423

Presented at
2020 AAAAI Annual Meeting
March 13–16, 2020
Philadelphia, PA

Improved Tolerability and Continued Immunomodulation Among Subjects Aged 4–17 Years Following 28 or 56 Weeks of Extended Daily Therapeutic AR101 Dosing

Dareen Siri,[1] Rita Kachru,[2] Noelle M. Griffin,[3]* Andrea Vereda,[4] Alex Smith,[3] Ellen Sher[5,6]

[1]Midwest Allergy Sinus Asthma, S.C./SWIA Clinical Research Center, Normal, IL; [2]David Geffen School of Medicine at UCLA, Los Angeles, CA; [3]Aimmune Therapeutics, Brisbane, CA; [4]Aimmune Therapeutics, London, UK; [5]Allergy Partners of NJ, Ocean, NJ; [6]Atlantic Research Center, Ocean, NJ; *At time of study

INTRODUCTION

- 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[1]
- In the international phase 3, randomized, double-blind, placebo-controlled PALISADE trial (NCT02635776), subjects treated with PTAH demonstrated increased tolerability to peanut protein[2]
- The baseline prevalence of allergic comorbidities, serum levels of peanut-specific immunoglobulin E (psIgE), skin prick test (SPT) wheal diameters, and highest tolerated doses of peanut protein in PALISADE subjects are indicative of a highly atopic and sensitized subject population
- ARC004 (NCT02993107) is an open-label follow-on study to PALISADE

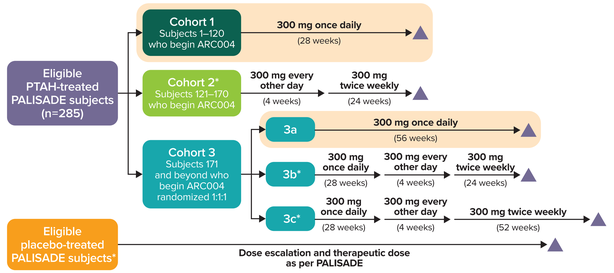
OBJECTIVE

- To assess the tolerability and immunomodulation of continued PTAH therapeutic dosing (300 mg/day) for an additional 28 weeks (~80 weeks total including PALISADE) or 56 weeks (~108 weeks total including PALISADE) compared with the initial 6 months of therapeutic dosing in PALISADE

METHODS

- Subjects aged 4–17 years at PALISADE enrollment who completed PALISADE and could tolerate ≥300 mg of peanut protein (≥443 mg cumulative) at the exit double-blind, placebo-controlled food challenge (DBFCPC) were eligible to continue PTAH 300 mg/day therapeutic dosing for 28 (Cohort 1 [C1]) or 56 weeks (Cohort 3a [C3a]) in ARC004 (**Figure 1**)

Figure 1. ARC004 Study Design



▲ Indicates the end of the study period. Subjects underwent a double-blind, placebo-controlled food challenge at this time.
*Data from these cohorts will be presented at another time.

Acknowledgments Editorial assistance and medical writing support were provided by The Curry Rockefeller Group, LLC and were funded by Aimmune Therapeutics.

References **1.** Aimmune Therapeutics Inc. *Full Prescribing Information for PALFORZIA [Peanut (Arachis hypogaea) Allergen Powder-dnfp].* Brisbane, CA: Aimmune Therapeutics Inc.; January 31, 2020. **2.** PALISADE Group of Clinical Investigators. AR101 oral immunotherapy for peanut allergy. *N Engl J Med.* 2018;379(21):1991-2001.

- At the end of the treatment periods, subjects completed an exit DBPCFC up to 2000 mg
- Data from the 300 mg/day therapeutic dosing periods and exit DBPCFCs were summarized using descriptive statistics and compared
- Data assessed included:
  - Safety: adverse events (AEs)
  - Efficacy: ability to tolerate 300, 600, 1000, and 2000 mg peanut protein with no more than mild symptoms at exit DBPCFCs
  - Immunologic changes: wheal diameter on peanut SPT, peanut-specific immunoglobulin E (psIgE) and immunoglobulin G4 (IgG4) concentrations, and psIgE/psIgG4 ratio

RESULTS

Study Population

- 110 PALISADE completers were assigned to ARC004 C1 and 32 to C3a, of which 94.5% and 81.3% completed the ARC004 exit DBPCFC, respectively
- Most subjects were between the ages of 4 and 11 years (64.1%), male (53.5%), and white (78.9%); 62 (43.7%) subjects reported asthma at baseline
- Baseline characteristics were overall balanced between the cohorts; more subjects in C1 (94.5%) were in North America compared to C3 (65.6%)

Safety

- Similar percentages of subjects experienced AEs of similar maximum severity during ARC004 compared with PALISADE; however, the total number of AEs was halved (**Table 1**)
- No deaths or life-threatening AEs occurred

Table 1. Summary of Treatment-Emergent AEs During PALISADE and ARC004 Therapeutic Dosing (Safety Population)

