Effect of high-dose subcutaneous spesolimab on skin manifestations: Results from the pivotal Effisayil 2 trial of flare prevention in generalized pustular psoriasis

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An analysis of patients with GPP receiving high-dose spesolimab showed more improvement in GPPGA scores vs placebo in the Effisayil 2 trial

AIM

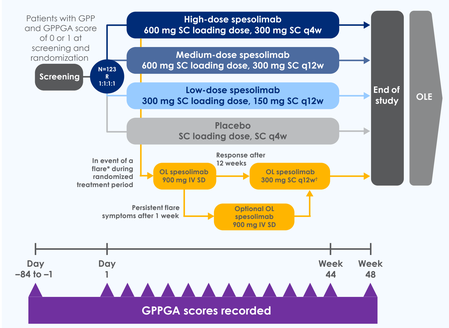
In this analysis of Effisayil 2, the effect of high-dose spesolimab or placebo on **GPP lesions** was assessed using subscores and total score on the **GPPGA scale**

INTRODUCTION

- **GPP is a chronic, rare, and potentially life-threatening skin disease**,[1–3] characterized by the extensive development of sterile pustules, and has recently been reclassified to the group of superficial/epidermal neutrophilic diseases
- **Current treatments are suboptimal in preventing flares**, which are a common and potentially life-threatening, but unpredictable, feature of GPP;[4] it is also important to address chronic skin manifestations that persist in many patients, even in the absence of flares
- **Spesolimab, a monoclonal antibody targeted specifically at the interleukin-36 receptor**, is effective and approved for the treatment of GPP flares[5-7] and has been evaluated for the prevention of flares in the pivotal, randomized, placebo-controlled Effisayil 2 trial (NCT04399837)[8]

METHODS

Effisayil 2 trial design



*Increase in GPPGA total score of ≥2 from baseline and GPPGA pustulation subscore ≥2; †Patients receiving OL spesolimab 300 mg SC q12w had the option to escalate to 300 mg SC q4w if they had an increase in the GPPGA pustulation subscore of ≥1 from any previous OL visit(s).

- GPPGA subscores for **erythema**, **pustulation** and **scaling/crusting** and GPPGA **total score** were compared between patients receiving **high-dose spesolimab (600 mg SC loading dose, 300 mg SC q4w)** and placebo
- Scores were recorded at **baseline** and over the **course of treatment** on the **GPPGA scale** from 0 (clear) to 4 (severe)[8]
- Patients were classified as having a **flare** if they had a **pustulation subscore of ≥2** and a **total score increase of ≥2** from baseline[8]
- Results were reported as proportions of patients with each score and flare at each time point and were analyzed descriptively

CONCLUSION

- Compared with placebo, high-dose SC spesolimab (600 mg SC loading dose, 300 mg SC q4w) resulted in a greater proportion of patients with GPP achieving and maintaining GPPGA scores of 0
- Compared with placebo, a lower proportion of patients receiving high-dose SC spesolimab had flares at Week 4 of treatment
- No patient receiving high-dose spesolimab had a flare after Week 4
- The difference between treatments was sustained over 48 weeks

RESULTS

The GPPGA scale

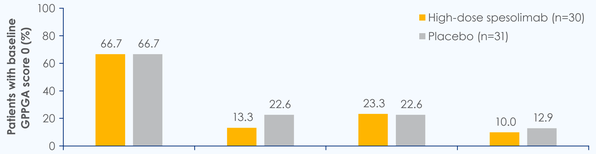
Score	Erythema	Pustulation	Scaling/crusting
0 (clear)	Normal or post-inflammatory hyperpigmentation	No visible pustules	No scaling or crusting
1 (almost clear)	Faint, diffuse pink, or slight red	Low-density occasional small discrete pustules (noncoalescent)	Superficial focal scaling or crusting restricted to periphery of lesions
2 (mild)	Light red	Moderate-dentisity grouped discrete small pustules (noncoalescent)	Predominantly fine scaling or crusting
3 (moderate)	Bright red	High-density pustules with some coalescence	Moderate scaling or crusting covering most or all lesions
4 (severe)	Deep fiery red	Very-high-density pustules with pustular lakes	Severe scaling or crusting covering most or all lesions

