Continuous Weekly Adalimumab is the Optimal Long-term Strategy for Patients with Moderate-to-Severe Hidradenitis Suppurativa: Results from the PIONEER Open Label Extension Trial

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Presented at the Fall Clinical Dermatology Conference - 36th Anniversary • Las Vega, Nevada • October 12 – 15, 2017

INTRODUCTION

- Adalimumab (originator) 40 mg weekly dosing (ADAew) is approved for treatment of moderate-to-severe hidradenitis suppurativa (HS).
- There are clinical circumstances where patients are obliged to temporarily discontinue or reduce this dose.
- This is a pooled analysis of 3 trials that evaluated 40 mg ADAew in patients with moderate-to-severe HS:
  - The phase-3 placebo-controlled PIONEER I & II trials evaluated the efficacy and safety of ADAew vs placebo.[1]
  - The subsequent open-label extension trial (OLE) (NCT01635764) determined the long-term safety and efficacy of ADAew.

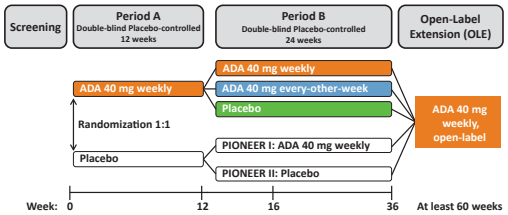
OBJECTIVE

- Determine the effectiveness of retreatment with ADAew in patients with moderate-to-severe HS, following dose withdrawal or reduction.

MATERIALS & METHODS

- In PIONEER I & II, patients randomized to 40 mg ADAew in the 12-week Period A were re-randomized at week 12 to 40 mg ADAew, 40 mg ADA every-other-week (eow), or placebo for 24 weeks (Period B) (**Figure 1**).
- At week 36 of the trial (week 24 of Period B), patients had the option to enter the OLE and receive 40 mg ADAew. Patients who discontinued during Period B due to loss of treatment response or lack/worsening of disease improvement could also enter the OLE at discontinuation.

Figure 1. Study Schematic of PIONEER I and II, and the OLE



Randomization: stratified by baseline Hurley Stage II vs III (PIONEER I & II) & baseline concomitant antibiotic use (PIONEER II). Re-randomization for Period A ADA patients: stratified by week 12 HiSCR status at entry into Period B, & by baseline Hurley Stage II vs III. Period A: patients started ADA at week 4 after 160 mg (week 0), 80 mg (week 2). Patients receiving placebo in Period A, and ADA or placebo in Period B, were not included in this analysis.
Abbreviations: ADA=adalimumab; HiSCR=Hidradenitis Suppurativa Clinical Response.

Table 1. PIONEER I and II Key Eligibility/Exclusion Criteria

Inclusion	Exclusion
• Adults, anti-TNFα-naïve, diagnosed with HS for ≥1 year prior to baseline	• No prior treatment with anti-TNF agents
• Inadequate response to oral antibiotics for the treatment of HS	• No other active skin disease that could interfere with assessment of HS
• Total abscess and inflammatory nodule (AN) count of ≥3	• Draining fistula count of >20 at baseline
• HS lesions in ≥2 body areas, one of which was Hurley Stage II or III	

- The primary outcome measure was HiSCR (Hidradenitis Suppurativa Clinical Response) defined as a ≥50% reduction in total abscess and inflammatory nodule (AN) count with no increase in abscess and draining fistula counts.
- PIONEER I & II results were pooled. Retreatment was evaluated for patients receiving ADAew in the OLE following withdrawal (placebo) or dose reduction (ADAeow) in Period B.
- The patients in this analysis from PIONEER I & II were intent-to-treat.
- Treatment groups are listed by treatment received in Period A/Period B/OLE.

RESULTS

Table 2. Baseline Patient Characteristics, PIONEER OLE

		ADAew/ew/ew N=88		ADAew/eow/ew N=90		ADAew/pbo/ew N=92	
		n	%	n	%	n	%
Sex	Female	56	63.6	60	66.7	50	54.3
	Male	32	36.4	30	33.3	42	45.7
Race	White	81	92.0	70	77.8	75	81.5
	Black	4	4.5	16	17.8	12	13.0
	Other	3	3.4	4	4.4	5	5.4
BMI,[a] kg/m²	<25 (normal weight)	14	15.9	19	21.1	20	22.0
	25 to <30 (overweight)	23	26.1	23	25.6	17	18.7
	30 to <40 (obese)	40	45.5	35	38.9	42	46.2
	≥40 (morbidly obese)	11	12.5	13	14.4	12	13.2
Nicotine user		52	59.1	55	61.1	48	52.2
Hurley Stage	II	42	47.7	47	52.2	51	55.4
	III	46	52.3	43	47.8	41	44.6
		Median	Range	Median	Range	Median	Range
Age, year		35.5	18-64	36.0	19-63	35.0	20-67
Lesion count	AN	9.0	3-71	9.0	3-78	10.0	3-50
	Draining fistulas	2.0	0-19	2.0	0-20	2.5	0-20
	Abscess	1.0	0-13	2.0	0-14	1.0	0-17
	Inflammatory nodules	7.0	0-69	7.0	2-76	8.0	0-38
Modified Sartorius Score		103.0	158-1093	100.0	139-433	107.0	162-397
Prior HS duration, years		10.3	1.0-40.4	8.5	1.1-32.9	8.2	1.1-43.5
Pain at worst, NRS		4.6	0-9.7	4.7	0-10.0	4.4	0-8.4
DLQI, range 0-30		16.0	2-30	14.5	1-30	14.0	0-30
hsCRP, mg/L		6.5	0.2-189.0	7.8	0.3-104.0	9.1	0.2-95.2

a. Data missing: BMI, ADAew/pbo/ew, n=1.
Abbreviations: ADA=adalimumab; ew=every-week dosing; eow=every-other-week dosing; pbo=placebo; BMI, body mass index; AN=total abscess and inflammatory nodule count; HS=hidradenitis suppurativa; NRS=numerical rating scale; DLQI=Dermatology Life Quality Index score; hsCRP=high-sensitivity C-reactive protein.

