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Vilobelimab induced C5a suppression correlates with clinical benefit and pain reduction in patients with ulcerative pyoderma gangrenosum

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Introduction & Objectives: Pyoderma gangrenosum (PG) is an inflammatory, rare, ulcerative skin disease with no approved treatment in Europe or the US. There is increasing evidence suggesting the role of human complement factor C5a, in the pathophysiology of this debilitating disease. Vilobelimab is a first-in-class anti-C5a monoclonal antibody, which specifically blocks the biological activity of C5a in human plasma with high selectivity and leaves the membrane attack complex (C5b-9) intact, an important component in protecting against pathogens. We present the relationship between pharmacodynamic suppression of C5a by vilobelimab and key clinical outcomes, including target ulcer closure and pain reduction, in patients with ulcerative PG.

Materials & Methods: Nineteen patients were treated biweekly in three escalating vilobelimab dosing groups; 800mg (n=6), 1600mg (n=6) and 2400mg (n=7) for 26 weeks. Vilobelimab plasma concentrations were measured at predefined time points. Efficacy was evaluated by Physician's Global Assessment (PGA-score), border elevation, and wound erythema of the target ulcer. Pain reduction was evaluated as change from baseline on Numeric Rating Score (NRS). Spearman correlation matrices were computed across all pharmacokinetic (PK), pharmacodynamic (PD), efficacy, and Patient-Reported Outcome (PRO) variables, and visualized using heatmaps displaying correlation coefficients and significance levels.

Results: Vilobelimab plasma concentrations demonstrated consistent PD suppression of C5a levels at Days 15, 43, and 99. The correlation between vilobelimab plasma levels and lowered C5a concentrations were statistically significant at all measured time points, with Spearman correlation coefficients (rho) of -0.665 (p=0.002) on Day 15, -0.782 (p=0.0002) on Day 43, and -0.846 (p=0.0001) on Day 99.

Vilobelimab concentrations and the corresponding levels of C5a suppression correlated with the improvement in clinical outcomes of wound healing, PGA score, and patient reported outcomes such as DLQI and pain NRS.

Vilobelimab exposure showed corresponding significant correlation with the target ulcer area reduction on Day 43 and Day 99 (rho: -0.561 and -0.517, p = 0.0297 and p = 0.0849, respectively) and with PGA-score reductions (rho: -0.504 and -0.572; p = 0.039 and p = 0.032, respectively).

Significant correlations between C5a reduction and wound healing were also observed. These included reduction in target ulcer area at Day 43 and Day 99 (rho: 0.514 and 0.635, p=0.050 and p=0.015, respectively) and PGA-score reduction at Day 43 and Day 99 (rho: 0.478 and 0.360, p=0.052 and p=0.170 respectively).

Pain reduction, as measured by the NRS showed associations with lowered C5a levels and higher vilobelimab plasma concentrations on Day 99 (rho: 0.412, p = 0.113 and rho: -0.600, p = 0.023 respectively).

Conclusion: The findings from this analysis demonstrate that pharmacodynamic suppression of C5a by vilobelimab is linked to clinically meaningful improvements in patients with ulcerative pyoderma gangrenosum. The increasing vilobelimab concentrations and the consequent suppression of C5a levels were correlated with

wound healing, and reduction of pain. These correlations underscore a critical role of C5a in the inflammatory pathophysiology of PG and support the therapeutic potential of vilobelimab as a targeted treatment.