Original Investigation

Safety and Efficacy of Anakinra in Severe Hidradenitis Suppurativa
A Randomized Clinical Trial

Vassiliki Tzanetakou, MD; Theodora Kanni, MD; Sophia Giatrakou, MD; Alexandros Katoulis, MD, PhD; Evangelia Papadavid, MD, PhD; Mihai G. Netea, MD, PhD; Charles A. Dinarello, MD, PhD; Jos W. M. van der Meer, MD, PhD; Dimitrios Rigopoulos, MD, PhD; Evangelos J. Giamarellos-Bourboulis, MD, PhD

IMPORTANCE Hidradenitis suppurativa (HS) is a common skin disorder in which excessive inflammation is believed to have an important role. There is no specific therapy for HS.

OBJECTIVE To investigate the safety and efficacy of the anti-inflammatory biological therapy anakinra in HS.

DESIGN, SETTING, AND PARTICIPANTS Double-blind, randomized, placebo-controlled clinical trial with a 12-week treatment phase and a 12-week follow-up phase. The setting was Attikon University General Hospital, a tertiary care institution in Athens, Greece. Participants were 20 patients with Hurley stage II or III HS. The study and the analysis were conducted between March 1, 2012, and February 28, 2014.

INTERVENTIONS Patients were randomized to receive injections from identical syringes containing placebo or anakinra subcutaneously once daily for 12 weeks. Peripheral blood mononuclear cells were isolated and stimulated for cytokine production before the beginning of treatment and at week 12 (the end of treatment) and week 24.

MAIN OUTCOMES AND MEASURES The primary endpoint was the effect of anakinra on HS disease severity. Secondary endpoints were the time to a new exacerbation and the production of cytokines.

RESULTS Among the 20 trial participants, 10 each were randomized to the group to receive anakinra or the placebo group. The mean (SD) ages were 42.8 (13.8) and 36 (11.3) years in the anakinra and placebo groups, respectively. The disease activity score was decreased at the end of treatment in 20% (2 of 10) of the placebo arm compared with 67% (6 of 9) of the anakinra arm (P = .04). Hidradenitis suppurativa clinical response at 12 weeks was achieved in 30% (3 of 10) of the placebo arm and in 78% (7 of 9) of the anakinra arm (P = .04). The production of interferon-γ by peripheral blood mononuclear cells in the anakinra arm was decreased, and the production of interleukin 22 was increased. The time to a new HS exacerbation was prolonged in the anakinra arm by log-rank test (log rank, 6.137; P = .01). No serious adverse events were reported.

CONCLUSIONS AND RELEVANCE Anakinra has the potential to be an effective and well-tolerated treatment for HS. Inhibition of interleukin 1 is a promising treatment strategy.

TRIAL REGISTRATION clinicaltrials.gov Identifier: NCT01558375

Published online November 18, 2015.
Hidradenitis suppurativa (HS) is a chronic disorder of skin areas rich in apocrine glands. Nodules appear in the affected locations, where they progressively become inflamed and rupture, with the release of pus. This process occurs repeatedly, leading to sinus tract formation and scarring. The disease course creates a frustrating situation for patients and their physicians. Traditional treatments include at least a 10-week course of antibiotics and surgical excision.

The mean Dermatology Life Quality Index (DLQI) in patients with HS is 8.9, which is among the highest for chronic inflammatory skin disorders. Hidradenitis suppurativa indiscriminately affects the global population. Although the exact epidemiology is unknown, the point prevalence is reported to range from 1% to 4%. A large epidemiological survey in France reported a 0.97% disease prevalence of HS.

The precise origin of HS is unknown. Smoking, dietary habits, and genetic predisposition have all been linked to HS. Hypotheses implicating autoimmune inflammatory mechanisms or specific deficiencies of the immune system in the pathogenesis of HS have been proposed. That excessive inflammation has an important role in HS was reinforced by the finding of positive therapeutic result after administration of tumor necrosis factor (TNF) antagonists in prospective studies.

Anakinra is a recombinant interleukin 1 (IL-1) receptor antagonist. It blocks the biological activity of naturally occurring IL-1 (IL-1α and IL-1β) by competitively inhibiting the binding of both IL-1α and IL-1β to the IL-1 type I receptor. Interleukin 1 is produced in response to various microbial and nonmicrobial stimuli and is a major mediator of the inflammatory response. The biological properties of anakinra and clinical and laboratory data suggesting overinflammation in HS prompted our investigation of whether the use of anakinra would be a novel safe and efficacious approach in the management of HS.

