

# 602 Systemic Reactions Associated with Food Oral Immunotherapy Versus Subcutaneous Immunotherapy in Clinical Practice

Kristina Nguyen, Warner W. Carr MD  
Allergy and Asthma Associates of Southern California, The Food Allergy Center

## ABSTRACT

**RATIONALE:** Subcutaneous immunotherapy (SCIT) to environmental allergens/venom has an established safety profile and is accepted as generally safe. Oral immunotherapy to foods (FOIT) is growing in popularity; however, safety concerns prevent many practicing Allergists from adopting this therapy. We compare the safety of SCIT and FOIT with a focus on systemic allergic reaction rates in a busy outpatient allergy clinic.

**METHODS:** A blinded retrospective chart review of 356 FOIT patients versus 742 SCIT patients in a single outpatient Allergy clinic from July 2016 to July 2019. The total number of SCIT and FOIT administrations were determined over the time period and the number of systemic reactions per patient and systemic reactions per exposure were calculated. A systemic reaction was defined as a reaction felt to be related to either SCIT or FOIT and required immediate therapy, such as administration of epinephrine.

**RESULTS:** For FOIT, 356 patients received 146,060 daily doses with a systemic reaction rate of 0.02% assuming 100% compliance. At 80% compliance, patients would have a reaction rate of 0.03%. For SCIT, 742 patients received 272,508 injections with a systemic reaction rate of 0.15%. Systemic reactions occurred in 34 patients (11.3%) on FOIT, while 105 SCIT patients (13.88%) experienced a systemic reaction.

**CONCLUSIONS:** FOIT yields no additional safety concerns compared to SCIT. As FOIT continues to gain popularity among Allergists, a strong safety profile helps to establish FOIT as standard of care for food allergy management. FOIT is a safe therapy that provides practicing Allergists another tool for treating their patients' disease.

## BACKGROUND

- Food allergy affects 5% of adults and 8% of children
  - Prevalence is increasing<sup>1</sup>
- DBPC studies have demonstrated that oral immunotherapy (FOIT) to peanut is effective<sup>2</sup>, and further studies in FOIT to other foods are still under investigation.
- Recent publications have also expressed concerns about the short-term and long-term safety of FOIT, especially with regards peanuts.<sup>3</sup>
- When appropriately dosed, SCIT has been a long-standing, well-established, and effective<sup>4</sup> therapy in the treatment of allergic diseases<sup>5</sup>

## METHODS

- A blinded retrospective chart review of 356 FOIT patients (aged 18 months to 36 years) and 742 SCIT patients (aged 4 to 74 years) from July 2016 to July 2019
- Customized per patient's living conditions, allergic reactions, or other limiting factors.
- Eligible FOIT Patients: **food specific SPT** (wheal  $\geq$  3mm), **food specific IgE**  $\geq$  0.35 kU/L, history of **food-associated reaction**, and/or **failed oral food challenge**.
  - Standardized up dosing regimen per food. Example protocol in Figure 1.
  - Day 1: Initial dose escalation up to a set dose as tolerated
  - Build-up every 1-4 weeks until maximum maintenance dose is reached.
- Eligible patients for SCIT required: **environmental SPT** (wheal  $\geq$  3mm), **environmental/venom IgE**  $\geq$  0.35 kU/L, and/or **anaphylactic reaction history**
  - Standardized up dosing regimen per clinical care guidelines.<sup>4</sup> Example protocol in Table 3.
  - Conventional build-up phase of 1-3 injections per week up to a maintenance dose after 3-6 months. Cluster schedules were not used.

