Induction and Maintenance Treatment with Risankizumab Leads to Symptomatic Relief in Patients with Moderate to Severe Crohn's Disease

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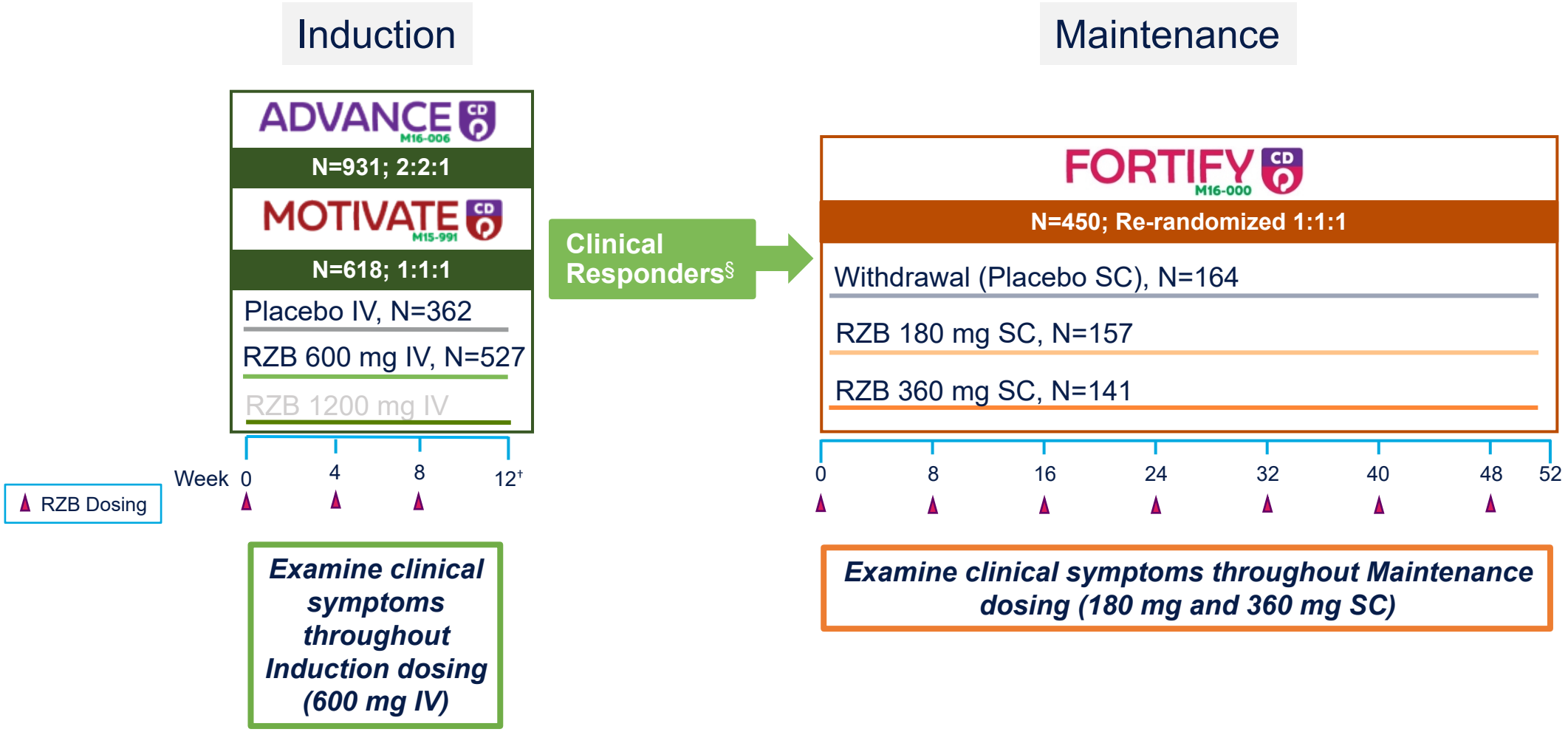
Introduction

- Abdominal pain (AP) and increased stool frequency (SF) comprise two of the most burdensome symptoms of Crohn's disease (CD)
- For patients, fast resolution of symptoms is an important goal in therapy.
- Risankizumab (RZB), was shown to be well-tolerated and superior to placebo for inducing and maintaining clinical remission and endoscopic response in patients with moderate to severe CD.[1,2]
- Here, the patient reported outcomes (PROs) of AP score (APS) and SF, and their correlation with endoscopic outcomes, were assessed during induction and maintenance treatment.

