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Clinical and Immunologic Characteristics of European Patients Screened for PALISADE (Peanut Allergy Oral Immunotherapy Study of AR101 for Desensitization in Children and Adults)

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BACKGROUND

- Double-blind placebo-controlled food challenge (DBPCFC) is considered the gold standard in diagnosis of food allergy[1,2]
- DBPCFCs were recently conducted during screening for PALISADE, a randomized, placebo-controlled, international phase 3 trial of AR101 for peanut allergy[3]
- Preliminary pre-randomization data on European patients performing DBPCFC for PALISADE are summarized here

METHODS

- Eligible subjects aged 4–55 years with a clinical history of IgE-mediated peanut allergy and evidence of peanut sensitization underwent a screening DBPCFC
  - Screening DBPCFCs included both a peanut challenge (defatted peanut flour) and a placebo challenge (oat flour) on separate days
  - The screening DBPCFC, an abbreviated version of the PRACTALL DBPCFC, progressed sequentially without repeating any dose (1, 3, 10, 30, and 100 mg of peanut protein). Doses were given at 20- to 30-minute intervals, but intervals could be increased to 60 minutes to observe emerging symptoms
  - DBPCFC stopping criteria were prespecified in the protocol, based on PRACTALL guidelines,[4] and required the presence of 1 or more investigator-determined dose-limiting symptoms (DLS), which were generally objective
  - Investigators graded the severity of allergic symptoms during DBPCFCs using National Cancer Institute Common Toxicity Criteria grading scales previously modified and established by the Consortium of Food Allergy Research
- Subjects who had DLS at or before the 100 mg (144 mg cumulative) challenge dose of peanut protein were eligible for the PALISADE study

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RESULTS

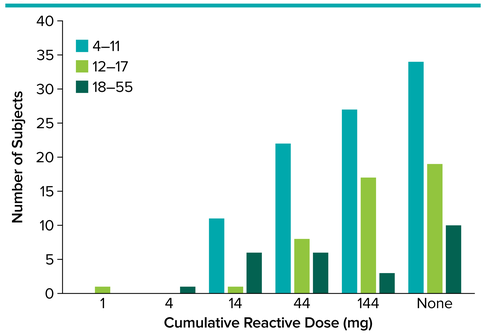
Table 1. European Subject Demographics

Characteristic	Population (N=166)
Mean age, years (SE); median (Q1, Q3)	11.4 (0.6); 10 (6, 15)
Male sex	59%
Peanut-specific IgE,* median (Q1, Q3), kU_A/L	13.2 (2.9, 72.3)
Ara h 1–specific IgE,* median (Q1, Q3), kU_A/L	0.9 (0.3, 17.8)
Ara h 2–specific IgE,* median (Q1, Q3), kU_A/L	8.1 (1.0, 38.1)
Peanut Skin Prick Test wheal diameter, median (Q1, Q3), mm	10.5 (8, 12.5)
Allergic rhinitis, n (%)	92 (55.4)
Asthma, n (%)	81 (48.8)
Atopic dermatitis, n (%)	86 (51.8)
Allergy to foods other than peanut, (%)	83 (50)

*n=163.

- 57% of the subjects were aged 4–11, 28% were aged 12–17, and 15% were adults
- 62% of the subjects experienced DLS at a cumulative median [IQR] 44 mg of peanut protein [44–144] (**Figure 1**)

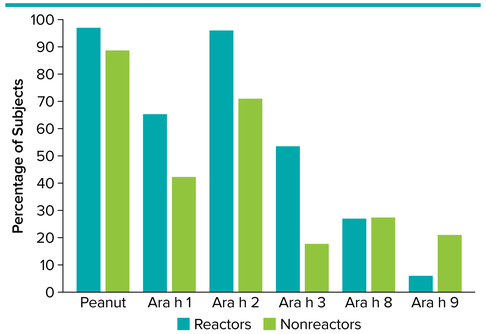
Figure 1. Cumulative Amount of Peanut Protein Causing DLS During the Screening DBPCFC, by Age (N=166)



DLS, dose-limiting symptoms.

