
Rapid and sustained response to spesolimab in five Chinese patients with generalized pustular psoriasis

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Dear Editor, Generalized pustular psoriasis (GPP) is a rare skin disease characterized by generalized sterile pustules with or without severe systemic symptoms. In China, systemic treatment with ciclosporin, retinoids and methotrexate is the main management strategy, but with poor outcomes and frequent recurrences. Several studies have indicated that the interleukin (IL)-36 pathway plays an important role in the occurrence and development of this disease,¹ which is further demonstrated by the efficacy and safety results for spesolimab (a monoclonal antibody, IL-36 receptor inhibitor) from some clinical trials.²⁻⁴ Previous randomized controlled trials for spesolimab have limited patient numbers, especially participants from the Chinese population, here we share our experience with spesolimab in five Chinese patients with GPP flare.

We treated five Chinese adult patients with spesolimab in our department from August 2022 to January 2023 who presented with a GPP flare. All the patients were diagnosed with GPP according to the European consensus statement.⁵ We used the Generalized Pustular Psoriasis Physician Global Assessment (GPPGA) and the Generalized Pustular Psoriasis Area and Severity Index (GPPASI) for the evaluation of efficacy of spesolimab at week 0, week 1, week 4 and week 16. Safety events were documented throughout the follow-up period.

Ethical approval was not applicable and all patients gave written, informed consent for participation and publication of their case details and images.

All patients received one single intravenous 900 mg spesolimab dose. The characteristics and clinical course for the five patients are listed in Table 1.

The five patients have a disease history of at least 1 year, and two of them had a history of coexisting lesions of psoriasis vulgaris (PV). All five patients had received systemic treatment prior to spesolimab, including adalimumab, methotrexate, acitretin and traditional Chinese medicine (such as *Tripterygium wilfordii*) with poor outcomes. All patients had

a GPPGA score >3 at admission, and two of them had a fever.

We observed a remarkable response to spesolimab with an almost resolution of pustules in 12 h in one patient (Figure 1), two patients achieved resolution of pustules in 24 h, one patient in 48 h, one patient in 96 h. A GPPGA score of 1 was achieved in two of five patients (40%) and the other three achieved a GPPGA score of 2 at week 1. Three patients achieved a score of 0 and two patients achieved a score of 1 at week 16 (Table 1).


It is important to point out that PV lesions appeared in two out of the five patients (patient 3 and patient 4) during the observation period after the resolution of pustules. Patient 3 was treated with acitretin 30 mg twice daily orally and patient 4 treated with methotrexate 10 mg once weekly orally to treat the PV lesions after 4 weeks of spesolimab therapy. In addition, we observed that the body temperature of patient 1 and patient 4 decreased to normal on the fifth and second day after spesolimab treatment, respectively.

We also evaluated our patients with the use of GPPASI, with total score ranging from 0 (least severe) to 72 (most severe). In our patients, an 83.5% improvement in GPPASI score was achieved in one patient at week 1, with the others scoring 75.0%, 61.6%, 47.3% and 47.2%. The mean percentage improvement of GPPASI score for those five patients was 62.9% at week 1, 92.5% at week 4 and 98% at week 16, which were shown in Figure 2. Our findings are of a greater improvement than those published in the phase I trial for spesolimab.¹

Although no severe adverse effects occurred, four out of five patients (80%) experienced various mild adverse events. One patient experienced numbness in hands and feet during the administration of spesolimab, which quickly relieved after the administration. One week after treatment, two patients had mild anaemia, two upper respiratory tract infections, two increases in their uric acid level and in one patient elevated liver enzymes, facial cutaneous infections, a urinary tract infection, an elevated platelet count and hypoproteinaemia were observed. A second case of a urinary tract infection occurred in patient 3 at week 4. Of all the adverse reactions, 92% occurred in the first week after treatment and all resolved after symptomatic treatment.

GPP flare is a recrudescence inflammatory disease with limited treatment options in China, the approval of spesolimab may change future treatment recommendations; however, we need more data about efficacy and safety to guarantee future clinical use. From our case series, Chinese patients with GPP showed a consistent, rapid and sustained response to spesolimab in line with previous published results.

Data are available on request from the corresponding author.