1. D'Haens G, Panaccione R, Baert F, Bossuyt P, Colombel JF, Danese S, et al. Risankizumab as induction therapy for Crohn's disease: results from the phase 3 ADVANCE and MOTIVATE induction trials. The Lancet. 2022 May;399(10340):2015–30.
2. Ferrante M, Panaccione R, Baert F, Bossuyt P, Colombel JF, Danese S, et al. Risankizumab as maintenance therapy for moderately to severely active Crohn's disease: results from the multicentre, randomised, double-blind, placebo-controlled, withdrawal phase 3 FORTIFY maintenance trial. The Lancet. 2022 May;399(10340):2031–46.

Study Objectives and Study Design



§ Clinical responders defined as patients with ≥ 30% decrease in average daily stool frequency (SF) and/or ≥ 30% decrease in average daily abdominal pain score (APS) and both not worse than baseline at week 12 of induction treatment
† The Week 12 visit in the induction studies correlates with the Week 0 visit in FORTIFY

Methods

PROs - During the screening period, patients were provided with an electronic diary in which to record CD-related symptoms throughout the study.

The diary was completed daily and reviewed at each study visit.

7-day average daily SF and average daily AP score were calculated.

Abdominal pain was rated as 0 = none, 1 = mild, 2 = moderate, 3 = severe.

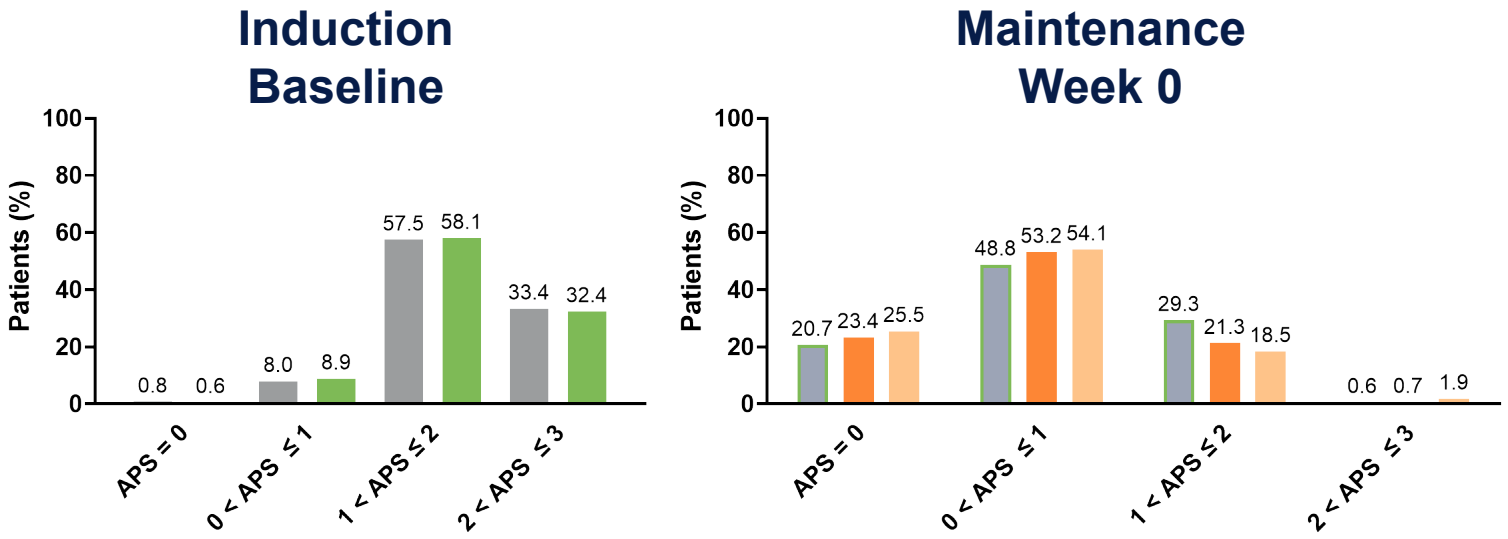
Tetrachoric correlation – appropriate to measure the correlation between two binary variables; used to determine the correlation between achieving SF (≤ 2.8) and APS (≤ 1.0) remission and endoscopic outcomes.

