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Placebo responders with moderate-to-severe hidradenitis suppurativa experience declines in inflammation as measured by C-reactive protein: a post hoc analysis of two double-blinded, randomized-controlled trials

Introduction

Hidradenitis suppurativa (HS) is a chronic inflammatory disorder characterized by inflamed nodules, abscesses, and tunnels. The Hidradenitis Suppurativa Clinical Response (HiSCR) is defined as a 50% reduction in nodule and abscess counts, without an increase in fistula or abscess counts.[1] High placebo response rates occur in some studies using HiSCR, which may result from underlying disease variability or intrarater inconsistency.[2,3] Prior research describes an association between the severity of skin disease and C-reactive protein (CRP) in patients with HS.[4] We studied whether patients who received placebo and achieved HiSCR had corresponding improvements in CRP, which could support the hypothesis that placebo responders have improvements in systemic inflammation that mirror improvements in their skin disease.

Methods

Clinical trial data from 2 phase III, double-blinded, randomized-controlled trials (PIONEER I and PIONEER II), as previously described, were obtained from Vivli, Inc. (Boston, Massachusetts).[5] We analyzed lesion counts and laboratory data between baseline and week 12. Statistical analyses were performed in RStudio (Boston, Massachusetts, version 1.4.1717).

Results

At trial initiation, 297 patients and 293 patients received adalimumab and placebo, respectively. Complete lesion count and laboratory data at the primary endpoint were available for 297 adalimumab recipients and 289 placebo recipients. Adalimumab recipients, when compared to placebo recipients, had significant decreases in CRP (–42.7%, interquartile range [IQR]: –65.1% to 4.26% vs. 4.35%, IQR: –28.8% to –53.8%, $P < .001$, Wilcoxon rank sum) and abscess counts (–58.3%, IQR: –83.3% to –16.7% vs. –25.0%, IQR: –60.0% to 13.3%, $P < .001$, Wilcoxon rank sum). Among all placebo recipients, 81 (27.6%) achieved HiSCR (Table 1). Placebo responders had lower nodules counts, Hurley scores, and International Hidradenitis Suppurativa Severity scores at baseline and median CRP levels (5.3 mg/L, IQR: 2.7–13.2 mg/L and 10.0 mg/L, IQR: 4.6–25.0 mg/L, respectively, $P = .001$, Wilcoxon rank sum). Placebo responders had modest declines in CRP compared to placebo nonresponders (–6.67%, IQR: –35.1% to 34.8% vs. 9.36%, IQR: –26.4% to 66.9%, $P = .0287$, Wilcoxon rank sum, one-sided test). Placebo recipients appeared to have a more normal distribution of improvement in nodules and abscesses and CRP when compared to adalimumab-treated groups (Fig. 1).

Discussion

In this post hoc analysis, placebo recipients who responded per HiSCR showed spontaneous modest improvement in systemic inflammation as measured by CRP. This is consistent with the hypothesis that patients with HS experience real variation, including improvement in their skin disease. The use of more stringent endpoints, such as the HiSCR 75, may reduce the rate of placebo responders.

Adalimumab recipients showed more uniform improvements in CRP regardless of clinical improvement, likely because of the medicine's effect on systemic inflammation. Our study is limited by the fact that HiSCR does not include assessments of draining tunnels.

Nonetheless, our finding that placebo responders had less severe disease and a lower CRP, relative to placebo nonresponders, complements prior research, describing how patients with less severe disease are more likely to clinically improve both spontaneously and in response to treatment.

What is known about this subject in regard to women and their families?

- Hidradenitis suppurativa is a chronic inflammatory disorder that presents with inflamed nodules, abscesses, and tunnels in the intertriginous areas.
- The disease disproportionately affects women and significantly impacts the quality of life of patients and their family members.

What is new from this article as messages for women and their families?

- Patients with hidradenitis suppurativa have a high systemic inflammatory burden that can be improved with treatment.
- Delays in diagnosis are common in hidradenitis suppurativa and since patients can benefit from systemic therapy on multiple health dimensions they should be encouraged to seek treatment.

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Table 1

Baseline characteristics of patients who received placebo by response to treatment