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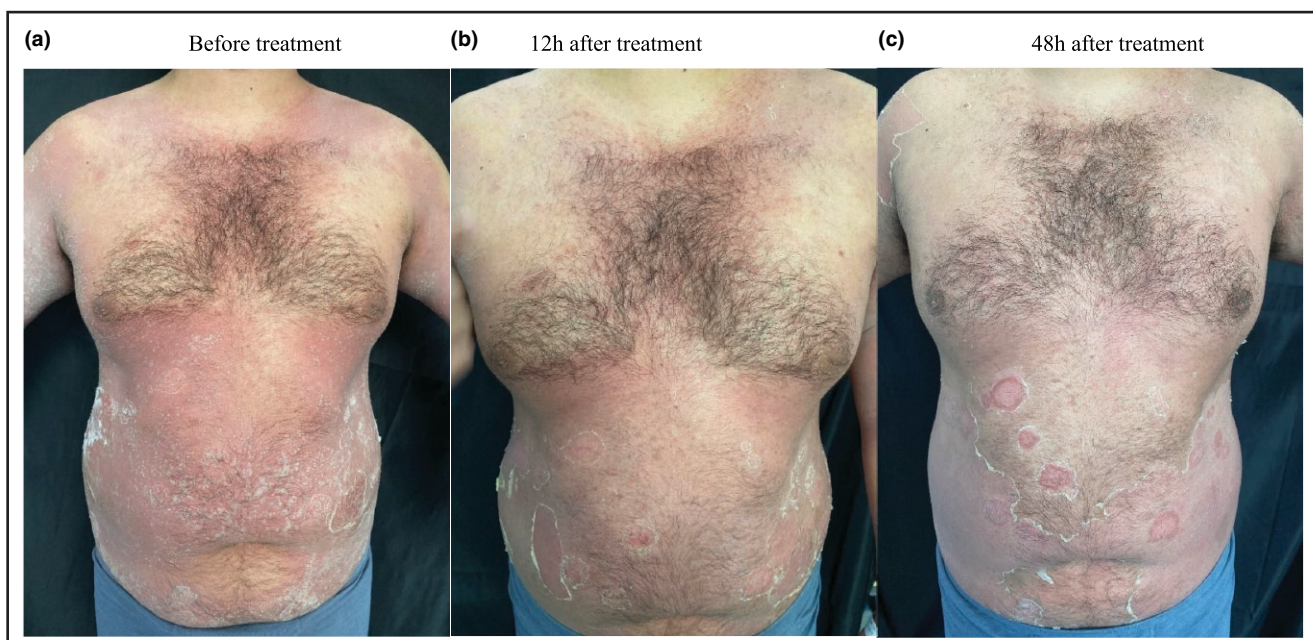
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Table 1 Characteristics and clinical information of five patients with generalized pustular psoriasis (GPP)

Variable	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Age, years	26	25	29	26	65
Sex	Woman	Woman	Man	Woman	Woman
Age at onset of GPP, years	12	1	29	26	64
Previous treatments	Adalimumab (1 year ago)	Acitretin (1.5 years ago)	Acitretin (within the past 2 weeks), methotrexate (4 years ago)	Methotrexate (1 year ago)	<i>Tripterygium wilfordii</i> (2 months ago)
PV history	Negative	Negative	Positive	Positive	Negative
Other medication history	Negative	9-valent HPV vaccine 1 month before	Negative	Negative	Negative
Family history	Negative	Negative	Positive	Negative	Negative
Accompanying symptom	Fever (39.2 °C)	Negative	Negative	Fever (37.5 °C)	Negative
PV lesions during the interval between GPP attacks	Negative	Negative	Positive	Positive	Negative
Treatment with spesolimab	Single dose 900 mg	Single dose 900 mg	Single dose 900 mg	Single dose 900 mg	Single dose 900 mg
Treatment after 4 weeks	None	None	Acitretin 30 mg twice daily	Methotrexate 10 mg once weekly	None
Resolution of pustules, h	14	24	12	96	44
GPPGA score					
Prior to treatment	3	3	3	3	3
Week 1	1	2	2	2	1
Week 4	1	0	1	1	1
Week 16	0	0	1	0	1
GPPASI score					
Prior to treatment	56.4	34.9	35.6	46.6	25.2
Week 1	9.3	18.4	18.8	17.9	6.3
Week 4	1.4	0	7.2	0.9	3.2
Week 16	0	0	2.2	0	0.8
Adverse effects	Numb hands and feet, mild anaemia, elevated liver enzymes, facial cutaneous infections	Mild anaemia, urinary tract infection	Upper respiratory tract infection, increase in uric acid levels, urinary tract infection	Upper respiratory tract infection, increase in uric acid levels, elevated platelet count, hypoproteinaemia	None

GPPGA, Generalized Pustular Psoriasis Physician Global Assessment; GPPASI, Generalized Pustular Psoriasis Area and Severity Index; HPV, human papillomavirus; PV, psoriasis vulgaris.

**Figure 1** Skin lesions on the thorax and abdomen of patient 3 (a) before and (b) after spesolimab treatment at 12 h and (c) at 48 h.

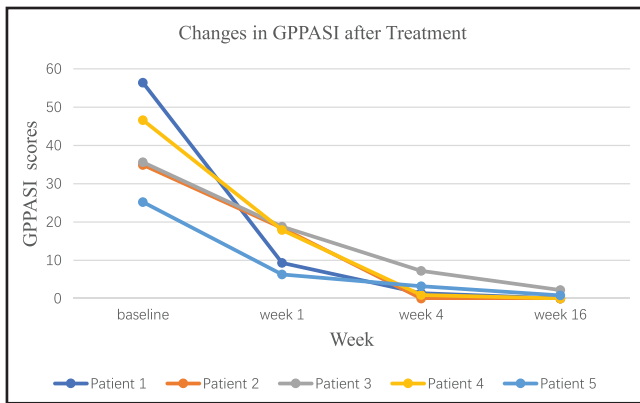


Figure 2 Changes in Generalized Pustular Psoriasis Area and Severity Index scores in five patients with generalized pustular psoriasis.

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