Briquilimab, an Anti-Human CD117 Antibody, Effectively Treats Epicutaneous Allergen-Induced Atopic Dermatitis in Mouse Model Expressing Chimeric Human/Mouse CD117

Mang Yu[1], Sambidhan Kattel[1], Andrew Wells[1], Revati Nerkar[1], Karl Meneses[1], Hye-Sook Kwon[1], Wendy W. Pang[1]
[1]Jasper Therapeutics, Inc., Redwood City, CA 94065, USA.

Background: Stem cell factor (SCF) signaling through c-Kit (CD117) is crucial in mast cell (MC) growth, differentiation, migration, survival, and activation. Inhibition of this pathway with briquilimab, a humanized aglycosylated monoclonal antibody against CD117 that potently inhibits SCF signaling, has the potential to treat MC-mediated diseases, including atopic dermatitis (AD).

Methods: In transgenic C57BL/6 mice expressing chimeric CD117 (hmCD117), consisting of human extracellular and mouse intracellular domains of CD117 in lieu of wild-type mouse CD117, AD was induced on back skin by epicutaneous (e.c.) sensitization (days 1-4) and challenge (days 15-18) using house dust mite antigen and Staphylococcus enterotoxin B (HDM/SEB). 50 mg/kg briquilimab was administered intraperitoneally either on day 6 to evaluate AD prophylaxis or on day 23 to evaluate AD therapeutic treatment. Control mice were administered PBS on day 6 or 23. The skin eruption score (ES), scaling score (SS), post-inflammatory hyperpigmentation score (HS), and skin histology were assessed on day 20 (prophylaxis model) or day 37 (therapeutic model).

Results: In control hmCD117 mice, briquilimab depleted skin MCs by 82% by day 20 (32□1 vs. untreated 180□4/mm^2, P<0.05). HDM/SEB hmCD117 mice exhibited significant skin eruption, scaling, and hyperpigmentation on day 20, as well as increased dermal MCs (258□30 vs. control 180□4/mm^2, P<0.05) and inflammatory leukocytes (1645□168 vs. control 56□4/mm^2, P<0.05). Prophylactic treatment with briquilimab of HDM/SEB hmCD117 mice on day 6 led to decreased dermal MCs (103□56 vs. untreated 258□30/mm^2, P<0.05), and decreased inflammatory leukocytes (519□122 vs. untreated 1645□168/mm^2, P<0.05), as well as marked improvements in skin ES (1□0.5 vs. untreated 2.8□0.3, P<0.05), SS (0.3□0.3 vs. untreated 2.7□0.3, P<0.05), and HS (0□0 vs. untreated 3.7□0.6, P<0.05), suggesting that briquilimab can prevent development of AD. Importantly, therapeutic treatment with briquilimab on day 23 in HDM/SEB hmCD117 mice, after AD was established, also led to improved skin ES by 85%, SS by 80%, and HS by 95% on day 37, accompanied by a 70% decrease in dermal mast cells and a 90% reduction in dermal inflammatory leukocytes (P<0.05 for all measures), indicating that briquilimab can reverse AD pathology.

Conclusions: This study provides early evidence that briquilimab may be a novel therapeutic agent for AD.