A Novel Immunosuppressive Drug (4SC-101) Improves TNBS-Induced Colitis in Mice

Leo R. Fitzpatrick1, Jeffrey S. Small1, George Zhang2 and Ruediger Jankowsky3

1. Penn State College of Medicine, Hershey PA  2. P&G Pharmaceuticals, Mason OH  3. 4SC AG, Martinsried Germany

This work was supported by P&G Pharmaceuticals.

4SC-101 is a proprietary component of 4SC-AG

ABSTRACT

Disease patients.

Methods

Histological evaluations were performed on coded H&E stained slides. Two observers, blinded to the treatment groups, scored each slide according to the method of Reuter et al. (1988). The macroscopic scores were calculated by the method of Reuter et al. (1988). The total length, distal (5 cm) segment weight, myeloperoxidase (MPO) and histological pathology. Kidney and spleen weights were also determined on study day 7.

During the study period, 5 mice did not complete the study due to morbidity or mortality. Therefore, 37 mice were available for tissue collection on day 7. On study day 7, mice were euthanized by exposure to carbon dioxide. The colons were analyzed for overall macroscopic damage, ulceration, adhesions, colonic thickness, loose stool/diarrhea.

Abstract: 4SC-101 is a novel immunosuppressive drug with excellent potential for the treatment of intestinal inflammation. 4SC-101 is a novel immunosuppressive drug that inhibits DHODH. This drug is a potent inhibitor of lymphocyte proliferation, and it is also active in rodent models of arthritis and other autoimmune conditions. Oral treatment with 4SC-101 (4SC-101) improved various parameters of TNBS-induced colitis. Oral treatment of mice with 4SC-101 improved various parameters of TNBS-induced colitis. Overall, the anti-colitis efficacy profile of 4SC-101 was similar to that of Dexamethasone. 4SC-101 is currently undergoing a clinical phase II trial in Crohn’s Disease patients.

CONCLUSION

SUMMARY

Oral treatment of mice with 4SC-101 improved various parameters of TNBS-induced colitis. Overall, the anti-colitis efficacy profile of 4SC-101 was similar to that of Dexamethasone. 4SC-101 is currently undergoing a clinical phase II trial in Crohn’s Disease patients.