

Combined Inhibition of Integrin $\beta 7$ and TL1A, Integrin $\beta 7$ and IL-23, or TL1A and IL-23 Are Superior to Their Constituent Monotherapies in Mouse TNBS-Induced Colitis

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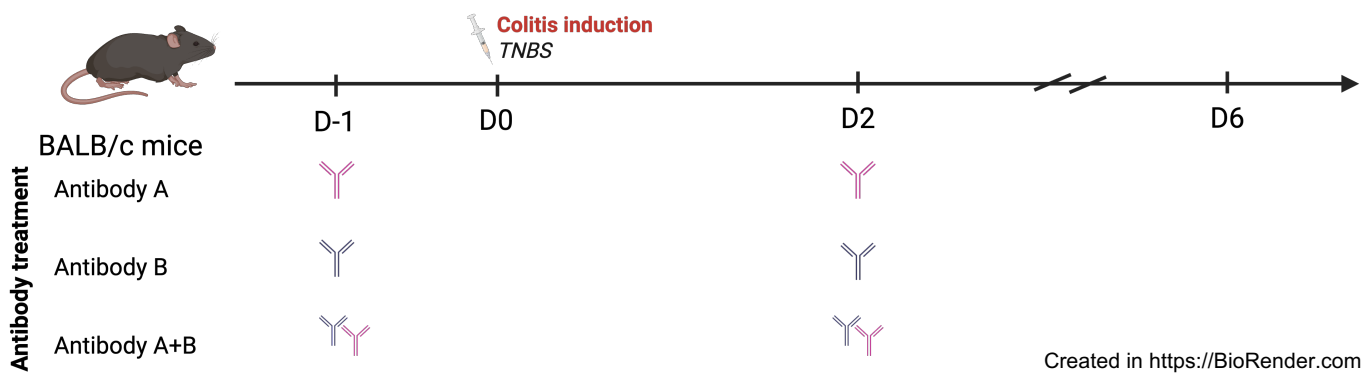
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Background

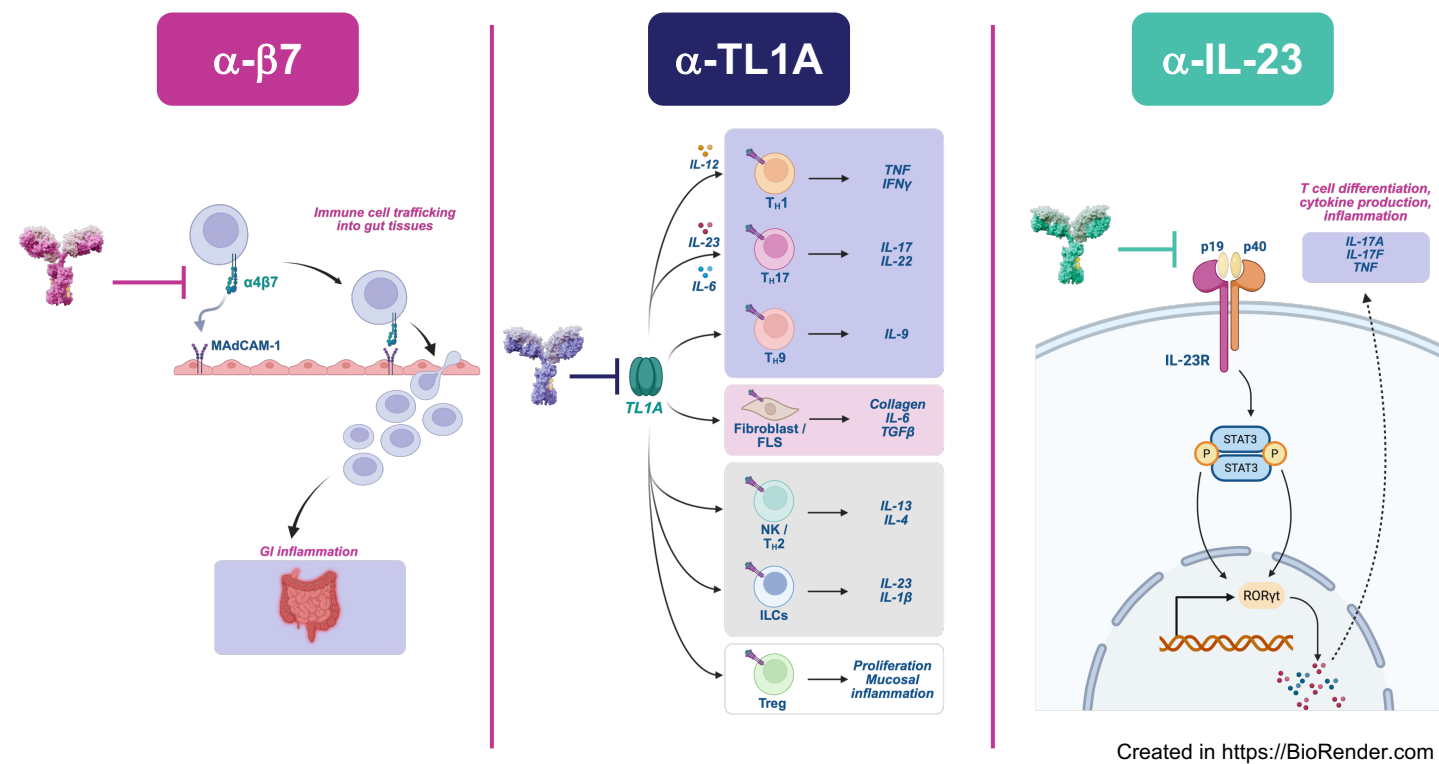
- Combined use of **targeted biologic agents** has the potential to break through the IBD treatment efficacy ceiling while avoiding the risks associated with broad immunosuppression.¹
- SPY001**, **SPY002**, and **SPY003** are investigational **half-life extended antibodies** against validated IBD targets (**$\alpha 4\beta 7$** integrin, **TL1A**, and **IL-23**, respectively)^{2,3,4} being evaluated as **monotherapies and in combination** to treat IBD in the SKYLINE-UC Phase 2 platform study in ulcerative colitis (UC; NCT07012395).