Characteristics and Demographics at the Baseline of Induction

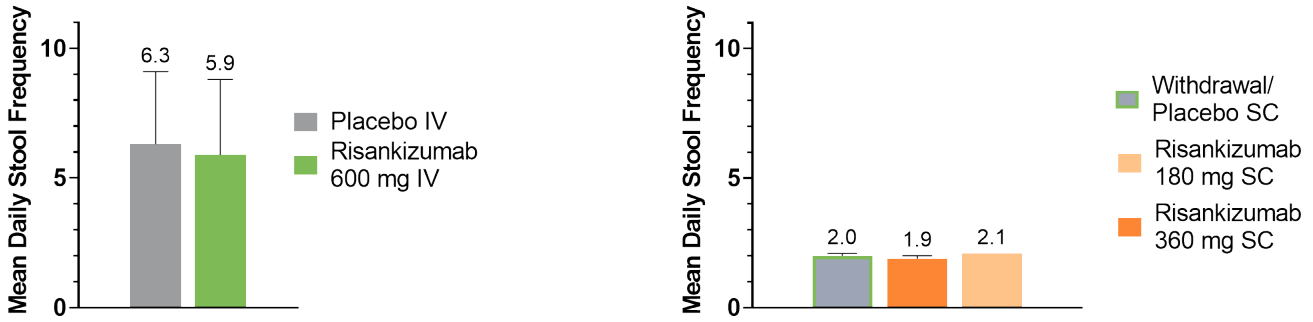
	ADVANCE + MOTIVATE Induction		FORTIFY Maintenance		
	Placebo (N=362)	Risankizumab 600 mg IV (N=527)	Withdrawal (Placebo SC) (N=164)	Risankizumab 180 mg SC (N=157)	Risankizumab 360 mg SC (N=141)
Female, n (%)	175 (48.3%)	246 (46.7%)	75 (45.7%)	89 (56.7%)	60 (42.6%)
Age, years, mean (SD)	38.3 (13.4)	39.0 (13.4)	38.0 (13.0)	39.1 (14.8)	37.0 (12.8)
Weight, kg, mean (SD)	71.6 (18.7)	70.9 (18.7)	71.8 (19.2)	69.2 (16.2)	70.4 (17.5)
Disease duration, years, mean (SD)	10.4 (8.8)	9.7 (8.5)	9.6 (8.8)	10.8 (10.2)	9.3 (8.1)
Disease location, n (%)					
Ileal only	45 (12.4%)	85 (16.1%)	23 (14.0%)	15 (9.6%)	15 (10.6%)
Colonic only	143 (39.5%)	190 (36.1%)	62 (37.8%)	70 (44.6%)	59 (41.8%)
Ileal-colonic	174 (48.1%)	252 (47.8%)	79 (48.2%)	72 (45.9%)	67 (47.5%)
Corticosteroid use, mean (SD)	117 (32.3)	167 (31.7)	51 (31.1%)	51 (32.5%)	42 (29.8%)
Biologics failure history, n (%)					
0	78 (21.5)	141 (26.8)	41 (25.0%)	44 (28.0%)	39 (27.7%)
1	129 (35.6)	192 (36.4)	60 (36.6%)	42 (26.8%)	51 (36.2%)
>1	155 (42.8)	194 (36.8)	63 (38.4%)	71 (45.2%)	51 (36.2%)
Anti-TNF failure history, n (%)					
0	6 (2.1)	26 (6.7)	4 (3.3%)	6 (5.3%)	11 (10.8%)
1	160 (56.3)	211 (54.7)	71 (57.7%)	52 (46.0%)	49 (48.0%)
>1	118 (41.5)	149 (38.6)	48 (39.0%)	55 (48.7%)	42 (41.2%)
Vedolizumab failure history, n (%)	85 (29.9%)	116 (30.1%)	31 (25.2%)	35 (31.0%)	31 (30.4%)
Ustekinumab failure history, n (%)	59 (20.8%)	79 (20.5%)	15 (12.2%)	18 (15.9%)	17 (16.7%)
Fecal calprotectin, mg/kg, median	1124	1065.5	794.5	1561	1543
hs-CRP, mg/liter, median	8.9	8	7.7	8.4	10.1
CDAI, mean (SD)	319.4 (64.9)	311.1 (62.8)	307.4 (64.9)	323.2 (67.6)	308.9 (61.1)
SES-CD, mean (SD)	14.5 (7.5)	14.6 (7.7)	14.0 (7.1)	14.7 (7.1)	14.3 (7.4)
Average daily stool frequency, mean (SD)	6.3 (2.8)	5.9 (2.9)	5.8 (2.7)	6.1 (3.2)	5.9 (2.6)
Average daily abdominal pain score, mean (SD)	1.9 (0.5)	1.9 (0.5)	1.9 (0.5)	2.0 (0.5)	1.8 (0.5)