Methods

Study Population

This study was a double-blind, randomized, placebo-controlled prospective clinical trial conducted between March 1, 2012, and February 28, 2014 (with similar dates for the analysis), by the Fourth Department of Internal Medicine and the Second Department of Dermatology and Venereology, University of Athens Medical School, at Attikon University General Hospital, a tertiary care institution in Athens, Greece. The trial had an initial 12-week treatment phase and a 12-week follow-up phase. The study was approved by the Attikon Hospital Ethics Committee, by the National Organization of Medicine, and by the National Ethics Committee.

The study inclusion criteria were (1) written informed consent provided by the patient, (2) age 18 years or older, (3) diagnosis of HS, and (4) Hurley stage II or III HS. Diagnosis of HS was based on the following criteria by the second international symposium organized by the Hidradenitis Suppurativa Foundation:

1. Disease onset after puberty
2. Involvement of at least 2 areas of the skin rich in apocrine glands, including left or right axillae, left or right inframammary areas, left or right femoral-inguinal fold, and left or right gluteal area (any other affected areas were taken into account during patient follow-up but were not considered in the study inclusion criteria); and
3. History of recurrent drainage of pus from the affected areas.

Hurley stage II HS was defined as recurrent abscesses with sinus tracts and scarring involving single or multiple widely separated lesions. Hurley stage III HS was defined as diffuse or almost diffuse involvement or multiple interconnected tracts and abscess.

Twelve study exclusion criteria were applied. These included (1) history of systemic lupus erythematosus, rheumatoid arthritis, or seronegative inflammatory arthritis; (2) prior administration of any type of TNF-blocking therapy over the last 6 months; (3) administration of any live (attenuated) vaccine over the last 4 weeks; (4) history of recurrent vein thrombosis or embolism compatible with antiphospholipid syndrome; (5) any present or smoldering infection; (6) hepatic dysfunction, defined as any value of transaminases, γ-glutamyl transpeptidase, or bilirubin greater than 2 times the upper normal limit; (7) history of hematological or solid tumor malignancy, arterial hypertension, liver cirrhosis, human immunodeficiency virus infection, or hepatitis B or C infection; (8) history of episodes mimicking demyelinating disorders or a definite diagnosis of multiple sclerosis; (9) any serum creatinine level above 1.5 mg/dL (to convert creatinine level to micromoles per liter, multiply by 88.4); (10) corticosteroid use, defined as daily intake of prednisone or equivalent exceeding 1 mg/kg over the last 3 weeks; (11) neutropenia, defined as less than 1000 neutrophils per microliter; and (12) pregnancy or lactation.

Study Procedures

Once a patient was considered eligible for the study, the following screening procedures were performed: (1) history and physical examination; (2) skin tuberculin test; (3) chest radiograph; (4) serology for human immunodeficiency virus and hepatitis virus B and C; and (5) testing for white blood cell
count, serum creatinine level, and liver biochemistry. Patients selected for enrollment were randomized at a 1:1 ratio to receive placebo or anakinra subcutaneously once daily for 12 weeks. The randomized sequence was generated by an independent biostatistician. Anakinra was provided in single-use, prefilled glass syringes with 27-gauge needles. The syringes contained 100 mg of anakinra in a volume of 0.67 mL. Identical placebo syringes contained 0.67 mL of sterile water for injection. The placebo and anakinra syringes were identical in appearance to ensure masking. After treatment, patients were followed up from week 13 to week 24. The patients and investigators were masked to the administered treatment. Once the follow-up of the last enrolled patient was completed, masking was lifted.

At the baseline visit, clinical characteristics of the patients were recorded, including demographics, weight, height, time since HS onset, and involved areas. Patient visits were scheduled at weeks 0, 4, 8, 12, 16, 20, and 24. Six evaluations were performed at the study visits. First, patients provided a self-assessment of their disease severity using a visual analog scale (VAS) ranging from 0 to 100 mm, where 0 represents no disease activity and 100 represents the worst activity they ever had. Patients provided one score for their overall disease impression and another score for pain. Second, patients completed the DLQI at weeks 0, 12, and 24. Third, the investigators counted the number of fistulas, nodules, abscesses, and scars at each affected area, and they scored the degree of inflammation from 0 to 3, where 0 represents absent, 1 represents minimal, 2 represents moderate, and 3 represents severe.

