DDW2025
Digestive Disease Week®

MAY 3–6, 2025 | SAN DIEGO, CA

IMU-856 vs. Placebo Efficacy Effects in Celiac Disease Patients Are Independent of Q-MARSH Scale at Baseline

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INTRODUCTION

IMU-856 is an orally administered, systemically acting small molecule modulator of SIRT-6, an enzyme with deacetylase and adenosine diphosphate-ribosyltransferase activity that protects against loss of tight junctions and histopathological damage.

IMU-856 is currently under development for the treatment of celiac disease and other gastrointestinal diseases. In a Phase 1b clinical trial, IMU-856 attenuated villous height deterioration during a gluten challenge and increased citrulline concentrations, a biomarker of intestinal epithelial activity.[1]

AIM

To evaluate the effect of baseline villous atrophy on the efficacy and pharmacodynamics of IMU-856 in patients with celiac disease.

METHOD

- Phase 1, double-blind, randomized, placebo-controlled study (ACTRN12620000901909)[1]
- Key inclusion criteria for Cohort C: 18–65 years with a BMI 18–35 kg/m^2, biopsy-proven celiac disease, and were gluten-free for at least 12 months with negative IgA-TG2 serology

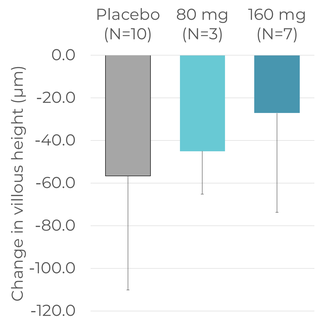
Cohort C: once-daily oral doses of IMU-856 (80 mg or 160 mg) or placebo for 28 days in patients with celiac disease with a gluten challenge on Day 14

  - Days 0–13: gluten-free diet
  - Day 14: gluten challenge (6 g once-daily) until Day 28

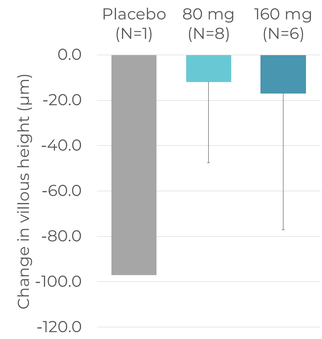
- Duodenal biopsy for histological analysis and blood collected at Baseline and Day 29
- Histological analysis performed at a central lab by three blinded slide readers

RESULTS

Change in villous height (baseline to Day 29)
Q-MARSH M0—M2

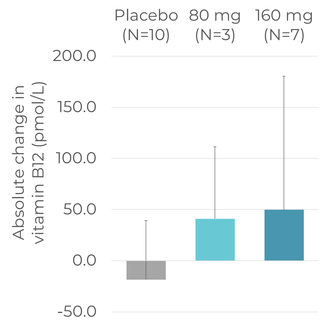


Q-MARSH M3a-c

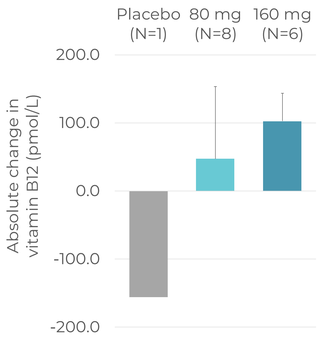


Data presented as mean (SD)

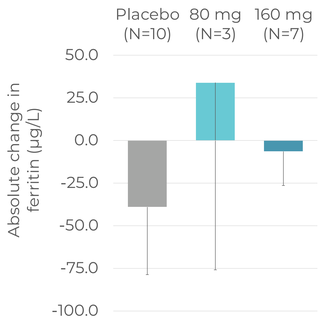
Change in vitamin B12 (baseline to Day 29)
Q-MARSH M0—M2



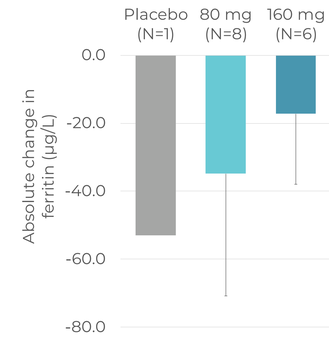
Q-MARSH M3a-c



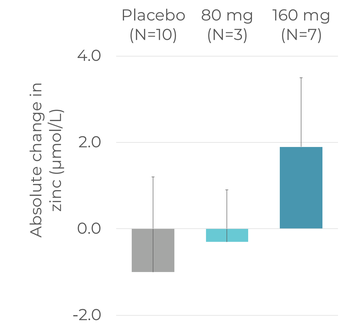
Change in ferritin (baseline to Day 29)
Q-MARSH M0—M2



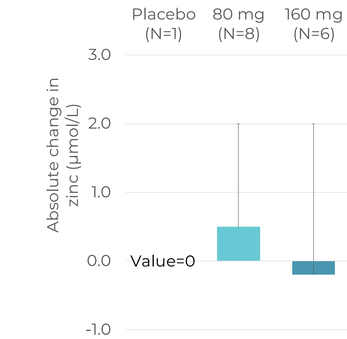
Q-MARSH M3a-c



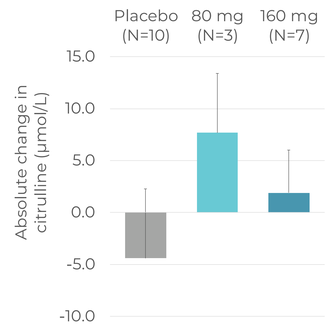
Change in zinc (baseline to Day 29)
Q-MARSH M0—M2



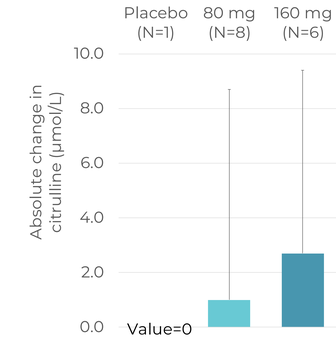
Q-MARSH M3a-c



Change in citrulline (baseline to Day 29)
Q-MARSH M0—M2



Q-MARSH M3a-c



CONCLUSIONS

Baseline Q-MARSH in patients with celiac disease did not appear to affect the efficacy (i.e., villous height) or pharmacodynamic effects (i.e., absorption parameters and an epithelial biomarker) of IMU-856 compared to placebo in a Phase 1b study using gluten challenge.

OUTLOOK

The results of this analysis support advancing IMU-856 into a Phase 2 trial in patients with ongoing active celiac disease.

REFERENCES

1. Daveson AJM, Stubbs R, Polasek TM, et al. Safety, clinical activity, pharmacodynamics, and pharmacokinetics of IMU-856, a SIRT6 modulator, in coeliac disease: a first-in-human, randomised, double-blind, placebo-controlled, phase 1 trial. *Lancet Gastroenterol Hepatol*. 2025;10(1):44-54.

ACKNOWLEDGEMENTS

We thank all investigators, study personnel, and participants in the trial.

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