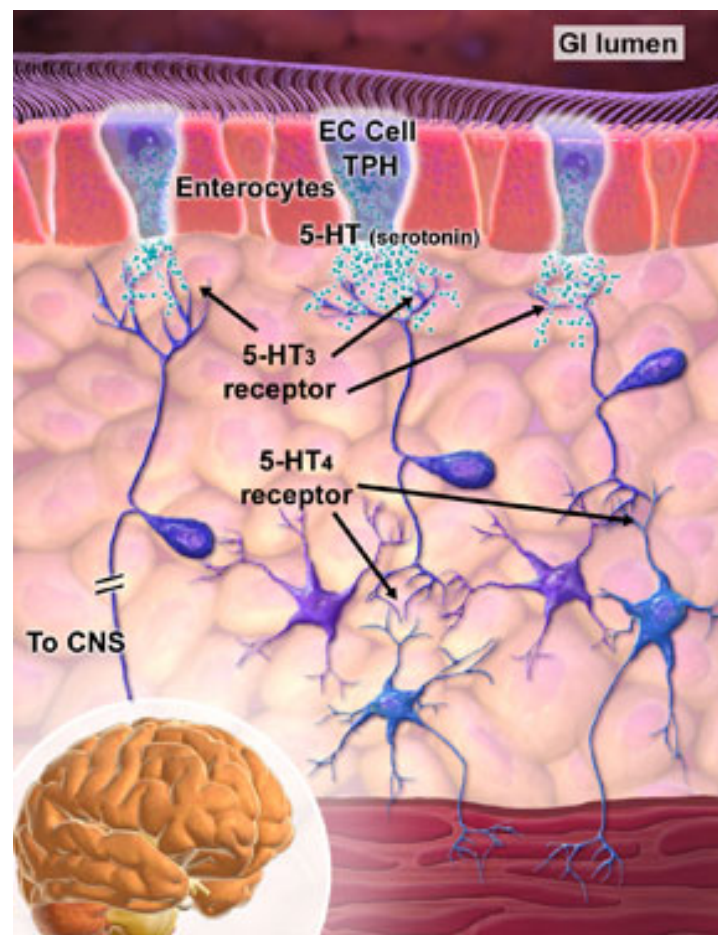

LX1031, a Novel Locally-Acting Inhibitor of Serotonin Synthesis, Significantly Improves Symptoms in Patients with IBS

Digestive Disease Week
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LX1031: A First-in-Class Oral Serotonin Synthesis Inhibitor (SSI) for IBS

- Serotonin regulates GI function
 - IBS therapies target 5-HT receptors
- Tryptophan hydroxylase (TPH)–rate limiting enzyme in serotonin production
- LX1031:
 - Orally active
 - Local inhibitor of GI TPH
 - Does not cross the blood–brain barrier



LX1031 Phase 2 Study Hypothesis

Inhibition of GI TPH by LX1031 is predicted to:

- Reduce serotonin production
 - Measured as metabolite—urinary 5-HIAA
- Benefit patients with IBS
- Correlate with 5-HIAA reduction

