Anti-Hemojuvelin Monoclonal Antibody Reverses Anemia and Exerts Disease-Modifying Effects in a Mouse Model of Inflammatory Bowel Disease

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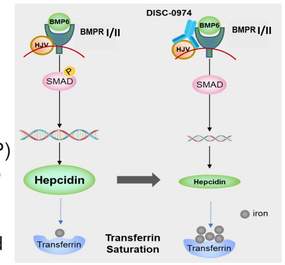
INTRODUCTION

Anemia is the most common complication of inflammatory bowel disease (IBD). Its etiology is multifactorial, caused by factors such as chronic inflammation, iron deficiency, intestinal blood loss, and reduced iron absorption.[1] Despite approved intravenous iron therapy, management of anemia in IBD patients remains a challenge in clinical practice.[2]

DISC-0974 is a humanized anti-hemojuvelin (HJV) monoclonal antibody. It was designed to disrupt the interaction between HJV and the bone morphogenetic protein (BMP) receptor complex, leading to decreased hepcidin expression and increased iron availability for enhanced erythropoiesis.



DISC-0974 is currently in clinical studies to treat anemia in patients with myelofibrosis (NCT05320198) and chronic kidney disease (NCT05745883).

AIM

The aim of this study was to evaluate the effect of DISC-0974 on improving anemia in a dextran sodium sulfate (DSS)-induced colitis mouse model.

METHODS

Chronic colitis was induced in female C57BL/6J mice by up to 4 cycles of DSS treatment. In each cycle, the mice were given drinking water containing 2.5% DSS for 4 days, followed by 3 days of washout (ie, no DSS in the drinking water).

For model development, the mice were euthanized after the completion of each DSS cycle.

For the efficacy study, at the start of the 2nd DSS cycle, either vehicle or DBIO-100 (murine analog of DISC-0974; 20 mg/kg) was administered intravenously on Day 7 and Day 17. Mesalamine, the first-line therapy of IBD, was used as a positive control. Mesalamine was administered at 100 mg/kg daily via oral gavage at the beginning of the 2nd DSS cycle on Day 7.

RESULTS

DSS-induced IBD mouse model characterization

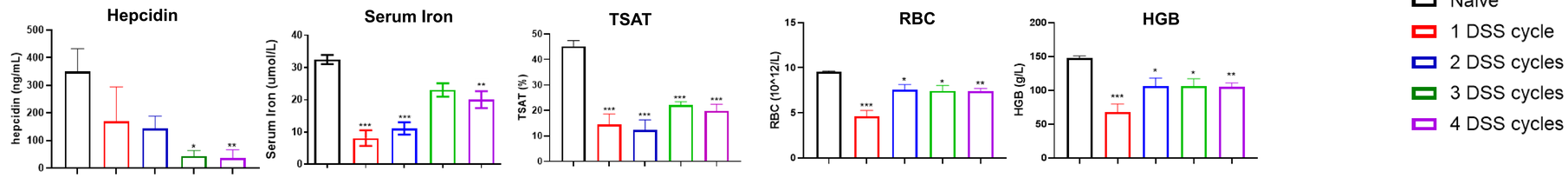


Figure 1. DSS-induced colitis mouse model is characterized by decreased serum hepcidin, iron, transferrin saturation (TSAT), as well as red blood cell (RBC) and hemoglobin (HGB) counts. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ vs Naive by 1-way analysis of variance (ANOVA). Values represent mean ± SEM.

DBIO-100 reduced hepcidin, improved iron availability, and ameliorated anemia in DSS-induced colitis mouse model

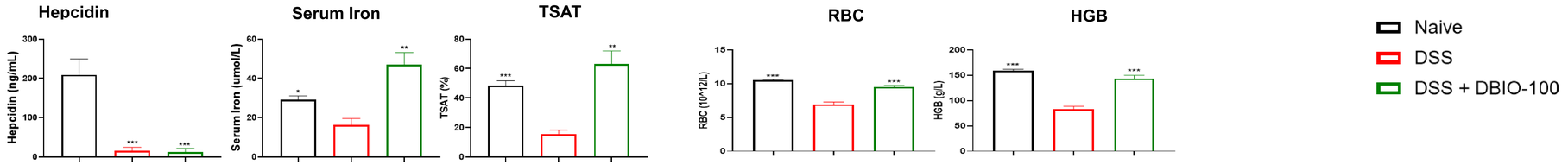


Figure 2. DBIO-100 reduced serum hepcidin, improved serum iron availability, and ameliorated anemia in DSS-treated mice. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ *vs* Naive by 1-way ANOVA. Values represent mean ± SEM.

DBIO-100 had disease-modifying effects in DSS-induced colitis mouse model

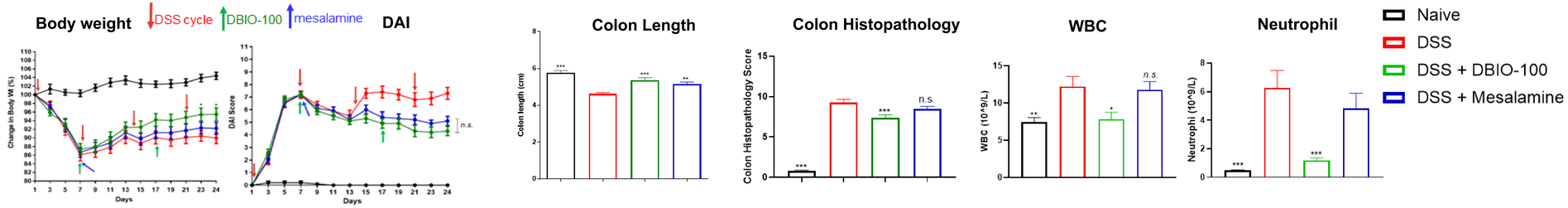


Figure 3. DBIO-100 had positive impacts on body weight, disease score (DAI), colon length, and colon histopathology; It also reduced white blood cell (WBC) and neutrophil counts . * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ vs Naive by 1-way ANOVA. Values represent mean ± SEM.

CONCLUSIONS

Taken together, this study demonstrated that DBIO-100, a mouse anti-HJV monoclonal antibody, not only reversed DSS-induced anemia and iron deficiency, but also exhibited disease-modifying therapeutic effects on chronic colitis in vivo. Of note, while some beneficial effects of DBIO-100 were equivalent to those of mesalamine, others showed superiority. The findings highlight the therapeutic potential of DISC-0974 in the treatment of anemia of chronic inflammatory disease such as IBD.

REFERENCES

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CONTACT INFORMATION

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