Adalimumab Efficacy in Hidradenitis Suppurativa Patients is Sustained at Least Three Years with Weekly Dosing: Results from a Phase 3 Open-Label Extension Study (PIONEER)

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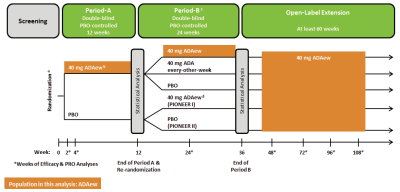
INTRODUCTION

- Hidradenitis suppurativa (HS) is a painful, chronic skin disease, characterized by recurrent inflamed nodules and abscesses, fistula formation, purulent drainage, and subsequent scarring.
- The PIONEER I and II phase 3 trials[1] evaluated treatment of patients with moderate-to-severe HS, with originator adalimumab (AbbVie) dosed every week. Adalimumab (ADA) is approved for a wide range of inflammatory diseases, including moderate-to-severe HS.
- The PIONEER trials were followed by a phase 3, open-label extension (OLE) trial (NCT01635764) designed to determine the long-term safety and efficacy of ADA in patients with moderate to severe HS.
- This analysis reports long-term results for patients who received weekly ADA weekly throughout PIONEER I and II, and continuing through the OLE to week 168.

METHODS

- Patients in this analysis entered the OLE if they completed Periods A and B or lost response during Period B of PIONEER I or II.
- In PIONEER I or II, patients were randomized to 40 mg weekly ADA at the start of the 12-week Period A, and upon completion of Period A, were re-randomized to 40 mg weekly ADA at the start of the 24-week Period B (**Figure 1**). Throughout the OLE, all patients received 40 mg weekly ADA.

Figure 1. Study Design for PIONEER I and II, and Open-Label Extension



a. Stratified by BL Hurley Stage II vs III (PIONEER I & II) & BL concomitant antibiotic use (PIONEER II). b. 160 mg week 0; 80 mg week 2; 40 mg from week 4. c. Re-randomization at entry to Period B, stratified by week 12 HiSCR status & BL Hurley Stage II vs III. d. 160 mg week 12; 80 mg week 14; 40 mg from week 16. ADA=adalimumab; ew=every week dosing; PBO=placebo; BL=baseline; PRO=patient-reported outcomes.

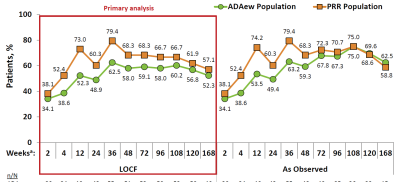
STATISTICAL ANALYSIS

- **ADAew Population**: patients who received continuous 40 mg weekly ADA in Periods A and B of PIONEER I or II and in the OLE.
- **PRR Population**: patients in the ADAew Population who either achieved HiSCR at week 12, or did not achieve HiSCR but achieved at least a partial response to treatment at week 12
  - HiSCR (Hidradenitis Suppurativa Clinical Response) was defined as ≥50% reduction in AN count with no increase in abscess count and no increase in draining fistula count relative to baseline
  - Partial response was defined as ≥25% reduction in total abscess and inflammatory nodule (AN) count relative to baseline, at the end of Period A in PIONEER I or II.
- All patients who were treated with ADA weekly in Periods A and B of PIONEER I and II, and entered the OLE, were included in the analysis.
- Missing values were handled by non-responder imputation (NRI) in Periods A and B of PIONEER I and II, and last-observation-carried-forward (LOCF) and observed case were used for both continuous and categorical variables.
- Results are reported as "study weeks," which consist of PIONEER + OLE weeks, shown consecutively.

RESULTS

- For patients who were randomized to weekly ADA in Period A of the 2 trials, the primary endpoint outcome (pooled data), was achievement of HiSCR at week 12 by 50.6% of patients (160/316), which was significantly higher than for patients randomized to placebo (26.8%; 85/317); *P*<0.001.
- In this analysis of results across PIONEER I and II (pooled data) into the OLE, 88 patients were in the ADAew Population and 63 were in the PRR Population.
- The HiSCR rate (LOCF) increased from baseline to week 48 in both populations and was maintained to week 108 (**Figure 2**).

Figure 2. Achievement of HiSCR

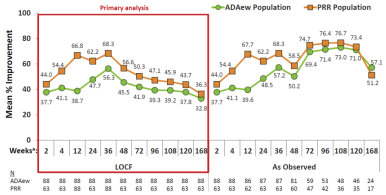


a. Weeks include PIONEER I or II + the OLE, listed consecutively.

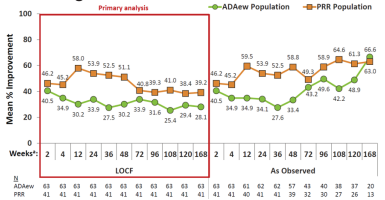
- The AN count, draining fistula count, and total fistula count (sum of draining fistulas and non-draining fistulas) (LOCF) decreased from baseline in both populations, and remained generally stable to study-week 168 (**Figure 3A-C**).