Table 3. Patient Status, PIONEER OLE

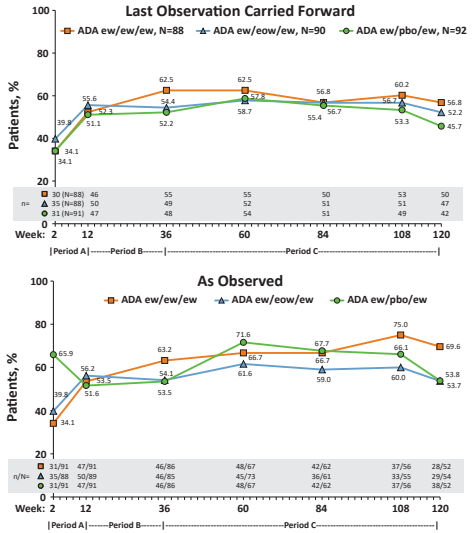
	ADAew/ew/ew N=88		ADAew/eow/ew N=90		ADAew/pbo/ew N=92	
Patient Status	n	%	n	%	n	%
Dosed	88	100	90	100	92	100
Completed study	37	42.0	44	48.9	44	47.8
Discontinued study	51	58.0	46	51.1	48	52.2
Primary reason:						
AE	7	8.0	11	12.2	5	5.4
Lack of efficacy	15	17.0	10	11.1	17	18.5
Withdrew consent	15	17.0	9	10.0	16	17.4
Lost to follow up	7	8.0	11	12.2	8	8.7
Exceeded protocol specified number of interventions	0	0	0	0	1	1.1
Protocol deviations	1	1.1	0	0	0	0
Other	6	6.8	5	5.6	1	1.1

Abbreviations: AE=adverse event

EFFICACY

- Patients sustained response to ADAew throughout PIONEER and the OLE, regardless of whether they experienced dose reduction or dose withdrawal during Period B (week 12-36).
- More patients who remained on ADAew throughout PIONEER and the OLE, achieved response as measured by HiSCR (**Figure 2**).

Figure 2. Patients Achieving HiSCR, n (%), by OLE Dose Groups

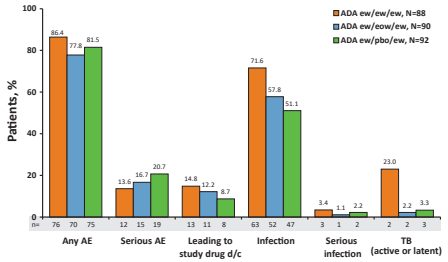


Abbreviations: ADA=adalimumab; ew=every-week dosing; eow=every-other-week dosing; pbo=placebo.

SAFETY

- The rate of any treatment-emergent adverse event (AE) was similar among the treatment groups (**Figure 3**). The rate of serious infections was low, and similar among the treatment groups.

Figure 3. Rate of Treatment-Emergent Adverse Events



Abbreviations: ADA=adalimumab; ew=every-week dosing; eow=every-other-week dosing; pbo=placebo; AE=adverse event; TB=tuberculosis; d/c=discontinued.

- Lymphoma was reported by one patient (ADAew/pbo/ew), non-melanoma skin cancer (NMSC) was reported by one patient (ADAew/pbo/ew), and malignancy other than lymphoma or NMSC, by 2 patients (one ADAew/eow/ew and one ADAew/pbo/ew).
- Serious AE infections for ADAew/ew/ew were reported by 3.4% of patients (cellulitis, n=1; pneumonia, n=2); for ADAew/eow/ew, 1.1% (vulval abscess, n=1), and for ADAew/pbo/ew, 2.2% (cellulitis, n=1; pilonidal cyst, n=1).
- There were no deaths in these 3 groups.

REFERENCES

1. Kimball A, et al. *N Engl J Med*. 2016;375:5.

DISCLOSURES

AKI received honoraria as a consultant and grants as an investigator from Janssen, AbbVie, Amgen, and Novartis and has received fellowship funding from Janssen. **MO** received honoraria from AbbVie for advisory board participation and speaker services, and from AbbVie, Gilead Science, and Crescendo Biosciences for consultant services. Dr. Okun was an AbbVie employee during this study. **GM** received a salary as AbbVie employees, and may have also received stocks and/or stock options.

AbbVie Inc. funded this study and participated in the study design; study research; collection, analysis and interpretation of data; and writing, reviewing and approving of this publication. All authors had access to the data, and participated in the development, review, and approval, and in the decision to submit this publication.

The authors would like to acknowledge Piyalal Karunaratne, former AbbVie employee, for statistical support, and Jody Bennett, employed by AbbVie, for medical writing support in the production of this publication.

CONCLUSIONS

- The optimal long-term strategy for managing HS patients with adalimumab appeared to be continuous weekly dosing, as either a short-term reduction of dose to every-other-week or treatment withdrawal (placebo) was associated with modest loss of long-term response.
- This conclusion is limited by the small number of evaluable patients in this analysis.
- No new safety risks were identified.

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