Mean Daily Abdominal Pain Score and Stool Frequency

APS



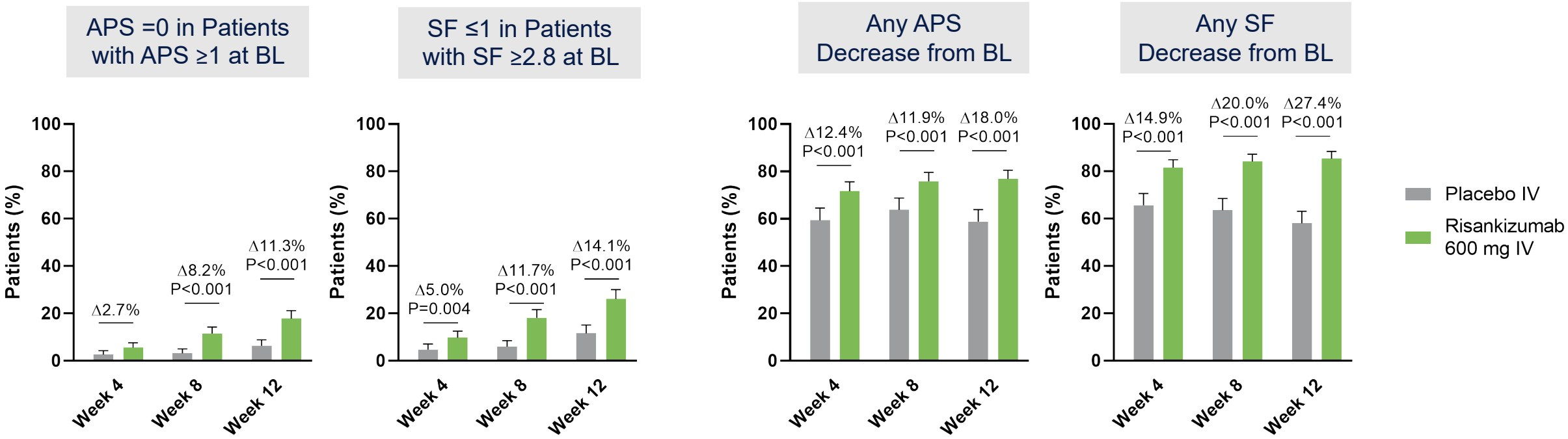
SF



Induction: ADVANCE + MOTIVATE ITT population which included randomized patients who received at least one dose of study drug during the 12-Week Induction Period and had SES-CD of ≥ 6 (≥ 4 for isolated ileal disease);
Maintenance: FORTIFY ITT population which included the randomized patients who received IV risankizumab for only one period of 12 weeks in the induction study and at least one dose of study drug in the sub-study 1 and had eligible SES-CD of had SES-CD of ≥ 6 (≥ 4 for isolated ileal disease) at baseline of induction study.

