Title (15 words/limit of 15 words)

Briquilimab Potently Inhibits Stem Cell Factor (SCF)/c-Kit Signaling, And Mast Cell (MC) Degranulation And Survival.

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Body (250 words/250 words limit)

Introduction:
SCF binding to c-Kit receptor regulates MC activation and survival. Briquilimab is an aglycosylated IgG1, antagonistic c-Kit monoclonal antibody (mAb) that blocks SCF binding to c-Kit and inhibits SCF/c-Kit signaling leading to MC apoptosis. We evaluated briquilimab's inhibition of MC degranulation and survival in comparison to a tool compound mAb that blocks c-Kit dimerization (JSP084) and the small molecule multi-tyrosine kinase inhibitor, imatinib. Briquilimab's effects on FcγR-mediated MC degranulation, antibody-dependent-cellular-cytotoxicity (ADCC), and complement-dependent cytotoxicity (CDC) were also evaluated.

Methods:
The primary human MC ($CD34^-FcεRI^+c\text{-}Kit^+$) cells were differentiated from mobilized peripheral $CD34^+$ cells and used to assess MC degranulation, cytokine release assay and MC survival rate. ADCC and CDC were measured using M-07e and UT-7 cells.

Results:
Both briquilimab and JSP084 inhibited *in vitro* IgE/FcεRI-mediated MC degranulation significantly more potently than imatinib. Briquilimab exhibited lower IC_{50} and was more potent than JSP084 at inhibiting MC degranulation. Briquilimab also reduced MC cytokine release, including TNFα and Th2-associated cytokines at 6h and 24h after IgE/anti-IgE challenge. Briquilimab at 100 nM almost completely inhibited SCF-dependent MC survival, but 100 nM of JSP084 only partially inhibited MC survival after 6 days of culture. Antibodies containing either wildtype Fc or a modified Fc region with enhanced FcγR binding affinity, but not briquilimab lacking FcγR binding ability via aglycosylation, induced FcγR-mediated MC degranulation. Additionally, briquilimab did not induce FcγR-mediated ADCC nor CDC.

Conclusion:
Briquilimab potently inhibits human IgE/FcεRI-mediated MC degranulation and MC survival in culture, and it does not induce FcγR-mediated MC degranulation, ADCC or CDC.