

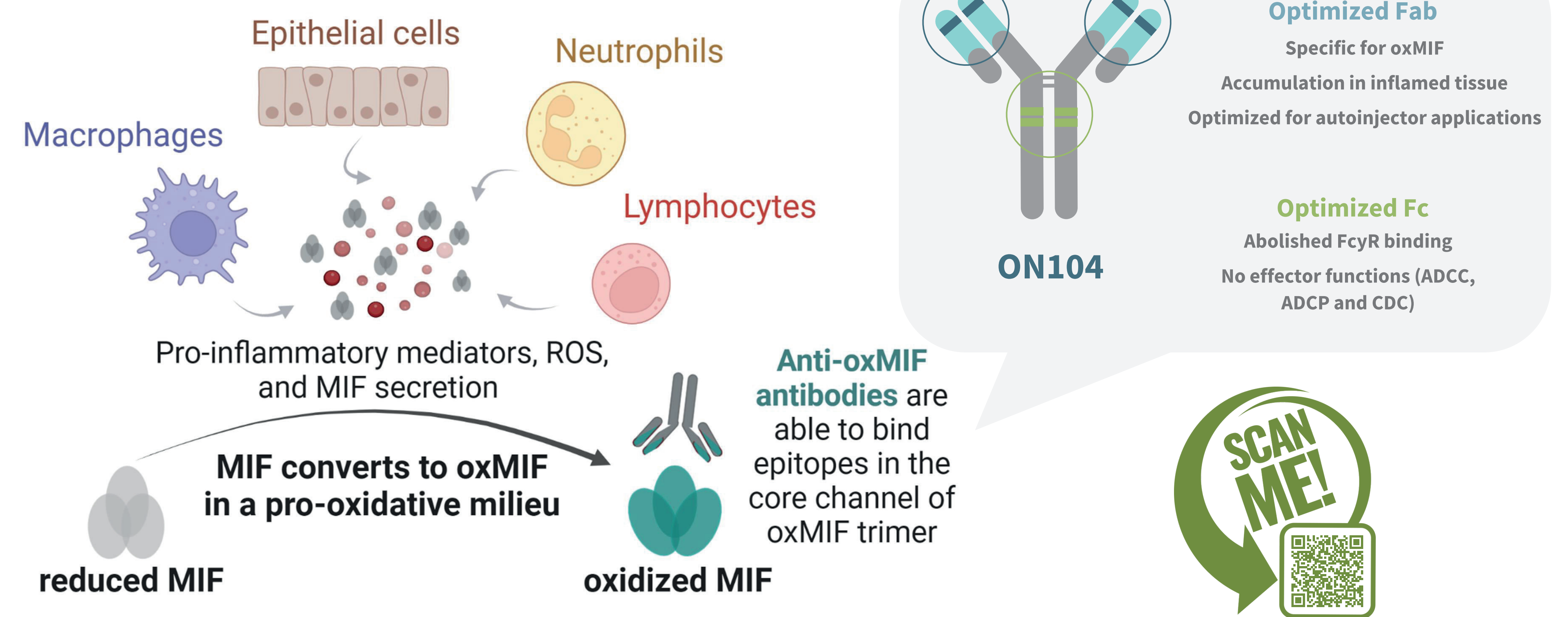
ON104, a novel antibody targeting oxidized Macrophage Migration Inhibitory Factor (oxMIF) shows efficacy in preclinical models of chronic inflammation

