
2023 SCSG
GI SYMPOSIUM

IBD Abstract Review DDW 2023

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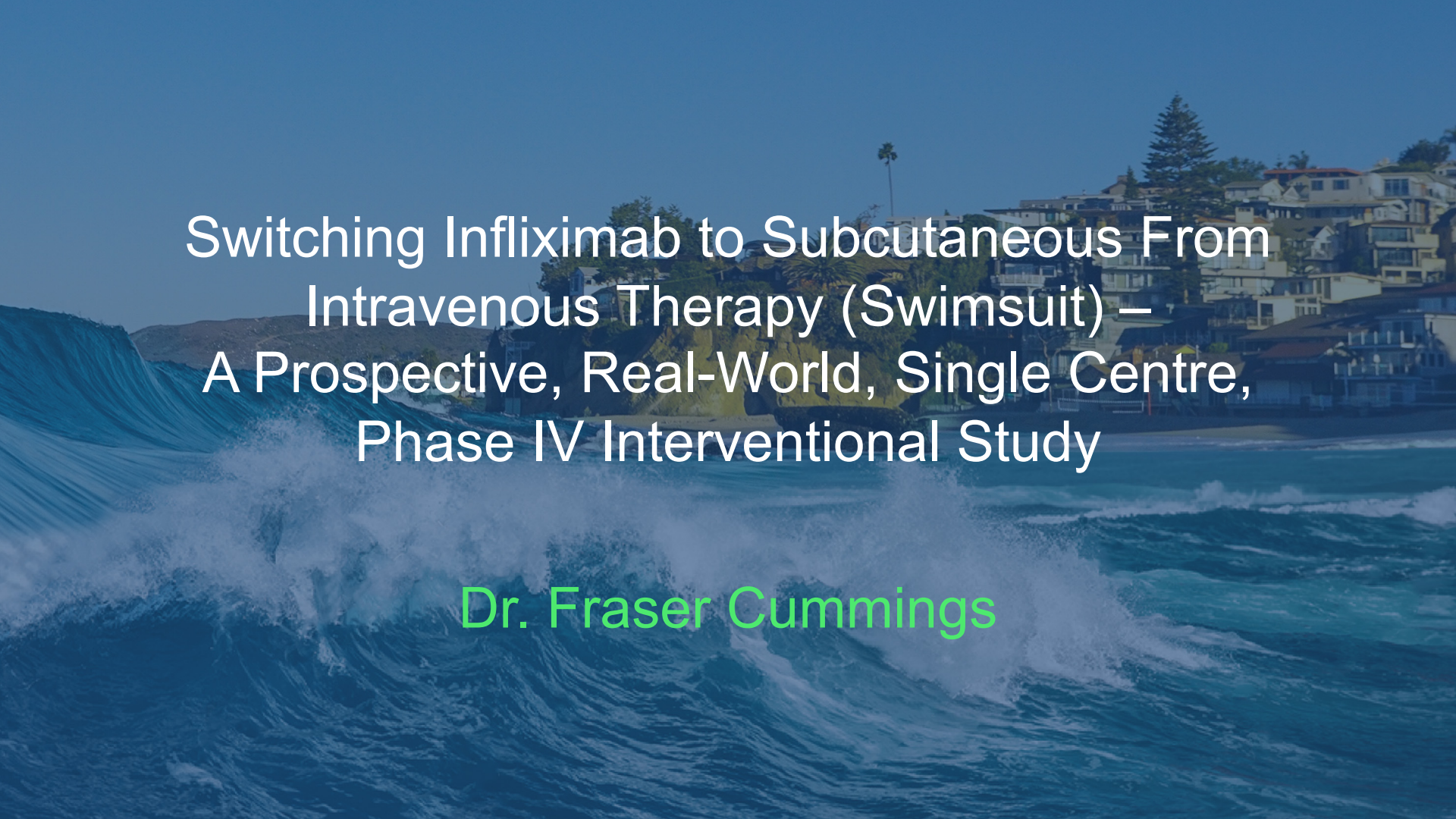
Disclosures

- None

Outline

- Established Drug Therapies
  - SC Infliximab (FDA approval submitted)
- New Drug Therapies
  - Risankizumab (Skyrizi)
  - Upadacitinib (Rinvoq)
  - Ozanimod (Zeposia)



Switching Infliximab to Subcutaneous From Intravenous Therapy (Swimsuit) – A Prospective, Real-World, Single Centre, Phase IV Interventional Study

Dr. Fraser Cummings

Background

- Subcutaneous (SC) infliximab (CT-P13) was approved in 2020 by the EMA for use in IBD. This offers patients greater choice, flexibility and the convenience of administering their treatment at home as well as other potential therapeutic benefits. We aim to evaluate the clinical outcomes of patients switching from intravenous (IV) infliximab to SC CT-P13.

Cummings, F et al. DDW Abstract. 2023.

Methods

- IBD patients established on IV infliximab (>4 doses) were offered the opportunity to switch to SC CT-P13.
- Patients who agreed to switch were followed up every 12 weeks for 24 weeks.
- Demographics, disease history, disease activity scores, IBD CONTROL PROM, SF36, calprotectin, standard blood tests, infliximab drug levels, antidrug antibodies (ADA) and adverse events were collected at each visit. The primary endpoint was the maintenance of clinical status at week 24 (W24).
- A failure to maintain clinical status was defined as an increase in disease activity scores (mHBI or SCCAI) of ≥3, and/or a decline in IBD-Control PROM score of ≥4 points at any time during the study period.

PROM: Patient reported outcome measures
SF: Short Form 36 questions about physical and mental questionnaire
SCCAI: Simple clinical colitis activity index
Cummings, F et al. DDW Abstract. 2023.

