Continuous and Daily OIT for Peanut Allergy: Results from a 2-Year Open-Label Follow-On Study

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I have no disclosures to report

Introduction:

- The FDA approval of Palforzia (PTAH) for peanut oral immunotherapy (OIT), has significantly changed treatment strategies for peanut allergic patients.
- Two phase 3 randomized placebo-controlled trials (PALISADE and ARTEMIS) have demonstrated the effectiveness of once-daily Palforzia dosing in desensitizing patients.
- This study (ARC004 trial) served as an exploratory open-label extension to the PALISADE study to assess the safety and efficacy of alternative peanut OIT maintenance regimens.

Study Demographics:

Focus of trial was on patients 4-17 years of age subsequently re-enrolled into ARC004 from the PALISAIDE trial.

261 of the 358 patients that were re-enrolled into the ARC004 trial completed the study, including 53.9% (55 of 102) from the PTAH-naïve group and 80.5% (206 of 256) from the PTAH-continuing group.

TABLE I. Demographic and baseline characteristics at ARC004 trial entry (safety population; N = 351)

Characteristic	PTAH-Naive (n = 100) ~52 wk	PTAH-Continuing (n = 251)				
		Daily dosing cohorts		Non–daily dosing cohorts*		
		Cohort 1 (n = 109) ~28 wk	Cohort 3A (n = 31) ~56 wk	Cohort 2 (n = 46) ~28 wk	Cohort 3B* (n = 31) ~56 wk	Cohort 3C* (n = 34) ~56-84 wk
Median age (y) (range)	9.5 (5-17)	11 (5-17)	9 (5-17)	10 (4-17)	9 (5-16)	9 (5-16)
Sex: male, n (%)	65 (65.0)	57 (52.3)	17 (54.8)	25 (54.3)	19 (61.3)	18 (52.9)
No. of systemic allergic reactions due to peanut during lifetime, n (%)						
0	27 (27.0)	36 (33.0)	9 (29.0)	11 (23.9)	11 (35.5)	12 (35.3)
1	32 (32.0)	43 (39.4)	14 (45.2)	20 (43.5)	14 (45.2)	12 (35.3)
2	19 (19.0)	17 (15.6)	6 (19.4)	7 (15.2)	2 (6.5)	2 (5.9)
3	8 (8.0)	8 (7.3)	1 (3.2)	3 (6.5)	3 (9.7)	5 (14.7)
>3	13 (13.0)	5 (4.6)	1 (3.2)	5 (10.9)	1 (3.2)	3 (8.8)
History of asthma, n (%)	47 (47.0)	47 (43.1)	14 (45.2)	28 (60.9)	16 (51.6)	16 (47.1)
Allergic rhinitis, n (%)	80 (80.0)	79 (72.5)	20 (64.5)	33 (71.7)	19 (61.3)	23 (67.6)
Atopic dermatitis, n (%)	56 (56.0)	67 (61.5)	22 (71.0)	32 (69.6)	18 (58.1)	17 (50.0)
Food allergies other than peanut, n (%)	64 (64.0)	67 (61.5)	17 (54.8)	35 (76.1)	16 (51.6)	22 (64.7)
Immunoglobulin and SPT results, median (IQR)						
Total IgE (IU/mL)	484.5 (258-1127)	345.0 (194-783)	371.0 (114-952)	463.0 (239-996)	580.0 (234-1034)	520.5 (204-739)
Peanut-specific IgE (kUA/L)	108.25 (32.9-277.8)	63.5 (20.9-247.5)	45.4 (2.73-220.5)	33.55 (5.82-187.5)	72.0 (10.5-259.0)	90.95 (35.1-301.0)
Peanut-specific IgG_4 (mgA/L)	0.5 (0.3-1.4)	6.1 (2.4-13.4)	7.4 (1.9-20.9)	5.5 (2.2-11.1)	9.8 (2.6-24.1)	9.4 (3.6-29.1)
Peanut-specific IgE/IgG_4 ratio	187.49 (44.55-401.94)	13.26 (2.33-32.50)	6.14 (0.70-21.01)	5.83 (2.37-19.46)	7.13 (2.61-14.86)	7.69 (2.26-33.61)
SPT mean wheal diameter (mm)	10.5 (8.5-13.5)	7.5 (5.5-10.0)	7.0 (4.0-9.5)	6.25 (4.0-9.0)	6.5 (4.5-10.0)	7.0 (5.0-8.5)
Single maximum dose tolerated at trial entry, n (%)						
1 mg	8 (8.0)	0	0	0	0	0
3 mg	17 (17.0)	0	0	0	0	0
10 mg	27 (27.0)	0	0	0	0	0
30 mg	20 (20.0)	0	1 (3.2)†	0	0	0
100 mg	21 (21.0)	0	0	1 (2.2)†	1 (3.2)†	0
300 mg	3 (3.0)	16 (14.7)	1 (3.2)	7 (15.2)	4 (12.9)	2 (5.9)
600 mg	2 (2.0)	25 (22.9)	10 (32.3)	10 (21.7)	4 (12.9)	7 (20.6)
1000 mg	2 (2.0)	68 (62.4)	19 (61.3)	28 (60.9)	22 (71.0)	25 (73.5)