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1 Study abstract

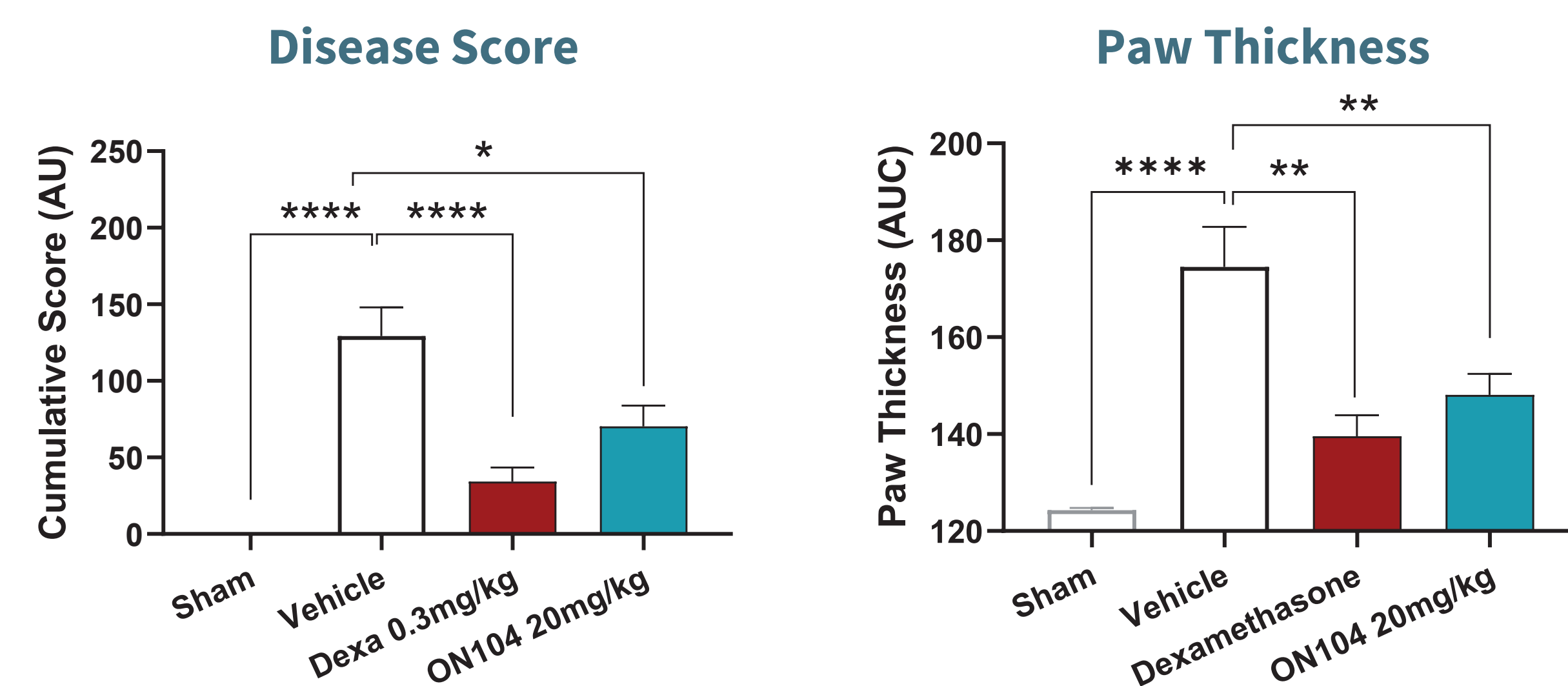
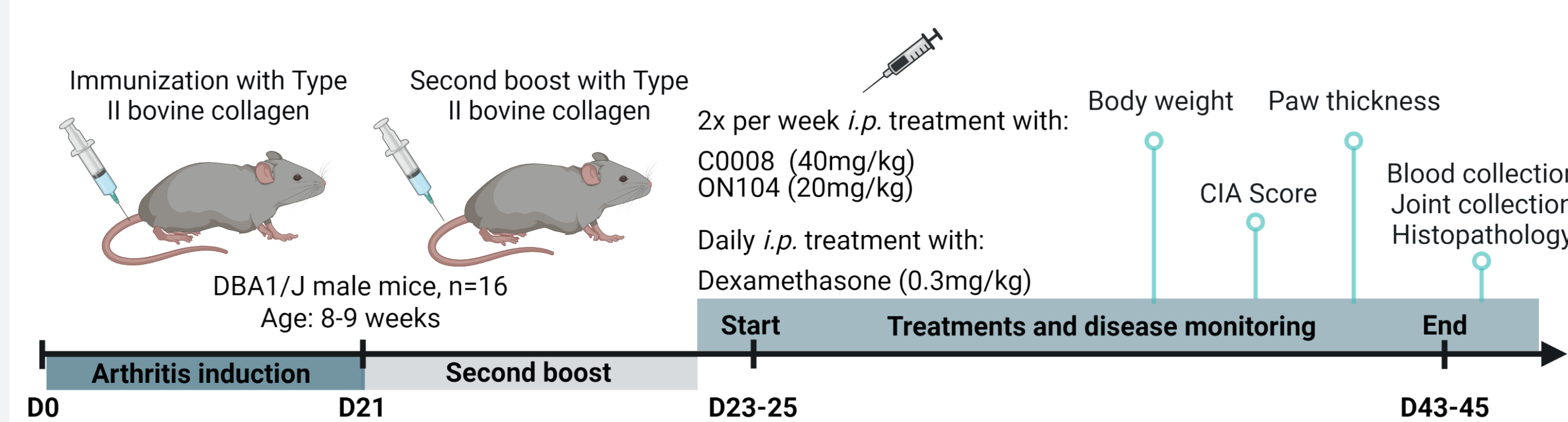
Macrophage Migration Inhibitory Factor (MIF) is a pleiotropic inflammatory cytokine, ubiquitously present in various tissues and the circulation of healthy subjects. MIF is a primary counter-actor of glucocorticoids that emerged as a pivotal regulator of chronic inflammation¹⁻⁵. During inflammation, **MIF converts into oxidized (ox)MIF** which was described as the **pathogenic and druggable isoform of MIF**⁶⁻⁷. ON104, a fully human antibody, was engineered to specifically neutralize oxMIF without triggering immune cell effector functions. ON104 was tested in three experimental models of chronic inflammatory diseases (CIDs): Glomerulonephritis (GN) in WKY rats, Collagen-Induced Arthritis (CIA) in DBA/1j mice; and adoptive T-cell transfer colitis in SCID mice. At disease onset, ON104 was administered at different doses twice a week for 1, 3, and 8 weeks in GN, CIA, and colitis, respectively. Clinical evaluations, blood and tissue sampling were done for all individual animals. In the GN model, ON104 significantly reduced proteinuria, hematuria, and CD68+ macrophage infiltration within the inflamed kidneys. During CIA, ON104 ameliorated the severity of arthritis as indicated by reduced paw thickness, and decreased disease score. Furthermore, treatment with ON104 substantially attenuated clinical signs of colitis by preventing body weight loss and restoring stool consistency compared to the vehicle-treated controls. **In conclusion**, our findings substantiate the role of oxMIF in the pathogenesis of autoimmune diseases. Thus, ON104 has the potential to become a well-tolerated therapeutic antibody for treating patients with CIDs.