LX1031 in Non-Constipating IBS Patients

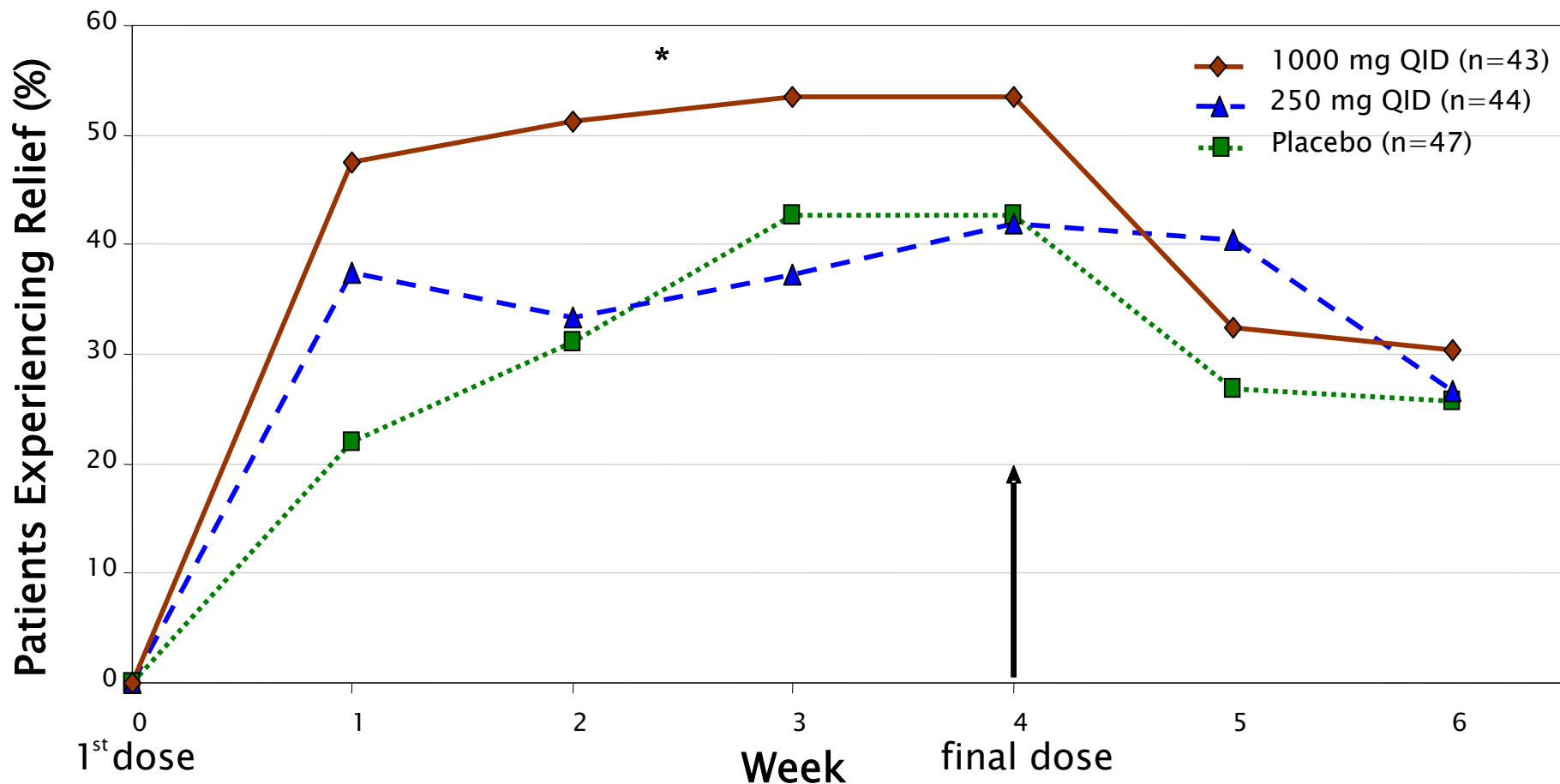
- Randomized, double-blind, placebo-controlled trial
 - Three arms 28 day treatment period:
 - Placebo (n=47)
 - LX1031 250 mg QID (n=44)
 - LX1031 1000 mg QID (n=43)
 - 2 week run-in period
 - 2 week follow-up period
- Patients
 - Average age: 48.1 years (range 21–68 years)
 - 16% Males, 84% Females
 - 23.9% IBS-Mixed
 - 76.1% IBS-Diarrhea
- 24-hour urinary 5-HIAA (n=74)
 - Baseline
 - Week 4
 - 2 week follow up

LX1031 Well Tolerated With Favorable Safety Profile; No Dose-Dependent Toxicities Observed

- Adverse Events (AEs)
 - Mild, self-limited and equally distributed overall
 - More frequent than placebo:
 - Nausea, diarrhea, dyspepsia, vomiting and headache
 - One serious adverse event unrelated to study drug
- 13 discontinuations
 - 7 due to AEs
 - Placebo (n=1), low dose (n=4), high dose (n=2)

Patients in High Dose Arm Showed Significant Improvement in Weekly Global Assessment Over 28 Day Treatment Period

