Inhibition

瑛Acalabrutinib

瑛Ibrutinib

瑛Remibrutinib

Immune Targets

Alarmins

IgG4

mAbs

Tregs

Microbiome

CLINICAL EVIDENCE

Dupilumab Clinic

Monotherapy

Single Agent Effects

瑛Reduces type 2 inflammatory biomarkers

瑛Improves atopic dermatitis & comorbidities

漾No consistent food desensitization alone

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Adjunct to OIT

Potential Benefits

瑛Improves tolerability during escalation

瑛Reduces allergic adverse events

瑛Enhances desensitization with OIT

Important Caveats

琢Incremental efficacy beyond OIT alone remains uncertain

琢Long-term remission data are currently lacking

PATHWAY TARGETS

Anti-IL-33 Upstream Therapy

琪Increased peanut tolerance in adults after single IV dose

琪Proven reduction in type 2 inflammatory biomarkers

Why Target IL-33?

Upstream Rationale

琪Epithelial-derived alarmin initiating type 2 cascade

琪Interrupts response before downstream IgE production

Clinical Evidence

Phase 2a Etokimab Trial (NCT02920021)

Profile & Limits

Opportunities & Caveats

瑛Targets earliest steps; potential to broadly suppress inflammation

漾Small studies with limited long-term safety and durability data

Unlike omalizumab (which neutralizes circulating IgE), anti-IL-33 therapy intervenes before Th2 polarization and IgE production, representing an upstream strategy that may modify allergic inflammation at its earliest stages.

🏷 Why Target JAK? Rationale & Advantages

- 瑛Oral administration & broad intracellular action
- 瑛Suppresses multiple type 2 cytokine pathways

瑛Demonstrated biologic effects on type 2 pathways

瑛Modulates allergic immune responses in early trials

In vitro work supports biologic plausibility: abrocitinib **suppressed effector T-cell activation while preserving Treg activation**, decreased **peanut-specific basophil activation**, and suppressed peanut-induced cytokine release (IL-5, -9, -10, -13) from PBMC.

Current Evidence Caveats

琢No FDA approval & early-stage clinical development (NCT05069831)

琢Limited human data for food allergy; long-term safety remains unknown

Clinical Data Early Evaluation

Unlike biologics that neutralize a single extracellular target (e.g., IgE or IL-33), JAK inhibitors act intracellularly to suppress signaling from multiple cytokines involved in type 2 immunity. This broad mechanism may offer therapeutic advantages but also raises important considerations regarding long-term safety.

CLINICAL EVIDENCE

BTK Inhibitors (remibrutinib, ibrutinib, acalabrutinib)

Why Target BTK?

Rationale & Advantages

瑛Preserves mast cells but prevents intracellular activation

瑛Acts within hours,

Clinical Data

Remibrutinib Phase 2

- 琐87% of subjects tolerated >600mg peanut protein in the high dose group
- 琐47% could tolerate >3000mg peanut protein

Current Evidence Caveats

- 琮No FDA approval currently for IgE-mediated food allergy
- 琮Evidence consists primarily of early-phase & pilot studies

Clinical Data

Acalabrutinib Phase 2

- 琐Median tolerated peanut dose: 29 mg to 4,044 mg
- 琐7 of 10 participants tolerated max dose with no symptoms

BTK inhibitors target the final common intracellular pathway downstream of FcεRI, providing a rapid approach to suppress IgE-mediated mast cell and basophil activation. Their rapid onset and marked threshold increases make them highly promising.

Clinical Evidence

IgG4 Monoclonal Antibody (IGNX001)

Overview

Therapeutic Profile

An investigational, peanut-specific IgG4 monoclonal antibody therapeutic designed for targeted intervention.

Active Formulations

Mixture of two high-affinity, engineered human IgG4 monoclonal antibodies directed against immunodominant epitopes of major peanut allergens **Ara h 2** and **Ara h 6**.

How It Works

Acts as blocking antibodies, competing with endogenous IgE for allergen binding. This prevents allergen-mediated cross-linking and subsequent degranulation.

Composition

Data suggest protection occurs through direct allergen neutralization rather than via inhibitory FcRIIb signaling, preventing mast cell and basophil degranulation and subsequent anaphylaxis.

Peanut Vaccines

瑛Evaluating safety and desensitization potential

瑛Phase I/IIa studies currently ongoing

HAL-MPE1

Modified Peanut Extract

瑛Chemically modified, aluminum hydroxide adsorbed extract

瑛Phase I studies enrolling, no data published

VLP Peanut

CuMVtt-based Vaccine

瑛Disguises major allergen (Ara h2) on nanoparticle surface

瑛Reduces allergenicity while promoting protective immunity

NCT03755713 (Astellas)

琼Completed and discontinued from further clinical development

琼Showed modest immune changes without significant clinical efficacy

ADJUNCTIVE STRATEGIES

Emerging Options

Probiotics

Nanoparticles

Microbial Therapies

Combination Biologics

OIT + Biologics

PATIENT-CENTERED FRAMEWORK

Choosing the Right Therapy

A collaborative framework aligning clinical data with patient values to choose the optimal therapeutic path.

Clinical Factors

- 瑛Patient Age
- 瑛Allergen Profile
- 瑛Baseline IgE Levels
- 瑛Asthma & Eczema
- 瑛EoE History

Patient Factors

Lifestyle & Preferences

- 瑛Family Goals
- 瑛Treatment Burden
- 瑛Financial Cost

Making Algorithm

FUTURE DIRECTIONS

Key Clinical Highlights

Durable Remission

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Combination Therapy

Precision Medicine

Biomarkers

Health Equity

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SUMMARY & TAKEAWAYS

Key Take-Home Messages

Food allergy management is rapidly evolving.

Omalizumab
Transformed treatment options for accidental exposure protection.

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Evolving Management

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OIT Profiles
Greatest desensitization but carries the highest adverse-event burden.

The Next Frontier

Combination biologic–immunotherapy approaches represent the future.

SLIT & EPIT Safety

Both options provide attractive and favorable safety profiles.

Selection and shared decision-making remain central to success.