Results

We approached 204 patients receiving IV infliximab, of which 120 patients switched to SC CT-P13. 24 patients had perianal disease at baseline. Median age was 38. The median time taken by patients (leaving home to returning home) to receive their infusions was 180 minutes (range 60 to 660). 96 participants were on concomitant immunomodulators (79 thiopurines, 17 methotrexate) and 105 were treated with SB2 preswitch (figure 1). The median duration of IV infliximab prior to switching was 45 months. 70 (58%) of the patients were on the standard dosing (5mg/kg Q8W) regimen. All patients were switched to 120mg of SC CT-P13 every other week, regardless of their baseline regimen. 11 (9.2%) patients discontinued the treatment prior to finishing the study. 75% (CI 0.65, 0.82) of the whole cohort reached the primary endpoint of maintaining clinical status at week 24. There was no statistically significant difference in disease activity scores or IBD-Control PROM between baseline and W24 (figure 2). 31 (25.8%) of the patients had evidence of immunogenicity at baseline (ADA of > 50ng/ml). Of the 89 patients with no immunogenicity at baseline, 69 (77.5%) maintained this at W24. The median serum infliximab levels increased by 72.8 % from baseline to W24 (3.05 µg/ml to 5.27 µg/ml (figure 3)). 81.7% of patients maintained their immunogenicity at W24 (figure 4). Patient satisfaction with SC CT-P13 was very high (figure 5).

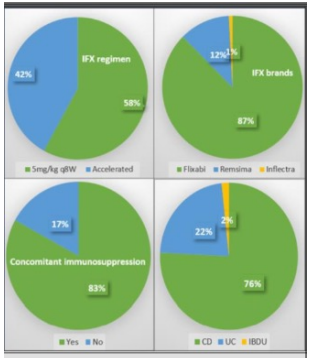


Figure 1- baseline characteristics

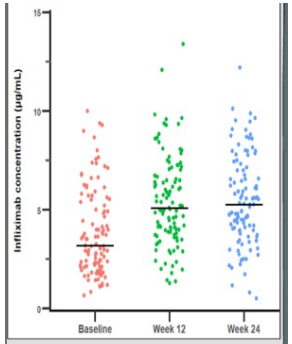
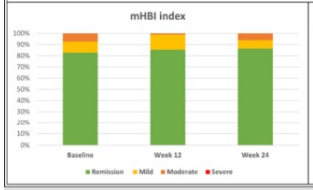


Figure 3 – IFX drug level before and after switch

	Baseline	Week 12	Week 24	Mean difference between week 0 and week 24 (95% CI)
mHBI, median (IQR)	2 (1, 3)	2 (1, 3)	1 (0, 3)	-0.22 (-0.61, 0.17)
SCCAI, median (IQR)	2 (1, 4)	2 (1, 3.5)	2 (1, 4)	-0.28 (-1.04, 0.49)
IBD-Control-8, median (IQR)	14 (12, 16)	14.5 (12, 16)	15 (12, 16)	-0.14 (-0.81, 0.52)
IBD-Control-VAS, median (IQR)	9 (8, 9)	9 (8, 10)	8.5 (7.3, 9.4)	-0.59 (-0.96, -0.22)



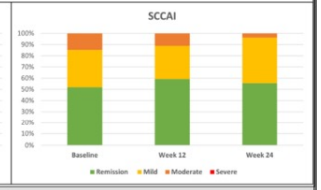


Figure 2 – Disease activity scores and PROMS

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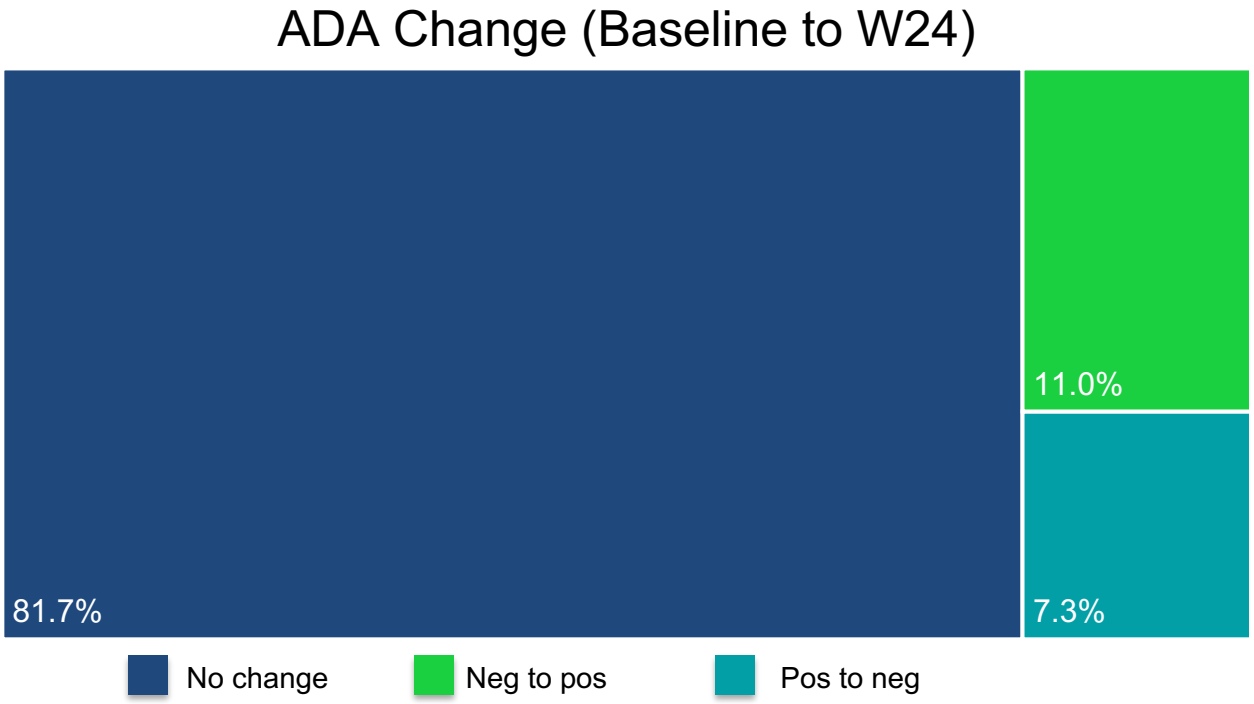

Figure 4 – ADA change after switch to SC.
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Conclusion

- Switching patients from IV to SC CT-P13 is safe, effective, and well-accepted with higher infliximab serum levels. The majority of the patients with no immunogenicity at baseline maintained this at W24.