IQR, Interquartile range; *SPT*, skin prick test.
Baseline values were relative to the start of ARC004.
*Participants in cohorts 3B and 3C underwent initial daily dosing for 28 wk.
†These patients did not meet the inclusion/exclusion criteria of the ARC004 study.

Methods:

- Participants who completed the PALISADE trial were invited to participate in the ARC004 trial.
- Patients initially in the placebo arm of PALISADE (PTAH-naïve patients) underwent up-dosing for 22-40 weeks and subsequent maintenance dosing at 300 mg/d for 24-weeks.
- Patients in the treatment arm of PALISADE who passed the end of study 300 mg OFC were enrolled into 1 of 5 cohorts with different dosing regimens.
- All patients at the end of the study were eligible for a double-blind placebo-controlled OFC to peanut, with a maximum dose of 2000 mg

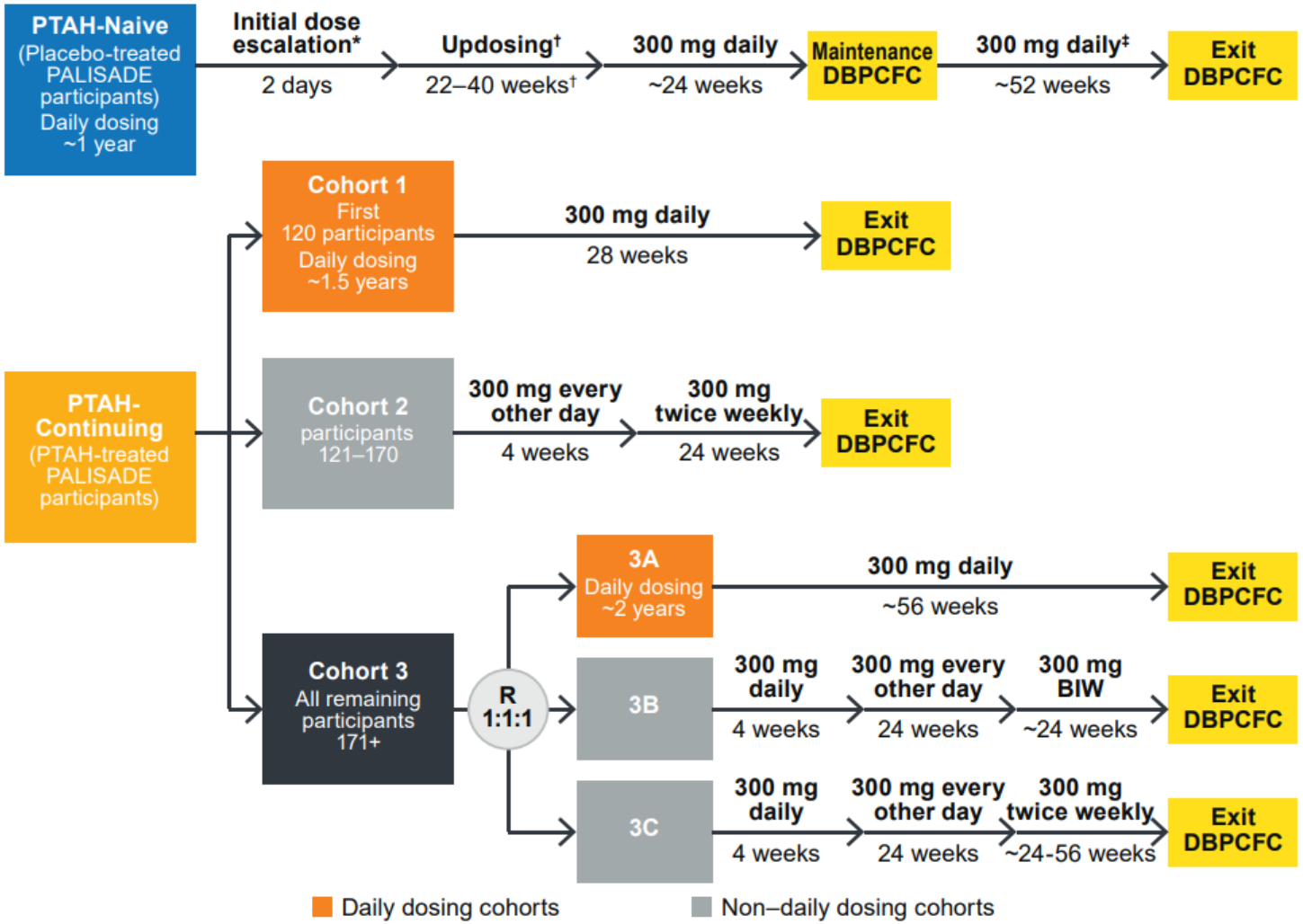

FIGURE 1. ARC004 Trial design. All treatments were administered as tolerated. *Day 1, 0.5- to 3-mg or 6-mg PTAH as tolerated; day 2, confirmation of ability to tolerate 3-mg PTAH. †From 3 mg to 300 mg daily, with dose escalation every 2 weeks. ‡Administration of daily or non–daily dosing regimens was contingent on results; planned regimens were every other day, twice weekly, once weekly, or every other week. Regimens less frequent than twice weekly were not instituted because of small cohort size *and at the recommendation of the Safety Monitoring Committee*. All ARC004 completers had the option of entering the open-label ARC008 study of daily PTAH.

Results: Desensitization

- Desensitization rates were higher in daily dosing cohorts compared to non-daily dosing cohorts.
  - Desensitization response rates, were highest in cohort 3A, which had the longest duration of daily dosing (56 weeks).
  - Desensitization response rates were lowest in cohort 2, which received q48 hr dosing for 4 weeks, followed twice weekly dosing for 24 weeks.

