Orismilast for the Treatment of Moderate to Severe Ulcerative Colitis:
A phase 2a, open-label, single-arm explorative clinical study

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INTRODUCTION

This study aims to evaluate the efficacy and safety of orismilast in patients with moderate to severe ulcerative colitis (UC). Orismilast, an oral B/D selective phosphodiesterase-4 (PDE4) inhibitor, is currently in development for the treatment of atopic dermatitis, psoriasis, and hidradenitis suppurativa. PDE4 receptors have also been shown to be upregulated in UC. This study (the UCORIS study) aims to explore the efficacy and safety of orismilast to guide future studies.

METHODS

Patients with a UC diagnosis currently on stable 5-ASA treatment and experiencing moderate to severe disease activity(defined as a MAYO endoscopic sub score of 2 or 3) were eligible for inclusion. Orismilast was administered twice daily for 12 weeks, with investigators allowed to individualize the dose based on treatment response and tolerability.

Descriptive statistics were applied to efficacy data from patients who completed treatment and patients who discontinued treatment prematurely. A last-observation-carried-forward approach was used for patients who discontinued treatment. The primary endpoint was clinical remission based on total Mayo score at week 12, defined as 2 points or lower with no individual sub-score above 1.

RESULTS

10 patients were included in the study. Of these, 4 have finished the full 12-week study period:

- 1 patient met the study's primary endpoint and achieved complete remission
- 2 out of 4 reached a Mayo endoscopic sub score of 0-1.

The remaining 6 discontinued prematurely:

- 3 due the adverse events
- 3 due to lack of efficacy

When looking at data from all patients included in the study trial:

- 3 out of 10 (30%) achieved complete remission

The most common adverse events were nausea (80%), abdominal pain (60%) and headache (20%).