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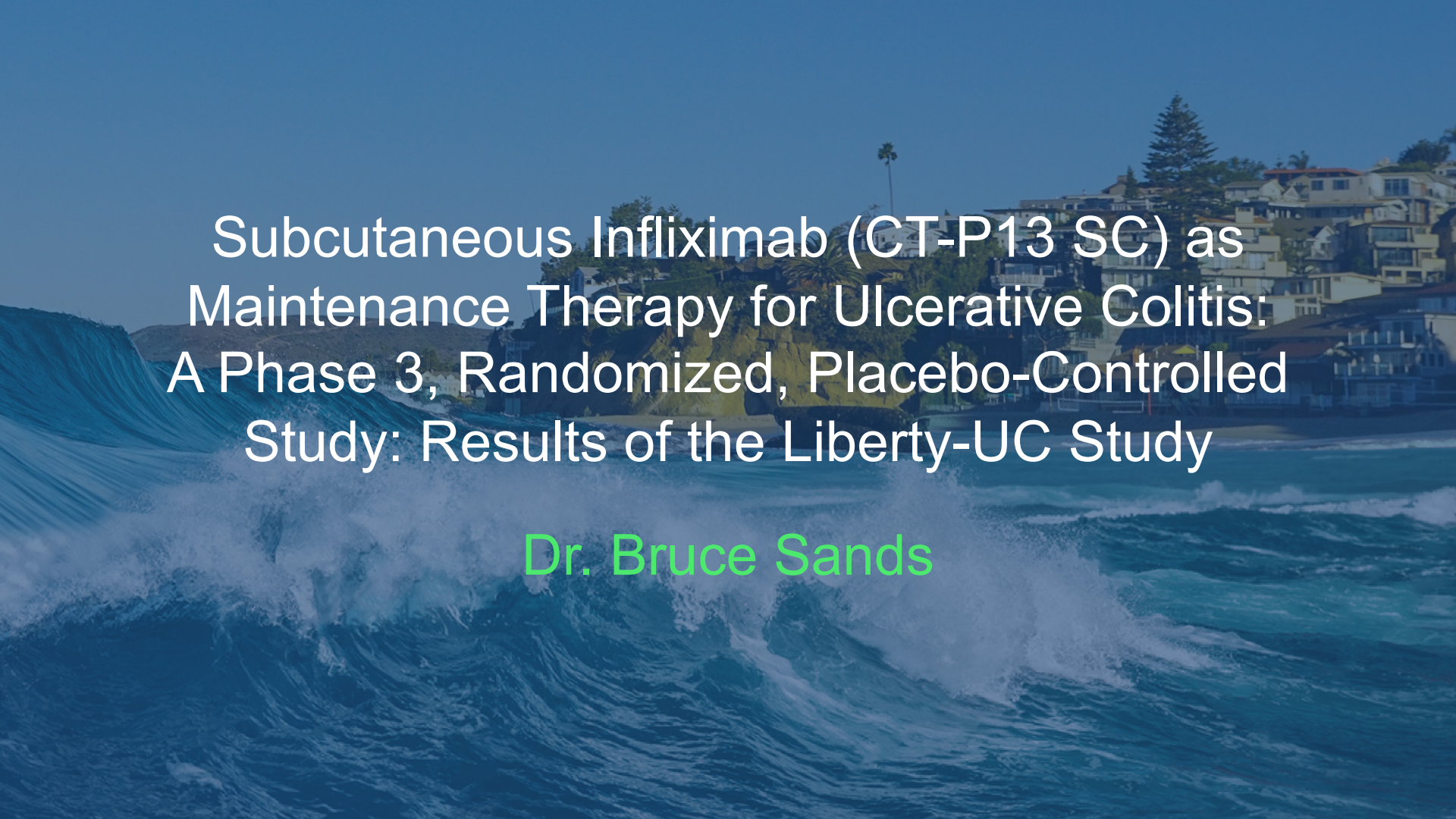

Subcutaneous Infliximab (CT-P13 SC) as Maintenance Therapy for Ulcerative Colitis: A Phase 3, Randomized, Placebo-Controlled Study: Results of the Liberty-UC Study

Dr. Bruce Sands

Background

- CT-P13 subcutaneous (SC) infliximab formulation was developed to provide patients with a convenient option for treatment. Previous studies have shown efficacy and safety of CT-P13 SC comparable to CT-P13 intravenous (IV) in inflammatory bowel disease (IBD) and rheumatoid arthritis. This study aimed to demonstrate superiority of CT-P13 SC over placebo in maintenance therapy after induction therapy of CT-P13 IV in patients with ulcerative colitis (UC).

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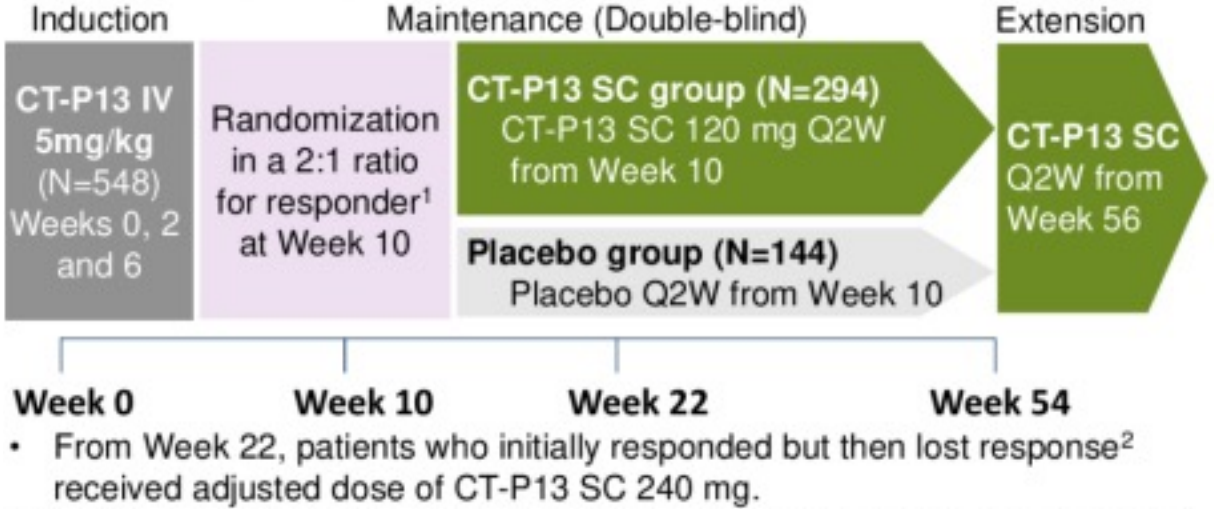
Figure 1. Study design



- From Week 22, patients who initially responded but then lost response[2] received adjusted dose of CT-P13 SC 240 mg.

