Adalimumab for Nail Psoriasis: Efficacy and Safety from the Open-Label Extension of a Phase-3, Randomized, Placebo-Controlled Trial

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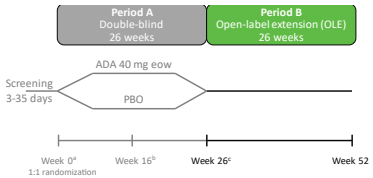
INTRODUCTION

- Treatments that are simultaneously effective in nail and skin psoriasis are needed as affected patients have worse quality of life and pain than patients with skin psoriasis alone.
- Management of nail psoriasis is challenging; the disease etiology and pathology are not fully understood and treatment guidelines are limited.[1,2] Topical agents have been minimally effective, but improvement in nail psoriasis has been reported following treatment of skin psoriasis with biologic therapies.[3]
- We evaluated the safety and efficacy of originator adalimumab (AbbVie) for fingernail psoriasis in the open-label-extension period (Period B) of a phase-3 trial of adalimumab (ADA) in patients with moderate-to-severe psoriasis who also had substantial, clinically impactful, moderate-to-severe fingernail psoriasis (clinicaltrials.gov NCT 02016482).

METHODS

- Patients with chronic, moderate-to-severe plaque psoriasis and fingernail psoriasis were enrolled. In 26-week Period A, patients were randomized 1:1 to 40 mg ADA every-other-week (ADAeow) after initial 80 mg dose, or matching placebo (PBO).
- From week 16, if the affected body surface area increased by ≥25% from baseline, patients were required to roll over to the 26-week Period B (early escape). Patients completing Period A at week 26 or who escaped early, entered Period B at week 26.
- At Period B entry (week 26), patients receiving PBO in Period A received an initial blinded dose of 80 mg ADA; patients receiving ADA in Period A received matching PBO. All received 40 mg ADAeow from weeks 27 through 51 (**Figure 1**).

Figure 1. Study Design



[a]Initial dose of ADA was 80 mg.
[b]Starting at week 16, if psoriasis-affected BSA increased ≥25% over baseline, patients were rolled over to Period B.
[c]Period-A ADA arm received matching PBO; Period-A PBO arm received blinded ADA 80 mg.
Abbreviations: ADA=adalimumab; eow=every-other-week dosing; PBO=placebo; BSA=body surface area.

KEY INCLUSION CRITERIA

- Adults diagnosed with both chronic, moderate-to-severe plaque psoriasis (with disease duration of at least 6 months) and moderate-to-severe psoriasis in at least one fingernail (any disease duration).
- BSA ≥10% and baseline target fingernail modified Nail Psoriasis Severity Index (mNAPSI)[4] ≥8; or BSA ≥5% with baseline target fingernail mNAPSI ≥8 and baseline total mNAPSI ≥20 (scale of total score 0 [no nail findings] to 130 [nail findings present in each nail]).
- Physician's Global Assessment of Fingernail (PGA-F) of at least moderate severity for fingernail psoriasis (scale 0 [clear] to 4 [severe]).
- Nail Psoriasis Physical Functioning Severity (NPPFS) score >3 (scale 0 [none] to 10 [severe]); or Nail Psoriasis Pain Numeric Rating Scale (NRS) score >3 (scale 0 [no pain] to 10 [severe pain]).

ENDPOINTS

- All efficacy variables assessed in Period A were also assessed in Period B (see list in **Table 3**). Period A primary and ranked secondary endpoints that were evaluated in Period B are reported here.
- Two intent-to-treat (ITT) patient populations were evaluated in Period B:
  - **Overall ITT_B Population:** all patients who received ≥1 study drug injection in Period B.
  - **Early Escape Population:** all patients who rolled over to Period B after experiencing worsening of disease from baseline in Period A.
- Period B treatment groups are identified by treatment received in Period A/Period B, ie, PBO/ADA and ADA/ADA.
- Missing data were handled in Period A by multiple imputation (MI), and in Period B by non-responder imputation (NRI) and by last observation carried forward (LOCF).

SAFETY

- Treatment-emergent adverse events (AEs) in Period B were analyzed for the ITT_B Population.

RESULTS

- 217 patients were randomized in Period A (108 to PBO; 109 to ADA).
  - 94/108 (87.0%) PBO/ADA and 94/109 (86.2%) ADA/ADA entered Period B (**Table 1**).
  - 81/94 (86.2%) PBO/ADA and 87/94 (92.6%) ADA/ADA patients completed Period B.

Table 1. Patient Disposition, Period B

Disposition, n (%)	PBO/ADA, N=94		ADA/ADA, N=94	
	n	%	n	%
Entered Period B	94	**100**	94	**100**
Completed Period B	81	**86.2**	87	**92.6**
Discontinued Period B; primary reason:	13	**13.8**	7	**7.4**
Adverse events	0	**0**	0	**0**
Withdrew consent	1	**1.1**	1	**1.1**
Lost to follow-up	2	**2.1**	0	
Lack of efficacy	6	**6.4**	4	**4.3**
All other reasons[a]	4	**4.3**	2	**2.1**

[a]Includes requirement for alternate therapy, and other reasons.

