Impact of Baseline Smoking Status and Body Mass Index in Patients with Hidradenitis Suppurativa Treated with Adalimumab or Placebo in 2 Phase 3 Studies

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INTRODUCTION

- Hidradenitis suppurativa (HS) is a chronic, inflammatory skin disorder associated with painful, deep-seated lesions in apocrine gland-bearing regions of the body[1–4]
- Patients with HS commonly have a higher body mass index (BMI) and a large proportion smoke tobacco, but the effect of these factors on treatment outcomes has been controversial[5]
- Originator adalimumab (ADA) is an anti-tumor necrosis factor monoclonal antibody approved for the treatment of moderate-to-severe HS[6]
  - Results from 2 phase 3, placebo-controlled trials, PIONEER I and PIONEER II, demonstrated the efficacy and safety of ADA[7]

OBJECTIVE

- This post hoc analysis evaluated the impact of baseline tobacco smoking status and BMI on the efficacy and safety of ADA in 2 phase 3, double-blind studies (PIONEER I and PIONEER II)

METHODS

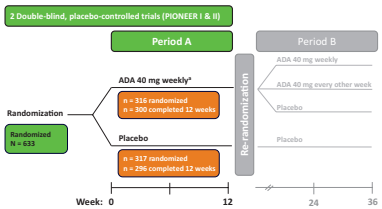
PARTICIPANTS

- Main inclusion criteria
  - Adults (male and female) ≥ 18 years of age, with a diagnosis of HS ≥ 1 year prior to baseline
  - HS lesions present in at least 2 distinct anatomical areas (eg, left and right axilla, or left axilla and left inguinocrural fold), 1 of which was Hurley Stage II or Hurley Stage III
  - Abscess and inflammatory nodule (AN) count ≥ 3, where the AN count equates to the sum of abscess and inflammatory nodules
- Main exclusion criteria
  - Previous anti-tumor necrosis factor therapy or ADA
  - Other active skin disease or condition (eg, bacterial, fungal, or viral infection) that could interfere with assessment of HS
  - At baseline visit, draining fistula count > 20
  - Treatment for HS with oral antibiotics within 28 days of baseline visit (except for PIONEER II subjects on stable doxycycline or minocycline only), or analgesics or prescription topical treatment for HS within 14 days of baseline visit

STUDY DESIGN AND TREATMENT

- Data were integrated from the first 12 weeks (Period A) of 2 phase 3 trials: PIONEER I and II
- In both studies, patients were randomized (1:1) to receive ADA or matching placebo **(Figure 1)**
  - Dose of ADA was 160 mg at week 0, 80 mg at week 2, and 40 mg weekly starting at week 4 for 12 weeks (Period A)
- In PIONEER II, concomitant doxycycline or minocycline up to 100 mg twice daily was permitted if patients took the antibiotic for > 28 days before baseline and maintained a consistent dosing regimen during the study
  - Concomitant antibiotic use was not permitted in PIONEER I

Figure 1. Study Design



[a]Starting at week 4 following 160 mg at week 0 and 80 mg at week 2.
In PIONEER II, patients who received placebo in period A received ADA 40 mg weekly in period B.
This analysis encompasses only the first 12 weeks, as depicted. ADA = adalimumab.

METHODS (CONTINUED)

PATIENT ASSESSMENT

- Patients were assessed in clinic at weeks 0, 2, 4, 8, and 12
- Data from both trials were integrated to evaluate the effect of baseline smoking status (yes or no) or BMI (< 30 or ≥ 30 kg/m^2)
- The primary endpoint in both studies was HS clinical response (HiSCR)
  - Defined as ≥ 50% reduction in AN count with no increase in abscess or draining fistula counts relative to baseline[8]
- Adverse events and overall rates of treatment-emergent adverse events (TEAEs) were also reported

STATISTICAL ANALYSIS

- All randomized patients were included in the integrated efficacy analyses
- Treatment difference for the proportion of patients achieving HiSCR was calculated using the Cochrane-Mantel-Haenszel test (2 tailed, α = .05)
  - Adjusted for study and baseline Hurley stage
- Treatment by subgroup interaction, was calculated using a logistic regression with HiSCR at week 12 as response variable, and treatment, subgroup, Hurley Stage, and treatment by subgroup interaction as factors