[1]Clinical response was defined as decrease in Modified Mayo score (MMS) from baseline of at least 2 points and at least 30% decrease in the rectal bleeding subscore of ≥1 or an absolute rectal bleeding subscore ≤ 1.
[2]Lost response was defined as, modified Mayr score ≥2 points and ≥30% from the Week 10 modified Mayo score (MMS) with actual value ≥5 points, and endoscopic subscore of ≥2 points.
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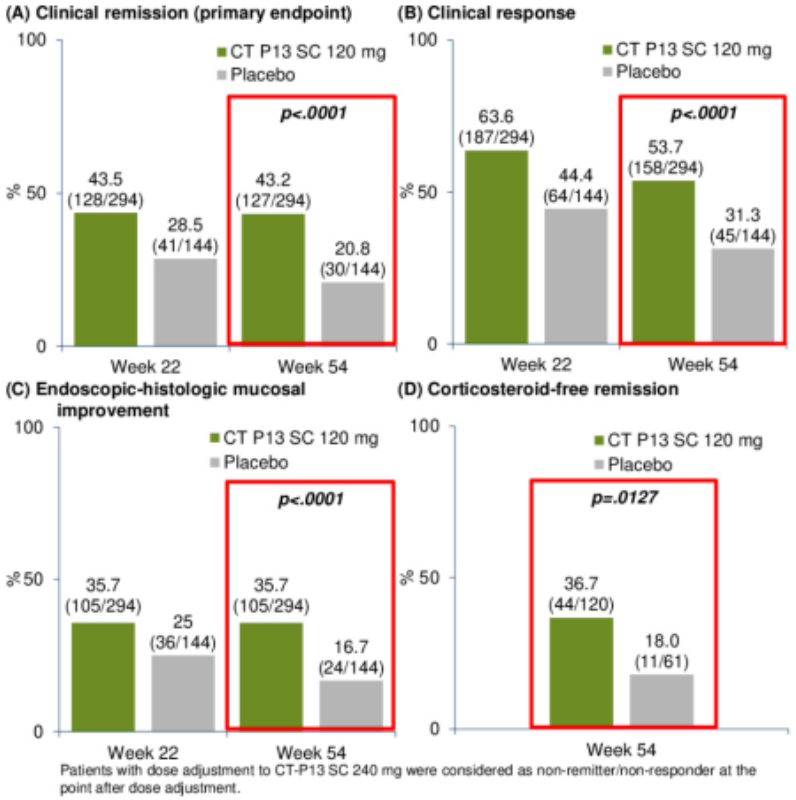
Figure 2. Proportion of patients achieving efficacy endpoints



Patients with dose adjustment to CT-P13 SC 240 mg were considered as non-remitter/non-responder at the point after dose adjustment.

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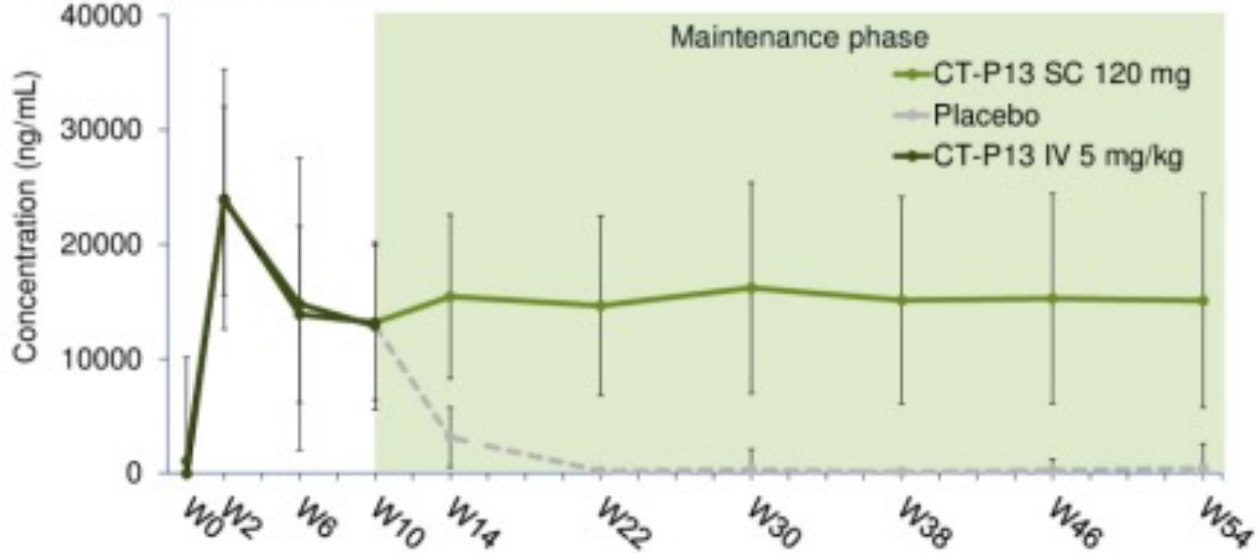
Figure 3. Mean (SD) pre-dose concentration of CT-P13



Patient whose does was adjusted to CT-P13 240mg were excluded from the time of dose adjustment.
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Table 3. Immunogenicity: Treatment period

Number of Patients (%)	CT-P13 SC 120 mg (N=296)	Placebo (N=140)
Positive Conversion in ADA, n*/N#(%)	183/287 (63.8)	123/134 (91.8)
Positive Conversion in NAb, n*/N$(%)	161/183 (88.0)	120/123 (97.6)

ADA, anti-drug antibody; NAb, neutralizing antibody; SC, subcutaneous;
Note. Data collected before initiation of dose adjustment for Placebo SC group are included in results. All data are included regardless of dose adjustment in CT-P13 SC group.
*Patients who reported at least one ADA of NAb positive after Week 0 study drug administration.
#Patients who have at least one immunogenicity result after Week 0 and have not any ADA positive result before Week 0.
$Patients who have at least one immunogenicity result after Week 0 and have not any NAb positive result before Week 0, among patients who have conversion in ADA.

