Phase 1b study of SOR102, a novel, orally delivered bispecific anti-TNF/anti-IL-23 domain antibody in patients with mild to severe ulcerative colitis

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Disclosures

Dr Vipul Jairath has:

- Held a consultancy/advisory role/board in AbbVie, Alimentiv, Arena Pharmaceuticals, Asahi Kasei Pharma, Asieris, AstraZeneca, Avoro Capital, Bristol Myers Squibb, Celltrion, Eli Lilly, Endpoint Health, Enthera, Ferring, Flagship Pioneering, Fresenius Kabi, Galapagos, Gilde Healthcare, GSK, Gilead, Innomar, JAMP Pharma Group, Janssen, Merck, Metacrine, Mylan, Pandion, Pendopharm, Pfizer, Protagonist, Prometheus Biosciences, Reistone Biopharma, F. Hoffmann-La Roche Ltd/Genentech, Inc., Roivant, Sandoz, Second Genome, Sorriso, Synedgen, Takeda, Toronto-Dominion Securities, Teva, Topivert, Ventyx, Vividion
- Been involved in speaker bureaus for AbbVie, Ferring, Bristol Myers Squibb, Fresenius Kabi, Galapagos, Janssen, Pfizer, Shire, Takeda

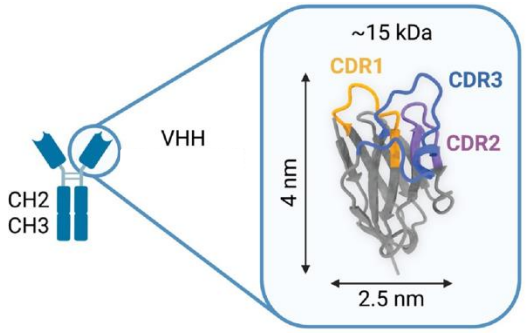
Therapeutic Ceiling of Monotherapies in IBD

- Multiple pathways drive the immune-mediated inflammatory process
- Limited remission rates for advanced therapies when used as single agents
- Mechanistic failure can develop over time for a single advanced therapies
- Advanced therapies used in succession tend to be less effective
- Emerging evidence from ulcerative colitis suggest that dual blockade of IL-23 and TNF is superior to either agent alone[1]

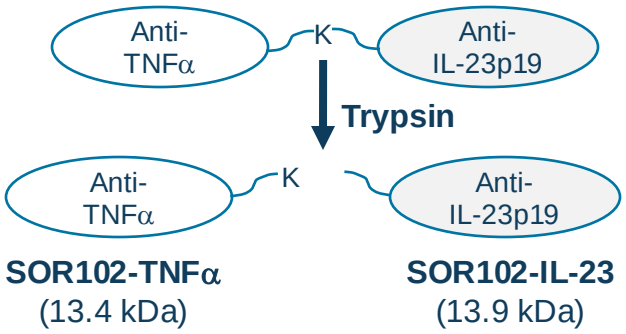
1. Feagan BG et al. Lancet Gastroenterol Hepatol 2023

Sorriso Single Domain Oral Antibody Platform

Heavy Chain Only VHH Single Domain Antibody[1]



SOR102[2]



SOR102-TNFα (13.4 kDa)