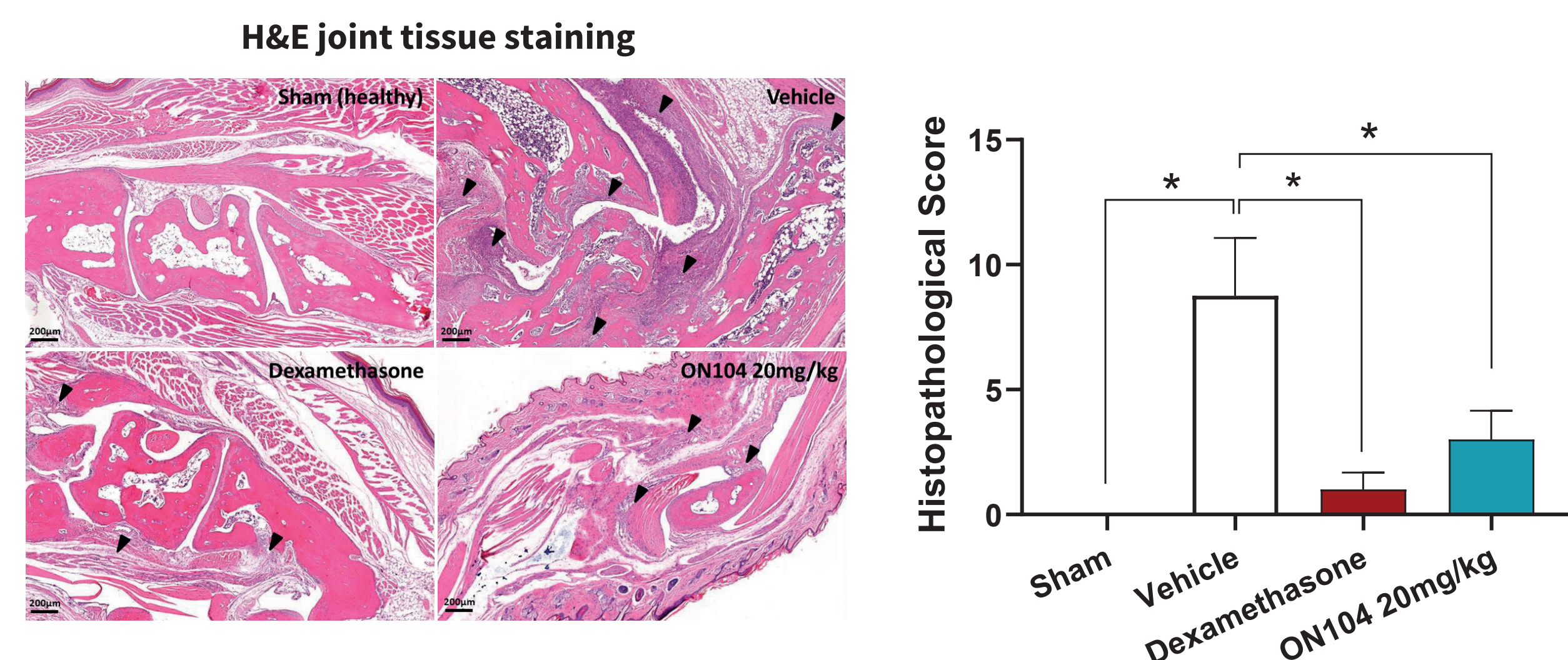
➔ oxMIF represents the disease-related and druggable isoform of MIF