Figure 1. Example FOIT Dosing Schedule for Peanut

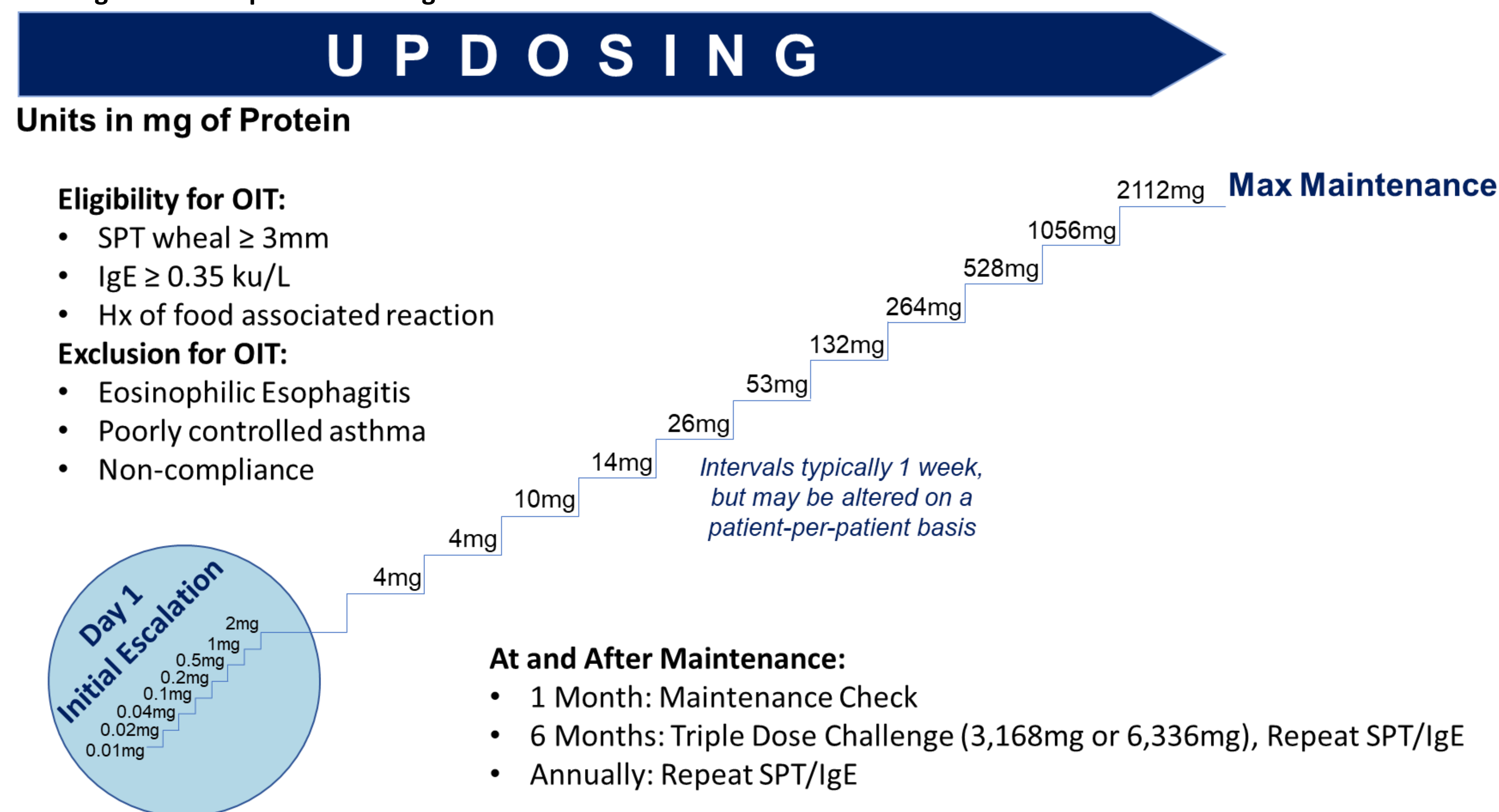


Figure 2. Graphs Comparing Per Patient and Per Dose Epinephrine Usage

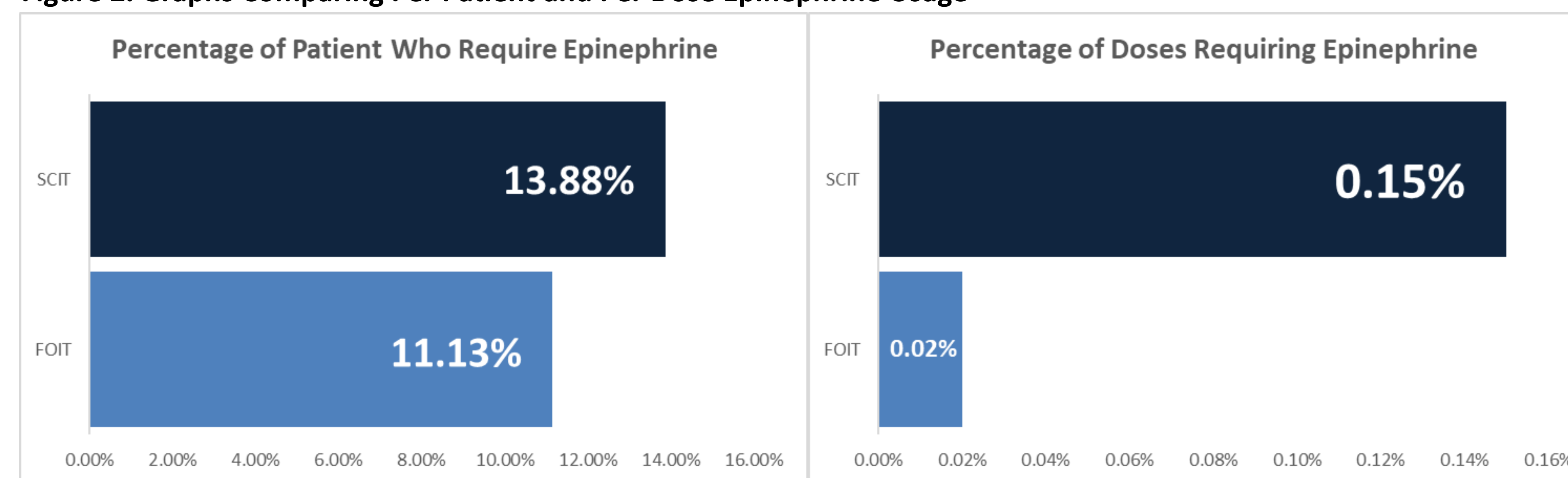


Table 1. FOIT Patient Demographics

Characteristics	Population (N=244)
Average Age	9.00
% Male	58.43%



Table 2. FOIT Efficacy Values and Safety Results

Efficacy Statistics	Abs	%	Epinephrine Incidence	Abs	%
# Graduated	292	82.02%	<b>100% Compliance</b>		
# Active	39	10.96%	Epi Count In-Office	23	0.01%
# Dropped	22	6.18%	Epi Count Out-Office	35	0.01%
# Transferred	3	0.84%	Total Epi Count	58	0.02%
<b>Pts Achieving Target</b>	356	93.06%	<b>80% Compliance</b>		
<b>Total Patients</b>	299		Epi Count In-Office	23	0.01%
<b>Reasons Patients Stop</b>			Epi Count Out-Office	35	0.02%
Taste Aversion/Anxiety	8	36.36%	Total Epi Count	58	0.03%
Reaction	8	36.36%	<b>Pts Requiring Epi</b>	39	10.96%
Other	6	27.27%	<b>Pts Requiring 2+ Epi</b>	7	2.34%

Table 3. Example SCIT Dosing Schedule

Dose Interval	Week	Dose of Venom
1-3x Per Week	1	0.1 mL of 0.01/0.03 ug/mL
	2	0.1 mL of 0.1/0.3 ug/mL
	3	0.1 mL of 1/3 ug/mL
	4	0.5 mL of 1/3 ug/mL
	5	0.1 mL of 10/30 ug/mL
	6	0.1 mL of 10/30 ug/mL
	7	0.5 mL of 10/30 ug/mL
	8	0.5 mL of 10/30 ug/mL
	9	1 mL of 10/30 ug/mL
	10	0.1 mL of 100/300 ug/mL
Weekly	11	0.2 mL of 100/300 ug/mL
	12	0.3 mL of 100/300 ug/mL
Every 2 Weeks	14	0.4 mL of 100/300 ug/mL
	16	0.5 mL of 100/300 ug/mL
Every 3 Weeks	19	0.75 mL of 100/300 ug/mL
	20+	1 mL of 100/300 ug/mL
Monthly	20+	1 mL of 100/300 ug/mL

Monthly maintenance to 3-5+ years

## RESULTS

- FOIT Age: 18 months to 36 years old, mean age at 9 years old. (Table 1)
- SCIT Age: 4 years to 74 Years old
- Of 356 FOIT patients, 145,060 doses were administered daily during the time frame.
