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Identifying Demographics and Baseline Clinical Characteristics Associated With Safety Outcomes During AR101 Therapy

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INTRODUCTION

- The prevalence of food allergy among children in the United States was estimated to be 7.6% in 2016[1] and is believed to be increasing[2]
- Peanut (*Arachis hypogaea*) Allergen Powder-dnfp (PTAH)—formerly known as AR101—is a first-in-class standardized oral biologic drug recently approved to mitigate allergic reactions that may occur with accidental exposure to peanuts in individuals 4–17 years of age with a confirmed diagnosis of peanut allergy[3]
- PTAH has been shown to induce and maintain desensitization to peanut in children and adolescents aged 4–17 years[4]
- The majority of adverse events reported in phase 2 and 3 clinical trials were allergic and mild/moderate in severity[4,5]

OBJECTIVE

- To identify demographic or baseline clinical characteristics associated with the likelihood of systemic reactivity during peanut oral immunotherapy with PTAH

METHODS

Study Design

- PTAH- and placebo-treated subjects aged 4–17 years who were enrolled in the randomized, double-blind, placebo-controlled PALISADE (North America and Europe; NCT02635776) and RAMSES (North America; NCT03126227) trials were included
- Inclusion criteria varied between the studies, with more stringent peanut sensitization and allergy history criteria required in RAMSES compared with PALISADE (**Table 1**)

Table 1. Key Inclusion Criteria in RAMSES and PALISADE

Inclusion Criteria	
RAMSES	**PALISADE**
History of physician-diagnosed IgE-mediated peanut allergy including onset of allergy symptoms within 2 hours of known oral exposure to peanut/peanut-containing food	Clinical history of allergy to peanuts or peanut-containing foods
Serum IgE to peanut ≥14 kU_A/L at screening and mean wheal diameter ≥8 mm compared with negative control on peanut SPT at screening	Serum IgE to peanut ≥0.35 kU_A/L within the past 12 months and/or wheal diameter ≥3 mm compared with negative control on peanut SPT at screening
No DBPCFC was conducted to assess for reactivity to peanut at screening	Dose-limiting symptoms after a single dose of peanut protein ≤100 mg at screening DBPCFC

DBPCFC, double-blind, placebo-controlled food challenge; IgE, immunoglobulin E; SPT, skin prick test.

Data Analysis

- Univariate and multivariate logistic regression analyses were run, controlling for treatment group (PTAH, placebo), to assess risk factors for any systemic allergic reactions of any severity, including these baseline variables:
  - Sex, age, race, region (Europe/North America), history of peanut-related anaphylactic reaction, atopic dermatitis, allergic rhinitis, asthma, multiple food allergies, peanut-specific immunoglobulin E (psIgE), peanut skin prick test wheal diameter
- For each variable, an odds ratio (OR; 95% CI) for the relative difference between dichotomized variable levels in the per-subject likelihood of experiencing a systemic allergic reaction of any severity was calculated

RESULTS

- Subject demographics and baseline clinical characteristics are shown in **Table 2**
  - More than half of the subjects were male and aged 4–11 years
  - Most subjects were white

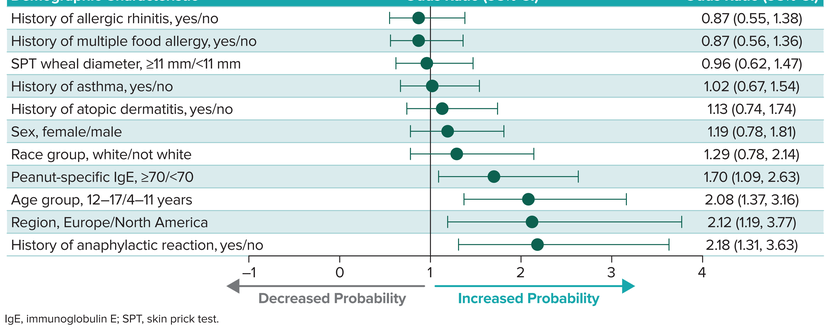
Table 2. Subject Baseline Demographics and Clinical Characteristics for RAMSES and PALISADE

