Measuring GPPGA, pain, symptom, and quality of life index scores in untreated generalized pustular psoriasis: Results from the placebo group of the Effisayil 2 trial

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Evaluation of disease burden in untreated patients with GPP revealed that GPP negatively impacts patients, even in the absence of acute flare events

AIM

- To evaluate the disease burden of untreated GPP by longitudinally analyzing patients from the Effisayil 2 trial who had been randomized to the placebo group and did not experience a GPP flare

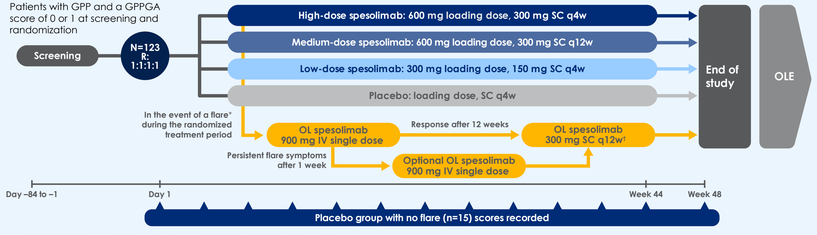
INTRODUCTION

- GPP is a rare, chronic, inflammatory, and potentially life-threatening skin disease that is characterized by episodic flares of widespread pustular eruptions and erythema[1–3]
- Many patients with GPP experience residual disease symptoms post flare episode[4]
- Effisayil 2 (NCT04399837) was a pivotal, randomized, placebo-controlled trial that evaluated the efficacy and safety of spesolimab (an anti–IL-36R monoclonal antibody[5]) SC in preventing GPP flares over 48 weeks[6]

METHODS

- In Effisayil 2, eligible patients with a history of GPP were randomized (1:1:1:1) to receive 1 of 3 SC spesolimab regimens or placebo for 48 weeks (**Figure 1**)

Figure 1. Study design[6]



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

- Chronic disease burden was assessed at baseline and at 4-week intervals using the GPPGA total score (range 0–4; 0=clear, 1=almost clear, 2=mild, 3=moderate, 4=severe), Pain VAS (continuous scale 0–100; severity of pain was evaluated using the categories, 0–4=no pain, 5–44=mild pain, 45–74=moderate pain, 75–100=severe pain), and PSS (range 0–16; 0=no symptoms, 4=mild symptoms, 8=moderate symptoms, 12=severe symptoms, 16=very severe symptoms); the DLQI was assessed at baseline and Weeks 4, 8, 12, 24, 36, and 48 (range 0–30; 0–1=no impact, 2–5=small impact, 6–10=moderate impact, 11–20=very large impact, 21–30=extremely large impact)
- This analysis included only patients who received placebo and did not experience a GPP flare
  - GPP flare was defined as an increase in the GPPGA total score of ≥2 from baseline and GPPGA pustulation subscore of ≥2. The use of medication with OL spesolimab IV or other investigator-prescribed medication was considered to be a GPP flare

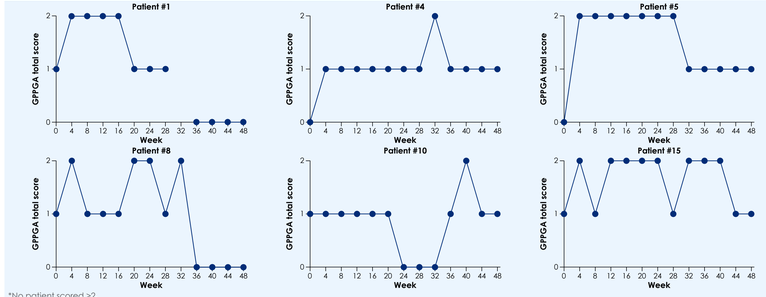
CONCLUSIONS

- Acute flare was reported in >50% (n=16/31) of patients in the placebo group over 48 weeks
- Despite not meeting the trial's definition of GPP flare, most of the 15 non-flare placebo patients showed clear evidence of underlying GPP disease activity
  - Nearly half did not have clear or almost clear skin and had moderate pain and symptoms
  - A small subset reported severe pain and symptoms
- The majority of patients who received placebo experienced a moderate to very large impact on QoL over the 48 weeks
- These findings suggest that untreated GPP negatively affects patients even in the absence of acute flare events

RESULTS

- Of 31 patients who received placebo in Effisayil 2, 16 experienced a GPP flare and 15 did not experience a flare over the 48-week period
- 40% (n=6/15) of non-flare placebo patients had ≥1 GPPGA total score of 2 (i.e. skin not clear or almost clear), and 4 of the 6 reported a score of 2 at ≥4 visits (for 3/4 patients, these visits were consecutive); no scores of 2 were reported at Week 48 (**Figure 2**)