  - 0.02% of FOIT exposure events required epinephrine
  - 11.3% of patients required at least one dose of epinephrine during therapy or after graduation
- Of 742 SCIT patients, 272,508 injections were administered daily during the time frame.
  - 0.15% of SCIT injections required epinephrine
  - 13.88% of patients required epinephrine associated with a systemic reaction
  - Epinephrine threshold was defined as an SR at Grade 2 or higher<sup>4</sup>, although some providers did administer epinephrine for certain Grade 1 symptoms<sup>4</sup> (i.e. urticaria, angioedema, cough, SOB) at their discretion. (Table 3)

## CONCLUSIONS

- FOIT at a busy allergy practice with a board-certified allergist provides no additional safety concerns per dose compared to SCIT.
- Per exposure (dose), less patients require epinephrine in FOIT compared to SCIT.
- FOIT treats a life-threatening disease process, while SCIT generally helps to improve quality of life disease processes.
- Board-certified allergists who are already comfortable with standardized therapies for SCIT may considering FOIT as a treatment option for their patients.

## IMPLICATIONS/NEXT STEPS

- Financial limitations, to both patients and practices, may inhibit implementation of FOIT in practices with established SCIT programs.
- FOIT appears effective and safe in the short-term, but long-term efficacy & safety data is limited.
- It is unclear how long patients need to remain on FOIT to maintain tolerance, or if long-term tolerance is achievable. Long term tolerance is achievable with SCIT.<sup>4</sup>
- Current data for FOIT is shifted towards a younger population base, while SCIT is encompasses a wider range of ages. How does this affect the data?

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