

# ON104, a novel bioengineered antibody targeting oxidized Macrophage Migration Inhibitory Factor (oxMIF) shows efficacy in two distinct models of experimental colitis



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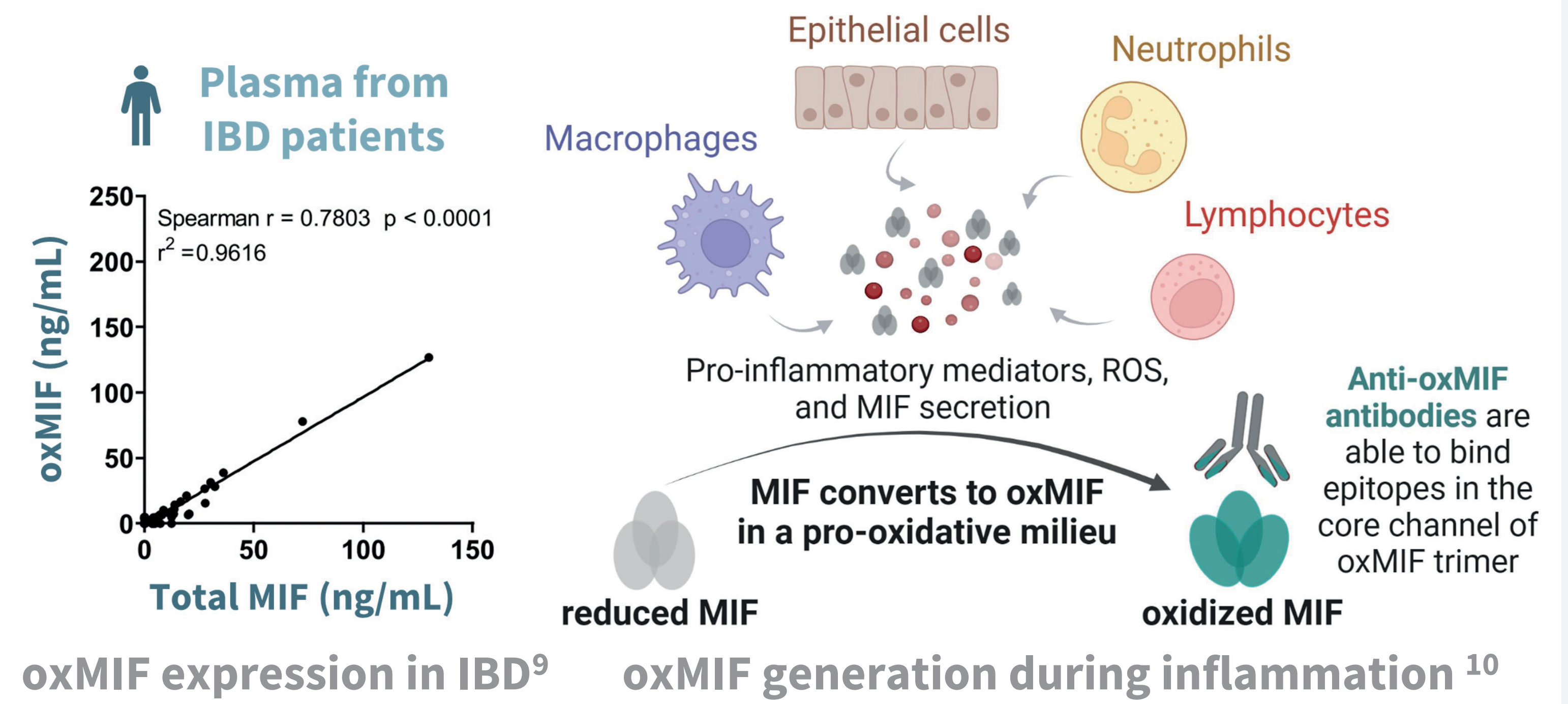
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## 1 Macrophage migration inhibitory factor

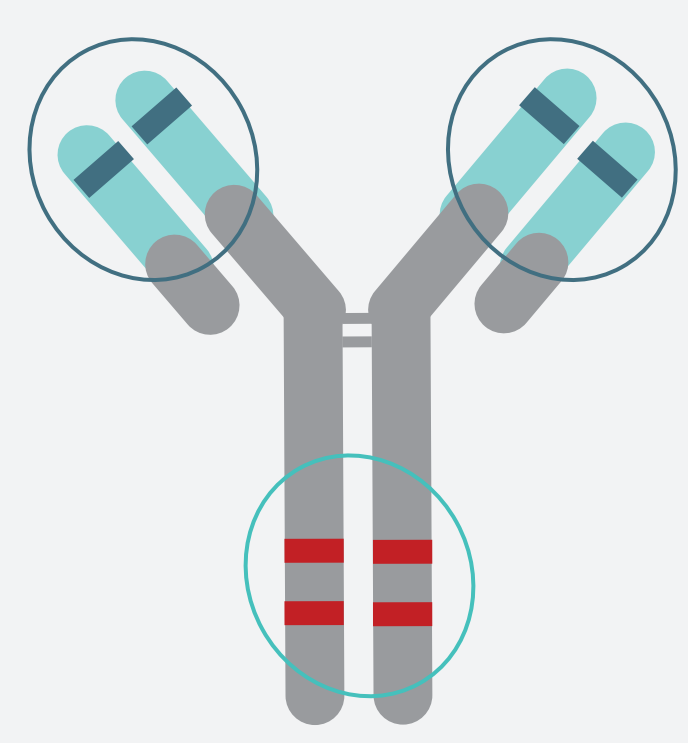
MIF is a pleiotropic inflammatory cytokine and a primary counter-actor of glucocorticoids that emerged as a pivotal regulator of chronic inflammation including inflammatory bowel diseases (IBD)<sup>1-5</sup>. MIF occurs in two immunologically distinct conformational isoforms: reduced MIF, ubiquitously present in various tissues and the circulation of healthy subjects, and oxidized MIF (oxMIF), described as the pathogenic and druggable isoform of MIF<sup>7-9</sup>.