Methods

- Anti-mouse **surrogates of SPY001, SPY002, and SPY003** were studied as monotherapies and as pairwise combinations in the TNBS murine colitis model

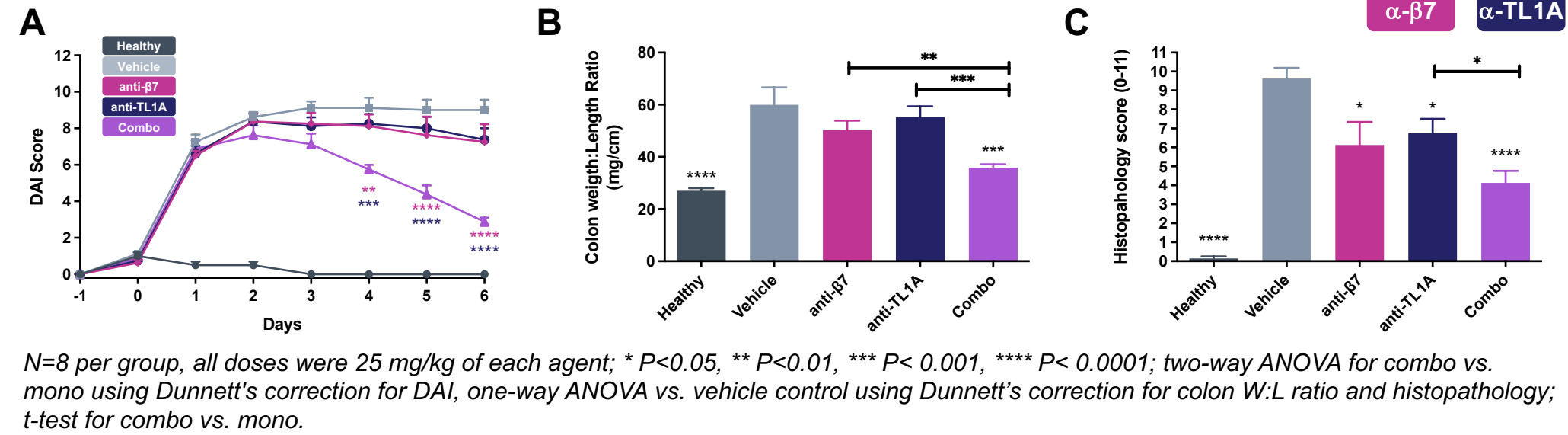


- BALB/c mice were dosed intravenously with test article (1 or 25 mg/kg) on Day -1 and Day 2, with Day 0 representing 2% TNBS administration.
- Histopathology was conducted only in the 25 mg/kg dose groups.