➔ ON104, a neutralizing anti-oxMIF mAb optimized for the treatment of chronic inflammation

2 In vivo POC | Collagen-induced arthritis



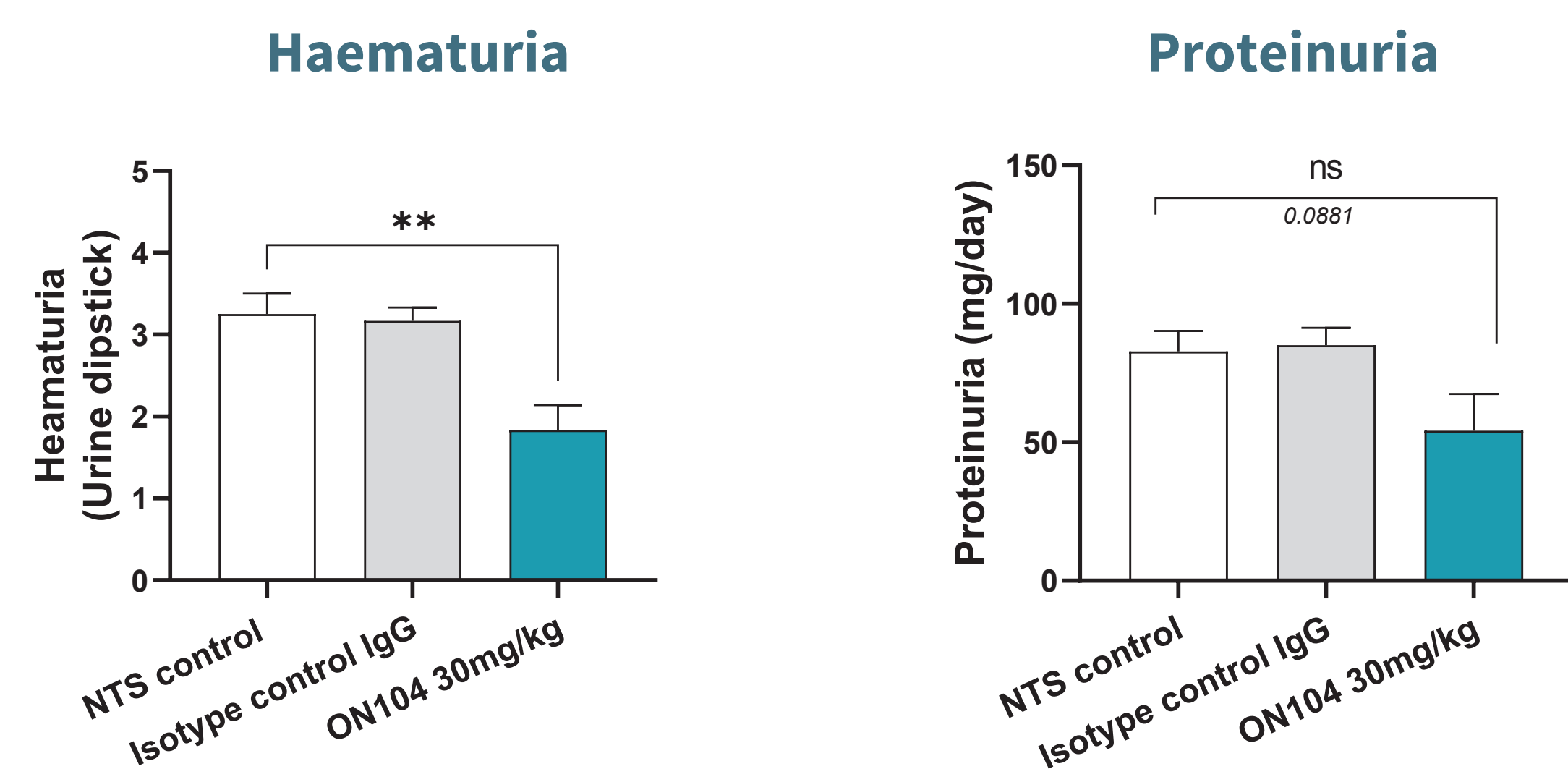
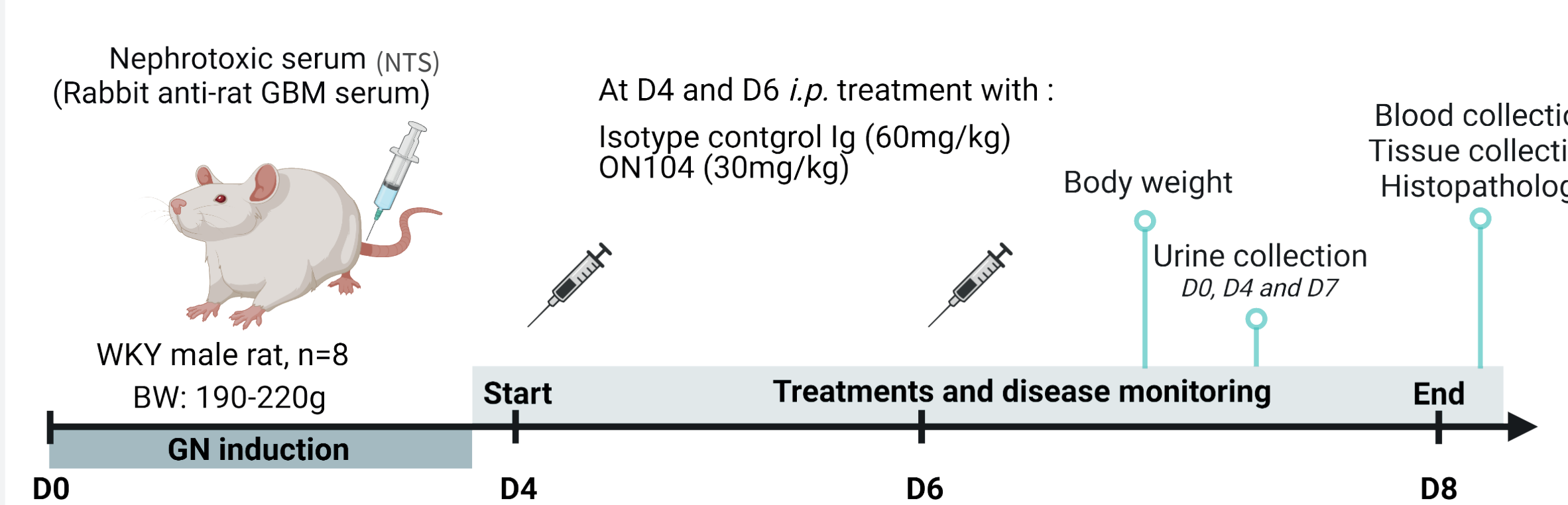
Histopathological evaluation