### Table. Baseline Characteristics of Patients Enrolled in the Study

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Placebo (n = 10)</th>
<th>Anakinra (n = 9)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>5</td>
<td>5</td>
<td>&gt; .99</td>
</tr>
<tr>
<td>Female</td>
<td>5</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Age, mean (SD), y</td>
<td>36.0 (11.3)</td>
<td>42.8 (13.8)</td>
<td>.26</td>
</tr>
<tr>
<td>Body mass index, mean (SD)</td>
<td>27.9 (6.8)</td>
<td>27.8 (5.1)</td>
<td>.98</td>
</tr>
<tr>
<td>Family history of HS, No. (%)</td>
<td>5 (50)</td>
<td>3 (33)</td>
<td>.65</td>
</tr>
<tr>
<td>Smoker, No. (%)</td>
<td>8 (80)</td>
<td>8 (88)</td>
<td>&gt; .99</td>
</tr>
<tr>
<td>Staphylococcus aureus nasal carriage, No. (%)</td>
<td>0</td>
<td>0</td>
<td>&gt; .99</td>
</tr>
<tr>
<td>Hypothyroidism, No. (%)</td>
<td>2 (20)</td>
<td>2 (22)</td>
<td>&gt; .99</td>
</tr>
<tr>
<td>Time since HS onset, mean (SD), y</td>
<td>11.1 (6.8)</td>
<td>12.3 (6.7)</td>
<td>.70</td>
</tr>
<tr>
<td>Exacerbations per month, median (range)</td>
<td>2 (1-16)</td>
<td>2 (1-10)</td>
<td>.31</td>
</tr>
<tr>
<td>Past treatment for HS, No. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incision and drainage</td>
<td>3 (30)</td>
<td>3 (33)</td>
<td>.71</td>
</tr>
<tr>
<td>Debridement</td>
<td>1 (10)</td>
<td>1 (11)</td>
<td></td>
</tr>
<tr>
<td>Antibiotic</td>
<td>9 (90)</td>
<td>6 (67)</td>
<td>.56</td>
</tr>
<tr>
<td>Anti–tumor necrosis factor</td>
<td>3 (30)</td>
<td>4 (44)</td>
<td>.65</td>
</tr>
<tr>
<td>Affected skin area, No. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Axillae</td>
<td>7 (70)</td>
<td>5 (56)</td>
<td>.65</td>
</tr>
<tr>
<td>Submammary or inframammary fold</td>
<td>2 (20)</td>
<td>2 (22)</td>
<td>&gt; .99</td>
</tr>
<tr>
<td>Inguinal and crural fold</td>
<td>7 (70)</td>
<td>9 (100)</td>
<td>.21</td>
</tr>
<tr>
<td>Perianal</td>
<td>2 (20)</td>
<td>2 (22)</td>
<td>&gt; .99</td>
</tr>
<tr>
<td>Gluteal</td>
<td>4 (40)</td>
<td>4 (44)</td>
<td>&gt; .99</td>
</tr>
<tr>
<td>Scrotum</td>
<td>2 (20)</td>
<td>1 (11)</td>
<td>&gt; .99</td>
</tr>
<tr>
<td>Pubic</td>
<td>1 (10)</td>
<td>3 (33)</td>
<td>.30</td>
</tr>
<tr>
<td>Lesion count, median (range)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inflammatory nodule</td>
<td>4 (3-10)</td>
<td>6 (4-23)</td>
<td>.55</td>
</tr>
<tr>
<td>Noninflammatory nodule</td>
<td>3 (0-13)</td>
<td>1 (0-23)</td>
<td>.19</td>
</tr>
<tr>
<td>Draining fistula</td>
<td>2 (0-23)</td>
<td>3 (1-40)</td>
<td>.36</td>
</tr>
<tr>
<td>Nondraining fistula</td>
<td>0 (0-1)</td>
<td>0 (0-7)</td>
<td>.73</td>
</tr>
<tr>
<td>Scar</td>
<td>6 (0-102)</td>
<td>0 (0-19)</td>
<td>.11</td>
</tr>
<tr>
<td>Hurley stage of HS, No.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>4</td>
<td>6</td>
<td>.37</td>
</tr>
<tr>
<td>III</td>
<td>6</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>HS severity, mean (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DLQI</td>
<td>14.3 (8.4)</td>
<td>20.7 (5.9)</td>
<td>.08</td>
</tr>
<tr>
<td>VAS score</td>
<td>55.0 (20.3)</td>
<td>67.0 (19.8)</td>
<td>.51</td>
</tr>
<tr>
<td>VAS score for pain</td>
<td>60.5 (21.7)</td>
<td>54.4 (22.9)</td>
<td>.65</td>
</tr>
<tr>
<td>Disease activity score</td>
<td>113.4 (94.9)</td>
<td>186.9 (112.9)</td>
<td>.14</td>
</tr>
<tr>
<td>Sartorius score</td>
<td>82.0 (58.9)</td>
<td>104.6 (54.2)</td>
<td>.40</td>
</tr>
</tbody>
</table>

