Mast cell reduction does not impair human cutaneous wound healing

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Background

Several studies in mice indicate a role for skin mast cells (MCs) in murine wound healing. The role and relevance of MCs in human skin wound healing remains unknown. *Barzolvolimab* (CDX-0159) inhibits SCF-dependent KIT activation. It reduces disease activity and depletes cutaneous MCs in patients with chronic inducible urticaria (CIndU) providing a unique opportunity to study the contribution of MCs to human wound healing.

Methods

CIndU patients (n=23) enrolled in a phase 1 trial received a single i.v. dose of *barzolvolimab* (3mg/kg). Full thickness skin wounds (3mm biopsy punches) were induced **predose** and **1, 4, 8,** and **12 weeks after treatment** (Fig. 1). Wound areas were determined daily after each biopsy. Skin MC numbers at the site and time of wounding were quantified on KIT-stained sections.

Figure 1. Study design

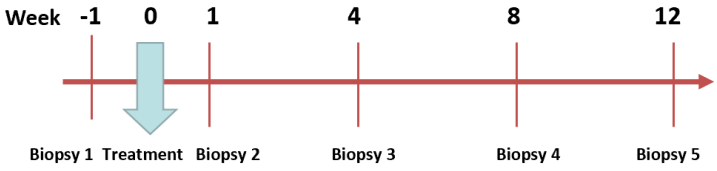
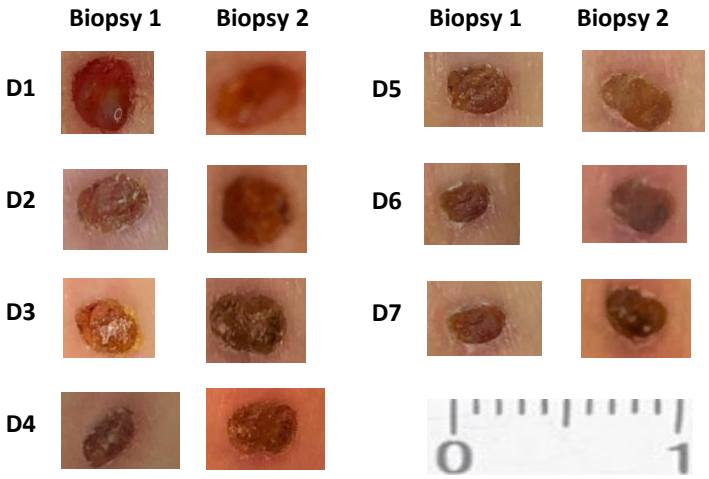


Figure 2. First 7 days (D1-D7) after Biopsy 1 (pre-treatment) and Biopsy 2 (post-treatment) with 1cm reference scale



Results

Skin MC numbers were significantly reduced after treatment with *barzolvolimab* (Fig. 3), from 9.9±3.1 MCs/mm2 at **baseline** to 3.9±3.1 (-61%), 1.9±2.7 (-81%), 0.9±1.5 (-91%), and 1.6±2.3 (-84%) MCs/mm2 at **week 1, 4, 8, and 12**.

Figure 3. MC reduction through treatment with *barzolvolimab*

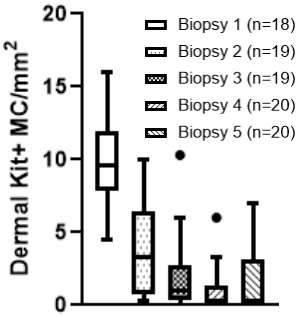
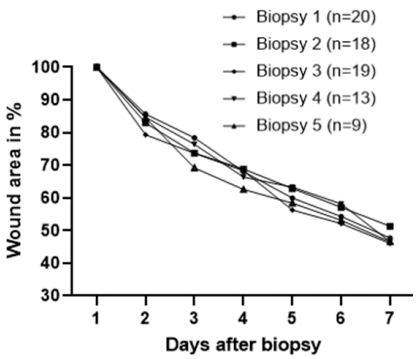


Figure 4. Mean wound area for each biopsy day 1-7



Skin wounds induced **before MC depletion** showed an average reduction of wound size to 48±12%, on day 7 after wounding, with complete closure by day 18±4.

Wound healing **in MC-depleted skin** was similar (Fig. 4, 5, 6), with an average time to closure of 17±4, 17±4, 18±5, and 17±7 days in wounds induced 1, 4, 8, and 12 weeks post-treatment. The average wound size reduction on day 7 after wounding, in wounds induced in the respective weeks after dosing, was 51±13%, 46±11%, 47±13%, and 47±14%.

Figure 5. Wound area 7 days after biopsy

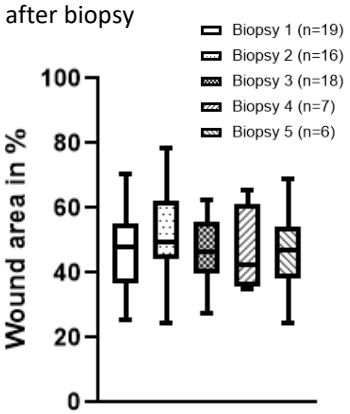
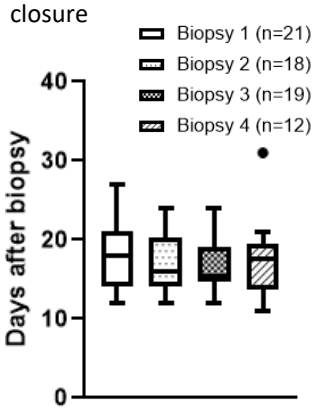


Figure 6. Days until wound closure



Conclusion

Our results suggest that in humans, the reduction of skin MCs does not affect the speed or duration of wound healing. This indicates that human MCs are dispensable for normal healing of small cutaneous wounds, different from skin wound healing in mice. Further investigation and analysis of wound colour, degree of erythema and pigmentation, will provide further information about the impact of MC reduction in humans concerning inflammation, vascularisation, pigmentation and scarring in wounds.