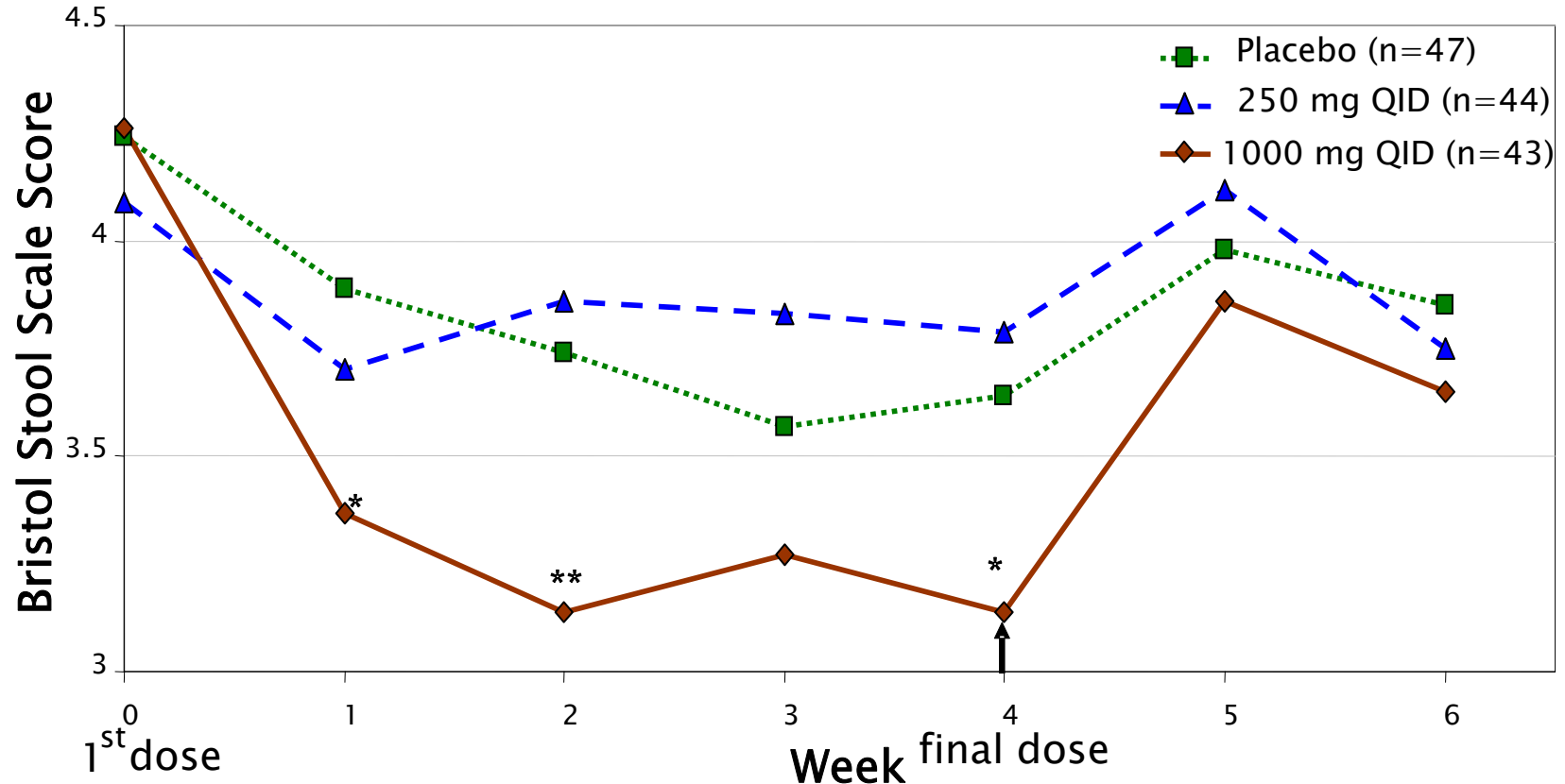
Adequate Relief of IBS Pain and Discomfort