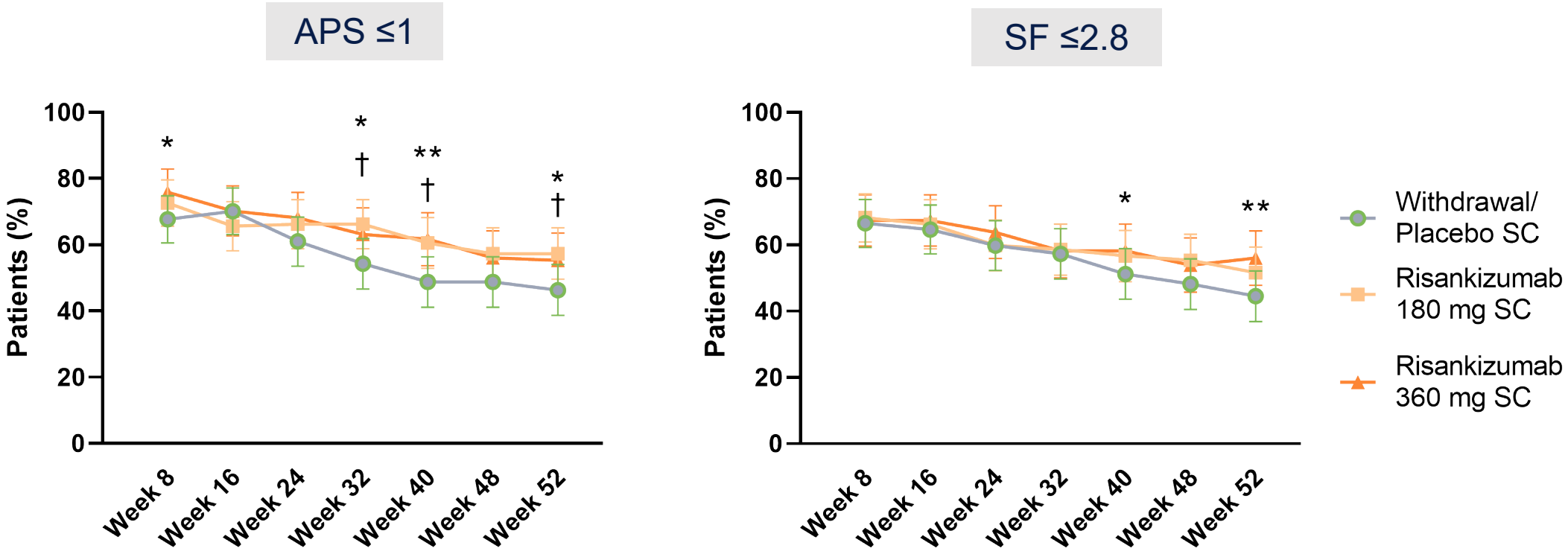
Proportion of Patients with Improved Clinical Symptoms Over Time - Induction