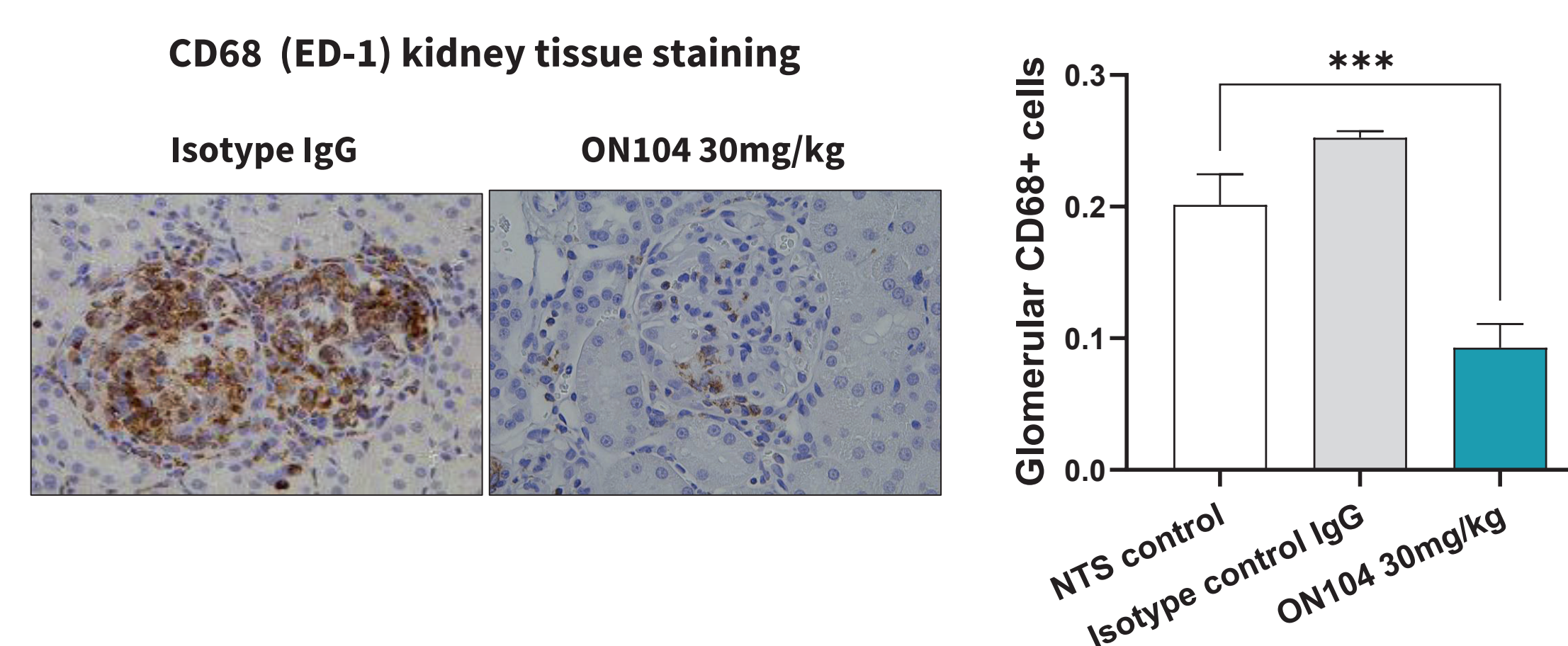
All data are expressed as mean ± SEM and analyzed by Mann-Whitney. n=4-6 animals for histological studies. *p<0.05; **p<0.01; ****p<0.0001

➔ ON104 significantly reduced disease severity and attenuates joint inflammation during experimental arthritis