* AUC analysis 1000 mg QID vs. Placebo $p < 0.05$

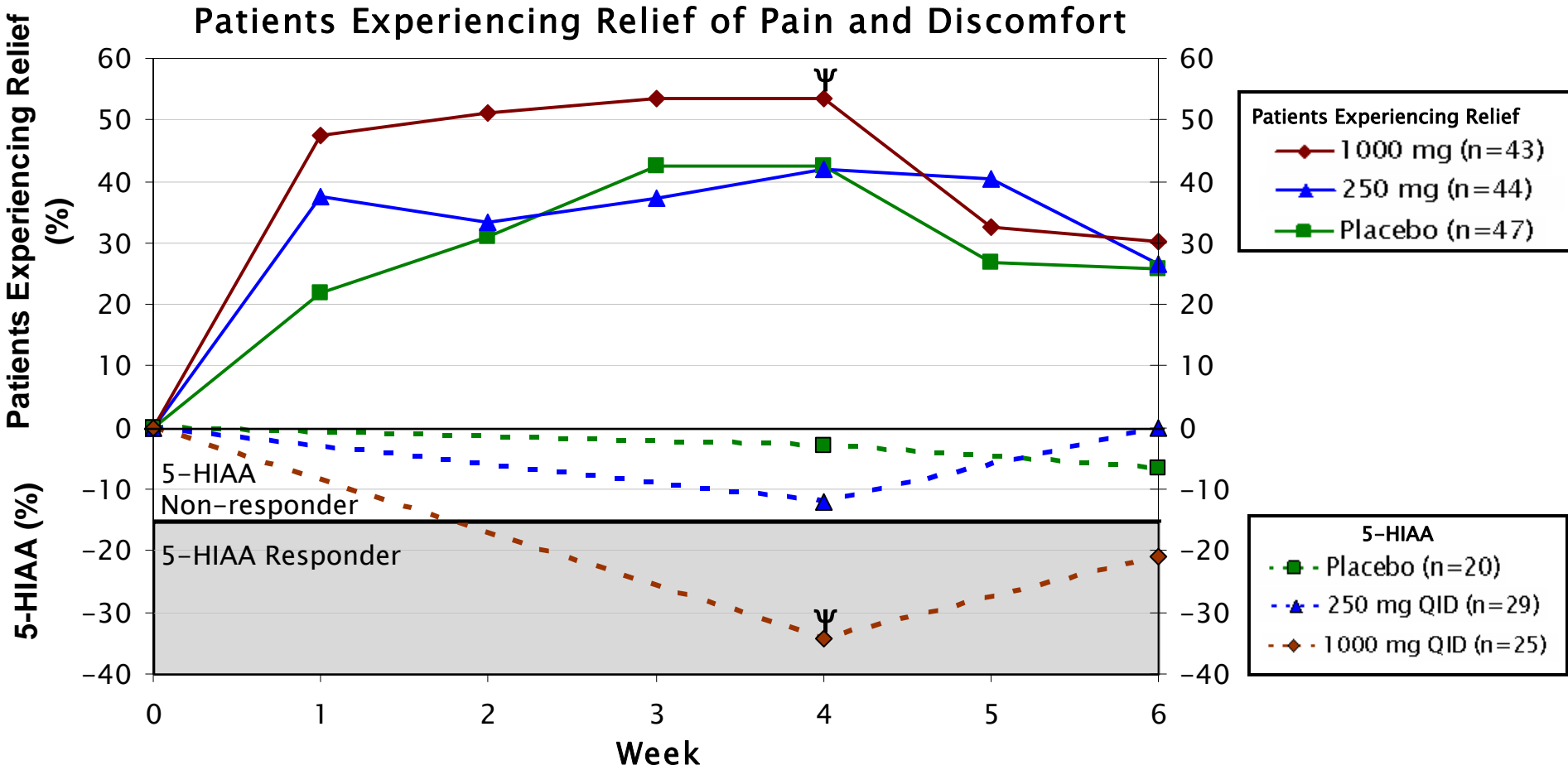
Patients in High Dose Arm Showed Significant Improvement in Stool Consistency (Bristol Stool Scale)

Stool Consistency–Bristol Stool Scale



* $p < 0.01$, ** $p < 0.001$ (1000 mg vs. Placebo)

Reduction in Urinary 5-HIAA Correlates with Adequate Relief of Pain and Discomfort