Figure 3. Improvement in Lesion Count

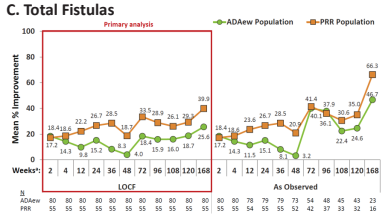
A. AN Count



B. Draining Fistulas



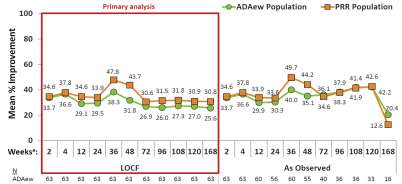
C. Total Fistulas



a. Weeks include PIONEER I or II + the OLE, listed consecutively. Mean improvement is relative to baseline.

- Improvement from baseline in pain (LOCF), indicated by mean percent decrease in NRS scores, remained generally stable in both populations to week 168 (**Figure 4**).

Figure 4. Improvement in Skin Pain

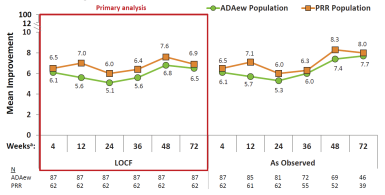


a. Weeks include PIONEER I or II + the OLE, listed consecutively.
Mean changes are relative to baseline. Change in numeric rating scale (NRS) at worst at each visit among patients with baseline NRS ≥3.

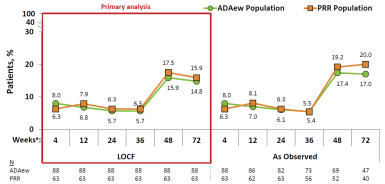
- In both populations, there was a clinically meaningful decrease in DLQI (LOCF) from baseline through week 72. (**Figure 5A**). The percentage of patients who achieved DLQI 0 or 1 increased from baseline to week 48 and was generally maintained to week 72 (**Figure 5B**).

Figure 5. Improvement in Dermatology Specific Quality of Life

A. Mean improvement from baseline



B. Achievement of DLQI 0 or 1



a. Weeks include PIONEER I or II + the OLE, listed consecutively. Mean changes are relative to baseline. DLQI 0 or 1=Dermatology Quality of Life Index, no effect of skin disease on quality of life.

SAFETY

- There were no adverse events of opportunistic infection excluding oral candidiasis, no events of tuberculosis, lymphoma, non-melanoma skin cancer, malignancy, or demyelinating disorder, and there were no deaths.

Table 2. Treatment-Emergent Adverse Events

Adverse Events, n (%)	ADAew Population N=88	PRR Population N=63
Any event	76 (86.4)	55 (87.3)
Leading to study drug discontinuation	13 (14.8)	10 (15.9)
Serious	12 (13.6)	9 (14.3)
Infections	63 (71.6)	45 (71.4)
Serious infections	3 (3.4) [a]	2 (3.2) [b]
Active or latent tuberculosis	2 (3.2)	2 (3.2)

a. Included pneumonia (n=2) and cellulitis of right leg (n=1).
b. Included pneumonia (n=1) and cellulitis of right leg (n=1).

CONCLUSIONS

- Data (LOCF) for the HS patient populations receiving weekly ADA spanning the PIONEER I and II studies and the OLE, confirm that weekly ADA treatment maintained long-term response, demonstrated by:
  - 52.3% of the ADAew Population and 57.1% of the PRR Population achieved HiSCR at week 168
  - Pain decreased starting at week 2, and was generally maintained to week 168 for both populations
  - Clinically meaningful improvement in DLQI at week 72 of 6.5
- The safety profile of long-term weekly ADA therapy in this analysis was consistent with the known ADA safety profile and no new safety risks were identified.

REFERENCES

1. Kimball, NEJM.

DISCLOSURES

C Zouboulis has received honoraria from AbbVie for participation on ad boards, as a consultant, investigator, and speaker; his department received grants from AbbVie and Novartis for his participation as an investigator. **M Okun** received compensation from AbbVie for consultation services and is a former AbbVie employee. He has served as a consultant for Gilead Sciences and Crescendo Biosciences. **R Gniadecki** has received honoraria from AbbVie, Janssen, Novartis, and Amgen for participation on advisory boards, as a investigator, and speaker; his department received grants from AbbVie, Janssen and Novartis for his participation as an investigator. **P Foley** has served as a consultant, investigator, speaker and/or advisor for and/or received travel grants from Galderma, LEO/Peplin, Ascent, Clinuvel, Janssen-Cilag, Eli Lilly, Australian Ultraviolet Services, Roche, CSL, 3M/iNova/Valeant, GSK/Stiefel, Abbott/AbbVie, Biogen Idec, Merck Serono, Schering-Plough/MSD, Wyeth/Pfizer, Amgen, Novartis, Celgene, Aspen, Boehringer Ingelheim and BMS. **C Lynde** has received honoraria as a principal investigator, speaker, and consultant for AbbVie, Amgen, Boehringer Ingelheim, Celgene, Eli Lilly, Janssen, Leo Pharma, Merck, Novartis, and Regeneron. **J Weisman** received research grants for investigator services from AbbVie, Allergan, Amgen, Astra Zeneca, Boehringer Ingelheim, Braintree, Celgene, Eli Lilly, Glaxo Smith Klein, Janssen, Leo Pharma, Merck, Novartis, Pfizer, Regeneron, Steifel, Tigercat; and received honoraria for service on advisory boards and speaker's bureaus from AbbVie, Amgen, Celgene, Eli Lilly, and Janssen. **P Karunaratne, D Williams** receive a salary as AbbVie employees, and may also receive stocks and/or stock options.

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