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Generalized pustular psoriasis (GPP) control is limited on traditional small-molecule therapy as measured by the GPP Physician Global Assessment (GPPGA) and Dermatology Life Quality Index (DLQI): Baseline data from the EFFISAYIL 2 trial

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Introduction & Objectives: GPP is a chronic inflammatory, potentially life-threatening skin disease. Most patients experience chronic skin symptoms between flares leading to significant patient burden. Spesolimab, an anti-interleukin-36 receptor monoclonal antibody, is approved to treat GPP in adults and pediatric patients aged ≥12 years and weighing ≥40 kg. EFFISAYIL 2 (NCT04399837) evaluated the efficacy and safety of subcutaneous (SC) spesolimab in GPP. Most patients entering the trial were receiving a traditional small-molecule therapy prior to randomization and all had a baseline GPPGA1 total score of 0 or 1. Here, we report the GPPGA total score and DLQI score at baseline stratified by small-molecule medication received prior to randomization in EFFISAYIL 2.

Materials & Methods: Patients were stratified by baseline medication use, including medications received by ≥5 patients or no medication. GPPGA was assessed as the proportion of patients with a score of 1. For DLQI, mean and standard deviation (SD) were calculated.

Results: Despite treatment with traditional small-molecule therapies before entering EFFISAYIL 2, most patients in each baseline medication group did not have clear skin (GPPGA total score=1) and all groups reported poor quality of life (mean DLQI>5). These observations were consistent with findings among patients who did not receive small-molecule therapy before randomization. The respective proportion of patients with a GPPGA total score of 1 by each medication group was: 95.6% (n=43) for acitretin, 84% (n=21) for cyclosporine, 66.7% (n=10) for methotrexate, and 80% (n=4) for any 2 small molecules (i.e., acitretin, methotrexate, cyclosporine), compared with 87.1% (n=27) for those not receiving prior small-molecule therapy. The mean (SD) DLQI scores at baseline were: 8.3 (5.6) for acitretin (n=45), 7.7 (7.4) for cyclosporine (n=25); 9.9 (7.4) for methotrexate (n=15), and 5.4 (7.2) for 2 small molecules (n=5); compared with 8.1 (6.1) for no therapy.

Conclusion: Despite being treated with traditional small-molecule therapy before randomization, many patients entering EFFISAYIL 2 still demonstrated incomplete skin clearance, as shown by GPPGA total score and DLQI scores, reflecting a moderate effect on a patient's life. These findings suggest that approved, targeted therapy should be considered to reduce the clinical burden of GPP.

1Burden AD, et al. *Br J Dermatol*. 2023;189(1):138-140.