- Demographic and baseline characteristics were generally comparable across the 2 treatment groups (**Table 2**). Patients showed substantial nail disease and pain at baseline.

Table 2. Key Demographics and Baseline Characteristics of Patients Entering Period B

Characteristic		PBO/ADA, N=94		ADA/ADA, N=94	
		N	%	N	%
Sex	Male	76	**80.9**	83	88.3
	Female	18	**19.1**	11	11.7
Race	White	90	**95.7**	89	94.7
	Asian	3	**3.2**	4	4.3
	Other[a]	1	**1.1**	1	1.1
BSA	5% to <10%	34	**36.2**	37	39.4
	≥10%	60	**63.8**	57	60.6
Scalp psoriasis		80	**85.1**	80	85.1
PsA		26	**27.7**	28	29.8
PGA-F	Moderate	53	**56.4**	44	46.8
	>Moderate	41	**43.6**	50	53.2
PGA-S[b]	Moderate	55	**58.5**	56	59.6
	>Moderate	39	**41.5**	37	39.4
		Mean	**SD**	**Mean**	**SD**
Age, years		**47.1**	11.44	**47.3**	11.82
BMI, kg/m^2		(n=93) **29.2**	6.88	(n=93) **29.6**	5.09
Duration of psoriasis, years		**18.7**	13.73	**20.7**	12.34
Duration of nail psoriasis, years		**12.0**	11.12	**12.4**	9.65
PASI score		**13.3**	9.87	**12.8**	9.00
Total fingernail mNAPSI score (range 0-130)		**58.6**	20.78	**57.0**	18.34
Total fingernail NAPSI score (range 0-80)		**46.6**	15.40	**48.0**	15.67
Nail Psoriasis Pain (NRS) score (range 0-10)		**5.7**	2.25	**5.0**	2.48
B-SNIPI, scalp component (range 0-20)		(n=16) **7.9**	5.82	(n=23) **9.7**	5.32
NPPFS score (range 0-10)		**5.2**	2.15	**5.2**	2.63
DLQI score (range 0-30)		(n=82) **12.3**	6.73	(n=81) **13.0**	7.31
Nail Psoriasis QoL score (range 0-10)		**5.2**	2.28	**4.9**	2.79

[a]Other includes Black (ADA/ADA) and multi-race (PBO/ADA). [b]1 patient had PGA-S mild. For all scores listed above, higher scores indicate higher disease severity or impairment. Abbreviations: PBO=placebo; ADA=adalimumab; BSA=body surface area; PsA=psoriatic arthritis; BMI=body mass index; PASI=Psoriasis Area Severity Index; PGA=Physician Global Assessment (-F=fingernail psoriasis, -S=skin psoriasis); NAPSI=Nail Psoriasis Severity Index (m=modified); NRS=Numeric Rating Scale; B-SNIPI=Brigham Scalp Nail Inverse Palmo-Plantar Psoriasis Index; NPPFS=Nail Psoriasis Physical Functioning Severity; DLQI=Dermatology Life Quality Index; QoL=quality of life.

EFFICACY IN PERIOD A

- Results at week 26 are shown in **Table 3**. All results were statistically significant (P<0.001 for all but B-SNIPI 50 scalp and mNAPSI=0; P<0.01).

Table 3. Efficacy Outcomes in Period A

	PBON=108	ADA, N=109
Primary Endpoint		
Percent of patients who achieved at least a 75% reduction in total fingernail mNAPSI (mNAPSI 75) relative to baseline	3.4%	46.6%
Ranked Secondary Endpoints		
Mean percent improvement from baseline in total fingernail NAPSI	11.5%	56.2%
Percent of patients who achieved total fingernail mNAPSI=0	0%	6.6%
Mean improvement from baseline in nail psoriasis pain (NRS; used to capture a patient's self-report of worst fingernail pain)	1.1	3.7
Mean improvement from baseline in NPPFS	0.8	3.7
Percent of patients who achieved B-SNIPI 50 scalp (at least 50% improvement in the scalp component of the Brigham Scalp Nail Inverse Palmo-Plantar Psoriasis Composite Index, among patients with a baseline scalp score of 6 or greater)[a]	0.4%	58.3%
Percent of patients who achieved PGA-F 0 (clear) or 1 (minimal), with ≥2 grades improvement from baseline[b]	6.9%	48.9%

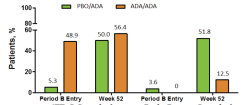
[a]Measured only at US and Puerto Rico sites. [b]Primary endpoint in US only, for US regulatory purposes. Abbreviations: PBO=placebo; ADA=adalimumab; NAPSI=Nail Psoriasis Severity Index (m=modified); NRS=numerical rating score; NPPFS=Nail Psoriasis Physical Functioning Severity; PGA-F=Physician's Global Assessment of fingernail.

