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Randomised Phase 3 trial of spesolimab in patients with ulcerative pyoderma gangrenosum: A study protocol

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Introduction & Objectives: Pyoderma gangrenosum (PG) is a rare, inflammatory, neutrophilic dermatosis, usually manifesting as rapidly progressive and painful skin ulcers, although rarer, atypical presentations exist. Interleukin-36 (IL-36) is thought to play a key role in PG pathogenesis.1 This randomised, placebo-controlled, multicentre, Phase 3 study will assess spesolimab, a novel, humanised monoclonal antibody against the IL-36 receptor, in patients with ulcerative PG who require systemic therapy (NCT06624670). The trial has been approved by independent ethics committees of participating centres.

Materials & Methods: Approximately 90 participants aged ≥18 years with a confirmed diagnosis of ulcerative PG, from 21 countries, will be included. In Part 1 of the trial (Weeks 0–26), participants will be randomised 2:1 to receive spesolimab plus low-dose oral corticosteroid (n=60), or placebo plus low-dose oral corticosteroid (n=30) (Figure 1). In Part 2 of the trial (Weeks 28–52), participants with a non-complete response will receive spesolimab; those with a complete response will be re-randomised 1:1 to receive either spesolimab or placebo. The primary endpoint is complete closure and re-epithelisation (PGAR-100) of the target ulcer up to Week 26, confirmed ≥2 weeks later. Secondary endpoints include PGAR-100 of the target ulcer at Week 26 and of any measurable ulcer at any time up to Week 26, confirmed ≥2 weeks later. Additional efficacy, safety and biomarker measures will also be assessed.

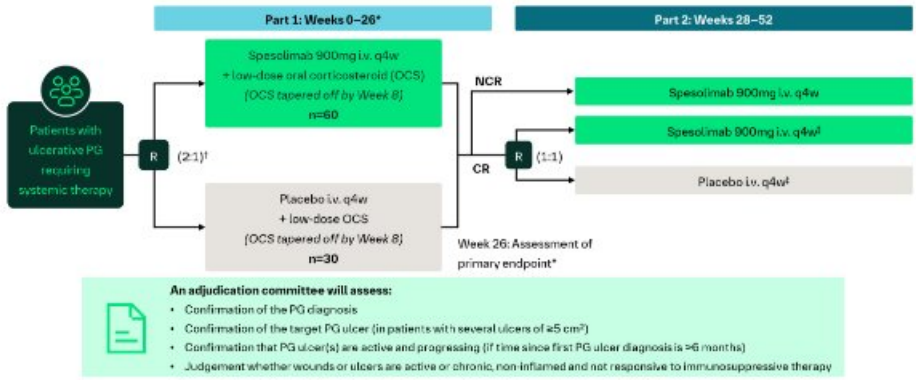
Results: The trial started in January 2025, with estimated trial completion in October 2026.

Conclusion: These results will provide safety and efficacy data on spesolimab as a potential treatment for ulcerative PG.

Reference:

\1. Guenin SH, Khattri S, Lebwohl MG. JAAD Case Rep. 2023;34:18–22.

Figure 1. Study design



*Confirmation of primary endpoint will occur at Week 28. †Randomisation stratified by target PG ulcer size categories (<40 cm² and ≥40 cm²) and presence of associated underlying inflammatory disease at baseline. ‡Trial participants who experience disease recurrence in the randomized double-blind arms in Part 2 can be offered open-label spesolimab 900 mg i.v. q4w at the time of recurrence. CR, complete response (i.e. complete closure of all PG ulcers); i.v., intravenous; NCR, non-complete response; OCS, oral corticosteroid; PG, pyoderma gangrenosum; q4w, every 4 weeks; R, randomisation.