Figure 2. GPPGA total score over time in non-flare placebo patients with ≥1 score of 2* (n=6)

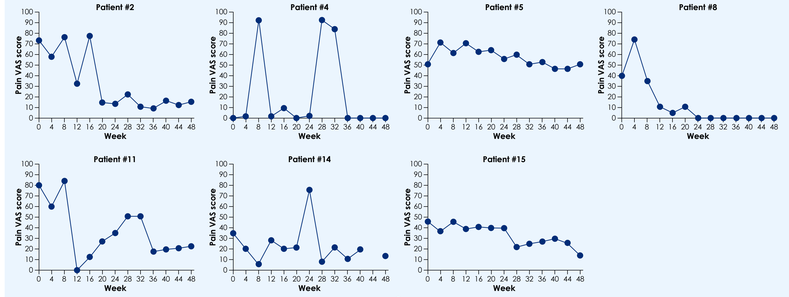


*No patient scored >2.

Placebo non-flare patients continued to experience GPP skin symptoms during the 48-week period

- 47% (n=7/15) of non-flare placebo patients had ≥1 "moderate" pain VAS score (score of 45–74), and 20% (n=3/15) had ≥1 "severe" pain VAS score (score of ≥75) over the 48-week period (**Figure 3**)

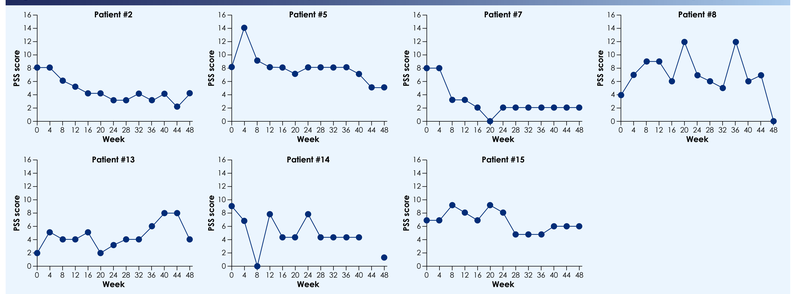
Figure 3. Pain VAS score over time in non-flare placebo patients who experienced ≥1 moderate or severe pain VAS score (n=7)



Placebo non-flare patients experienced moderate and severe pain during the 48-week period

- 47% (n=7/15) of patients had ≥1 "moderate" PSS score (score of 8–11) and 13% (n=2/15) had ≥1 "severe" PSS score (score ≥12) over the 48-week period (**Figure 4**)

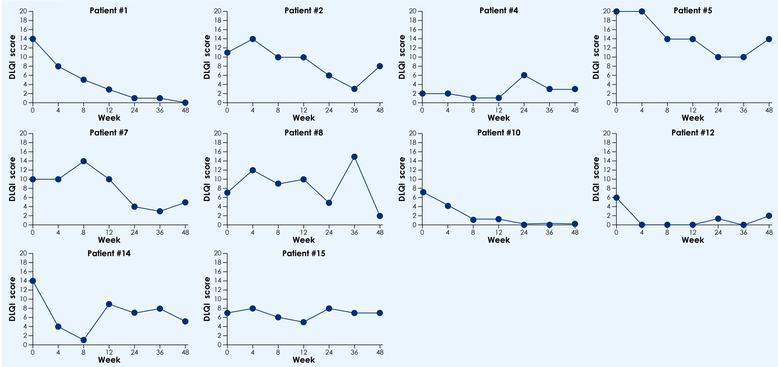
Figure 4. PSS score over time in non-flare placebo patients with moderate or severe PSS score (n=7)



Placebo non-flare patients experienced moderate and severe PSS scores during the 48-week period

- "Moderate" (score 6–10) and "very large" (score 11–20) effects on QoL were reported at least once in 67% (n=10/15) and 40% (n=6/15) of patients, respectively (**Figure 5**)

Figure 5. DLQI in non-flare placebo patients who reported ≥1 moderate or very large effect on QoL (n=10)



Placebo non-flare patients experienced moderate and very large effects on QoL during the 48-week period

Abbreviations

DLQI, Dermatology Quality of Life Index; GPP, generalized pustular psoriasis; GPPGA, Generalized Pustular Psoriasis Physician Global Assessment; IV, intravenous; OL, open-label; OLE, open-label extension; PSS, Psoriasis Symptom Scale; q4w, once every 4 weeks; q12w, once every 12 weeks; QoL, quality of life; R, randomized; SC, subcutaneous; VAS, Visual Analog Scale.

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