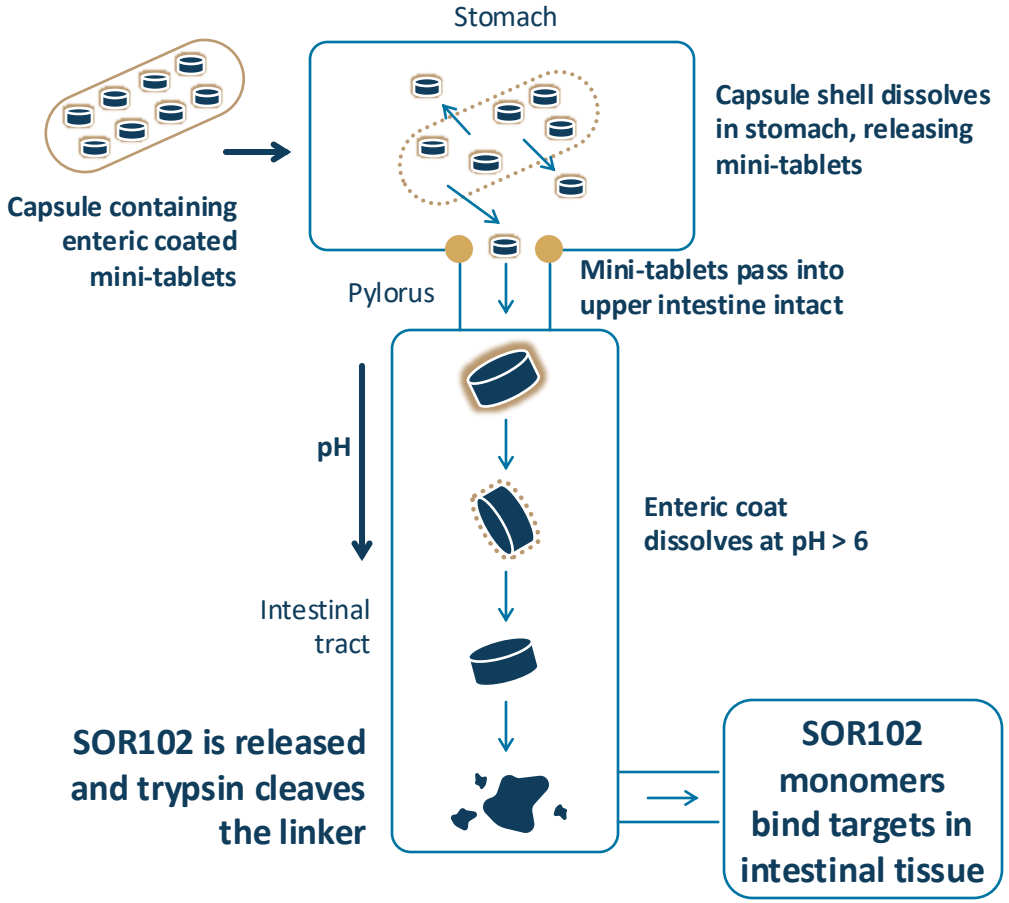
SOR102-IL-23 (13.9 kDa)

SOR102

Mechanism of Action

- Picomolar affinity to TNFα and IL-23p19
- Humanized and **GI stabile (eg protease resistant)**
- SOR102 can bind TNF and IL-23 simultaneously
- Endogenous trypsin cleaves the linker, releasing active VHH monomers to engage each target in tissue

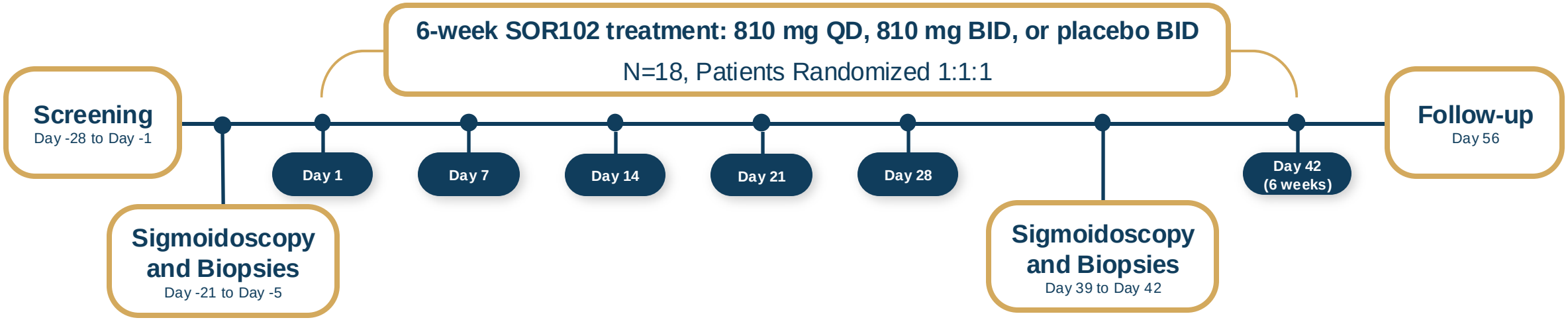
Oral Delivery to Intestinal Tissue[3]



1. Modified from Shen et al 2022, Trends in Molecular Medicine (28) 11:1006 – 1007; 2. Roberts et al 2021, Nat Sci Rep 11 (1):19422; 3. Crowe et al 2019, Drug Dev Ind Pharm, 45 (3):387-394.