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Conclusion

- CT-P13 SC was more effective than placebo for clinical remission, clinical response, endoscopic histologic mucosal improvement, and corticosteroid-free remission at Week 54 in patients with moderately to severely active UC. No new safety concerns were identified. These results demonstrate that the CT-P13 SC provides both a robust clinical benefit and the convenience of SC administration to patient with moderately to severely active UC.

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Additional Risankizumab Treatment Is Effective in Patients With Moderately to Severely Active Crohn's Disease Who Did Not Achieve CDAI Clinical Response With the Initial 12-Week Induction Treatment: Results From the Advance, Motivate, and Fortify Study

Dr. Marla Dubinsky

Background

- Risankizumab (RZB), an anti-interleukin-23 monoclonal antibody, has demonstrated efficacy and was well tolerated as both induction and maintenance therapies in primary analyses of patients with moderately to severely active Crohn's disease (CD). In this post hoc analysis of the ADVANCE, MOTIVATE, and FORTIFY studies, we evaluated the efficacy and safety of 12 additional weeks of RZB treatment in patients who did not achieve clinical response per Crohn's Disease Activity Index (CDAI) after an initial 12 weeks of induction intravenous (IV) treatment.

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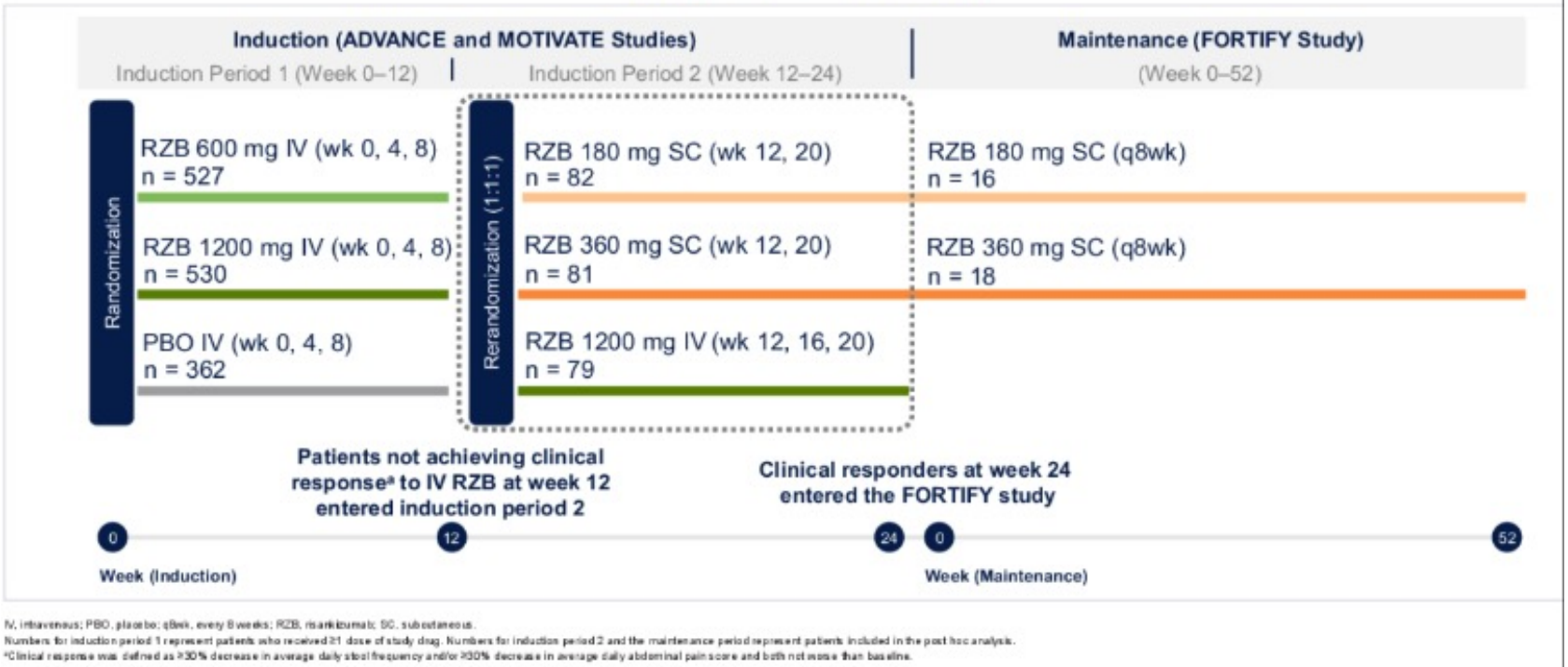
Figure 1. Study Design



IV, intravenous; PBO, placebo; q8wk, every 8 weeks; RZB, risankizumab; SC, subcutaneous.
Numbers for induction period 1 represent patients who received ≥1 dose of study drug. Numbers for induction period 2 and the maintenance period represent patients included in the post hoc analysis.
[a]Clinical response was defined as ≥30% decrease in average daily stool frequency and/or ≥30% decrease in average daily abdominal pain score and both not worse than baseline.

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Methods

- This post hoc analysis evaluated efficacy endpoints at week 24 of the induction studies and week 52 of the maintenance study in patients who did not achieve CDAI clinical response (≥100-point reduction in CDAI from baseline) at week 12 of the induction studies. Endpoints included CDAI clinical response, CDAI clinical remission, endoscopic response, and endoscopic remission. Data from the ADVANCE and MOTIVATE studies were pooled. As-observed data were reported were reported for the induction period; non-responder imputation with no special handling for data missing due to COVID-19 was used for the maintenance period.