➔ Targeting oxMIF represents a promising treatment option for patients with chronic inflammatory diseases such as IBD<sup>9,10</sup>

## 2 OncoOne's optimized anti-oxMIF mAb ON104

ON104: for chronic inflammatory diseases treatment

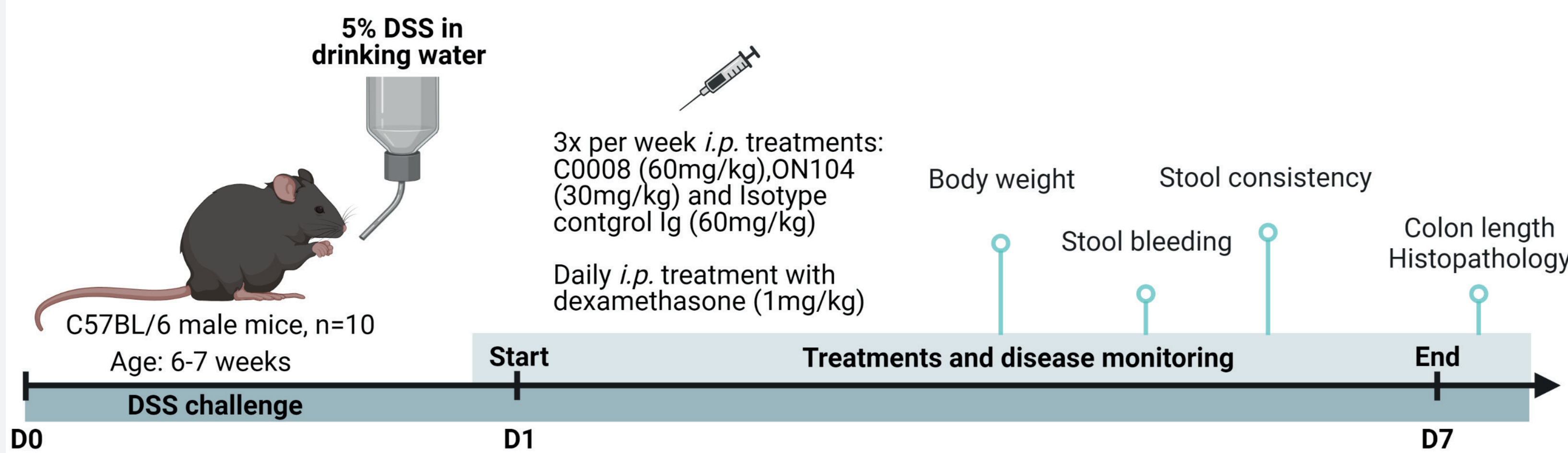


oxMIF-binding Fab with optimized variable domains

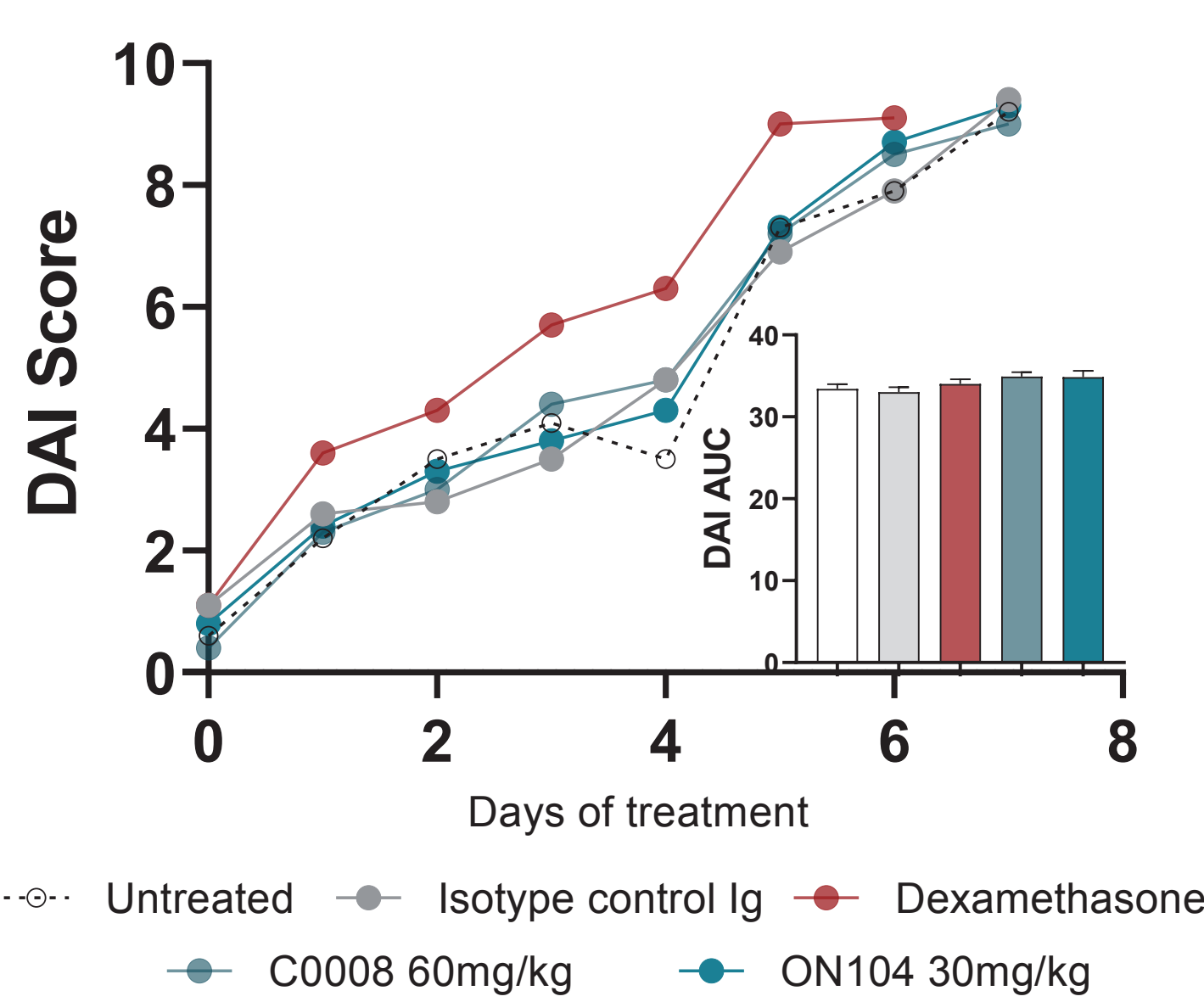
Optimized Fc To abolish FcγR binding and effector functions

ON104 vs. benchmark C0008 (Imalumab)  
Hydrophobicity ↓  
Aggregation ↓  
Pharmacokinetics ↑  
Biodistribution ↑