(GPPGA scale[8])

Baseline characteristics and GPPGA scores

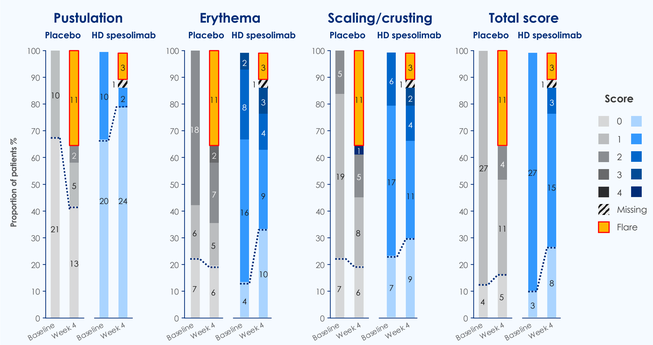
Patients from Effisayil 2 in this analysis[10]:

Mean age: 40 years; Sex: 62% female; Race: 36% White, 64% Asian; *IL36RN* status: 23% *IL36RN* mutation



The proportions of patients with a baseline score of 0 for each GPPGA subscore and total score were generally similar between treatment groups

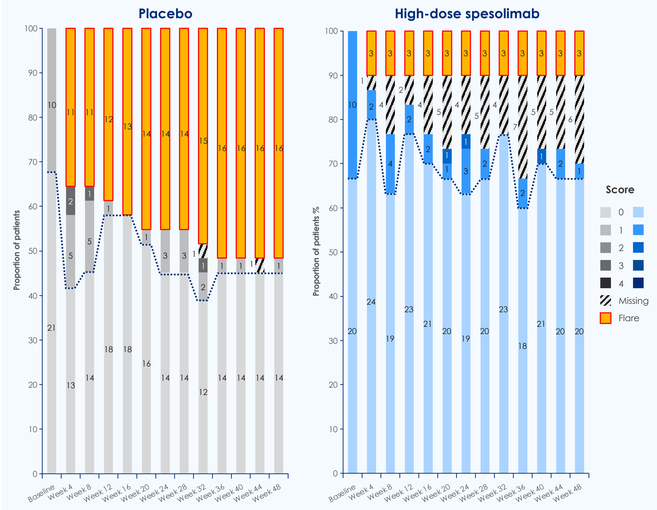
GPPGA scores with high-dose spesolimab compared with placebo



Missing data were due to patient non-attendance at the visit or to treatment discontinuation. Flares in patients who subsequently scored 0 at the next time point were not considered as flares.

The proportion of patients with a GPPGA score of 0 increased with high-dose spesolimab but decreased or remained similar with placebo at Week 4. The proportion of patients with GPP flares was lower with high-dose spesolimab than with placebo

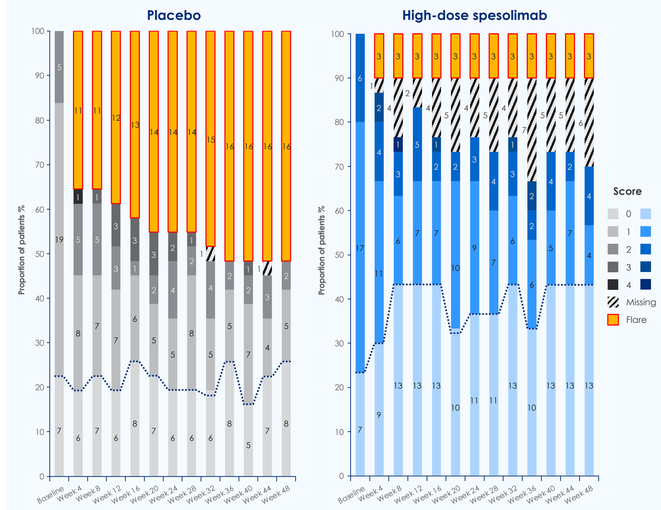
GPPGA pustulation subscores over 48 weeks



Missing data were due to patient non-attendance at the visit or to treatment discontinuation. Flares in patients who subsequently scored 0 at the next time point were not considered as flares.