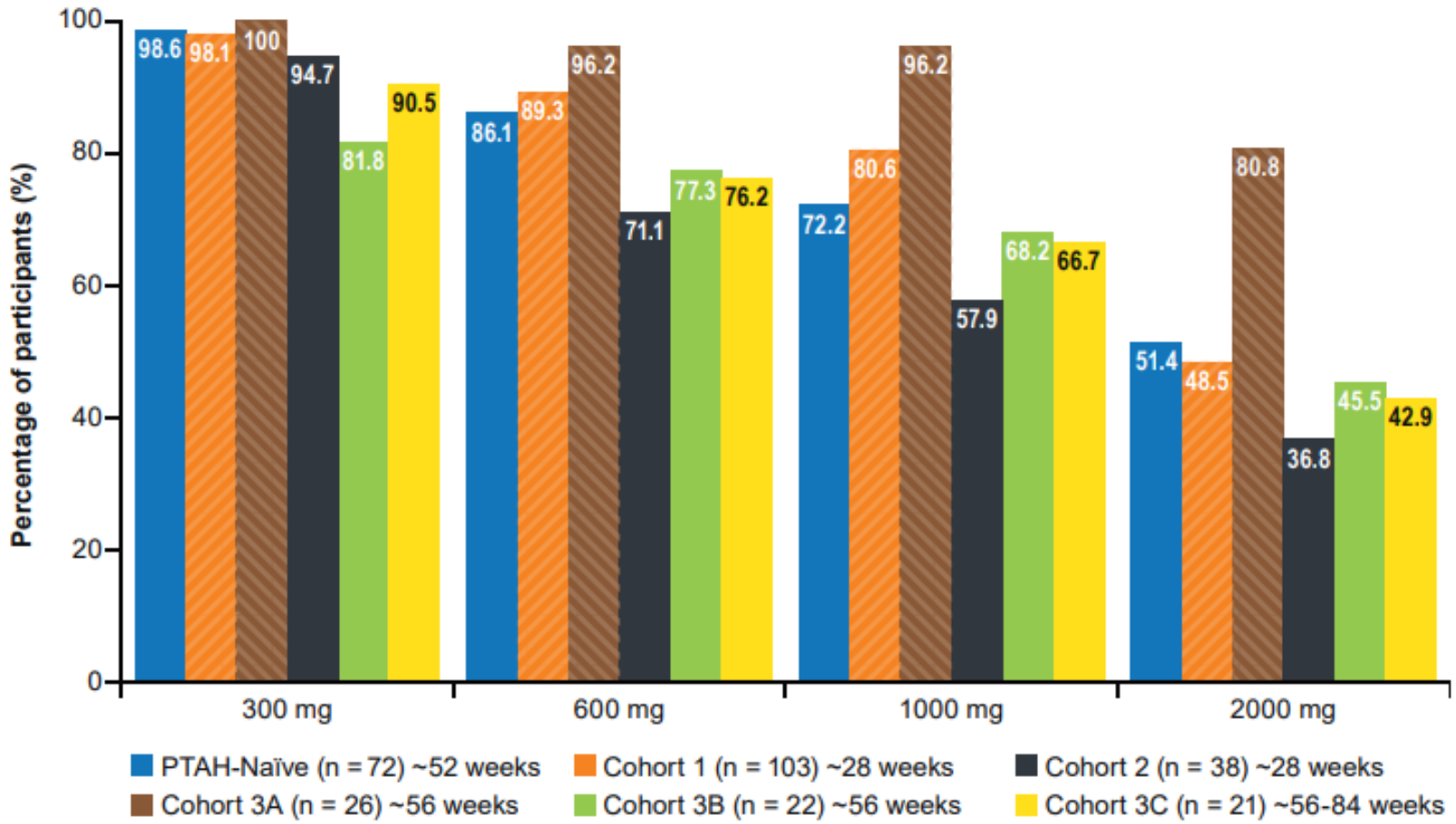

FIGURE 3. Desensitization rates based on the single highest tolerated dose at the exit DBPCFC (completer population; N = 282). Hatch marked bars indicate daily dosing cohorts.

Results: Safety and Tolerability

- Most patients in both the PTAH-continuing cohorts and PTAH-naïve cohort experienced at least one adverse reaction.
- When exposure-adjusted for adverse events, rates were lower in daily dosing cohorts vs. Non-daily dosing cohorts.
- 18 patients (6.1%) from the non-daily dosing cohorts reverted to daily dosing due to adverse events.
- However, the incidence of severe adverse events was low in both daily (2.1%) and non-daily (2.7%) dosing cohorts.