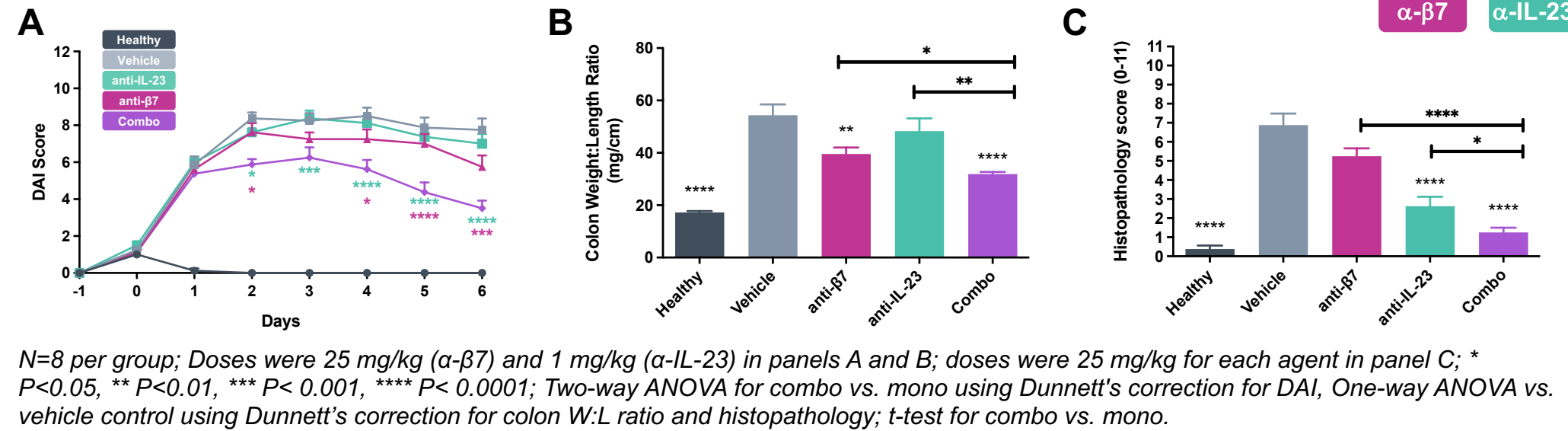


Results

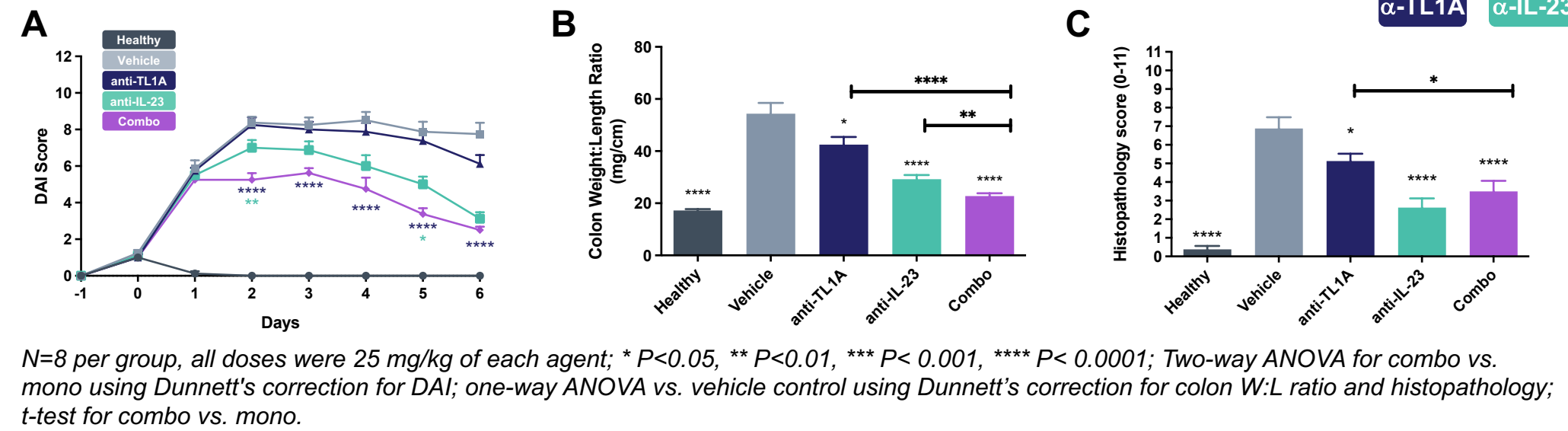
Combining anti- $\beta 7$ + anti-TL1A therapy results in superior efficacy compared to either monotherapy alone



Combining anti- $\beta 7$ + anti-IL-23 therapy results in superior efficacy compared to either monotherapy alone



Combining anti-TL1A + anti-IL-23 therapy results in superior efficacy compared to either monotherapy alone



Conclusions

- Combination therapy with anti- $\beta 7$ + anti-TL1A, anti- $\beta 7$ + anti-IL-23 or anti-TL1A + anti-IL-23 resulted in **additive to synergistic efficacy relative to constituent monotherapies** as assessed by disease activity score in mouse TNBS-induced colitis.
- Combination effects were **supported by additional endpoints** including weight:length ratio and histopathology.
- These preclinical results support advancement of the **combinations of SPY001, SPY002, and SPY003** into the **SKYLINE-UC Phase 2 platform study** in UC which started in mid-2025.



Phase 2 *platform* trial initiated to evaluate SPY001, SPY002, SPY003 and pairwise combinations in ulcerative colitis.



UC	
Monos	SPY001
	SPY002
	SPY003
Combos	SPY120 (SPY001 + SPY002)
	SPY130 (SPY001 + SPY003)
	SPY230 (SPY002 + SPY003)
	Placebo

References

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- Zhu, E. *et al.* A Novel Monoclonal Antibody Drug Candidate SPY001 Targeting Integrin $\alpha 4\beta 7$ for the Treatment of IBD: In Vitro Properties and Non-Human Primate Pharmacokinetics and Safety. *UEGW*, PP1103 (2024).
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Disclosures: All authors own equity in Spyre Therapeutics, Inc.