Characteristic		RAMSES (N=505)	PALISADE[a] (N=496)
Sex, n (%)	Female	185 (36.6)	212 (42.7)
	Male	320 (63.4)	284 (57.3)
Age,[b] median (Q1, Q3), years		9 (7.0, 12.0)	9 (7.0, 12.5)
Age group, n (%)	4–11 years	340 (67.3)	327 (65.9)
	12–17 years	165 (32.7)	169 (34.1)
Race,[c] n (%)	American Indian or Alaska Native	3 (0.6)	1 (0.2)
	Asian	93 (18.4)	49 (9.9)
	Black or African American	22 (4.4)	9 (1.8)
	Native Hawaiian or Pacific Islander	5 (1.0)	1 (0.2)
	White	400 (79.2)	389 (78.4)
	Other	28 (5.5)	47 (9.5)
psIgE, median (Q1, Q3), kU_A/L		93.5 (42.7, 200.5)	71.3 (19.7, 202.0)
Peanut SPT, median wheal diameter (Q1, Q3), mm		13.5 (10.5, 18.5)	11.0 (9.0, 15.0)
History of peanut anaphylactic reaction, n (%)		311 (61.6)	358 (72.2)
History of allergic rhinitis, n (%)		381 (75.4)	356 (71.8)
History of atopic dermatitis, n (%)		299 (59.2)	308 (62.1)
History of asthma, n (%)		253 (50.1)	262 (52.8)
History of multiple food allergies, n (%)		309 (61.2)	325 (65.5)

[a]Only subjects aged 4–17 years were reported in this analysis. [b]Age was calculated relative to the date of informed consent. [c]Subjects reporting >1 category were included in all reported categories.
psIgE, peanut-specific immunoglobulin E; Q1, first quartile; Q3, third quartile; SPT, skin prick test.

- A systemic allergic reaction of any severity was experienced by 89 of 709 PTAH-treated subjects (12.6%) and 13 of 292 subjects (4.5%) receiving placebo
  - Among these subjects, mild, moderate, and severe systemic allergic reactions occurred in 38 (5.4%), 46 (6.5%), and 5 (0.8%) subjects treated with PTAH, and 5 (1.7%), 8 (2.7%), and 0 (0.0%) placebo subjects, respectively
- Factors increasing the likelihood of experiencing a systemic allergic reaction included (**Figure 1**):
  - History of anaphylactic reaction (yes/no; OR: 2.18, 95% CI: 1.31–3.63)
  - European region (Europe/North America; OR: 2.12, 95% CI: 1.19–3.77)
  - Age group (aged 12–17/4–11 years; OR: 2.08, 95% CI: 1.37–3.16)
  - Baseline psIgE group (≥70/<70 kU_A/L; OR: 1.70, 95% CI: 1.09–2.63)
    - Similar trends were observed when age and psIgE were analyzed as continuous variables
- These factors were associated with an increased likelihood of systemic allergic reactions in the multivariate analysis as well
- The 95% CIs for the other variables investigated crossed the threshold of OR=1.00, suggesting no difference in risk of systemic allergic reactions between these variables (**Figure 1**)

Figure 1. Probability of Systemic Allergic Reaction (Mild, Moderate, and Severe) by Baseline Characteristics



IgE, immunoglobulin E; SPT, skin prick test.

CONCLUSIONS

- Several factors were identified that may increase the risk of a systemic allergic reaction while on PTAH treatment, including a history of peanut-related anaphylactic reaction, older age group (≥12–17 years vs 4–11 years), higher baseline peanut-specific IgE (≥70 kU_A/L), or residing in a European vs North American region
  - The difference observed in systemic allergic reaction risk rates between European and North American children may reflect regional differences regarding the definition of anaphylaxis[6]; it may also be due to differences in practice standards for epinephrine use between Europe and North America, with higher rates reported in North America[7]
- None of the identified risk factors preclude patients from potential treatment; however, awareness of these potential risk factors can contribute to shared decision-making discussions when considering PTAH treatment

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