RESULTS

PARTICIPANTS: BASELINE SMOKING AND BMI

- This integrated analysis included 633 randomized patients **(Table 1)**
  - Of these, 596 patients completed the first 12 weeks of the study (ADA, n = 300; placebo, n = 296)
  - 2 patients in the placebo group discontinued without receiving a dose
- At baseline, the majority of patients reported smoking or had a BMI ≥ 30 **(Table 1)**

Table 1. Baseline Demographics and Disease Characteristics

Characteristic	ADA (n = 316)	Placebo (n = 317)	Total (N = 633)
Age, years			
Mean (SD)	35.5 (10.4)	37.0 (11.8)	36.2 (11.1)
Sex, n (%)			
Female	199 (63.0)	218 (68.8)	417 (65.9)
Male	117 (37.0)	99 (31.2)	216 (34.1)
Duration of HS, n (median)			
< 9.18 years	163 (51.6)	153 (48.3)	316 (49.9)
≥ 9.18 years	153 (48.4)	164 (51.7)	317 (50.1)
Lesion counts, mean (SD)			
AN	12.4 (10.3)	13.1 (13.0)	12.8 (11.7)
Abscesses	2.4 (3.1)	2.6 (3.5)	2.5 (3.3)
Inflammatory nodules	10.0 (9.2)	10.5 (11.9)	10.3 (10.6)
Non-draining fistulas	5.5 (11.7)	5.9 (8.5)	5.7 (10.2)
Draining fistulas	3.8 (4.7)	3.8 (4.8)	3.8 (4.8)
Hurley Stage, n (%)			
II	166 (52.5)	170 (53.6)	336 (53.1)
III	150 (47.5)	147 (46.4)	297 (46.9)
Modified Sartorius score, mean (SD)	128.6 (109.9)	134.6 (93.2)	131.6 (101.8)
BMI, kg/m^2, N (%)			
< 30	133 (42.1)	113 (35.6)	246 (38.9)
≥ 30	182 (57.6)	202 (63.7)	384 (60.7)
Missing	1 (0.3)	2 (0.6)	3 (0.5)
Smoking Status, N (%)			
Yes	186 (58.9)	201 (63.4)	387 (61.1)
No	130 (41.1)	115 (36.3)	245 (38.7)
Unknown	0 (0)	1 (0.3)	1 (0.2)

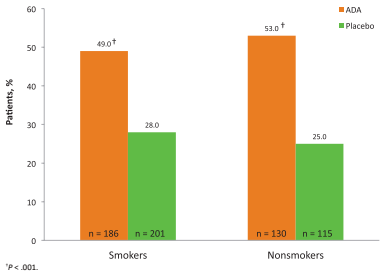
ADA = adalimumab; AN = sum of inflammatory nodules and abscesses; BMI = body mass index; HS = hidradenitis suppurativa; SD = standard deviation.

RESULTS (CONTINUED)

ACHIEVEMENT OF HiSCR BY SMOKING STATUS

- Among those patients who smoked, a significantly greater proportion of patients who received ADA achieved HiSCR compared with patients who received placebo (91/186 vs 56/201, respectively; $P < .001$) **(Figure 2)**
- Among nonsmokers, a significantly greater percentage of patients who received ADA achieved HiSCR compared with patients who received placebo (69/130 vs 29/115, respectively; $P < .001$) **(Figure 2)**
- The treatment effect is consistent across smoking subgoups with no significant treatment-by-subgroup interactions ($P = .343$)

Figure 2. Achievement of HiSCR in Both Smokers and Nonsmokers Who Received ADA

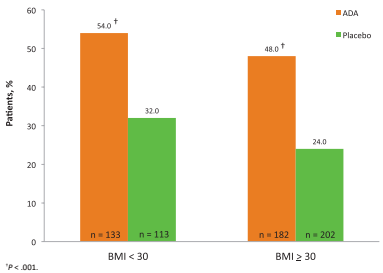


†P < .001.

