Regulation of Mast Cell Activity by KTN0158, a Humanized anti-KIT Monoclonal Antibody

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Introduction

- KTN0158 is a humanized immunoglobulin G1 kappa (IgG1k) monoclonal antibody (mAb) that specifically binds KIT (c-KIT, mast/stem cell factor growth factor, CD117).
- Mast cells have been implicated in a variety of allergic and inflammatory diseases such as asthma and rheumatoid arthritis as well as fibrosis (Metcalfe et al., 1997).
- Mast cell infiltrates are associated with tumors and may have roles in tumor promotion or rejection depending on the setting (Theoharides and Conti, 2004).
- KIT signaling in mast cells appears to play an important role in the development of plexiform neurofibromas in neurofibromatosis type 1 (NFI; Steaser et al., 2012).

Methods

- Effects of KTN0158 on SCF-Induced KIT Activation and Signaling in H526 Small Cell Lung Cancer Cells
- KTN0158 Inhibits SCF-Induced Secretion of TNFα and GM-CSF in the LA2D Mast Cell Line

Results

- KTN0158 Inhibits SCF-Induced Secretion of TNFα and GM-CSF in the LA2D Mast Cell Line
- KTN0158 is a potent inhibitor of SCF-mediated effects on cytokine secretion

Conclusions

- KTN0158 is a potent inhibitor of SCF-induced KIT signaling.
- KTN0158 modulates SCF-mediated effects on degradation and cytokine production in the mast cell line LA2D.
- KTN0158 treatment decreased mast cell numbers in dog skin indicating that sufficient concentrations of KTN0158 were achieved in skin to inhibit KIT signaling in mast cells.
- Collectively, these data suggest that KTN0158 can modulate mast cell function via KIT and may provide therapeutic benefit in mast cell-related diseases such as NFI.
- Studies to investigate the potential benefit of KTN0158 in mast cell-related diseases such as NFI and to evaluate safety are planned.

References


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