3 In vivo POC | Glomerulonephritis



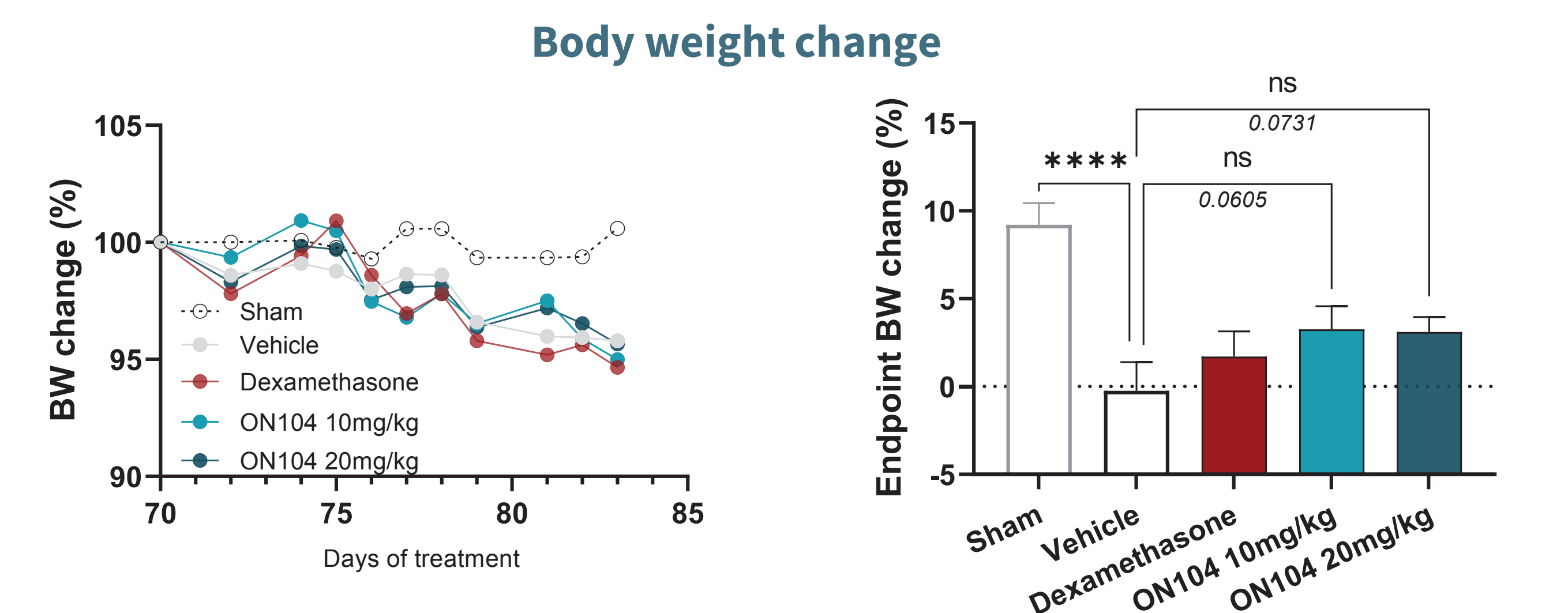
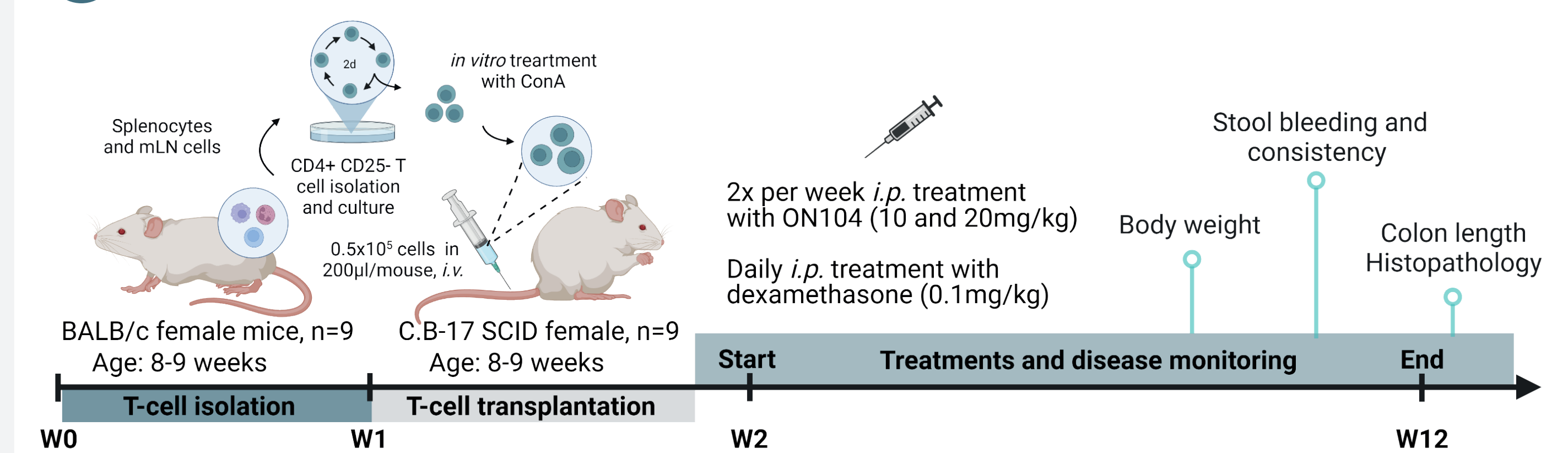
Macrophage infiltration