ACHIEVEMENT OF HiSCR BY BMI

- For patients with BMIs < 30, HiSCR was achieved by a significantly greater proportion of patients who received ADA compared with placebo (72/133 vs 36/113, respectively; $P < .001$) **(Figure 3)**
- For patients with BMIs ≥ 30, HiSCR was achieved by significantly more ADA-treated patients when compared with placebo (88/182 vs 48/202, respectively; $P < .001$) **(Figure 3)**
- The treatment effect is consistent across BMI subgroups with no significant treatment-by-subgroup interactions ($P = .522$)

Figure 3. Achievement of HiSCR in Patients with BMI < 30 and BMI ≥ 30 Who Received ADA



†P < .001.

TREATMENT-EMERGENT ADVERSE EVENTS

- The most frequently reported TEAEs in the ADA population were hidradenitis, followed by headache, upper respiratory tract infections, and nasopharyngitis
- Patients who received ADA reported fewer TEAEs than patients who received placebo, regardless of smoking status **(Table 2)** or BMI category **(Table 3)**
- Overall rates of TEAEs were similar in patients who received ADA, regardless of smoking status or BMI

Table 2. Treatment-Emergent Adverse Event Rates in Smokers and Nonsmokers

	Yes		No	
Characteristic	ADA (n = 186) n (%)	Placebo (n = 201) n (%)	ADA (n = 130) n (%)	Placebo (n = 113) n (%)
Any AE	105 (56.5)	135 (67.2)	70 (53.8)	67 (59.3)
Any SAE	4 (2.2)	7 (3.5)	2 (1.5)	4 (3.5)
Any AE leading to discontinuation of study drug	4 (2.2)	2 (1.0)	1 (0.8)	8 (7.1)
Any Severe AE	11 (5.9)	15 (7.5)	6 (4.6)	4 (3.5)
Any infection	50 (26.9)	68 (33.8)	29 (22.3)	28 (24.8)
Any serious infection	1 (0.5)	1 (0.5)	1 (0.8)	1 (0.9)

AE = adverse event; SAE = serious adverse event.

Table 3. Treatment-Emergent Adverse Event Rates by BMI Category (< 30 and ≥ 30)

	< 30		≥ 30	
Characteristic	ADA (n = 133) n (%)	Placebo (n = 113) n (%)	ADA (n = 182) n (%)	Placebo (n = 200) n (%)
Any AE	70 (52.6)	64 (56.6)	105 (57.7)	138 (69.0)
Any SAE	2 (1.5)	3 (2.7)	4 (2.2)	8 (4.0)
Any AE leading to discontinuation of study drug	2 (1.5)	5 (4.4)	3 (1.6)	5 (2.5)
Any severe AE	6 (4.5)	7 (6.2)	11 (6.0)	12 (6.0)
Any infection	35 (26.3)	30 (26.5)	44 (24.2)	65 (32.5)
Any serious infection	1 (0.8)	1 (0.9)	1 (0.5)	1 (0.5)

AE = adverse event; SAE = serious adverse event.

CONCLUSIONS

- Patients with HS who received treatment with ADA had a greater clinical response than patients who received placebo, irrespective of baseline smoking status or BMI
  - The clinical response observed with ADA was not affected by smoking status or BMI
  - Patients may not have appropriately declared themselves as smokers, which may have affected the proportion of smokers who achieved clinical response
- Overall rates of TEAEs were similar in patients who received ADA, regardless of smoking status or BMI

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DISCLOSURES

A Garg has served as a consultant for AbbVie Inc., Eli Lilly, Janssen, and Pfizer. **H van der Zee** has served as a consultant for AbbVie and InflaRx. **Z Geng** and **GD Mulder** are full-time employees of AbbVie, and may own stock and/or stock options. AbbVie, funded this study and participated in the study design, study research, data collection, analysis and interpretation of data, and writing, reviewing, and approving this poster for presentation. All authors had access to the data; participated in the development, review, and approval of the poster; and agreed to submit the abstract and subsequent poster to EADV for consideration. Editorial assistance, funded by AbbVie, provided by Kristy A Grabowski, PhD, of JB Ashtin.

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