MOR106, an anti-IL-17C antibody, reduces severity of atopic-dermatitis-like skin inflammation in Flaky Tail model

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Introduction

Interleukin-17C (IL-17C) is a distinct member of the IL-17-family that is induced in inflamed epithelia. IL-17C drives skin inflammation in an autocrine manner by binding to its receptor IL17RA/IL17RE complex, which is predominantly present on epithelial cells. Several lines of evidence point towards a role of IL-17C in driving disease activity in psoriasis1 but its role in other inflammatory skin diseases remains to be elucidated. Using the MOR106 anti-IL17C antibody, we recently showed that increased skin IL-17C expression plays a role in the development of atopic dermatitis (AD) and is associated with cutaneous inflammatory responses in the calcipotriol-induced mouse model of AD1,2. In addition, anti-IL-17C suppresses development of experimental psoriasis in a IL-23-driven murine skin inflammation model. MOR106 is a human IgG1 monoclonal antibody derived from the MorphoSys Yanti® library that potently and selectively binds to human and mouse IL-17C, thereby inhibiting the binding of IL-17C to its IL-17RE receptor and thus its biological activity. MOR106 attenuates progression of clinical signs in FT mice

![Image](image1.png)

**Figure 1.** FT mice treated with MOR106 have less hair loss in the shoulder & neck region and less skin association under the neck.

**Figure 2.** MOR106 reduces progression of skin severity score.

**Figure 3.** MOR106 reduces eyelid inflammation (blepharitis).

**Objective & Method**

We sought to further strengthen the evidence for IL-17C as a disease relevant cytokine in AD by evaluating its role in established disease. To this end, we evaluated the therapeutic administration of the anti-IL-17C antibody MOR106 in the Flaky Tail (FT) mutant mouse strain which spontaneously develops atopy and progressive overt dermatitis due to a defective skin barrier.3

- Study outline
  - FT mutant mice
    - (MOR106 treated + IgG control) 6-weeks old, with overt dermatitis age 9-10 weeks

- Randomized - Groups (n=10/group)
  1. FT mutant mice + isotype Ab (30 mg/kg) (i.p. twice weekly x 6 weeks)
  2. FT mutant mice + MOR106 (3 mg/kg) (i.p. twice weekly x 6 weeks)
  3. FT mutant mice + MOR106 (30 mg/kg) (i.p. twice weekly x 6 weeks)
  4. FT mutant mice + DEX (2 mg/kg) (i.p. twice weekly x 6 weeks)

- WT 3 age-matched C57BL/67 strain mice used as wildtype control mice

- All assessments were essentially done as described before.3

- Statistical analyses were performed with a one-way analysis of variance (ANOVA) and Dunnett post hoc test. *: p<0.05; **: p<0.01; ***: p<0.001

**MOR106 reduces acanthosis & mast cell infiltration in FT lesional skin**

![Image](image2.png)

**Figure 4.** Histomorphometric analysis of H&E stained lesional skin demonstrated a significant reduction of acanthosis upon treatment with MOR106 with a similar effect to dexamethasone (DEX) treatment.

**Figure 5.** MOR106 reduces number of mast cells in FT lesional skin. Data represent the number of mast cells counted per high power field (HPF) in paraffin-embedded tissue sections stained with toluidine blue.

**MOR106 reduces serum IgE and Th2 cytokines in FT mice**

![Image](image3.png)

**Figure 6.** MOR106 reduces the increased serum IgE levels in FT mice.

**Figure 7.** Inflammation in FT mice is characterized by increased Th2/Th17 cytokines. MOR106 reduced mainly the Th2 cytokines.

Conclusions

- Administration of the IL-17C neutralizing antibody MOR106 significantly attenuated the development of established AD-like inflammation in the flaky tail model of spontaneous dermatitis, with effects comparable to the treatment with a high dose of dexamethasone.

- Inhibiting IL-17C activity is a potential novel therapeutic paradigm for treating AD. MOR106 is currently evaluated in a Phase 1 study in healthy volunteers and patients with AD (NCT02739009).

References

3. Vandeghinste N et al. (2017). IL-17C drives skin inflammation in calcipotriol-induced rodent model of atopic dermatitis. Poster #PO239 EADV 2017 congress