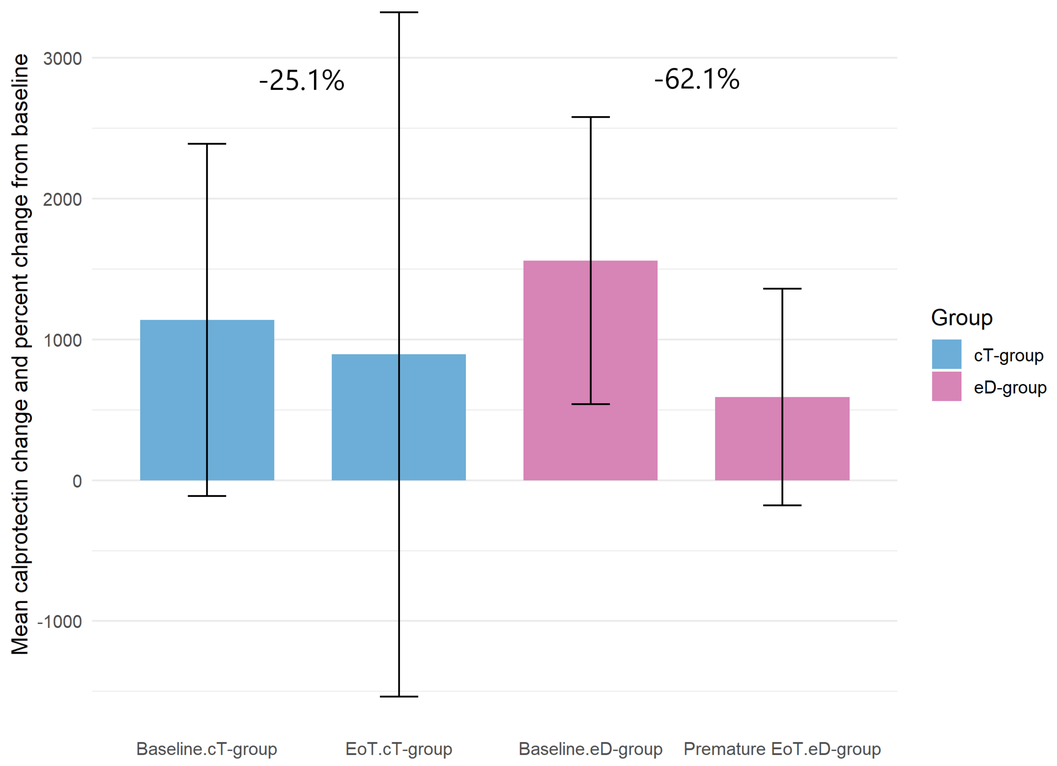


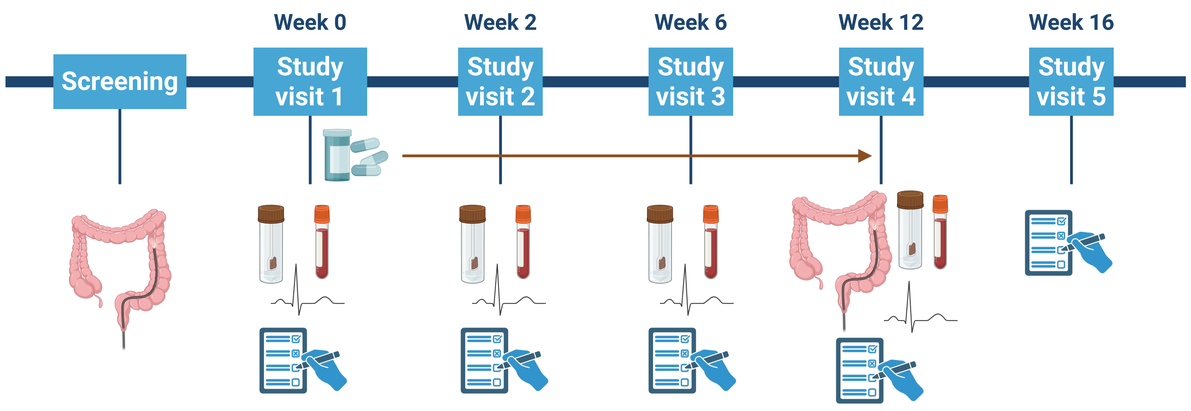
Figure 2: The mean calprotectin change and percent change from baseline in patients receiving treatment with orismilast. Results are shown for the completed trial group and the early discontinuation group.

CONCLUSION

This proof-of-concept study suggests that orismilast exhibits therapeutic potential in moderate-to-severe ulcerative colitis, with three patients achieving complete remission. However, sustained treatment was limited, as only one patient demonstrating both clinical and endoscopic response completed the full 12-week regimen. Notably, nausea emerged as a more prevalent adverse event in ulcerative colitis patients compared to its reported incidence in atopic dermatitis, psoriasis, and hidradenitis suppurativa.

Effective management of this adverse event may be critical to optimizing the tolerability of orismilast or other PDE4 inhibitors, potentially expanding their role in the treatment of ulcerative colitis.