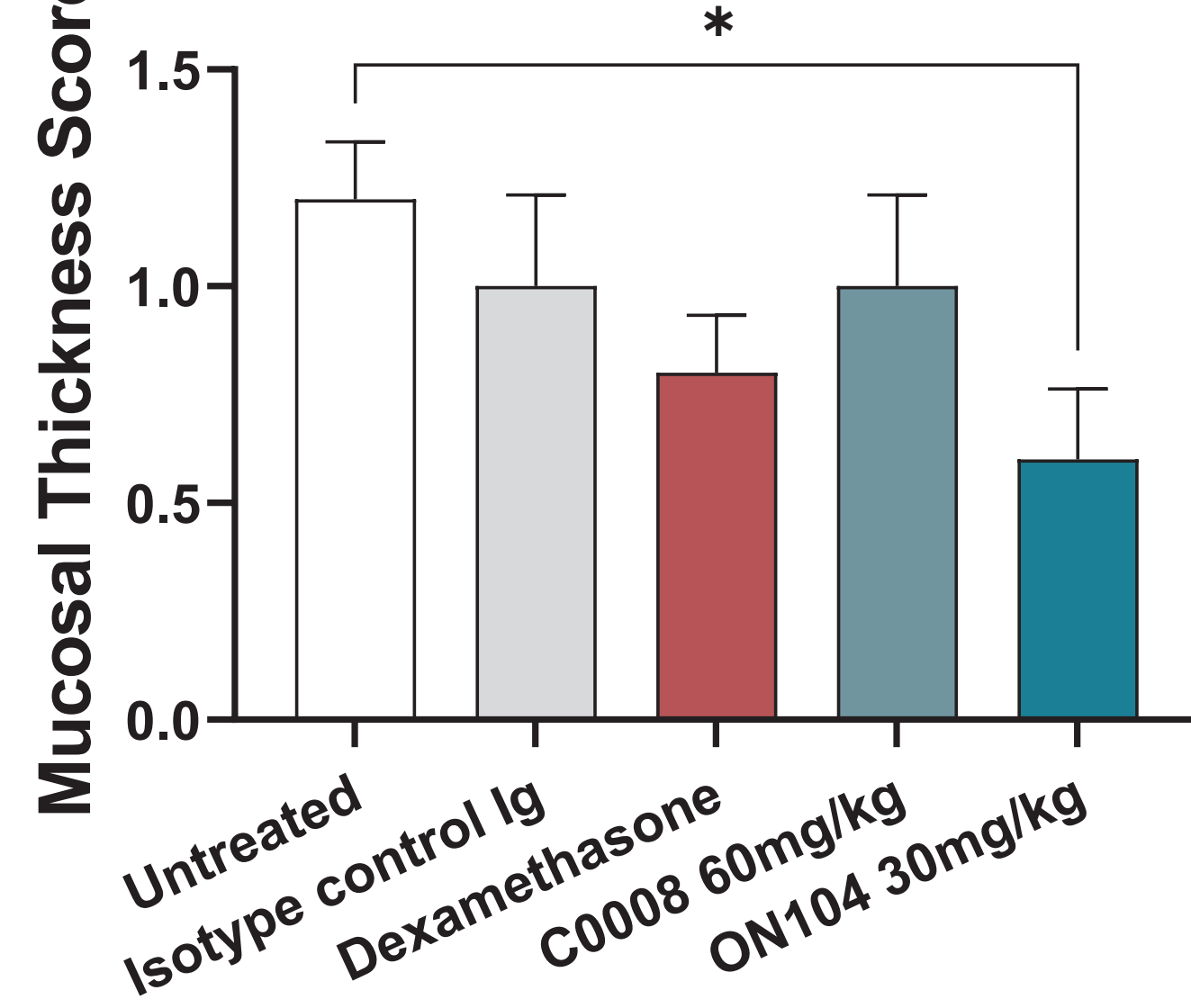
## 3 In vivo POC | DSS-induced colitis



### Disease activity index



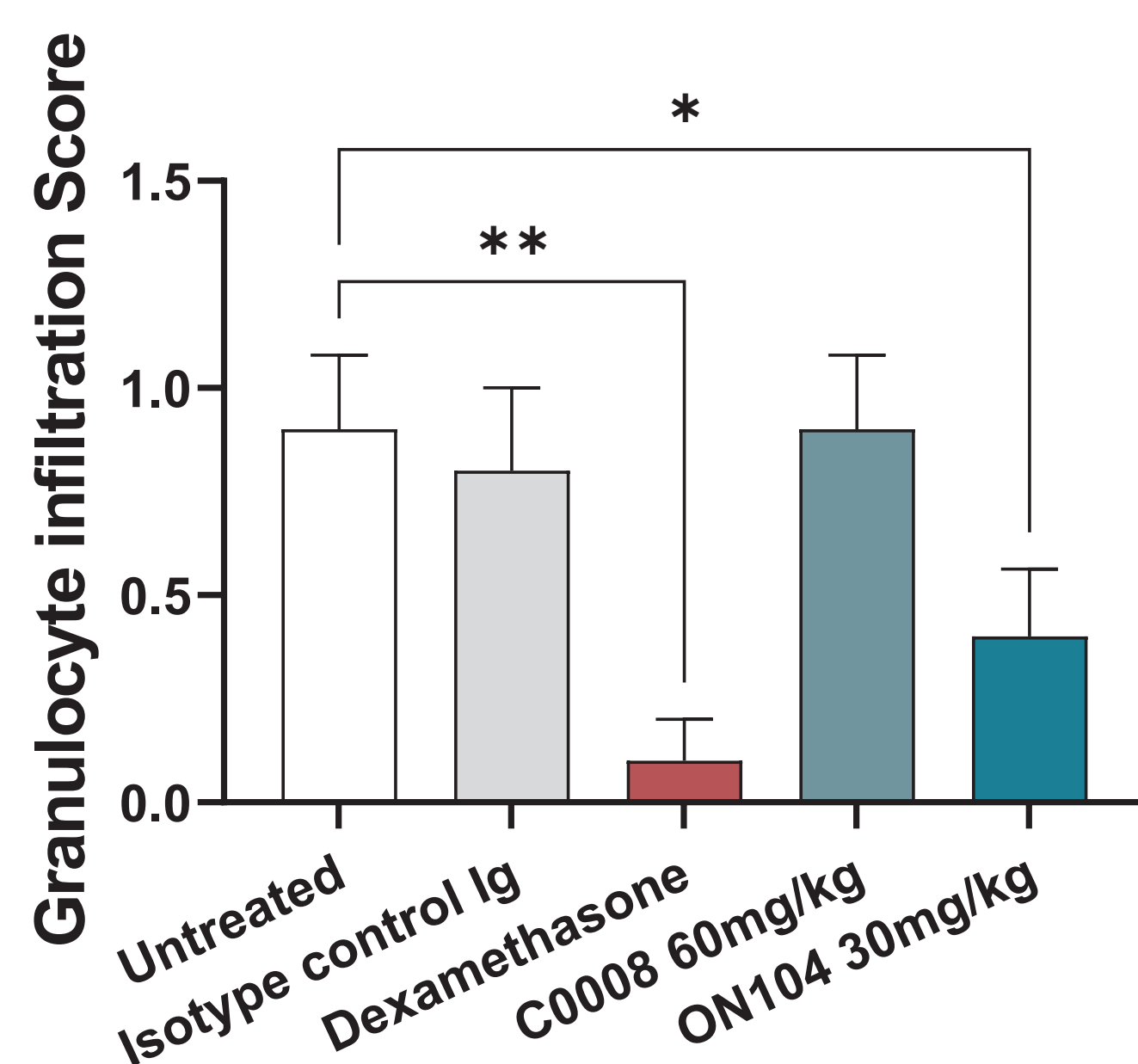
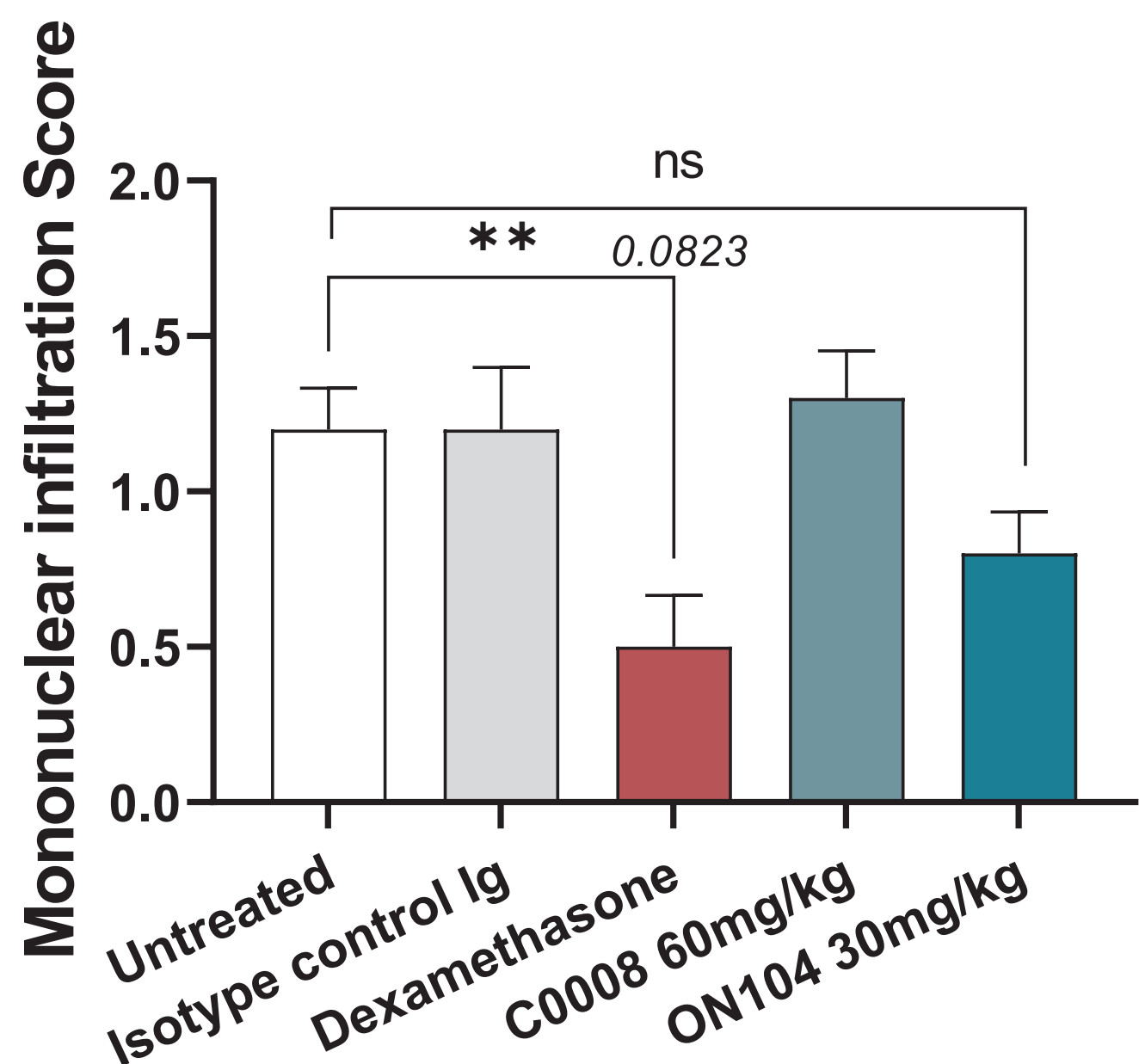
### Mucosal damage



Data are presented as mean ± SEM and analyzed by one-way ANOVA Fischer's LSD post-test. \* p<0.05

➔ ON104 significantly reduced colon tissue injury during acute DSS-induced colitis

