Targeting IL-31 in dystrophic epidermolysis bullosa: nemolizumab-ilto for persistent pruritus in a five-patient case series

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Background: Pruritus is among the most burdensome manifestations of dystrophic epidermolysis bullosa (DEB). Repetitive scratching may exacerbate skin injury and perpetuate an itch-scratch cycle in patients already affected by chronic wounds and skin fragility. Interleukin-31 (IL-31) is implicated in DEB-associated pruritus, providing a mechanistic rationale for targeted IL-31 receptor blockade.

Objective: To describe pruritus and clinical wound outcomes following off-label treatment with nemolizumab-ilto, an IL-31 receptor alpha antagonist, in patients with DEB and persistent pruritus despite multiple prior therapies.

Methods: This single-center case series included five patients aged 11–19 years at treatment initiation with genetically characterized DEB, including four with molecular findings consistent with recessive DEB and one with dominant DEB. Across the cohort, previous therapies included antihistamines, doxepin, topical corticosteroids, topical calcineurin inhibitors, and dupilumab. Nemolizumab-ilto was administered subcutaneously as an initial 60-mg dose as two 30-mg injections, followed by 30 mg every four weeks. Nemolizumab was added to ongoing antipruritic and wound-care regimens, and concomitant therapies were documented. Patients or caregivers completed a follow-up pruritus assessment at a time point ranging from 1 to 10 months after starting nemolizumab, depending on the individual patient. At this time four patients self-reported and one caregiver reported current and

pretreatment pruritus intensity using a 0–10 numerical rating scale (NRS). Wound appearance was evaluated by clinical examination and photographs.

Results: Recalled pretreatment pruritus scores ranged from 7 to 10 **(mean, 9.4)** and decreased to 1–6 at follow-up **(mean, 4.0)**. All five patients experienced reductions of at least 4 points, with a mean reduction of 5.4 points (range, 4–9). Individual scores decreased from 10 to 6, 10 to 6, 10 to 1, 10 to 6, and 7 to 1; two patients achieved a follow-up score of 1. All five patients also demonstrated clinical and photographic improvement in wound appearance, although wound healing was not formally quantified. No adverse events were reported.

Conclusion: Nemolizumab-ilto was associated with consistent reductions in pruritus across five genetically characterized patients with DEB. Concurrent improvement in wound appearance supports the hypothesis that reducing IL-31-mediated pruritus and scratching may decrease secondary mechanical skin injury. Although the uncontrolled design, retrospective recall of pretreatment pruritus, heterogeneous follow-up, and concomitant therapies preclude causal inference, these findings provide a clinically relevant signal supporting prospective evaluation of IL-31 receptor blockade in DEB using standardized longitudinal itch and wound outcomes.

Figure 1. Change in general pruritus intensity following nemolizumab treatment. Each row represents one patient. Pretreatment scores were retrospectively recalled at the follow-up assessment. All five patients experienced a reduction of at least 4 points on the 0–10 numerical rating scale.