EFFICACY IN PERIOD B (FIGURE 2A-G)

- **Overall ITT_B Population:** At week 52, response rates for the various efficacy endpoints were maintained for patients who continued ADA in Period B, and improved for patients who switched from PBO in Period A to ADA in Period B.
- **Early Escape Population:**
  - 188 patients were in the Early Escape Population (94 PBO/ADA; 94 ADA/ADA).
  - Patients who experienced worsening of disease from baseline in Period A and continued ADA in Period B had less improvement than those who switched from PBO in Period A to ADA in Period B.
  - Only 8 patients in the ADA/ADA group, vs. 56 in the PBO/ADA group, experienced worsening of disease from baseline in Period A and needed to escape early to Period B.

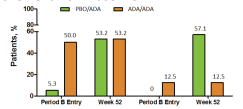
Figure 2. Efficacy Outcomes in Period B for Two Populations ≥

A. Achievement of mNAPSI 75



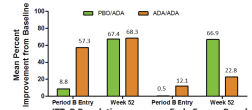
NRI. Missing at week 52 (n): ITT_B 14 PBO/ADA, 8 ADA/ADA; Early Escape 7 PBO/ADA, 2 ADA/ADA.

B. Achievement of PGA-F 0 or 1, with ≥2 Grades Improvement from Baseline



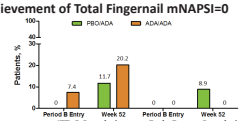
NRI. Missing at week 52 (n): ITT_B 14 PBO/ADA, 8 ADA/ADA; Early Escape 7 PBO/ADA, 2 ADA/ADA.

C. Improvement from Baseline in Total Fingernail NAPSI



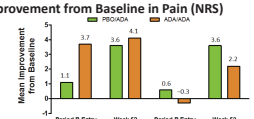
LOCF.

D. Achievement of Total Fingernail mNAPSI=0



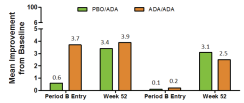
NRI. Missing at week 52 (n): ITT_B 14 PBO/ADA, 8 ADA/ADA; Early Escape 7 PBO/ADA, 2 ADA/ADA.

E. Improvement from Baseline in Pain (NRS)



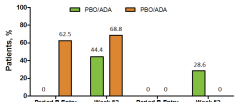
LOCF.

F. Improvement from Baseline in NPPFS



LOCF.

G. Achievement of ≥B-SNIPI 50 (scalp)



NRI. Missing at week 52 (n): ITT_B 3 PBO/ADA, 2 ADA/ADA; Early Escape 3 PBO/ADA, 1 ADA/ADA.

SAFETY

- Approximately half of the patients experienced a treatment-emergent AE in Period B (**Table 4**). The rates of serious AEs and serious infections were low. There were no AEs of tuberculosis, malignancy, or AEs leading to study-drug discontinuation; and no deaths.

Table 4. Safety in Period B

Adverse Events (AE), n (%)	Period A		Period B	
	PBO/ADA N=108	ADA/ADA N=109	PBO/ADA N=94	ADA/ADA N=94
Any AE	61 (56.5)	64 (58.7)	44 (46.8)	47 (50.0)
Serious AEs	5 (4.6)	8 (7.3)	3 (3.2)	3 (3.2)
Infections	30 (27.8)	32 (29.4)	25 (26.6)	30 (31.9)
Serious infection[a]	2 (1.9)	4 (3.7)	2 (2.1)	1 (1.1)
Tuberculosis	0	0	0	0
Malignancy	0	0	0	0
Leading to study drug discontinuation	3 (2.8)	6 (5.5)	0	0
Death	0	0	0	0
Special interest[b] AEs				
Allergic reaction[c]	2 (1.9)	1 (0.9)	1 (1.1)	0
Worsening/new onset of psoriasis	7 (6.5)	2 (1.8)	4 (4.3)	1 (1.1)
Injection-site reaction	3 (2.8)	4 (3.7)	2 (2.1)	2 (2.1)

[a]Serious infections: Period A pneumonia (n=2 PBO), and bronchitis, diverticulitis, endocarditis, erysipelas (n=1 each ADA); Period B influenza (n=1 ADA/ADA), lung infection (n=1, PBO/ADA), and diverticulitis (n=1, PBO/ADA). [b]AEs of special interest in <2 patients in a treatment group: Period A oral candidiasis, congestive heart failure, intestinal perforation, and hematologic disorders including pancytopenia (ADA); Period B diverticulitis, myocardial infarction, and hematologic disorders including pancytopenia (PBO/ADA). [c]Included angioedema and anaphylaxis. Abbreviations: PBO=placebo; ADA=adalimumab.

CONCLUSIONS

- For psoriasis patients with concomitant nail disease who received 40 mg ADA every-other-week treatment for 26 weeks in Period A, treatment response was maintained from entry to Period B through week 52.
- Patients receiving PBO in Period A, who switched to 40 mg ADA every-other-week treatment in Period B, eventually reached a similar response at week 52, to those receiving continuous ADA treatment.
- No new safety risks were identified with 40 mg ADA every-other-week treatment for 52 weeks.

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