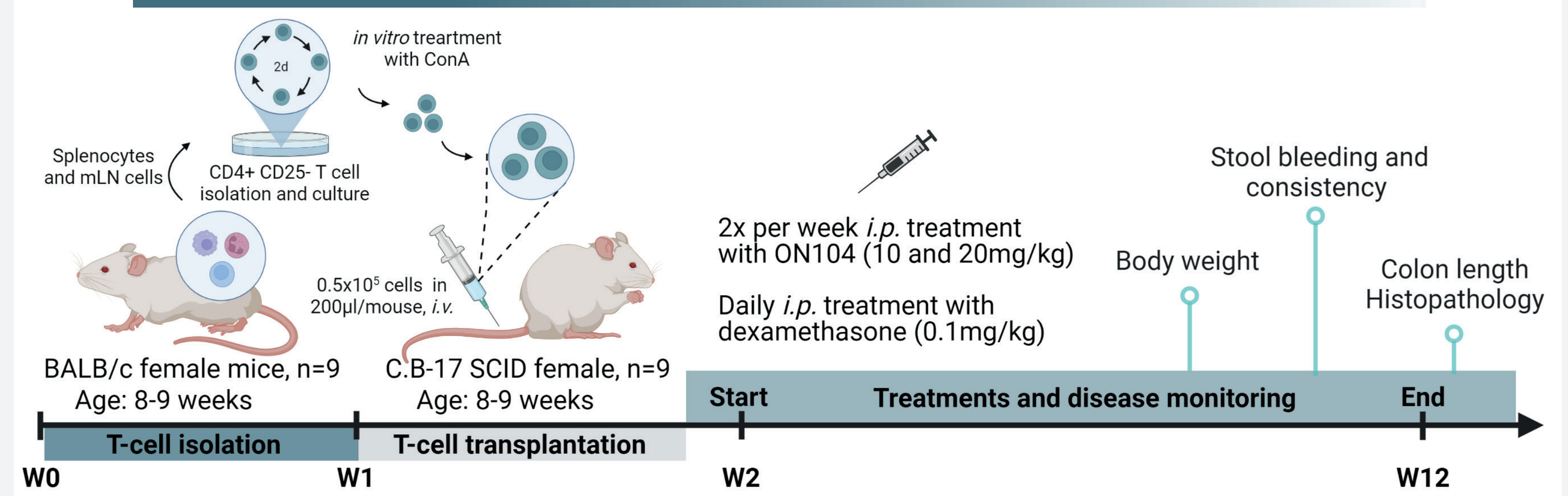
### Mucosal immune cell infiltration



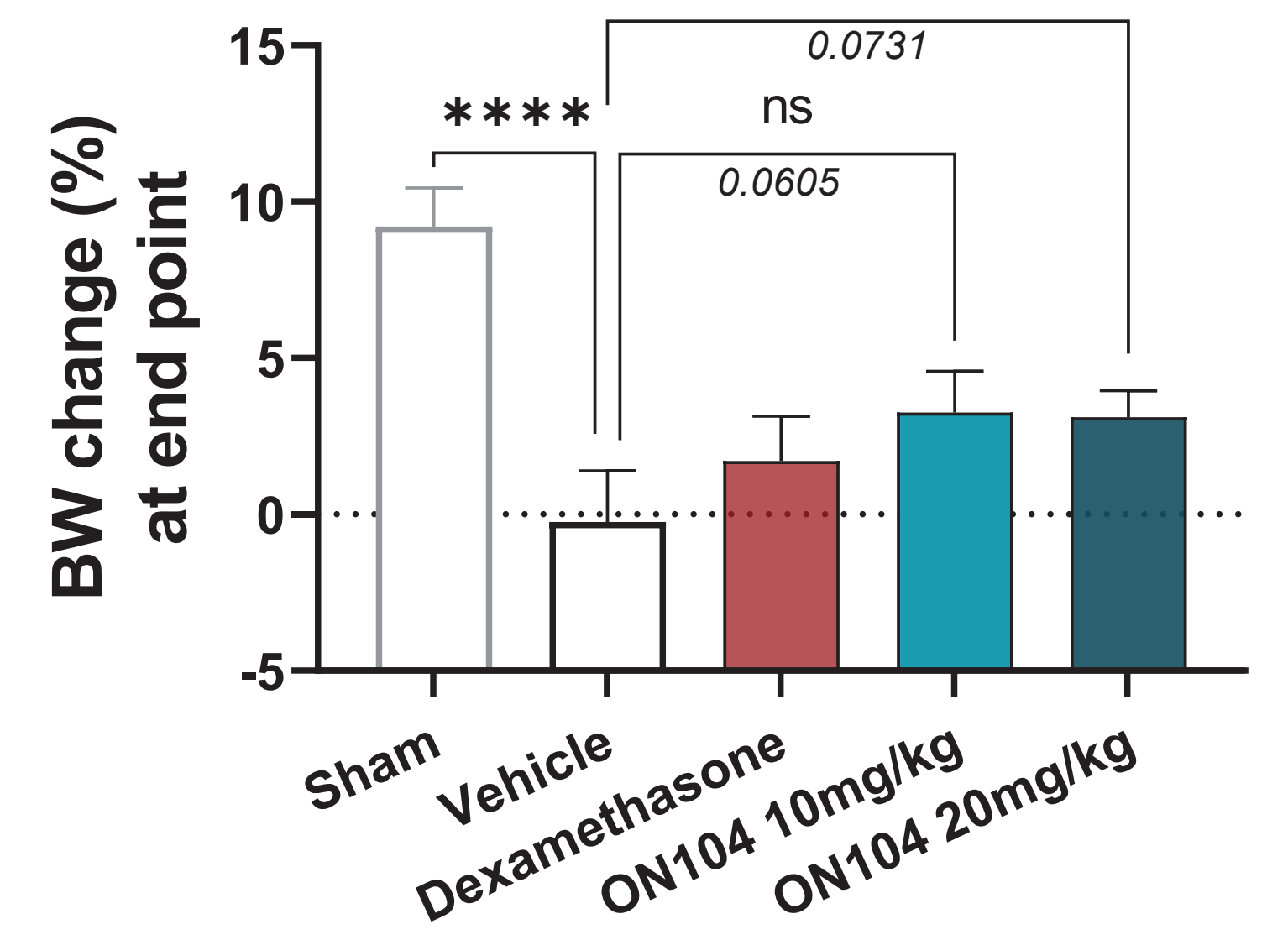
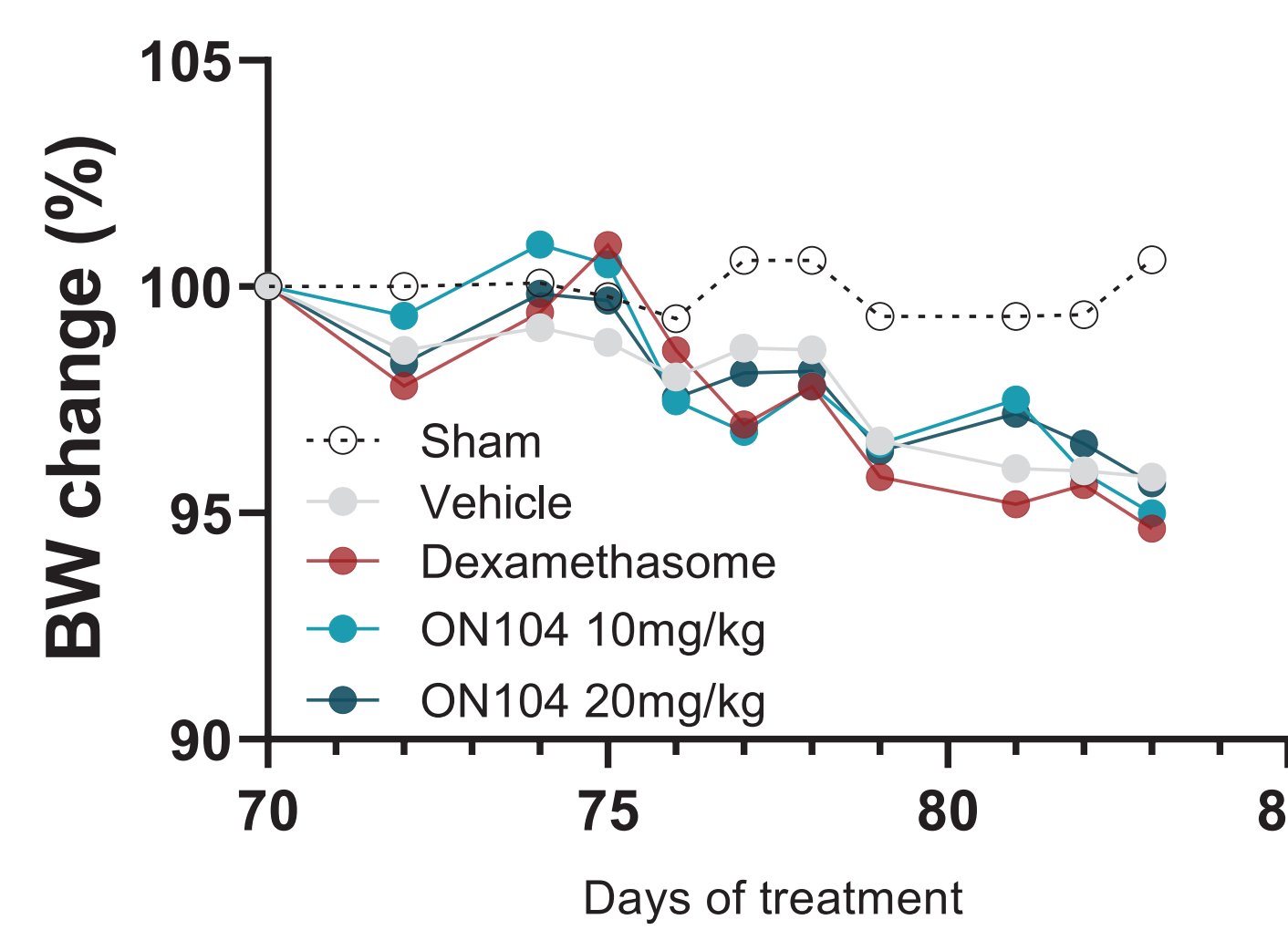
Data are presented as mean ± SEM and analyzed by one-way ANOVA followed by Fischer's LSD test. n.s.: non-significant, \* p<0.05, \*\* p<0.01