Induction



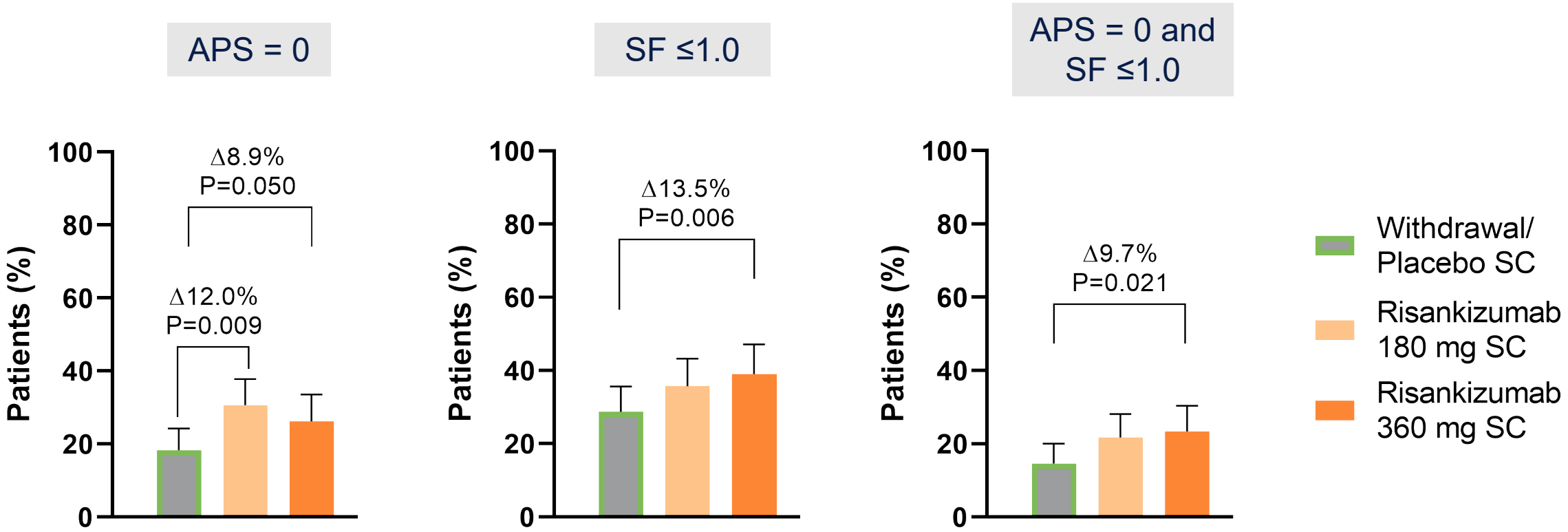
Proportion of Patients with Clinical Symptom Remission Over Time - Maintenance