Greater proportions of patients with a GPPGA pustulation subscore of 0 were maintained with high-dose spesolimab vs placebo at Week 24 and Week 48. There were no new flares with high-dose spesolimab after Week 4

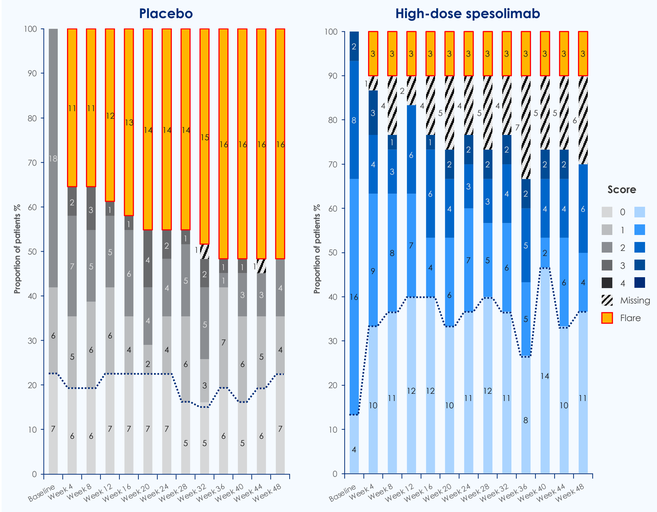
GPPGA scaling/crusting subscores over 48 weeks



Missing data were due to patient non-attendance at the visit or to treatment discontinuation. Flares in patients who subsequently scored 0 at the next time point were not considered as flares.

Greater proportions of patients with a GPPGA scaling/crusting subscore of 0 were maintained with high-dose spesolimab vs placebo at Week 24 and Week 48. There were no new flares with high-dose spesolimab after Week 4

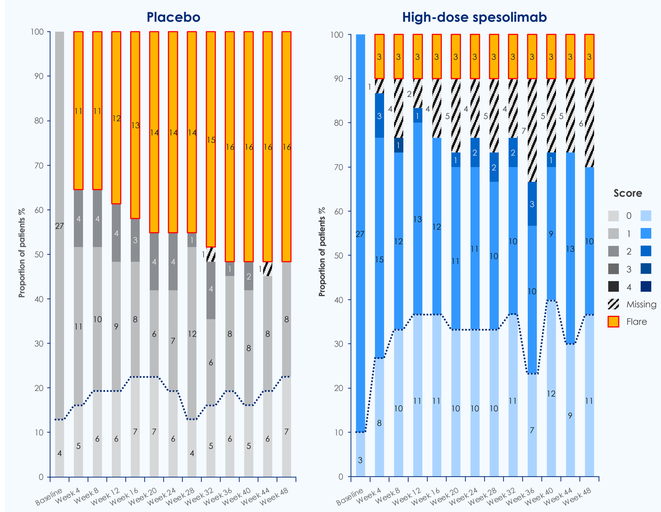
GPPGA erythema subscores over 48 weeks



Missing data were due to patient non-attendance at the visit or to treatment discontinuation. Flares in patients who subsequently scored 0 at the next time point were not considered as flares.

Greater proportions of patients with a GPPGA erythema subscore of 0 were maintained with high-dose spesolimab vs placebo at Week 24 and Week 48. There were no new flares with high-dose spesolimab after Week 4

GPPGA total scores over 48 weeks



Missing data were due to patient non-attendance at the visit or to treatment discontinuation. Flares in patients who subsequently scored 0 at the next time point were not considered as flares.

Greater proportions of patients with a GPPGA total score of 0 were achieved and maintained with high-dose spesolimab vs placebo over 48 weeks. There were no new flares with high-dose spesolimab after Week 4

Abbreviations

GPP, generalized pustular psoriasis; GPPGA, GPP Physician Global Assessment; HD, high-dose; IV, intravenous; OL, open-label; OLE, open-label extension; q4w, every 4 weeks; q12w, every 12 weeks; R, randomization; SC, subcutaneous; SD, single dose

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