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RESULTS

Patients

- Baseline demographics and characteristics among patients who did not achieve CDAI clinical response at entry of induction period 2 were generally similar across treatment groups **(Table 1)**

Table 1. Demographics and Characteristics at Baseline of Induction Period 1

Characteristic	RZB 1200 mg IV n = 79	RZB 180 mg SC n = 82	RZB 360 mg SC n = 81
Male	40 (50.6)	46 (56.1)	47 (58.0)
Age, years, mean (SD)	40.6 (13.7)	39.2 (12.8)	40.9 (12.8)
Disease duration, years, mean (SD)	12.8 (9.8)	10.9 (9.6)	9.9 (8.8)
Disease location			
Ileal only	13 (16.5)	21 (25.6)	16 (19.8)
Colonic only	18 (22.8)	23 (28.0)	24 (29.6)
Ileal-colonic	48 (60.8)	38 (46.3)	41 (50.6)
Corticosteroid use	22 (27.8)	36 (43.9)	38 (46.9)
Immunomodulator use	15 (19.0)	21 (25.6)	14 (17.3)
Biologics failure history			
0	18 (22.8)	20 (24.4)	20 (24.7)
1	24 (30.4)	33 (40.2)	21 (25.9)
>1	37 (46.8)	29 (35.4)	40 (49.4)
Ustekinumab failure history, n/N (%)	17/61 (27.9)	13/62 (21.0)	19/61 (31.1)
FCP, mg/kg, median (range)	482 (30, 24013)	623 (30, 8811)	803 (35, 14052)
hsCRP, mg/L, median (range)	5.6 (0.2, 98.6)	5.0 (0.2, 94.2)	8.2 (0.2, 115.0)
CDAI, mean (SD)	305.6 (64.6)	295.1 (60.9)	300.5 (69.3)
SES-CD, mean (SD)	14.8 (7.5)	13.1 (8.1)	13.8 (7.3)

CDAI, Crohn's Disease Activity Index; FCP, fecal calprotectin; hsCRP, high-sensitivity C-reactive protein; IV, intravenous; PBO, placebo; RZB, risankizumab; SES-CD, Simple Endoscopic Score for Crohn's Disease.
Data were pooled from the ADVANCE and MOTIVATE studies, which included randomized patients who received ≥1 dose of study drug in induction period 2 with baseline eligible SES-CD of ≥5 (≥4 for isolated ileal disease) and did not achieve CDAI clinical response.
Data presented as n (%) unless stated otherwise.

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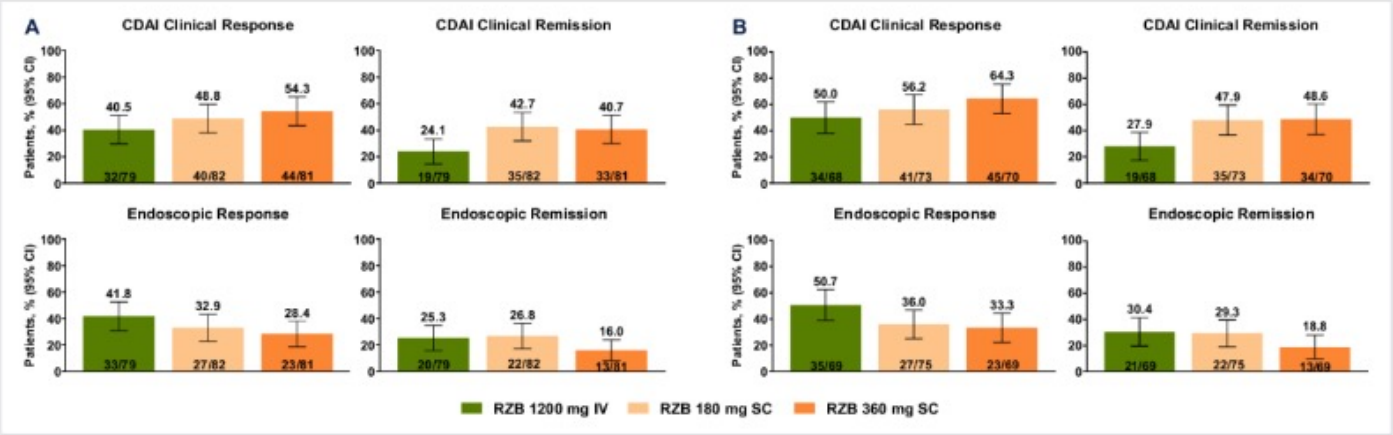
RESULTS CONTINUED

Efficacy

- After 12 additional weeks of RZB therapy, at least half of patients achieved clinical response and more than a third achieved endoscopic response **(Figure 2)**; the proportion of patients achieving clinical response and clinical remission were numerically higher with subcutaneous dosing
- In the maintenance study, response rates were generally sustained or increased further among patients who continued RZB treatment **(Figure 3)**

Figure 2. Proportion of Patients Achieving Clinical and Endoscopic Outcomes at Week 24 of Induction: A. NRI-NC B. As Observed



CDAI, Crohn's Disease Activity Index; IV, intravenous; NRI-NC, noncompleter imputation with no special data handling for missing data due to COVID-19; PBO, placebo; RZB, risankizumab; SC, subcutaneous; SES-CD, Simple Endoscopic Score for Crohn's disease.
CDAI clinical response, reduction of CDAI ≥100 points from baseline of the induction study; CDAI clinical remission, CDAI <150 points; Endoscopic response, ≥50% decrease in SES-CD from baseline (or for patients with isolated ileal disease and a baseline SES-CD of 4, ≥2-point reduction from baseline), as scored by a central reviewer; Endoscopic remission, SES-CD ≤4 and ≥2-point reduction vs baseline and no subscore >1 in any individual variable, as scored by a central reviewer.