SOR102-101[1]: Phase 1b Study Design

Randomized, Double-Blinded, Placebo-Controlled in Mild to Severe UC



- SOR102-101 was a 3-part FIH study
  - Part 1 (Single Ascending Dose) and Part 2 (Multiple Dose) in healthy volunteers showed no safety or tolerability concerns at SOR102 doses above Phase 1b dose levels; results were presented previously[2]
- Part 3 was a Phase 1b, randomized, placebo-controlled, double-blinded, double-dummy, multiple dose exploratory study
- **Key Inclusion Criteria:**
  - Mayo Score of 4 to 12, including Mayo ES of ≥2 as determined by central reader *and* RBS of ≥1 and SFS of ≥1
- **Key Exclusion Criteria**:
  - Prior primary efficacy failure or secondary loss of response to >1 biologic or new small molecule therapy *or*
  - Prior primary non-response, secondary loss of response or contraindication to anti-TNFα, anti-IL-12/23 or anti-IL-23

1. NCT06080048; 2. Jairath V et al. UEG Journal 2024;12(S8):72-73.

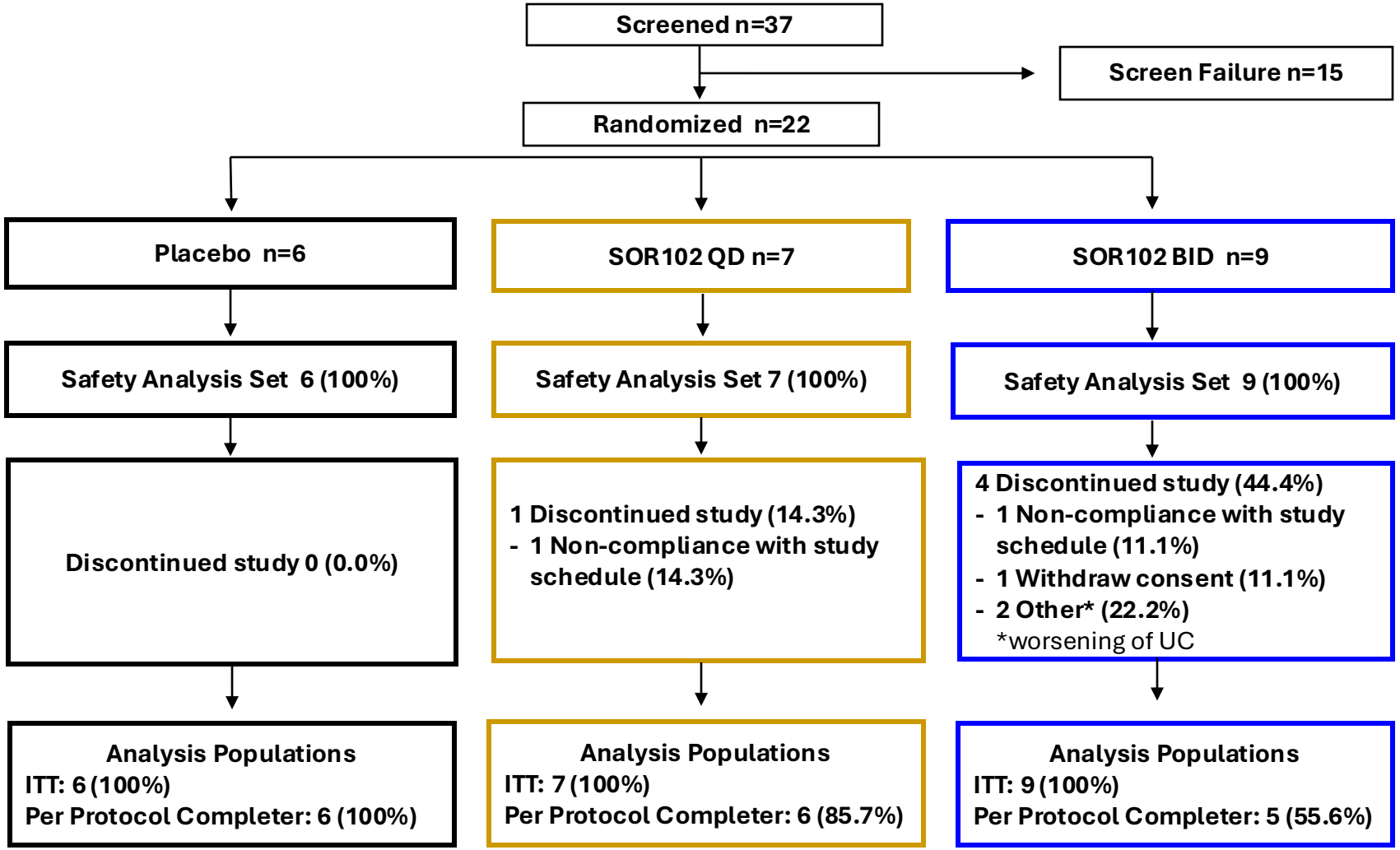
SOR102 Phase 1b Study Objectives & Endpoints