➔ ON104 successfully reduced local inflammation during acute DSS-induced colitis

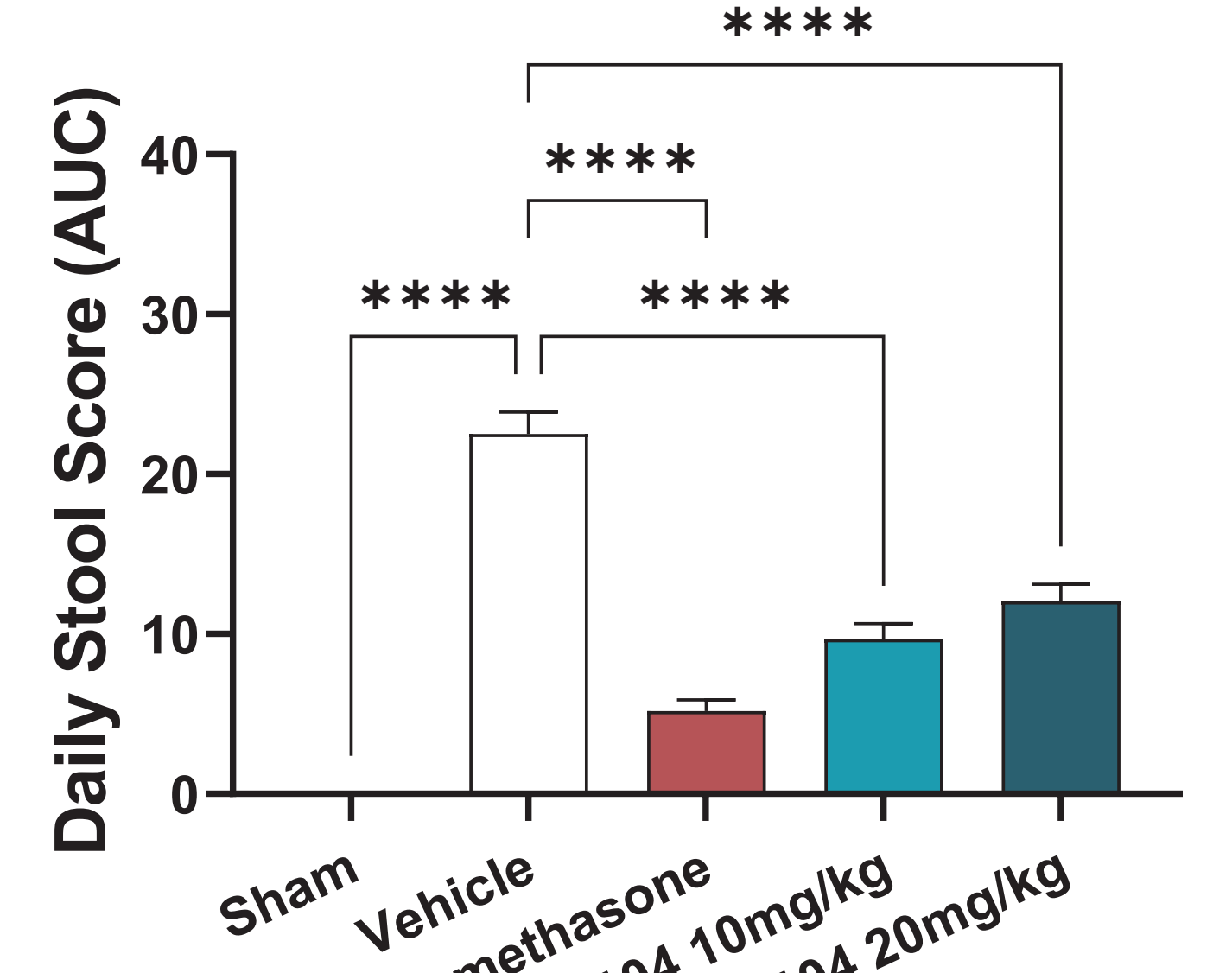
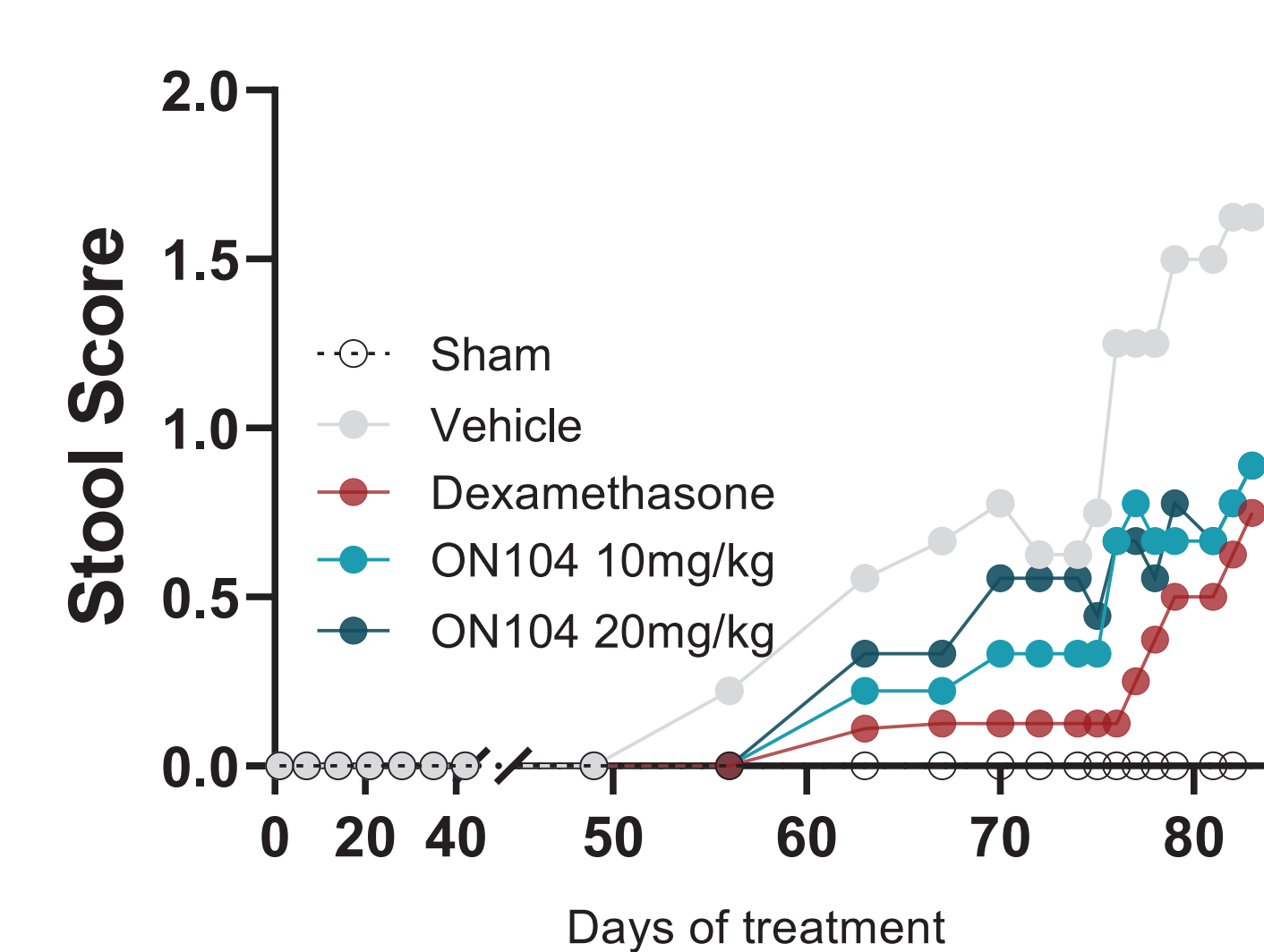
## 4 In vivo POC | T cell transfer-induced colitis