Abbreviations: DLQI, Dermatology Life Quality Index; HS, hidradenitis suppurativa; VAS, visual analog scale.

* Calculated as weight in kilograms divided by height in meters squared.
Patients with Hurley stage II or III hidradenitis suppurativa were randomized to placebo (n = 10) or anakinra (n = 9) for 12 weeks, followed by another 12 weeks of follow-up. The effect of anakinra treatment on disease severity was compared over the weeks of treatment and follow-up using the disease activity score, Sartorius score, visual analog scale (VAS) score, VAS score for pain, and Hidradenitis Suppurativa Clinical Response (HiSCR). *P* values are for comparisons between the 2 treatment arms. Only statistically significant differences are noted.

**Figure 2. Change in Hidradenitis Suppurativa Severity Over Time**

- **Disease activity score**
  
  - Placebo: Orange line
  - Anakinra: Blue line
  - *P* = .07

- **Sartorius score**
  
  - Placebo: Orange line
  - Anakinra: Blue line

- **VAS score**
  
  - Placebo: Orange line
  - Anakinra: Blue line

- **VAS score for pain**
  
  - Placebo: Orange line
  - Anakinra: Blue line

- **HiSCR**
  
  - Placebo: Orange line
  - Anakinra: Blue line
  - *P* = .001
  - *P* = .04
  - *P* = .28

Patients with Hurley stage II or III hidradenitis suppurativa were randomized to placebo (n = 10) or anakinra (n = 9) for 12 weeks, followed by another 12 weeks of follow-up. The effect of anakinra treatment on disease severity was compared over the weeks of treatment and follow-up using the disease activity score, Sartorius score, visual analog scale (VAS) score, VAS score for pain, and Hidradenitis Suppurativa Clinical Response (HiSCR). *P* values are for comparisons between the 2 treatment arms. Only statistically significant differences are noted.
baseline visit. The HiSCR was not proposed as a scoring system in increase in abscesses or draining fistulas compared with the lesion count (sum of abscesses and inflammatory nodules) and was defined as at least a 50% reduction in the inflammatory degree of individual lesions performed at each study visit.

Committee. Because it has been developed as a salient scoring system for HS, it was applied retrospectively based on the count of individual lesions performed at each study visit.

Laboratory Investigation
Peripheral blood mononuclear cells (PBMCs) were isolated after centrifugation of the obtained venous blood sample over a Ficoll-Hypaque gradient and stimulated for the production of TNF, IL-1β, IL-6, IL-10, IL-17, IL-22, and interferon-γ (IFN-γ). These methods had been reported in detail elsewhere. The HiSCR was not proposed as a scoring system for HS when this trial was submitted for approval by the National Organization for Medicines and by the National Ethics Committee. Because it has been developed as a salient scoring system for HS, it was applied retrospectively based on the count of individual lesions performed at each study visit.

Study End Points
The primary end point was the safety and efficacy of anakinra in patients with Hurley stage II or III HS based on decreased disease activity scores from the baseline visit to the end of treatment. Furthermore, the 2 study arms were compared regarding their DLQI, VAS score, development of serious adverse events, and HS severity (disease activity score, Sartorius score, and HiSCR) over the course of their visits.

Secondary end points were the effects of anakinra on the time to a new exacerbation of HS and on the ex vivo function of PBMCs. This latter effect was defined by the difference in cytokine production by PBMCs between the 2 study arms over the course of the study visits.