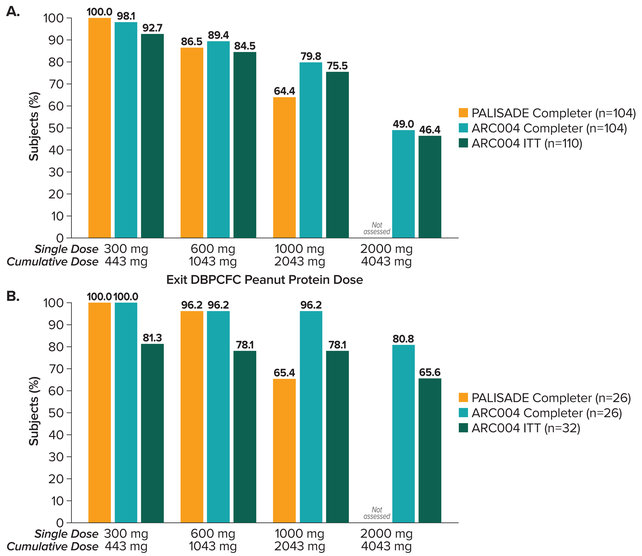
	Cohort 1 (n=110)		Cohort 3a (n=32)	
Subjects With ≥1 AE, n (%)	PALISADE	ARC004	PALISADE	ARC004
≥1 AE	97 (88.2)	91 (82.7)	29 (90.6)	27 (84.4)
Maximum AE severity				
Mild	60 (54.5)	58 (52.7)	20 (62.5)	15 (46.9)
Moderate	35 (31.8)	30 (27.3)	9 (28.1)	12 (37.5)
Severe	2 (1.8)	3 (2.7)	0	0
Unrelated AEs	48 (43.6)	44 (40.0)	10 (31.3)	12 (37.5)
Related AEs	49 (44.5)	47 (42.7)	19 (59.4)	15 (46.9)
Total number of events (events/patient-year)	739 (13.5)	416 (5.6)	348 (21.4)	147 (4.7)
Anaphylactic reactions	5 (4.5)	7 (6.4)	3 (9.4)	5 (15.6)
Mild	3 (2.7)	1 (0.9)	3 (9.4)	2 (6.3)
Moderate	2 (1.8)	4 (3.6)	0	3 (9.4)
Severe	0	2 (1.8)	0	0
Serious AEs[a]	1 (0.9)	1 (0.9)	0	0

[a]No deaths or life-threatening AEs occurred. AEs, adverse events.

Efficacy

- The ability to tolerate cumulative doses of peanut protein was sustained or improved between PALISADE and ARC004 exit DBPCFCs (**Figure 2**)
- A greater percentage of subjects in both C1 and C3a tolerated doses >300 mg peanut protein during ARC004 exit DBPCFC than at PALISADE exit DBPCFC
- Of note, tolerability of doses >300 mg peanut protein were also high among subjects in the ARC004 intent-to-treat (ITT) population, counting those not completing the challenge as failures

Figure 2. Efficacy of Continued PTAH Therapeutic Dosing: Tolerated Doses at Exit DBPCFC in (A) Cohort 1 and (B) Cohort 3a

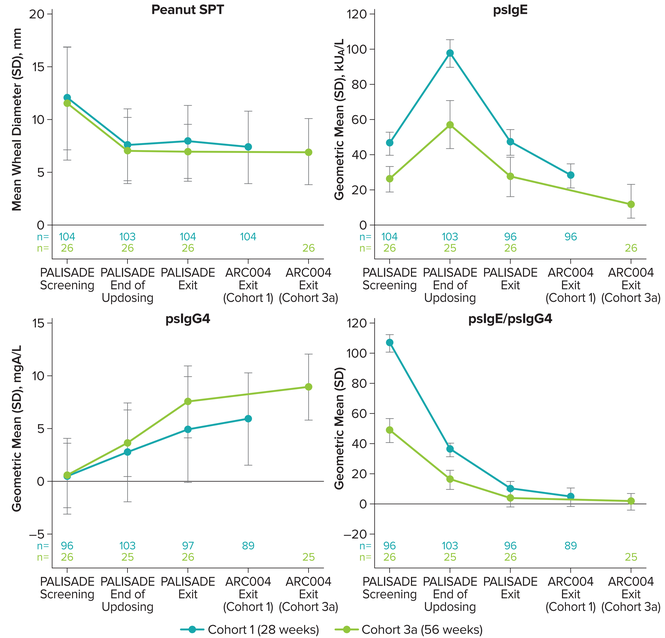


DBPCFC, double-blind placebo-controlled food challenge; ITT, intent-to-treat ; PTAH, Peanut (*Arachis hypogaea*) Allergen Powder-dnfp.

Immunologic Changes

- Changes in immune markers continued from PALISADE exit to ARC004 exit (**Figure 3**)
  - Reduction in SPT wheal size from baseline to PALISADE exit was maintained through ARC004 exit
  - psIgE continued to decrease from PALISADE exit to ARC004 exit
  - psIgG4 continued to increase from PALISADE exit to ARC004 exit
  - The psIgE/psIgG4 ratio continued to decrease from PALISADE exit to ARC004 exit

Figure 3. Changes in Immune Markers Between Baseline, End of Updosing, and Exit During PALISADE and ARC004 (Completer Population)



psIgE, peanut-specific immunoglobulin E; psIgG4, peanut-specific immunoglobulin G4; SPT, skin prick test.

CONCLUSIONS

- An additional 28 or 56 weeks of 300 mg daily AR101 therapeutic dosing resulted in:
  - An increase in the percentage of subjects tolerating higher doses of peanut protein during exit DBPCFC
  - An overall reduction in the number and rate of AEs experienced, despite incomplete desensitization during the first year of therapeutic dosing
  - Continued reduction in immunologic reactivity consistent with ongoing immunomodulation

Disclosures **DS** reports clinical research for Aimmune Therapeutics and DBV Technologies; consultant fees from Aimmune Therapeutics, Regeneron/Sanofi, DBV Technologies, Mylan, and Kaleo. **RK** reports clinical research support from Aimmune Therapeutics and DBV Technologies. **NMG** was an employee of Aimmune Therapeutics at the time of this study. **AV** and **AS** are employees of Aimmune Therapeutics. **ES** reports speakers bureau, advisory boards, and clinical research support, Aimmune Therapeutics; speakers bureau and clinical research support, Regeneron; advisor, DBV Technologies; and advisory board and speakers bureau, Kaleo.