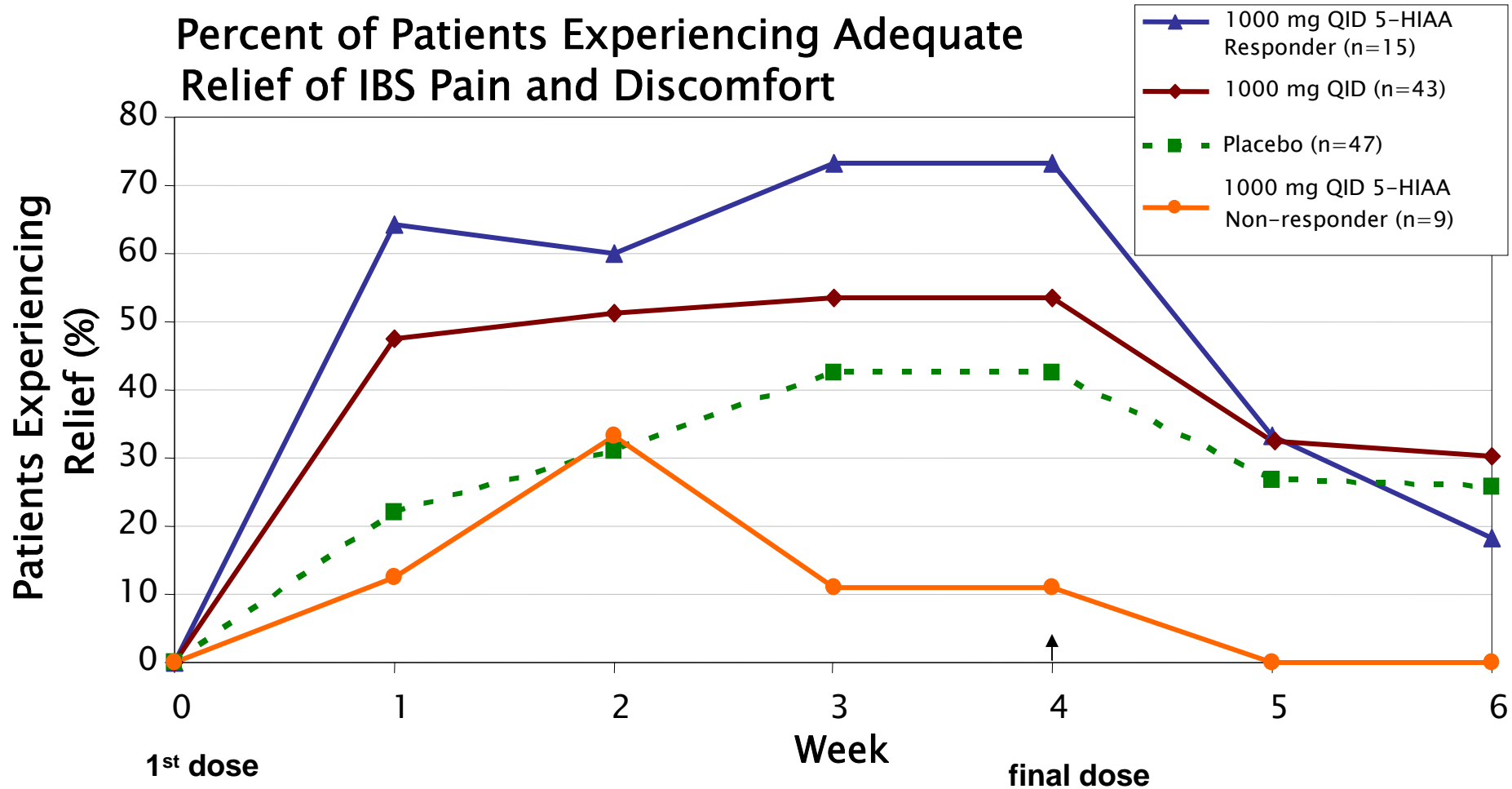
Median Percent Change from Baseline in Urinary 5-HIAA