Primary Objective	Secondary Objectives
To evaluate the safety and tolerability of multiple doses of SOR102 in patients aged 18 to 75 years with mild to severe active Ulcerative Colitis (UC)	• To determine the concentration of SOR102 and its monomers in serum, urine, and feces • To assess the incidence of positive Anti-Drug Antibody (ADA) to SOR102 and its monomers

Exploratory Objectives	Exploratory Endpoints
Mayo Score Clinical Response	Decrease from study baseline total Mayo score of ≥ 3 points and ≥30%, plus a decrease in rectal bleeding subscore of ≥1 point or an absolute rectal bleeding subscore of 0 or 1
Modified Mayo Score Clinical Response	Decrease from study baseline total Mayo score of ≥2 points and ≥30%, plus a decrease in rectal bleeding subscore of ≥1 point or an absolute rectal bleeding subscore of 0 or 1
Symptomatic Remission	SFS=0 or 1 without worsening and RBS=0
Endoscopic Improvement	MES of 0 or 1 at Day 42
UC-100 Score[1] mean change from baseline	UC-100 score at Day 42

1. UC-100 Score: a composite measure of disease activity calculated from the weighted sum of the Mayo stool frequency subscore, Mayo endoscopic score, and Robarts Histological Index (Jairath V et al. Lancet Gastroenterol Hepatol 2019;4:63–70)

Patient Disposition



Discontinuations: 1 discontinued after 5 days of dosing (QD); 1 had evidence of improvement (BID); 3 were treatment failures (BID) with significant disease burden at baseline

Summary of UC Baseline Characteristics
Safety Analysis Set

	Placebo (N=6)	SOR102 810mg QD (N=7)	SOR102 810mg BID (N=9)	Total (N=22)
Age, years	53 (17)	49 (18)	49 (16)	50 (16)
Sex, female	3 (50)	2 (29)	7 (78)	12 (55)
Extensive Disease (Pancolitis)	2 (33)	2 (29)	1 (11)	5 (23)
Full Mayo score	8 (6, 9)	9 (6, 10)	7 (6, 11)	8 (6, 11)
Modified Mayo score	6 (4, 7)	7 (5, 8)	5 (4, 9)	6 (4, 9)
Number (%) of patients with MES=3	1 (17)	6 (86)	5 (56)	12 (55)
FCAL, median	453.5 (69, 6001)	1559.0 (322, 3893)	1302.0 (12, 5483)	1226.0 (12, 6001)
CRP, median	2.90 (2.9, 157.8)	7.30 (5.3, 56.5)	5.80 (2.9, 38.6)	5.60 (2.9, 157.8)
Prior use of biologics	0 (0)	2 (29)[1]	0 (0)	2 (9)
Concomitant UC meds at baseline				
None	0 (0.0)	1 (14)	1 (11)	2 (9)
Corticosteroids	1 (17)	1 (14)	2 (22)	4 (18)
Aminosalicylates	5 (83)	6 (86)	8 (89)	19 (86)