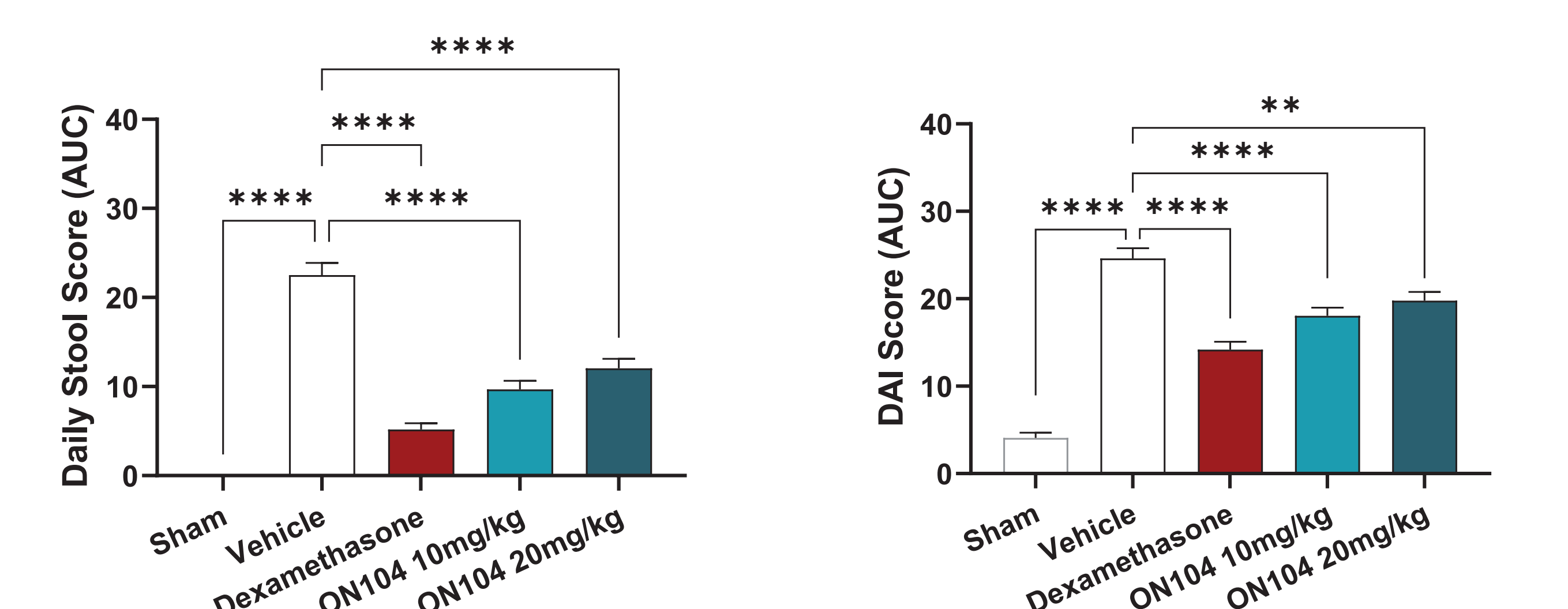
All data are expressed as mean ± SEM and analyzed by one-way ANOVA followed by Uncorrected Dunnett's test. **p<0.01; ***p<0.001

➔ ON104 successfully reduces clinical signs of kidney injury and glomerular inflammation

4 In vivo POC | T cell transfer-induced colitis



Stool consistency



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 significantly ameliorates clinical signs of chronic colitis

5 Summary

- Oxidized (ox)MIF is a promising target in CIDs
- Anti-oxMIF antibody ON104 shows *in vivo* efficacy in three different models of CIDs

6 Conclusion

- ON104 represents a promising new treatment option for patients with CIDs, either as monotherapy or in combination with reduced doses of glucocorticoids.

References
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