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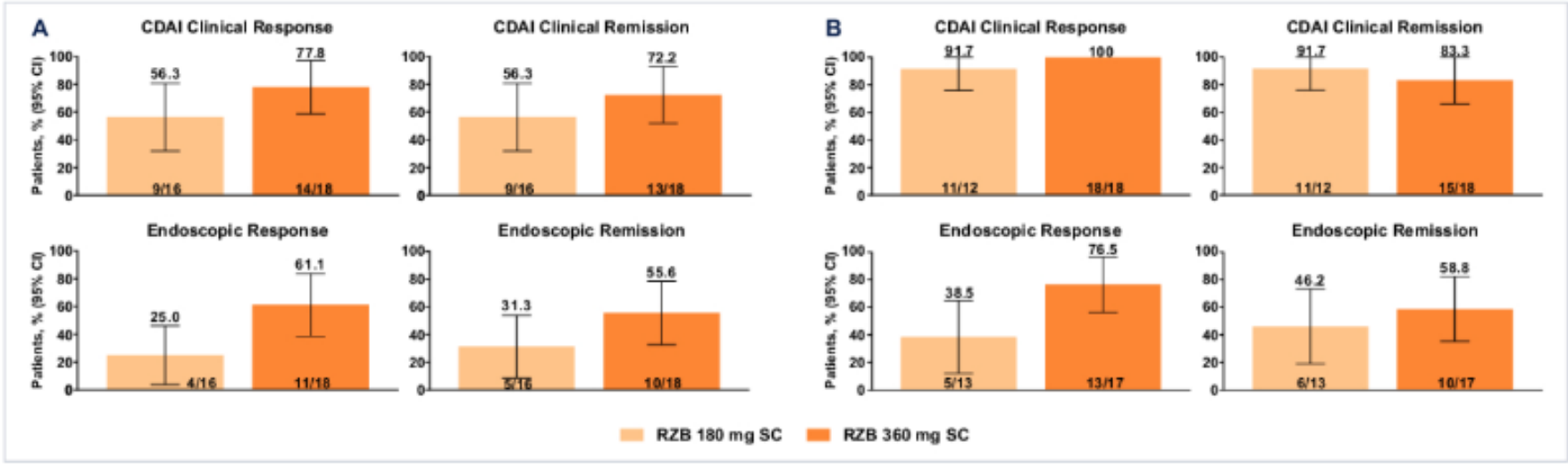
Figure 3. Proportion of Patients Achieving Clinical and Endoscopic Outcomes at Week 52 of Maintenance: A. NRI-NC B. As Observed



CDAI, Crohn's Disease Activity Index; NRI-NC, nonresponder imputation with no special data handling for missing data due to COVID-19; PBO, placebo; RZB, risankizumab; SC, subcutaneous; SES-CD, Simple Endoscopic Score for Crohn's disease.
CDAI clinical response, reduction of CDAI ≥100 points from baseline of the induction study; CDAI clinical remission, CDAI <150 points; Endoscopic response, >50% decrease in SES-CD from baseline (or for patients with isolated ileal disease and a baseline SES-CD of 4, ≥2-point reduction from baseline), as scored by a central reviewer. Endoscopic remission, SES-CD ≤4 and ≥2-point reduction vs baseline and no subscore ≥1 in any individual variable, as scored by a central reviewer.

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Conclusion

- In patients with moderate-to-severe CD who did not achieve CDAI clinical response following 12 weeks of induction therapy, an additional 12 weeks of RZB treatment led to improvements in clinical and endoscopic outcomes up to week 52 of the maintenance study. RZB was well tolerated during the prolonged induction and maintenance periods, and no new safety findings were identified.

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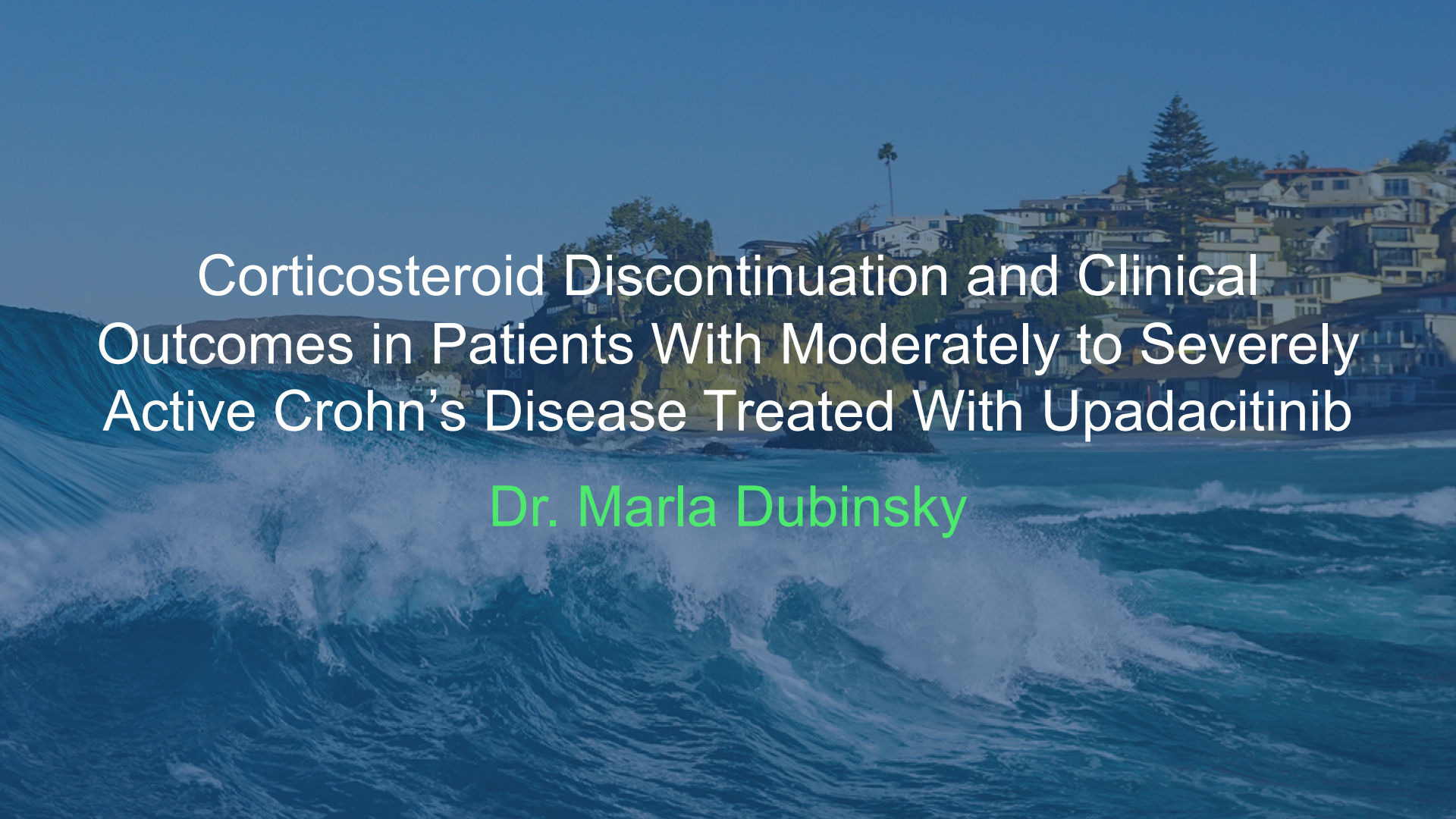