Data are n (%), mean (SD), or median (min, max); FCAL=fecal calprotectin; CRP=C-reactive protein

1. One patient received adalimumab, and one patient received mirikizumab, both in clinical trials

Overall Summary of TEAEs
Safety Analysis Set

	Placebo (N=6)	SOR102 810mg QD (N=7)	SOR102 810mg BID (N=9)	Total (N=22)
Total Number of TEAEs	5	2	6	13
Number of patients with ≥1 TEAE	3 (50)	2 (29)	5 (56)	10 (46)
Number of patients with TEAEs leading to study discontinuation	0 (0)	0 (0)	2 (22)	2 (9)
Number of patients with ≥1 SAE	0 (0)	0 (0)	1 (11)	1 (5)
Number of patients with SAEs leading to study discontinuation	0 (0)	0 (0)	1 (11)[1]	1 (5)
Number of patients with ≥1 TEAE by maximum severity				
Mild	1 (17)	1 (14)	2 (22)	4 (18)
Moderate	2 (33)	1 (14)	2 (22)	5 (23)
Severe	0 (0)	0 (0)	1 (11)	1 (5)
Number of patients with ≥1 TEAE by relationship to Treatment				
Possibly related	0 (0)	0 (0)	1 (11)[2]	1 (5)
Not related	5 (83)	2 (29)	5 (55)	12 (55)

1. Worsening of UC that led to hospitalization
2. Abdominal pain of mild severity

PK and Immunogenicity Results

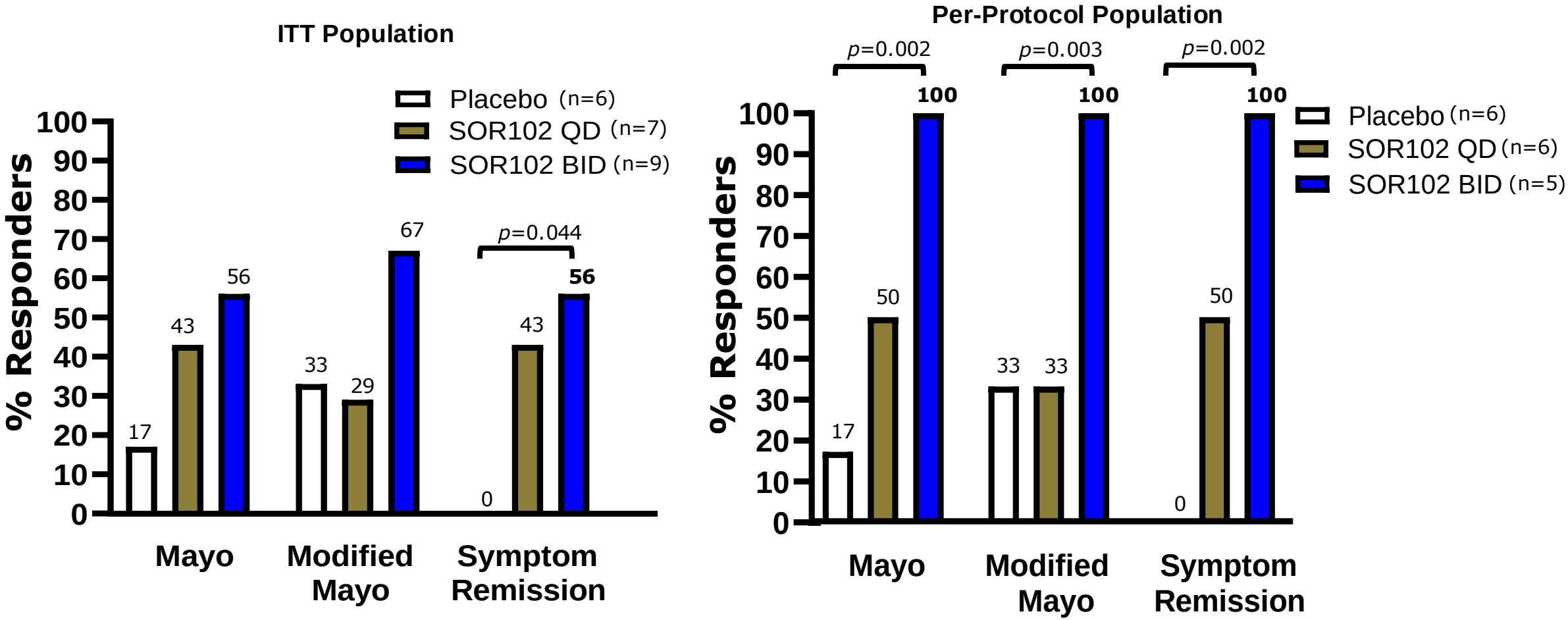
- Serum PK
  - One patient in the SOR102 QD arm had detectable SOR102-IL-23 monomer levels in serum
  - All other samples were below LLOQ for SOR102 and monomers