Maintenance

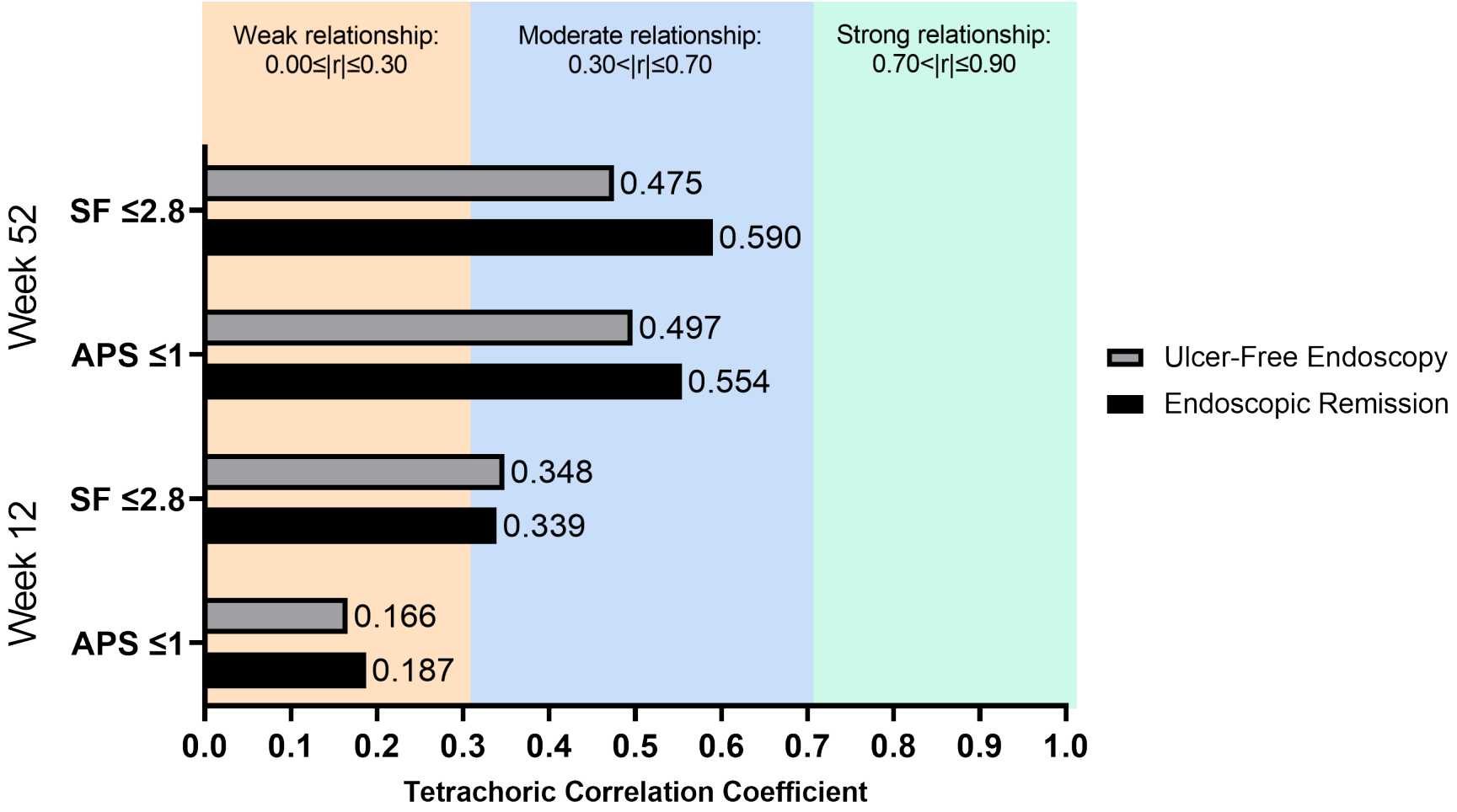


† Withdrawal (Placebo SC) vs. RZB 180 mg
* Withdrawal (Placebo SC) vs. RZB 360 mg
†, * p≤0.05; ** p ≤0.01

Resolution of Clinical Symptoms at Week 52



Correlation§ Between Achieving APS ≤1 or SF ≤2.8 and Endoscopic Outcomes



Endoscopic Response = decrease in SES-CD > 50% from Baseline of the induction study (or for subjects with isolated ileal disease and a SES-CD of 4 at Baseline of the induction study, at least a 2-point reduction from Baseline of the induction study), as scored by central reviewer
Ulcer Free Endoscopy = SES-CD ulcerated surface subscore of 0 in subjects with SES-CD ulcerated surface subscore ≥1 at baseline of the induction study, as scored by a central reviewer

§Tetrachoric correlation - describes the linear relation between two continuous variables that have each been measured on a dichotomous scale.

Safety Summary

Induction and maintenance treatment with risankizumab was generally well-tolerated, as previously reported.[1,2]

No new safety signals were observed

The safety profile was generally consistent with that observed in risankizumab studies in other immune-mediated inflammatory diseases

1. D'Haens G, Panaccione R, Baert F, Bossuyt P, Colombel JF, Danese S, et al. Risankizumab as induction therapy for Crohn's disease: results from the phase 3 ADVANCE and MOTIVATE induction trials. The Lancet. 2022 May;399(10340):2015–30.
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Conclusions

CD-related symptomatic PROs improved with RZB induction therapy

Both maintenance doses were effective in resolving abdominal pain; however, only the 360 mg SC RZB maintenance dose was significantly different than withdrawal (placebo SC) for improving daily SF and the combined endpoint of complete resolution of AP and SF ≤1

Symptom improvements and endoscopic outcomes were weakly correlated after induction and moderately correlated during maintenance, underscoring the importance of an objective measure to assess disease activity.

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