Power of the Study
The study was powered for the primary end point, aiming to disclose a significant difference between the 2 study arms according to the disease activity score used by the investigators of a previous trial. Based on the hypothesis that 10% of the placebo arm and 60% of the anakinra arm would have a decreased disease activity score at the end of treatment, 0.75 power at a 1-sided 0.1 level of significance was needed, with 10 patients randomized to each arm. Under these conditions, the actual computed power is 0.8, and the actual α level is .05.

Statistical Analysis
Comparisons of baseline demographic characteristics between the study arms were performed by the t test for quantitative variables and by the Fisher exact test for qualitative variables. The number of patients who had a decreased disease activity score at the end of treatment from baseline was compared between the study arms by the Fisher exact test. Percentage changes in the disease activity score, Sartorius score, VAS, and DLQI at each visit from the baseline visit at week 0 were calculated and expressed as the mean (SE). For each enrolled patient, curves of the changes over time in the disease activity score, Sartorius score, and VAS were plotted. The area under the curve was calculated by the linear trapezoidal rule. Comparisons of areas under the curve between the study arms were performed by the Mann-Whitney test. Comparisons of DLQI questions between the study arms were also performed by the Mann-Whitney test. Comparisons of the HiSCR between the study arms were performed by the Fisher exact test. The time to a new exacerbation was compared between the study arms by the log-rank test. Cytokine production was expressed as the mean (SE) and was compared by the Mann-Whitney test. P < .05 was considered statistically significant.

Results
Study Population
The study inclusion was discontinued when 20 patients were enrolled, including 10 patients randomized to the placebo arm and 10 patients randomized to the anakinra arm. No patient was taking oral corticosteroids. Because 1 patient randomized to anakinra treatment was lost to follow-up, the per-protocol analysis included 10 patients in the placebo arm and 9 patients in the anakinra arm (Figure 1). The 2 study arms did not differ in demographic characteristics or disease severity (Table).
Shown are concentrations at week 0 (baseline), week 12 (the end of treatment), and week 24 (the end of follow-up). Peripheral blood mononuclear cells of patients randomized to placebo (n = 10) and to anakinra (n = 9) were isolated and stimulated with bacterial lipopolysaccharide (LPS), phytohemagglutinin (PHA), and heat-killed isolates of *Candida albicans* (*C* *albicans*) and of *Staphylococcus aureus* (*S* *aureus*). Only statistically significant differences are noted.

\( ^a \ P = .03 \) vs baseline.

\( ^b \ P = .046 \) vs baseline.

\( ^c \ P = .02 \) vs placebo.

\( ^d \ P = .04 \) vs placebo.

\( ^e \ P = .02 \) vs baseline.
Primary End Point
The disease activity score was decreased at the end of treatment (week 12) in 2 of 10 placebo-treated patients (20%) compared with in 6 of 9 anakinra-treated patients (67%) (P = .04). The change over time in the disease activity score was only slightly decreased among patients treated with placebo compared with patients treated with anakinra (P = .07). The Sartorius score and VAS score did not differ over time between the study arms (Figure 2). The components of the HiSCR were prospectively counted as described in the trial protocol (Supplement 1), and the HiSCR was retrospectively assessed. At week 12, the HiSCR was positive in 30% (3 of 10) of patients randomized to placebo compared with in 78% (7 of 9) of patients randomized to anakinra (P = .04). The HiSCR was positive in 33% (3 of 9) of patients randomized to placebo and in 10% (1 of 10) of patients randomized to anakinra at week 24 (P = .28).

The change in overall DLQI at weeks 12 and 24 from baseline at week 0 was not different between the study arms. However, the results differed for question 7 (related to clothing) and for question 9 (related to sexual intercourse), demonstrating improvement in patients treated with anakinra. However, these differences were not statistically significant (P = .05 for question 7 and P = .06 for question 9) (eFigure 1 in Supplement 2).

Characteristic photographs of 2 patients with considerable improvement in skin lesions after anakinra treatment are shown in eFigure 2 in Supplement 2. The use of anakinra in patients with HS was safe. No serious adverse events were recorded, and no statistically significant differences in adverse events were observed between the study arms. One patient randomized to the anakinra arm discontinued treatment after 4 weeks because of diarrhea. Another patient manifested swelling at the injection site, and a third patient developed vaginal candidiasis. Among the placebo arm, sinusitis was recorded in 1 patient.

Secondary End Points
Compared with the placebo arm, the time to a new HS exacerbation was significantly prolonged in the anakinra arm (P = .01). This result is shown in Figure 3.