Characteristic	Total patients	Did not achieve HiSCR	Achieved HiSCR	*P* value
Participants, *n* (%)	293 (100)	212 (72.4)	81 (27.6)	
CRP, mg/L, median (IQR)	9.2 (3.8–23.1)	10.0 (4.6–25.0)	5.3 (2.7–13.2)	.001*
Sex, *n* (%)				
Female	202 (68.9)	141 (66.5)	61 (75.3)	.19
Male	91 (31.1)	71 (33.5)	20 (24.7)	
Race/ethnicity, *n* (%)				
Asian	7 (2.4)	6 (2.8)	1 (1.2)	.67
Black	42 (14.3)	31 (14.6)	11 (13.6)	
White	232 (79.2)	165 (77.8)	67 (82.7)	
Other	12 (4.1)	10 (4.7)	2 (2.5)	
Family history, *n* (%)	67 (22.9)	49 (23.1)	18 (22.2)	.99
BMI, kg/m^2, mean ± SD	33.7 ± 8.1	34.2 ± 7.9	32.3 ± 8.6	.08
Age, y, mean ± SD	37.1 ± 11.8	37.6 ± 12.1	35.8 ± 11.0	.22
Hurley score, *n* (%)				
2	161 (54.9)	106 (50.0)	55 (67.9)	.008*
3	132 (45.1)	106 (50.0)	26 (32.1)	
IHS4 score, median (IQR)	22 (11–40)	24 (13–43)	14 (8–27)	<.001*
Total number of abscesses and inflammatory nodules, median (IQR)	9 (5–16)	11 (6–17)	8 (5–13)	.016*
Total number of abscesses, median (IQR)	1 (0–3)	1 (1–3)	1 (1–3)	.18
Total number of inflammatory nodules, median (IQR)	7 (4–13)	7.5 (4–14)	6 (4–10)	.05*
Total number of draining fistulas, median (IQR)	2 (0–5)	2 (0–6)	1 (0–3)	<.001*

P values were calculated with χ^2 for categorical variables, with Welch 2 sample *t*-test for normally distributed continuous data, and with Wilcoxon rank sum test for nonnormally distributed continuous data. BMI, body mass index; CRP, C-reactive protein; HiSCR, Hidradenitis Suppurativa Clinical Response; IHS4, International Hidradenitis Suppurativa Severity Score System; IQR, interquartile range; SD, standard deviation.

* Statistically significant.

Conflicts of interest

The authors made the following disclosures: S.J.G. reports prior paid employment from Merck & Co., Inc. The other authors have no conflicts of interest.

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Author contributions

SJG takes responsibility for the integrity and accuracy of the data analysis. SJG, MLP, and ABK participated in design, writing, and review of the manuscript.

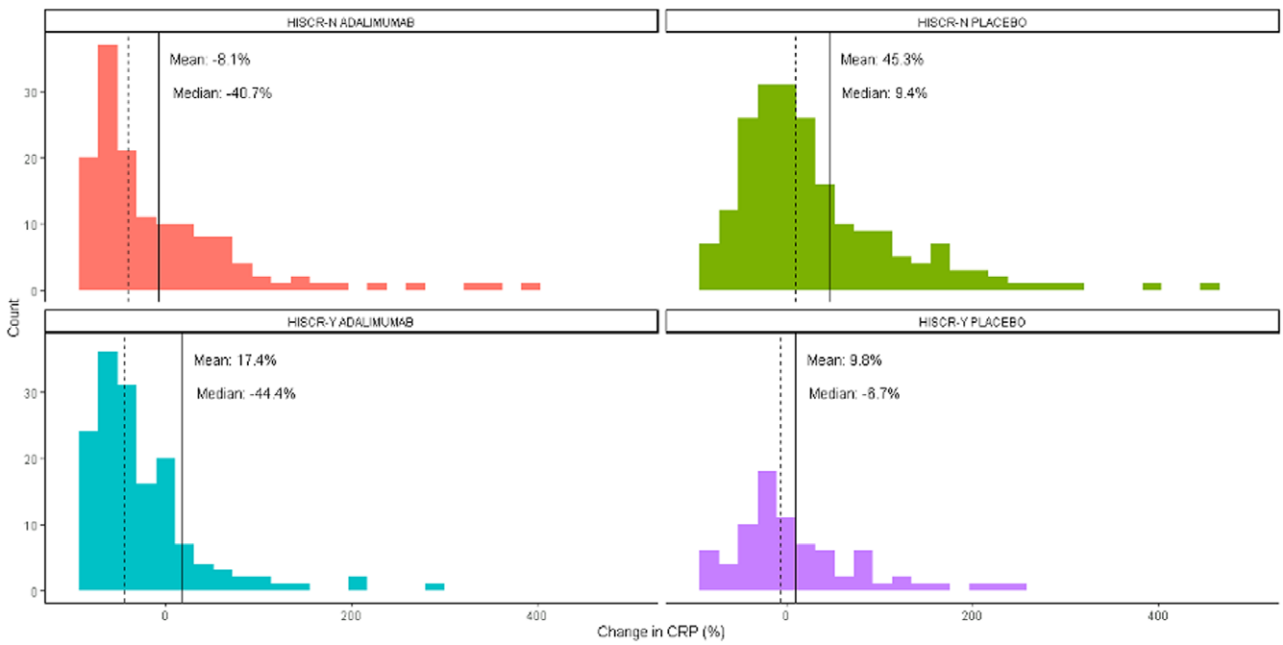

Fig. 1. Percent change in C-reactive protein by treatment group and response.

Data availability

This article is based on research using data from the data contributors AbbVie, which has been made available through Vivli, Inc. Vivli has not contributed to or approved, and is not in any way responsible for, the contents of this publication.

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