

ISM5411, A NOVEL GUT-RESTRICTIVE PROLYL HYDROXYLASE-2 INHIBITOR FOR INFLAMMATORY BOWEL DISEASE: RANDOMIZED, DOUBLE-BLINDED, PLACEBO-CONTROLLED FIRST-IN-HUMAN PHASE I STUDY TO EVALUATE SAFETY, TOLERABILITY AND PK PROFILES

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Poster

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ISM5411, an oral gut-restrictive PHD2 inhibitor designed to stabilize HIF-1 α and protect intestinal mucosal barrier, demonstrated safety and tolerability in a first-in-human Phase I study in 76 healthy subjects across single doses of 50-1000 mg and multiple doses of 200-800 mg daily for 14 days.

KEY POINTS

- No serious adverse events or deaths occurred; one Grade 1 rectal hemorrhage led to discontinuation in the 200 mg cohort but was judged unrelated to ISM5411, and all other treatment-emergent adverse events in ISM5411 groups were Grade 1
- ISM5411 was rapidly absorbed and metabolized to ISM5411-M15 with very low plasma exposure and more than 30% fecal excretion in prototypic form, demonstrating the intended gut-restrictive pharmacokinetic profile
- Systemic erythropoietin levels increased post-dose then decreased with most changes within normal range, and no clear trend was observed in systemic VEGF levels across cohorts
- ISM5411 is advancing to a Phase 2a proof-of-concept study in ulcerative colitis patients to evaluate safety, pharmacokinetics, and clinical efficacy following completion of Phase I studies in Australia and China

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