Cytokine production by PBMCs is shown in Figure 4. The greatest differences were found for IFN-γ, which was decreased in the anakinra arm, and for IL-22, which was increased in the anakinra arm. Moreover, the production of TNF and of IFN-γ was increased during the follow-up period in the placebo arm but not in the anakinra arm. The production of IL-22 was increased from baseline after stimulation with phytohemagglutinin in 6 of 10 patients with a positive HiSCR at week 12 and in 1 of 9 patients with a negative HiSCR at week 12 (P = .06).

Discussion
To our knowledge, the present study is the first double-blind, randomized trial assessing the safety and efficacy of anakinra in HS. Using the disease activity score and the newly proposed HiSCR, the results indicate that anakinra attenuates the severity of HS. Most of the clinical efficacy of anakinra was shown from week 8 onward. The Sartorius score was not helpful in demonstrating this clinical benefit, probably because it includes scoring for nondraining fistulas. The benefit of treatment with anakinra was prolonged, with a significantly longer time to a new exacerbation of HS during the 12-week follow-up period. Therefore, there was no sign of setback after discontinuing anakinra, although the disease activity score gradually rose after 16 weeks. This finding differs from an observation in the open-label study by Leslie et al, who reported rebound of HS in 4 patients after anakinra cessation. In addition, the literature on blockade of IL-1 in HS describes 6 patients, 3 of whom responded to the treatment. To date, the most effective treatment for HS has been anti-TNF therapy. Studies have been published on 3 anti-TNF preparations (etanercept, infliximab, and adalimumab). It is clear from these studies that not all patients respond to these interventions. In the first large trial of weekly treatment with the monoclonal antibody adalimumab, considerable efficacy was shown. Although the primary end point based on physicians' global assessment score change demonstrated a treatment benefit of 17.9% in the adalimumab group compared with 3.9% in the placebo group, patients treated with adalimumab experienced notable improvement in all secondary study outcomes (ie, reduced total number of inflammatory nodules and decreased DLQI and modified Sartorius score). While the size of the present study was limited, the response rate was approximately 44% (4 of 9) based on differences between the placebo and anakinra arms, with a considerable delay in the time to a new exacerbation.

A major question that we cannot answer at this time is whether patients who show an insufficient response to anti-TNF treatment benefit from anakinra therapy. Likewise, it is unknown whether we can predict which patients will benefit from which interventions. In a separate study, Kan et al demonstrated that high concentrations of IL-1β and TNF are present in the drainage from lesions of patients with HS. Some patients exhibit mainly TNF in their drainage, whereas others predominantly show IL-1β. In others, the drainage contains both cytokines. In future studies, such data should be considered to gain insight into whether personalized treatment (ie, the cytokine intervention directed toward the most prominent cytokine) is successful.

In the present study, anakinra efficacy was related to modulated cytokine production of PBMCs. The output of the proinflammatory cytokines TNF, IL-6, and IFN-γ progressively increased over the 24-week study period in the placebo arm, which did not occur in the anakinra arm. Moreover, the production of IL-22 was significantly increased among anakinra-treated patients, suggesting the contribution of IL-22 to an improved epithelial cell defense through the release of defensins. In the present study, modulatory effects on cytokine production were still observed at week 24, which may explain the benefit of anakinra in prolonging the time to a new HS exacerbation during the follow-up period between weeks 13 and 24. The described correlation between treatment benefit and improved function of T117 and T122 helper T cells provides new insights into the pathogenesis of HS because T117 cells drive neutrophil chemotaxis, and HS is characterized by cycles of purulence from the affected lesions.
Conclusions

Anakinra therapy was safe in patients with HS. Injection site pain and mild infections reported herein are within the drug safety profile.\(^{29,30}\) The main limitation of the present study was the few patients involved owing to the fact that this was a pilot study to validate the effect of an anti-IL strategy in HS. Despite the few enrolled patients, the results of anakinra use to treat HS are promising.

**REFERENCES**

8. van der Zee HH, de Ruiter L, van den Broecke DG, Dik WA, Laman JD, Prens EP. Elevated levels of tumour necrosis factor (TNF-α), interleukin (IL)-1β and IL-10 in hidradenitis suppurativa skin: a rationale for targeting TNF-α and IL-1β. *Br J Dermatol*. 2011;164(6):1292-1298.