TABLE II. Summary of treatment-emergent AEs (safety population; N = 351)

	PTAH-Naive (N = 100) ~52 wk			PTAH-Continuing (N = 251)				
				Daily dosing cohorts		Non–daily dosing cohorts*		
AE	IDE/updosing (n = 100)	Daily dosing (n = 85)	Total (n = 100)	Cohort 1 (n = 109) ~28 wk	Cohort 3A (n = 31) ~56 wk	Cohort 2 (n = 46) ~28 wk	Cohort 3B* (n = 31) ~56 wk	Cohort 3C* (n = 34) ~56-84 wk
Any AE, n (%)*	94 (94.0)	76 (89.4)	98 (98.0)	90 (82.6)	27 (87.1)	36 (78.3)	28 (90.3)	33 (97.1)
AEs by grade/severity, n (%)								
1: mild	41 (41.0)	45 (52.9)	37 (37.0)	58 (53.2)	15 (48.4)	22 (47.8)	13 (41.9)	12 (35.3)
2: moderate	51 (51.0)	30 (35.3)	58 (58.0)	29 (26.6)	12 (38.7)	14 (30.4)	15 (48.4)	18 (52.9)
3: severe	2 (2.0)	1 (1.2)	3 (3.0)	3 (2.8)	0	0	0	3 (8.8)
Treatment-related AEs, n (%)	81 (81.0)	43 (50.6)	86 (86.0)	47 (43.1)	15 (48.4)	25 (54.3)	14 (45.2)	24 (70.6)
Serious AEs, n (%)	0	0	0	1 (0.9)	0	0	1 (3.2)	1 (2.9)
Serious treatment-related AEs, n (%)	0	0	0	0	0	0	0	0
AEs leading to discontinuation, n (%)	7 (7.0)	2 (2.4)	9 (9.0)	3 (2.8)	1 (3.2)	0	2 (6.5)	1 (2.9)
Allergic reactions, n (%)	83 (83.0)	48 (56.5)	89 (89.0)	53 (48.6)	17 (54.8)	25 (54.3)	21 (67.7)	28 (82.4)
Total exposure (participant-years)	43.76	85.53	129.29	73.74	31.53	25.95	30.08	42.49
Exposure-adjusted AE rates†	54.80	18.13	30.54	12.94	17.54	20.69	13.86	30.10
Exposure-adjusted treatment-related AE rates‡	36.65	12.16	20.45	5.64	4.66	13.41	3.39	20.60

*Participants in cohorts 3B and 3C underwent initial daily dosing for 28 wk.

†Participants with >1 AE were counted only once using the highest severity and closest relationship to study product.

‡Exposure-adjusted event rates were defined as the total number of events divided by the total number of participant-years at risk during the period.

