AQX-1125 is a small molecule next generation SHIP1 activator. It has many of the inflammatory effect of AQX-1125, a small molecule SHIP1 activator. Here we tested the effect of prophylactic or therapeutic AQX-1125 administration in a murine model of bleomycin induced pulmonary inflammation and fibrosis.

Methods: The efficacy of AQX-1125, administered by oral gavage (3, 10 or 30 mg/kg), was assessed in bleomycin (BLM) induced lung injury in male CD-1 mice. In the prophylactic investigation, bleomycin (0.1 U/mouse) was administered two hours after the third dose of AQX-1125. For therapeutic investigation, AQX-1125 administration was started on Day 13 after bleomycin administration (0.05 IU/mouse). AQX-1125 administration continued once per day throughout the remainder of the studies. Twenty-one-days (prophylactic investigation), or 28-days (therapeutic investigation) after bleomycin administration, mice were sacrificed and bronchoalveolar lavage (BAL) cellular content, lung edema, myeloperoxidase, TGFB, histopathology, collagen deposition and mortality. Determinations were made.

Results: In the 21-day prophylactic model, AQX-1125 significantly (p<0.05) suppressed bleomycin-induced collagen deposition, inflammation and mortality. However, therapeutically administered AQX-1125 also dose-dependently reduced the mortality to bleomycin over the duration of the study. In addition, therapeutic AQX-1125 (3, 10 or 30 mg/kg) significantly (p<0.05) attenuated the bleomycin-induced collagen deposition in the airways by 45% and 82%, respectively, which correlated with significantly suppressed leukocyte infiltration of the airways, lung tissue, edema, myeloperoxidase activity, TGFB concentration and the histopathology score (p<0.05).

Conclusion: Therapeutic or prophylactic SHIP1 activation with AQX-1125 inhibits mortality, leukocyte accumulation, edema, inflammatory mediator and collagen content of the airways in a murine model of bleomycin-induced fibrosis. Thus, AQX-1125 has the potential to be developed as a treatment for fibrotic disease.

Efficacy of AQX-1125 on body weight in the therapeutic 28-day BLM-induced lung fibrosis model

Figure 9. Efficacy of AQX-1125 on body weight in the therapeutic 28-day BLM-induced lung fibrosis model.