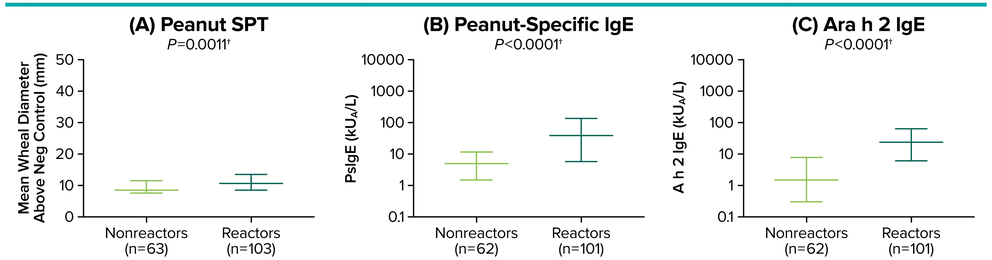
- 38% of the subjects did not experience DLS up to a cumulative reactive dose of 144 mg (nonreactors)
- Ara h 2, followed by Ara h 1 and Ara h 3, was a major peanut allergen in the reactive group (**Figure 2**)

Figure 2. Percentage of Subjects With Positive (≥0.35 kU_A/L) IgE



- Median peanut wheal diameter, peanut-specific IgE, and Ara h 2–specific IgE were statistically significantly greater in reactive subjects compared with nonreactive subjects (**Figure 3A–C**)

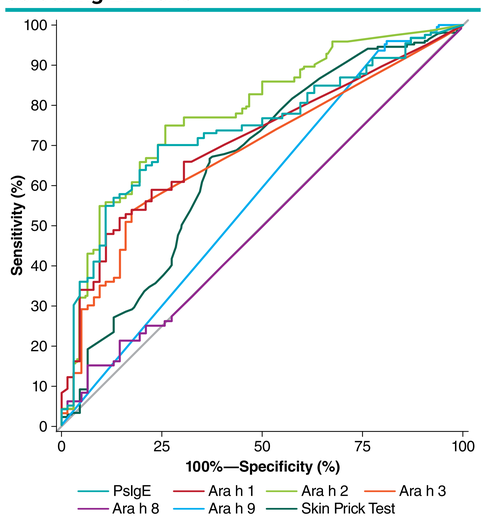
Figure 3. Immune Parameters Among Reactors and Nonreactors to the Screening DBPCFC*



*Medians and IQR shown. †Mann-Whitney 2-tailed t-test. SPT, skin prick test.

- In our analysis, Ara h 2–specific IgE demonstrated greater accuracy compared with peanut-specific IgE and peanut wheal diameter, for discriminating reactors from nonreactors to DBPCFC, based on receiver operating characteristic curve analysis (**Figure 4**)

Figure 4. ROC Curves Predicting Reaction to a Cumulative 144 mg of Peanut Protein During Screening DBPCFC



ROC Association Statistics				
ROC Model	Area	Standard Error	95% Wald Confidence Limits	
PsIgE	0.7407	0.0394	0.6636	0.8179
Ara h 1	0.7094	0.0376	0.6357	0.7832
Ara h 2	0.7816	0.0374	0.7082	0.8550
Ara h 3	0.6840	0.0358	0.6138	0.7542
Ara h 8	0.5072	0.0363	0.4360	0.5783
Ara h 9	0.5761	0.0288	0.5197	0.6326
Skin Prick Test	0.6586	0.0453	0.5698	0.7474

PsIgE, peanut-specific IgE; ROC, receiver operating characteristic.