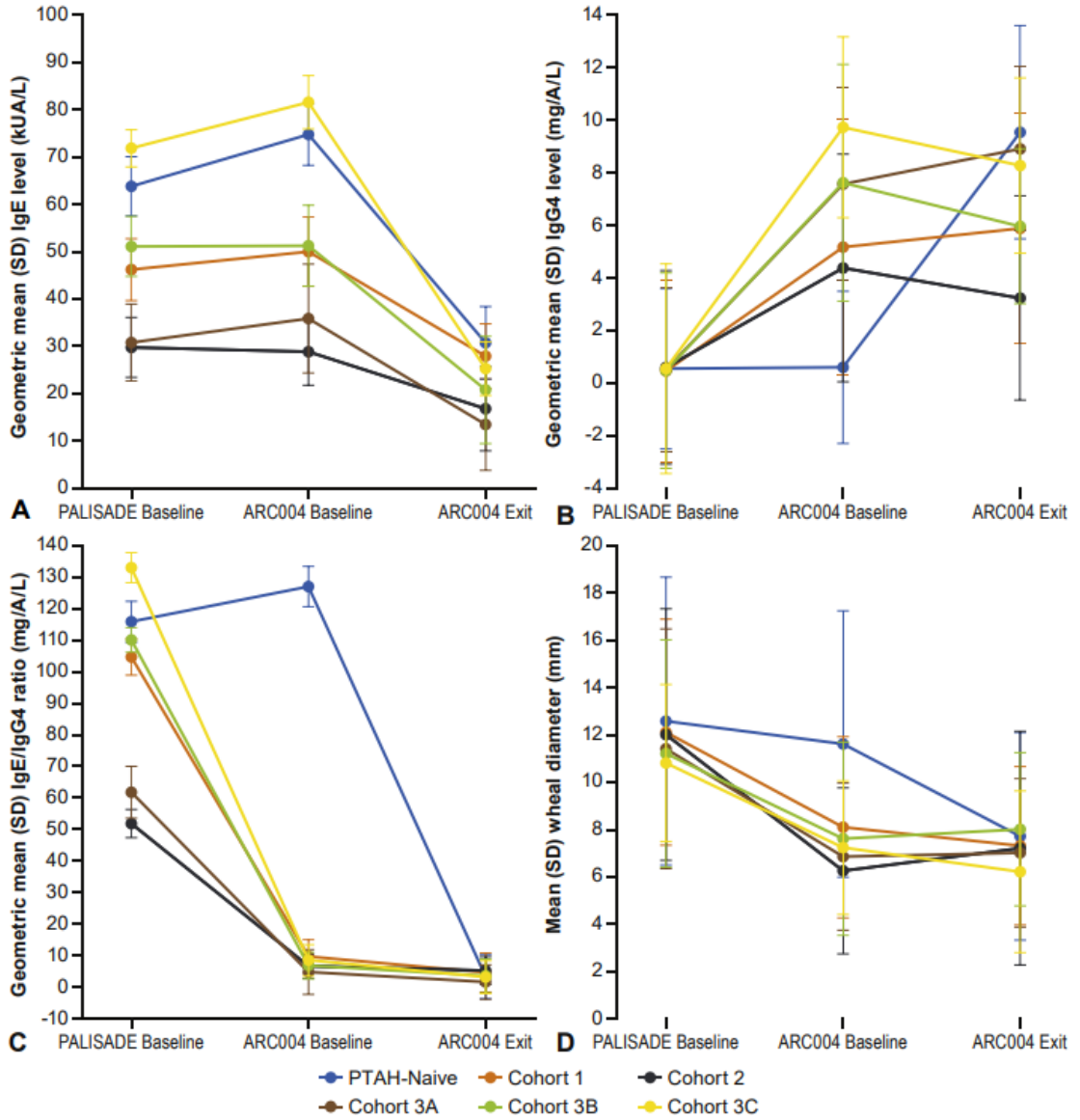

FIGURE 4. Peanut-specific IgE and IgG_4 levels and SPT wheal diameter: baseline vs trial exit. Geometric mean values for (**A**) peanut-specific IgE, (**B**) IgG_4, and (**C**) IgE/IgG_4 ratio at PALISADE baseline, ARC004 baseline, and ARC004 study exit. (**D**) The SPT mean wheal diameter at PALISADE baseline, ARC004 baseline, and ARC004 study exit. *SPT,* Skin prick test. PALISADE baseline values for peanut-specific IgE and IgG_4 and mean SPT wheal diameter were defined as the last available measurement before the first dose of the trial product on day 1 of the ARC004 trial for the PTAH-naive group and as day 1 of the PALISADE trial for participants in the PTAH-continuing cohorts.

Summary:

- Continued daily dosing of PTAH beyond 1 year appears to be safe and effective.
- Biomarkers suggest further improvement in immunomodulation beyond the first year of OIT.
- Daily dosing of PTAH has less exposure-adjusted adverse events and fewer severe systemic allergic reactions, compared to other regimens.
- After approximately 2 years of continued daily treatment with PTAH, 80% of participants were desensitized to 2000 mg of peanut protein.

Future Directions

- This study was limited by the open-label trial design, as well as the age restriction to 4-17 years of age.
- Future studies are needed to assess long-term impacts on tolerance and immunomodulation of these alternative dosing regimens.
- Additional subjective data from patients and caretakers could help provide additional insight into compliance with alternative dosing regimens.
- Follow-up studies exploring efficacy in patients with comorbid conditions and younger patient populations is needed.

Questions?