- Immunogenicity
  - 2 subjects (1 Placebo, 1 QD) were ADA+ for both monomers at Baseline
  - 6 subjects (4 QD, 2 BID) developed ADA+ responses after SOR102 dosing
    - Anti-TNF monomer only =1, Anti-IL-23 monomer only = 2, Both = 3
  - Most ADA titers were low ($\leq$1:240) and not associated with clinical response

LLOQ=lower limit of quantification

Mayo/Modified Mayo Clinical Response and Symptomatic Remission

ITT and Per-Protocol Population Responder Analyses

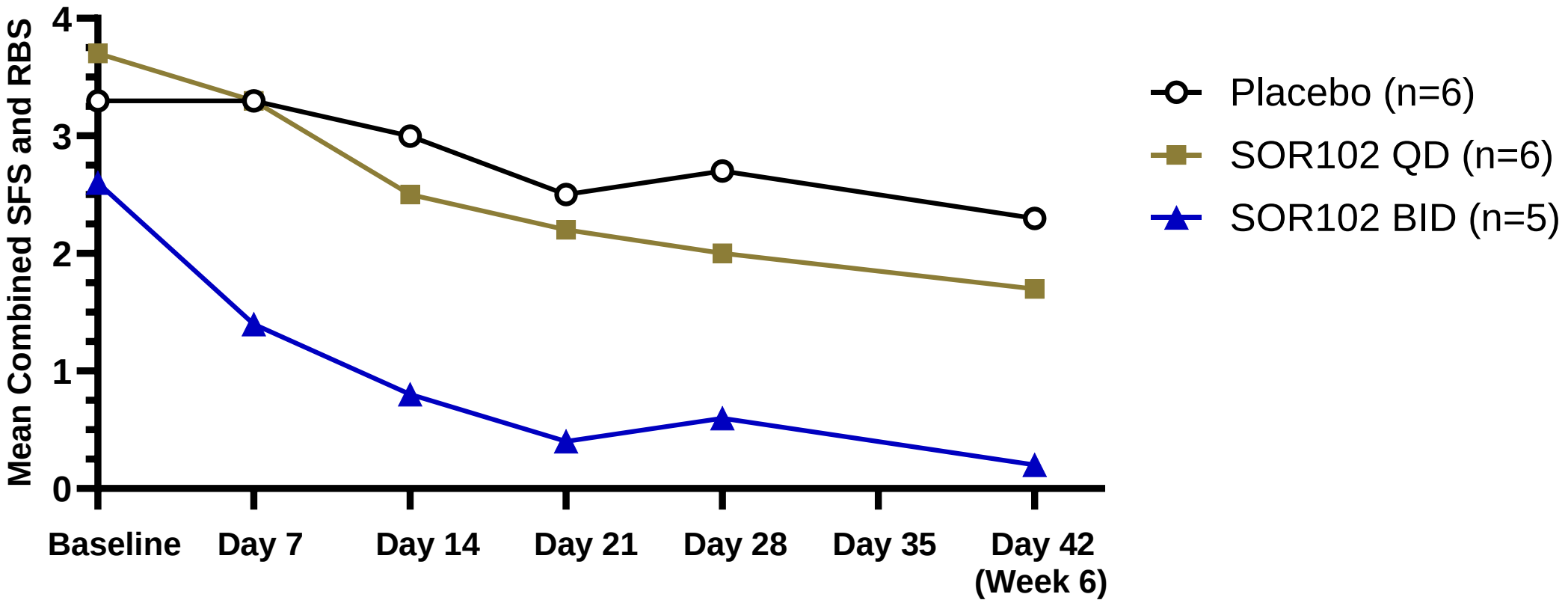


SOR102 BID demonstrated symptom improvement as early as Week 1 in the Per-Protocol Population