STUDY TIMELINE



RESULTS

Change in Total Mayo Score after 12 Weeks of Treatment

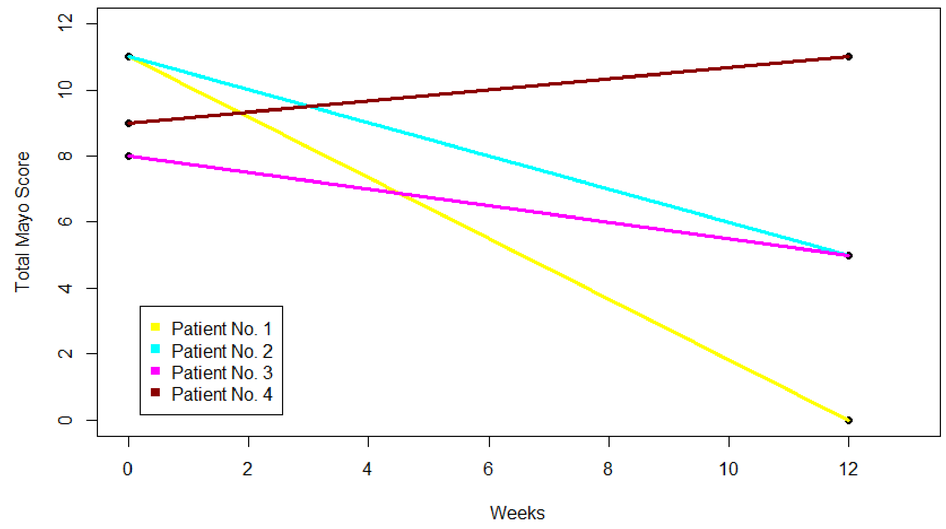
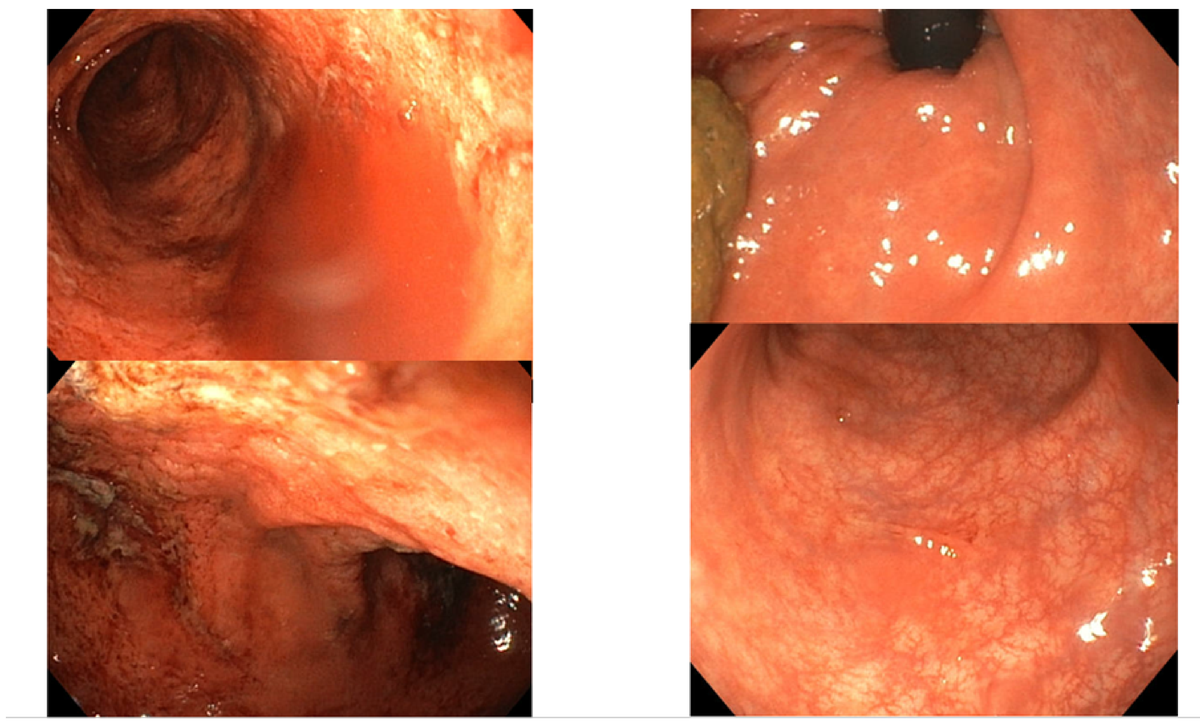


Figure 1: Changes in Total Mayo Score from baseline to the end of the study at Week 12. Results from the four patients who completed the full 12 weeks of treatment are presented.



Picture 1: From the endoscopic assessment performed on patient no. 1, who achieved complete remission after 12 weeks of treatment with orismilast.

ACKNOWLEDGEMENTS

This study was an investigator-sponsered study funded by a grant from UNION therapeutics, who also provided the investigational product (orismilast).