

1 **Spesolimab treatment in a patient with generalized pustular psoriasis: a case report with 12-**
2 **month follow-up and literature review**

3 **Running head:** Generalized pustular psoriasis and spesolimab

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24 Rosa María Zazueta-López has participated in protocols with Boehringer. Angel Kevin Garza-

1 Elizondo and Diana Paola Flores-Gutierrez have nothing to disclose. Esperanza Welsh has been a
2 consultant and/or speaker for Johnson & Johnson, La Roche Posay, Pierre Fabre, and Leo Pharma.
3 The company donated the drug employed in this case.

4 **Data availability:** The data that support the findings of this study are available from the
5 corresponding author upon reasonable request.

6 **Ethics statement:** The patient was informed that all the data were anonymized and understood that
7 the material may be published in a journal and seen by public. A written consent was obtained.

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9 Dear Editor, Diagnosing and treating generalized pustular psoriasis (GPP) is a challenge for
10 dermatologists due to its severity, low prevalence, and limited therapeutic options.
11 Treatment for GPP includes acitretin, methotrexate, and ciclosporin.¹ Some biological
12 agents such as TNF- α inhibitors, IL-17 inhibitors, and IL-23 inhibitors have been employed
13 in GPP but with less effectiveness than the one achieved in plaque psoriasis. Recently, new
14 therapeutic options have been developed.²

15 The role of interleukin-36 (IL-36) has been studied in various immune-mediated diseases
16 including GPP. Spesolimab is a humanized monoclonal antibody that antagonizes the IL-36
17 receptor. Recent studies have shown notable improvement and remission rates in patients
18 with GPP. These recent studies have reported a maximum follow-up of 16 weeks.^{3,4} We
19 present the case of a Hispanic patient with GPP and plaque psoriasis treated with
20 spesolimab with 12 months of follow-up and review the current evidence of spesolimab in
21 GPP.

22
23 Case presentation

24 A 63-year-old man with a 50-year history of plaque psoriasis presented to our outpatient
25 clinic with a 2-month history of fever, fatigue, and a generalized pustular rash. He had a
26 history of two previous GPP episodes (14 and 9 years before) that were treated with
27 acitretin. The patient remained on acitretin since the last episode but halted it a year prior
28 due to fatigue and hair loss. A month prior to evaluation with us, a dermatologist prescribed
29 methotrexate without response. At the initial evaluation, the patient presented fever,

1 fatigue, and intense itching. He presented generalized erythematous plaques with
2 abundant pustules. The pustules were not restricted to the plaques (Figure 1). A punch
3 biopsy confirmed the diagnosis of GPP. The patient started spesolimab treatment with a
4 dose of 900mg (IV) and a second dose was administered one week later.

5
6 In the first follow-up 7 days after the first dose, the patient presented a notable
7 improvement. At the next appointment 2 weeks later, the patient presented complete
8 remission. Up to the 12-month follow-up, the patient did not have any recurrence of his
9 GPP and had minimal psoriasis plaques (Figure 2).

10
11 We performed a literature review of GPP and spesolimab on September 4, 2023, through
12 PubMed with keywords “generalized pustular psoriasis” AND “spesolimab”. Of the 26
13 results, we excluded 23 articles that were reviews or outcomes of the same clinical trial. We
14 included 3 articles (Table 1) with 57 patients with GPP treated with spesolimab.³⁻⁵

15 The Effisayil 1 clinical trial included patients with moderate-severe GPP and compared
16 treatment with spesolimab (n=35) versus placebo (n=18). Response (Generalized Pustular
17 Psoriasis Physician Global Assessment -GPPGA- pustulation subscore of 0 at week 1) was
18 found in the spesolimab group in 54% of patients versus 6% in the placebo group.⁴ Patients
19 with a GPPGA ≥ 2 on the 8th day were eligible for a second dose of spesolimab, and patients
20 without response in the placebo groups were eligible to receive spesolimab in the open-
21 label phase. At week 4, a 75% or greater decrease in the Generalized Pustular Psoriasis
22 Area and Severity Index (GPPASI 75) was achieved in 51% of patients initially
23 randomized to spesolimab and in 40% of the patients receiving spesolimab after being
24 initially assigned to placebo. The longest follow-up time was 12 weeks. Of the 51 patients
25 who received spesolimab, 12% presented a serious adverse event.⁴

26 A case series by Ran et al.³ reported five patients with a GPPGA of 3 treated with
27 spesolimab and reported a follow-up for 16 weeks. This case series employed a single dose
28 of 900 mg. Symptom improvement was noted in less than 96 hours. Three patients got a
29 score of 0 at week 16, and two patients a score of 1 at week 16. Four patients had mild
30 adverse effects. Müller et al.⁵ reported a patient who, despite treatment with prednisolone,

1 methotrexate, and infliximab, had recurrent GPP. The patient received spesolimab which
2 significantly reduced itching and pustule formation after 3 days. A second dose was
3 administered after 1 week. This allowed a complete remission of pustules and a reduction
4 of erythema, but follow-up time is not specified in this case report. No adverse events were
5 reported.⁵

6 Our review found limited cases of GPP treated with spesolimab but with a high response
7 rate to the biologic. Reported adverse events were frequent but in most of the cases mild.
8 Most articles do not mention previous history of plaque psoriasis (present in around 50% of
9 patients with GPP) or the effect of spesolimab on it. The Effisayil 1 trial did not include the
10 plaque psoriasis response in their efficacy endpoints.⁴ In conclusion, we report a Hispanic
11 patient with a 1-year follow-up and remission of their GPP and important improvement of
12 their plaque psoriasis after two doses of spesolimab. Although GPP has shown an effective
13 response to spesolimab, more reports are needed to establish the long-term effect on GPP
14 patients with and without a history of plaque psoriasis.

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16 **References**

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1 **Figure legends**

2 Figure 1. (a and b) Generalized pustular psoriasis at initial evaluation.

3 Figure 2. (a) Follow-up 2 weeks after spesolimab; (b) 12-month follow-up.

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5 Table 1. Articles included in the literature review of generalized pustular psoriasis and
6 spesolimab.

AUTHOR	YEAR	PATIENTS	DOSES	FOLLOW-UP TIME	ADVERSE EVENTS
Bachelez et al. ⁴	2021	51 patients*	Single or two 900 mg IV doses	12 weeks follow-up	Pyrexia (n=5), upper respiratory (1), urinary infections (1), otitis externa, folliculitis, drug rash with eosinophilia and systemic symptoms (DRESS) (2), worsening of chronic plaque psoriasis (1), squamous-cell carcinoma of the skin (1), urinary (1) and respiratory (1) infections and arthritis (1).
Ran et al. ³	2023	5 patients*	Single 900 mg IV dose	16 weeks follow-up	Upper respiratory (2) and urinary tract (2) infection, mild anemia (2), increase in uric acid (2), elevated liver enzymes (1) and platelet count (1), hypoproteinaemia (1), numb hands and feet (1), and facial cutaneous infections (1).
Müller VL and Kreuter A ⁵	2023	1 patient*	Two 900 mg IV doses	Not specified	None
Current report	2023	1 patient	Two 900 mg IV doses	12-month follow-up	None

1 * Plaque psoriasis history not reported.

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Figure 1
156x103 mm (x DPI)



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Figure 2
146x117 mm (x DPI)

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