Ψ correlation $p = 0.0271$

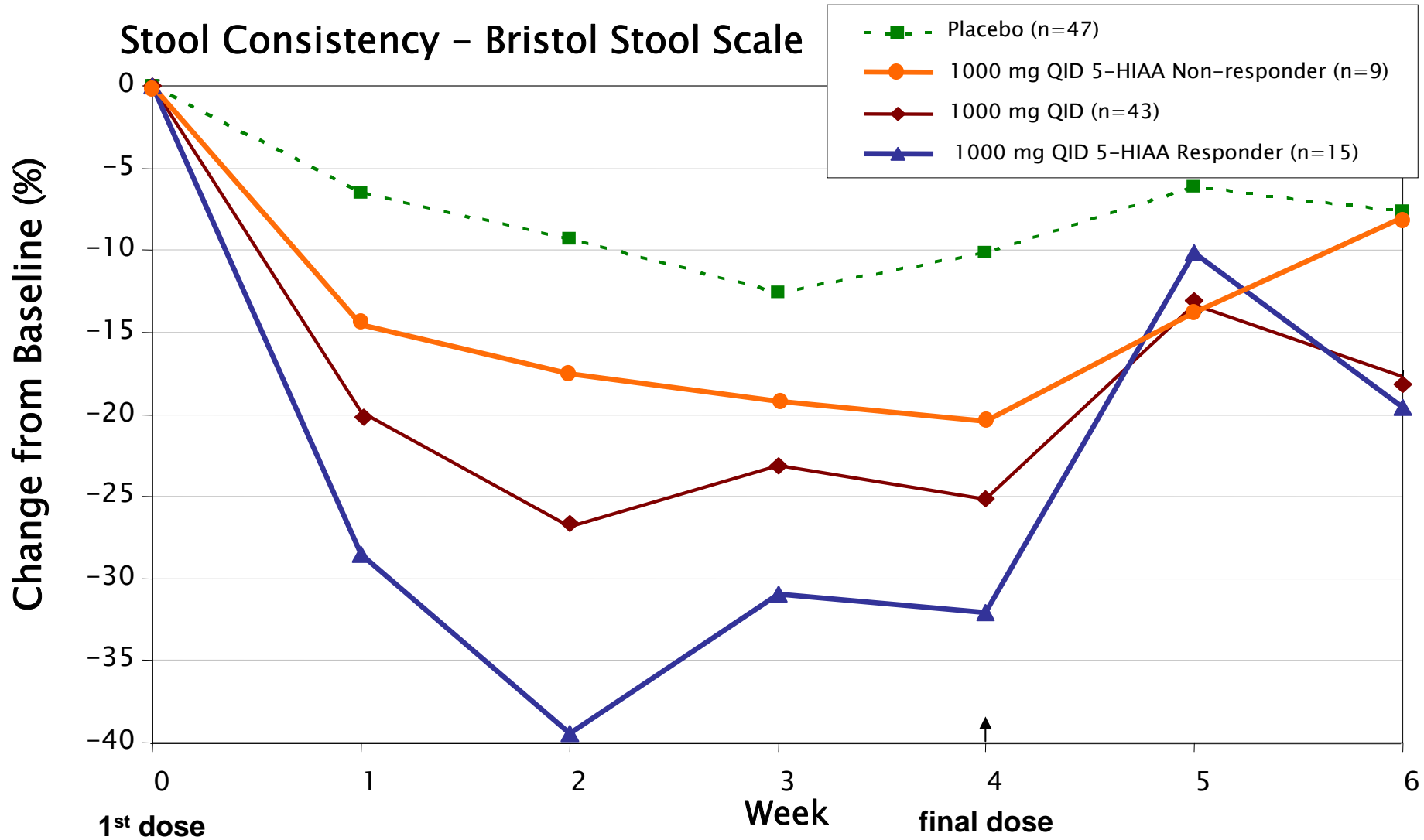
Clinical Response and Biomarker Response: 5-HIAA Reduction At Week 4

- Two groups of patients defined by biomarker response
 - 5-HIAA biomarker responder
 - $\geq 15\%$ reduction in 5-HIAA
 - 5-HIAA biomarker non-responder
 - $< 15\%$ reduction in 5-HIAA

High Dose 5-HIAA Biomarker Responders Show Enhanced Improvement in Global Outcome