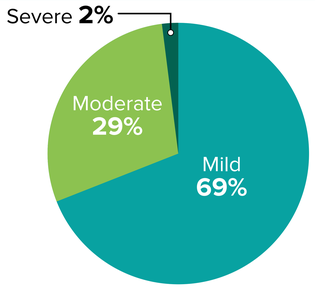
Table 2. Symptoms Occurring in ≥5% of Subjects During DBPCFC

Symptom, n (%)	Subjects Who Experienced an Adverse Event (n=103)	Adverse Events per Dose of FC
Mouth tingling/itching	65 (63.1)	145 (33.3)
Abdominal Pain/Cramping/Discomfort	60 (58.3)	88 (20.2)
Nausea	48 (46.6)	56 (12.8)
Other	48 (46.6)	102 (23.4)
Rhinorrhea/nasal congestion	46 (44.7)	50 (11.5)
Vomiting	44 (42.7)	44 (10.1)
Pruritus/itching	41 (39.8)	52 (11.9)
Conjunctivitis	31 (30.1)	33 (7.6)
Hives	28 (27.2)	32 (7.3)
Throat tightness/discomfort	27 (26.2)	48 (11)
Rash	24 (23.3)	25 (5.7)
Cough	15 (14.6)	17 (3.9)
Skin flushing	15 (14.6)	15 (3.4)
Sneezing	13 (12.6)	13 (3.0)
Facial swelling	10 (9.7)	10 (2.3)
Angioedema	10 (9.7)	11 (2.5)
Wheezing	9 (8.7)	10 (2.3)

*Total doses were 436. FC, food challenge.

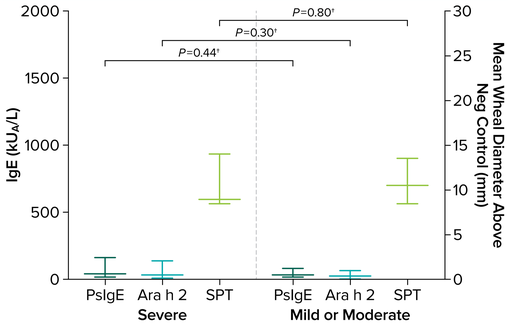
- The majority of the symptoms experienced were mild (**Figure 5A**)

Figure 5A. Symptom Severity During the Screening DBPCFC



- Peanut-specific IgE, Ara h 2–specific IgE, and peanut mean wheal diameters were not different in subjects with severe symptoms compared with subjects with mild or moderate symptoms (**Figure 5B**)

Figure 5B. Immune Parameters by Severity of Worst Symptom During the Screening DBPCFC*



*Medians and IQR shown. †Mann-Whitney 2-tailed t-test.
PsIgE, peanut-specific IgE; SPT, skin prick test.

- Nearly 15% of the reactive subjects received at least one dose of adrenaline. 21 doses of adrenaline were administered, with 9 subjects receiving 1 dose and 6 receiving 2 doses

CONCLUSIONS

- The majority of patients screened for PALISADE were children. Many of them were allergic to foods other than peanut, and most had at least one other atopic condition
- The majority of the screened patients were highly sensitive to peanut, reacting to 144 mg (cumulative) or less of peanut protein, but 38% of patients did not react at this dose
- Ara h 2–specific IgE, peanut-specific IgE, and peanut mean wheal diameters were significantly elevated in subjects reacting to the screening DBPCFC, compared with nonreactors. However, these parameters were not linked with the severity of the reaction
- Sensitization to Ara h 8 or Ara h 9 did not discriminate between reactors and nonreactors in our sample population
- Most of the symptoms appearing during the DBPCFC were either mild or moderate, and adrenaline was used in nearly 15% of the patients

IMPLICATIONS/FUTURE DIRECTIONS

- Even if allergic to multiple foods, patients and their families were nonetheless keen to participate in the trial
- The possibility of allowing higher amounts of peanut in the screening DBPCFC should be considered in future clinical trials with AR101
- This unique dataset of DBPCFCs will provide valuable data for future study