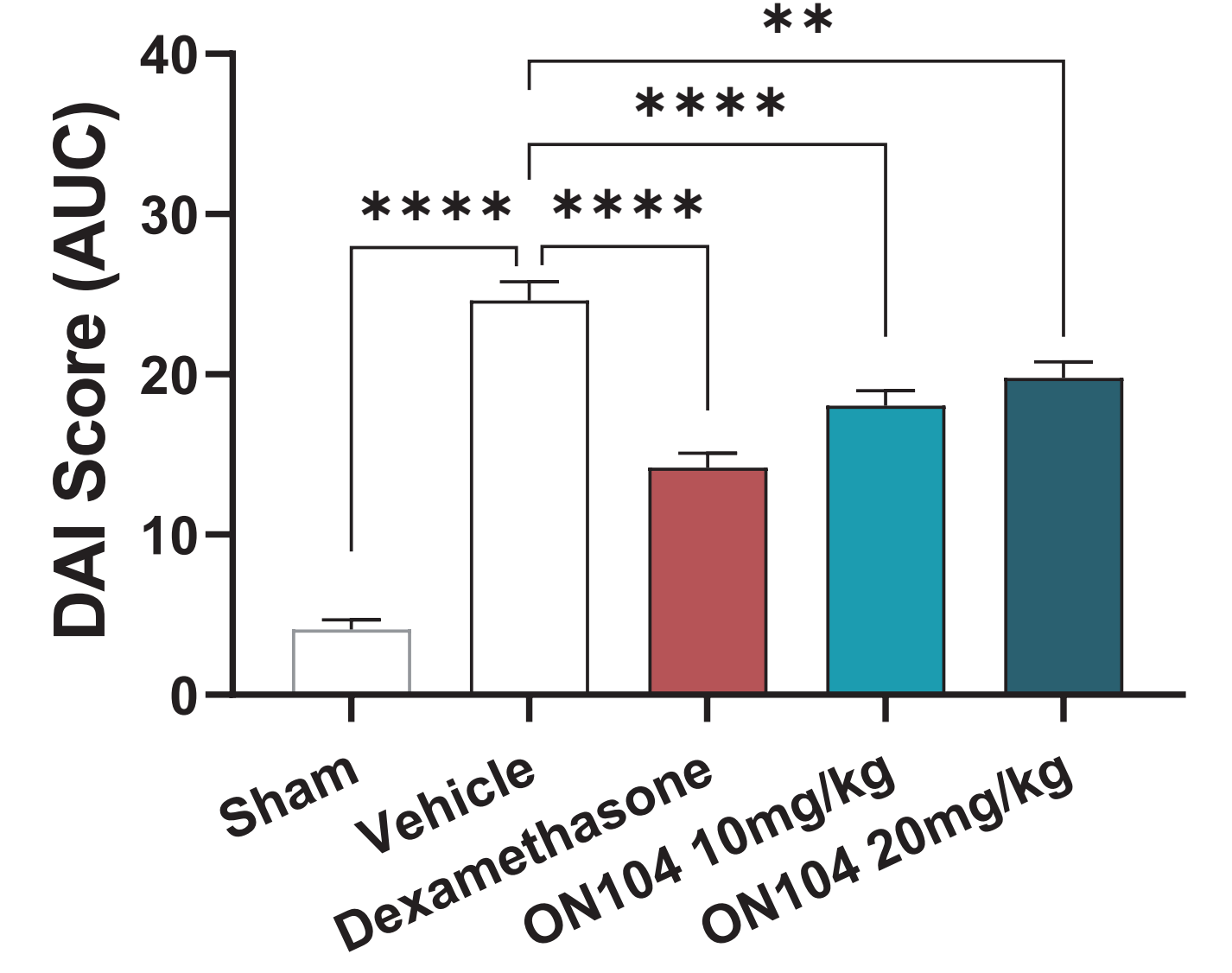
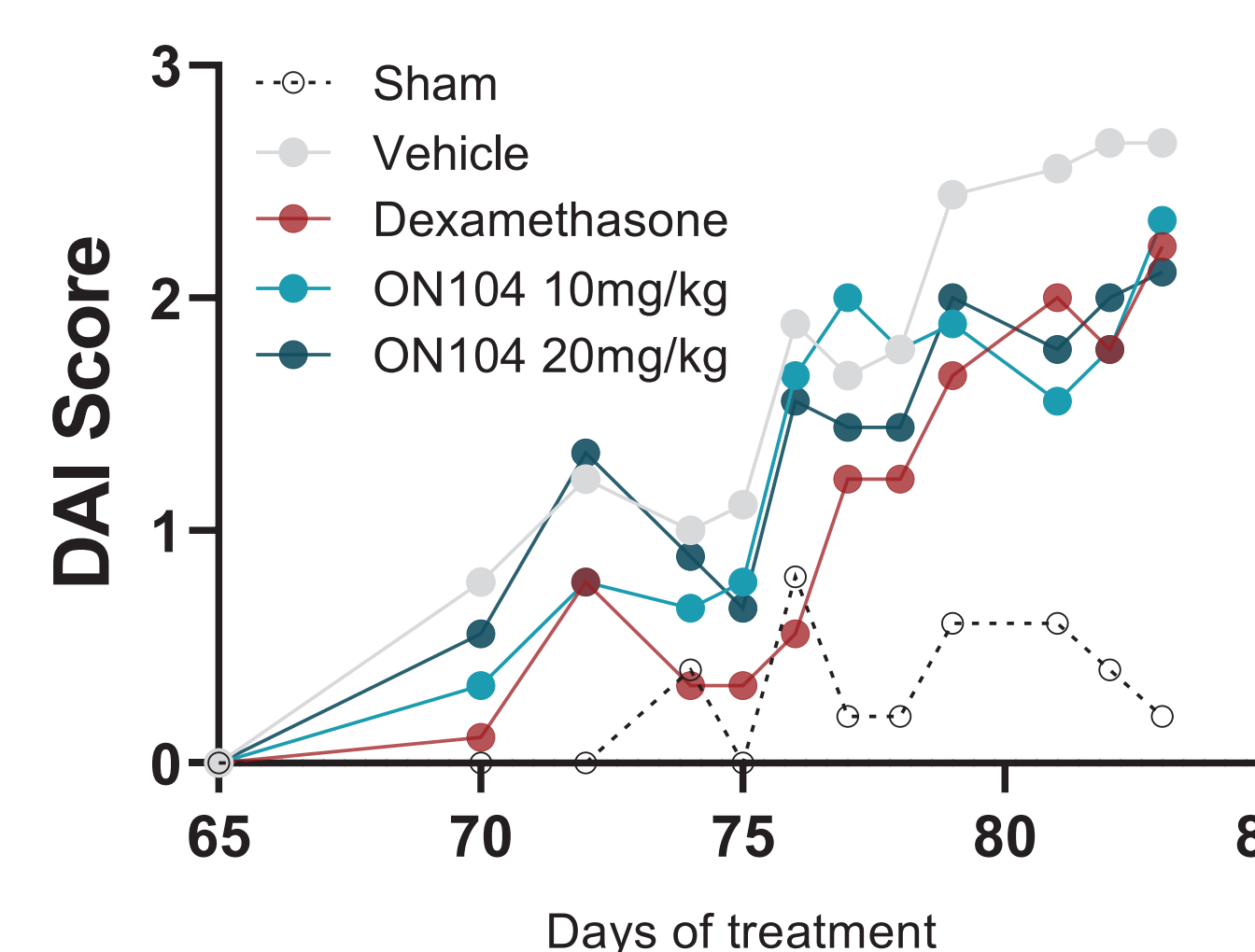
### Body weight change



### Stool consistency



### Disease activity index



Data are presented as mean ± SEM and analyzed by one-way ANOVA followed by Fischer's LSD test. n.s.: non-significant, \*\* p<0.01, \*\*\*\* p<0.0001

➔ ON104 reduced clinical symptoms of chronic colitis

## 5 Summary & conclusion

- oxMIF plays a role in experimental colitis
- ON104 improves clinical sign of colitis by ↓ colonic immune cell infiltration and ↓ tissue injury