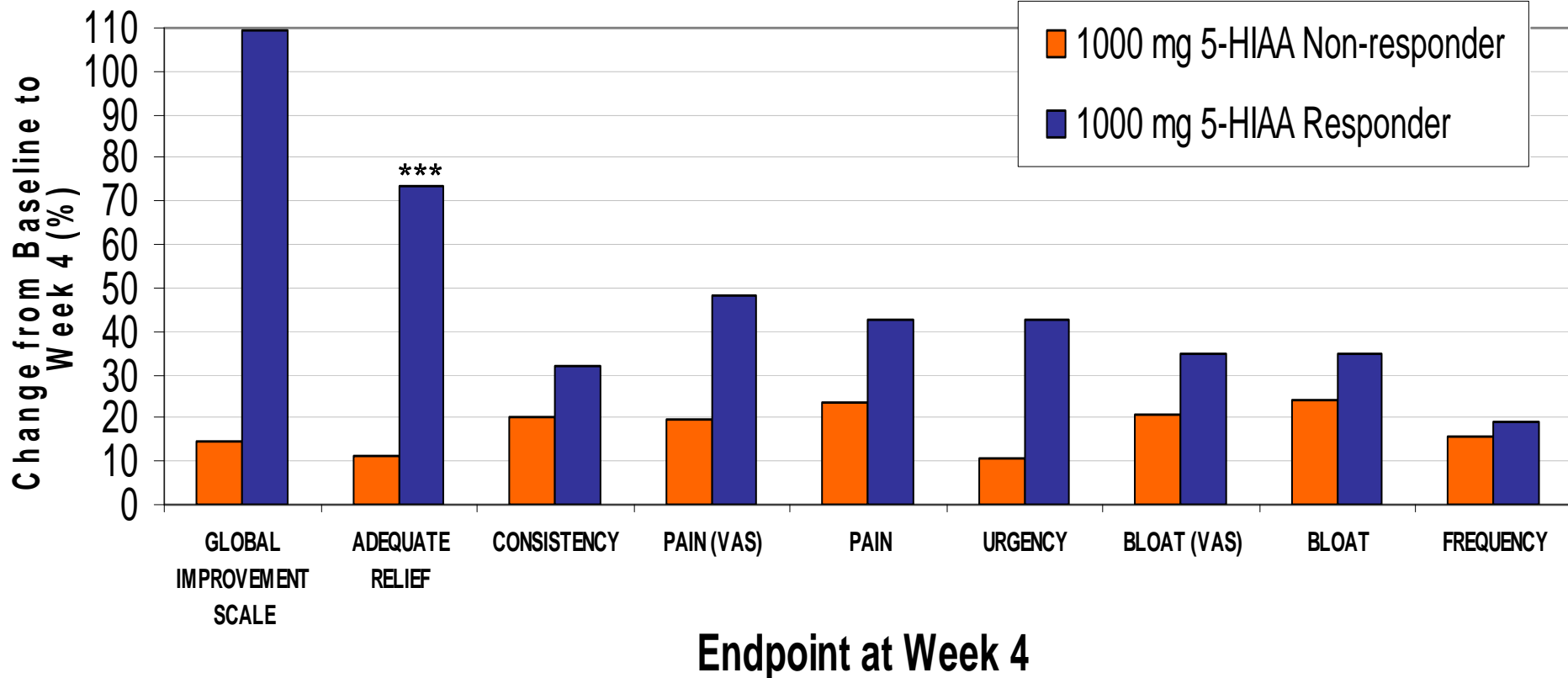


High-Dose 5-HIAA Biomarker Responders Show Improved Stool Consistency



High-Dose 5-HIAA Biomarker Response Corresponds With Clinical Benefit in Multiple Parameters