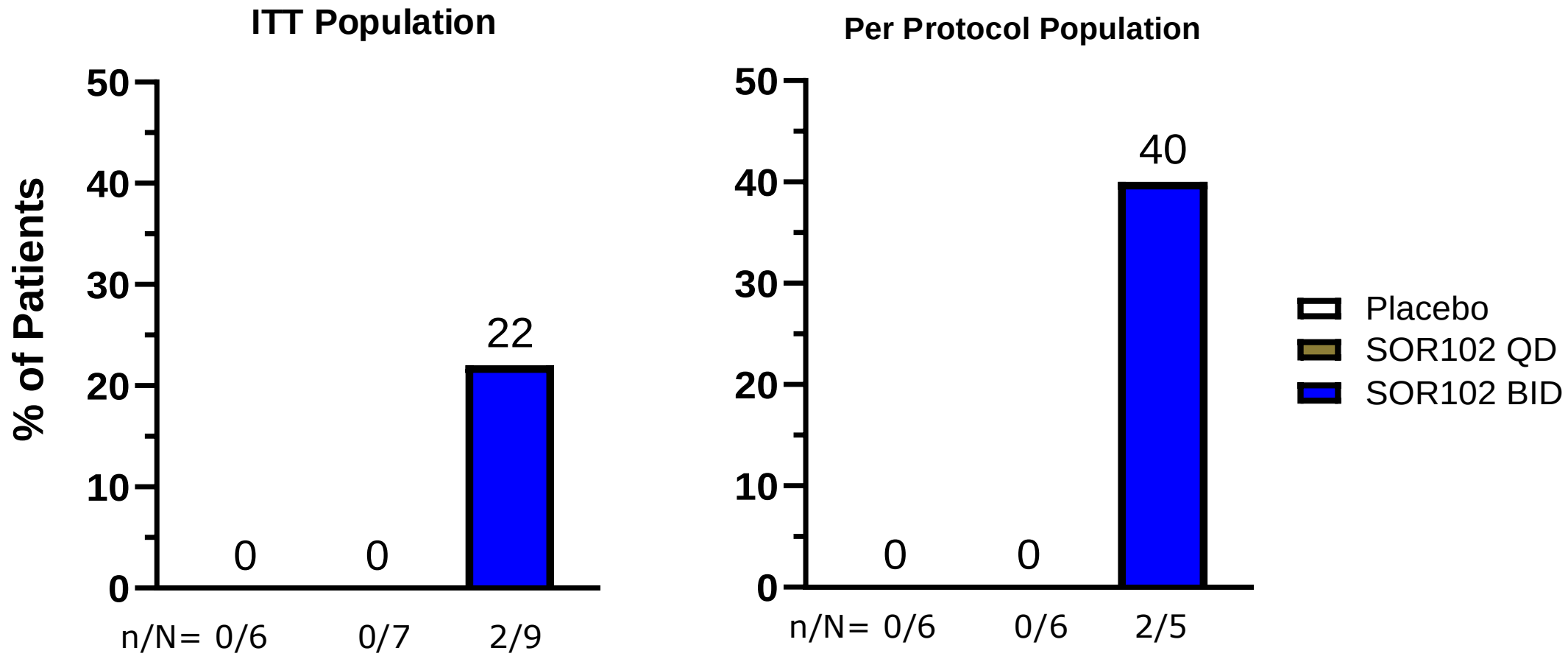
Mayo Score Clinical Response: Decrease from study baseline total Mayo score of ≥3 points and ≥30%, plus a decrease in rectal bleeding subscore of ≥1 point or an absolute rectal bleeding subscore of 0 or 1; **Modified Mayo Score Clinical Response**: Decrease from study baseline total Mayo score of ≥2 points and ≥30%, plus a decrease in rectal bleeding subscore of ≥1 point or an absolute rectal bleeding subscore of 0 or 1; **Symptomatic Remission**: SFS=0 or 1 without worsening, and RBS=0