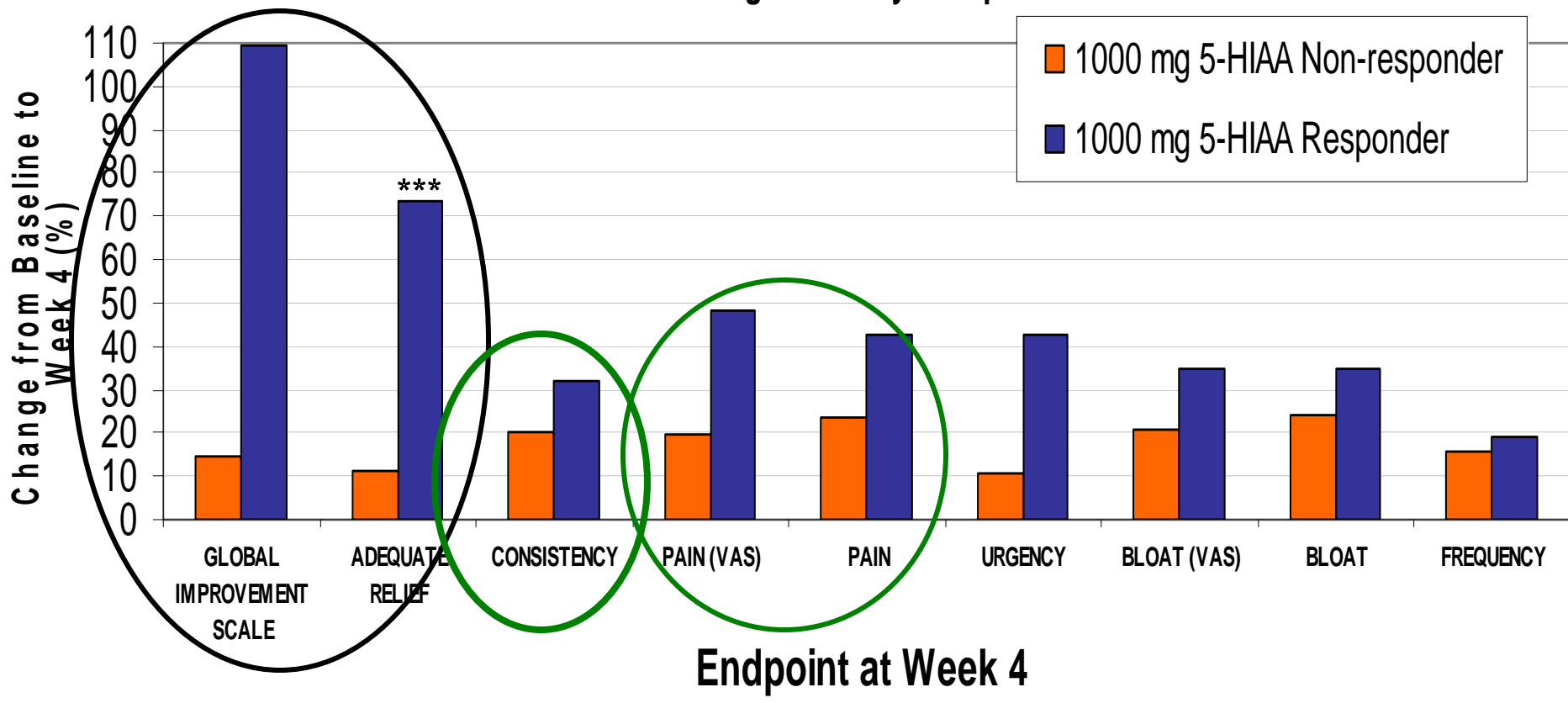
Percent Improvement from Baseline to Week 4 in Efficacy Endpoints
1000 mg Sub-study Group



*** p < 0.001

High-Dose 5-HIAA Biomarker Response Corresponds With Clinical Benefit in Multiple Parameters

Percent Improvement from Baseline to Week 4 in Efficacy Endpoints
1000 mg Sub-study Group



*** p<0.001

LX1031, a Novel SSI, Demonstrates Clinical Benefit in Patients with Non-Constipating IBS

- LX1031 was safe and well tolerated
- Benefits in high dose LX1031 arm:
 - Rapid, durable improvement in global assessment
 - Improved stool consistency
- 5-HIAA biomarker: a potential guide to IBS therapy
 - 5-HIAA reduction correlates to improvements in global assessment
 - High dose 5-HIAA biomarker responders exhibit enhanced clinical benefits across multiple endpoints