Rapid Improvement in UC Symptoms
Completer Population Combined SFS, RBS

SOR102 BID demonstrated clear symptomatic improvement within 2 weeks



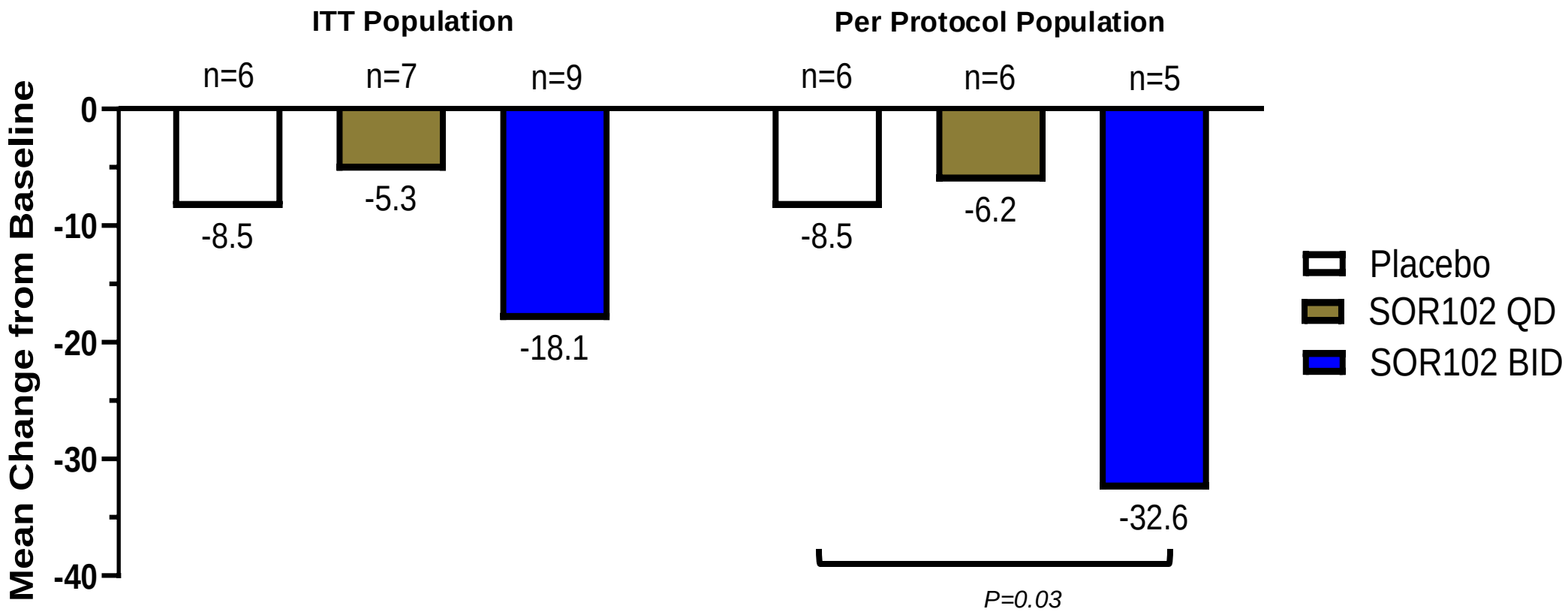
Endoscopic Improvement
ITT and Per-Protocol Population Responder Analyses



Endoscopic Improvement: MES of 0 or 1 at Day 42

Improvement in UC-100 Score[1]

ITT and Per-Protocol Population Mean Change from Baseline



Conclusions

- SOR102 was safe and well tolerated
- In most samples tested, there were no detectable levels of SOR102 or monomers in serum
- ADA titers were low in most patients and not associated with decreased clinical response
- Efficacy across multiple endpoints was observed in the SOR102 BID arm compared to QD and placebo, despite the short treatment duration
- Further clinical development of SOR102 is warranted

Acknowledgements

We would like to thank the:

- **Patients, their families and their caregivers** for their participation in this trial
- **Study investigators and their team members** for their support during the trial conduct