Corticosteroid Discontinuation and Clinical Outcomes in Patients With Moderately to Severely Active Crohn's Disease Treated With Upadacitinib

Dr. Marla Dubinsky

Background

- Corticosteroids (CS) may be used for induction of remission in Crohn's disease (CD); however, side effects, toxicities, and low rates of mucosal healing may limit their long-term use. Safety and efficacy of upadacitinib (UPA), an oral selective Janus kinase inhibitor, were evaluated among patients with CD receiving UPA with CS at baseline in phase 3 clinical trials.

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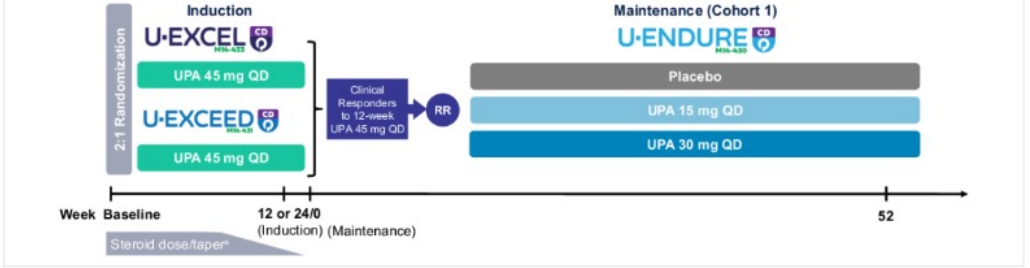
Methods

Figure 1. Study Design



QD, once daily; RR, rerandomized; UPA, upadacitinib.
[a]Clinical response was defined as ≥30% decrease in average daily very soft or liquid stool frequency and/or ≥30% decrease in average daily abdominal pain score (both not worse than baseline).
[b]Endpoints include clinical remission by stool frequency/abdominal pain score or by Crohn's Disease Activity Index (CDAI), enhanced clinical response, decrease of at least 100 points in CDAI from baseline, endoscopic remission, and endoscopic response.

- In the U-EXCEL (patients with or without biologic failure) and U-EXCEED (patients with biologic failure) induction studies, patients with moderately to severely active CD received UPA 45 mg once daily (QD) or placebo (PBO) for 12 weeks **(Figure 1)**
- Patients with clinical response[a] to 12 weeks of UPA 45 mg QD were rerandomized in the U-ENDURE maintenance study to receive UPA 30 mg QD, UPA 15 mg QD, or PBO for 52 weeks **(Figure 1)**
- A corticosteroid taper began at week 4 of the induction studies and, if not completed, continued during maintenance
- Efficacy endpoints included the proportion of patients who discontinued corticosteroid use at week 12 (induction) or for ≥90 days prior to week 52 (maintenance), and achieved clinical and endoscopic endpoints[b] at week 12 and week 52
- This analysis included patients taking corticosteroids at baseline of induction or week 0 of maintenance (end of induction)

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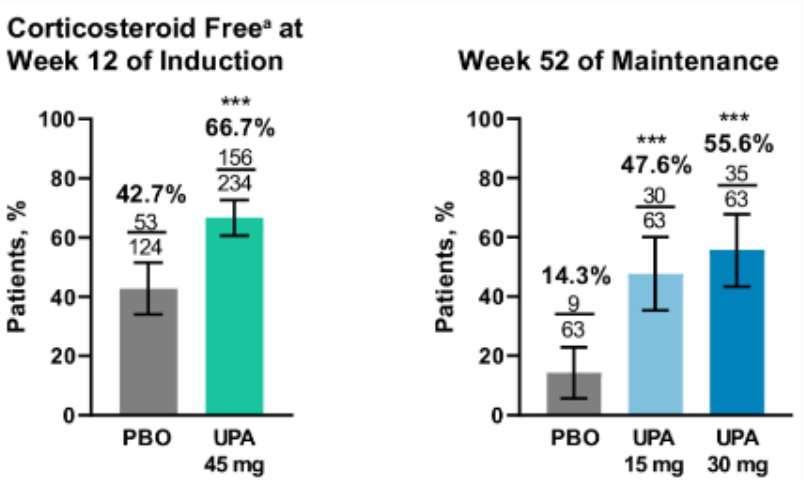
Figure 2. Reduction in Corticosteroid Use at Week 12 and Week 52



Denominators represent the number of patients included in the intent-to-treat analysis who were taking corticosteroids at baseline of the induction studies or week 0 of maintenance

PBO, placebo; UPA, upadacitinib.
Data are percent of patients (95% CI). Values above bars are percent of patients and n/N.
***P <.001 vs PBO.
[a]Induction: patients who discontinued corticosteroid use by week 12, in patients taking corticosteroids at baseline. Maintenance: patients who discontinued corticosteroid use at the week 52 visit, in the patients taking corticosteroids at baseline or week 0 of maintenance.

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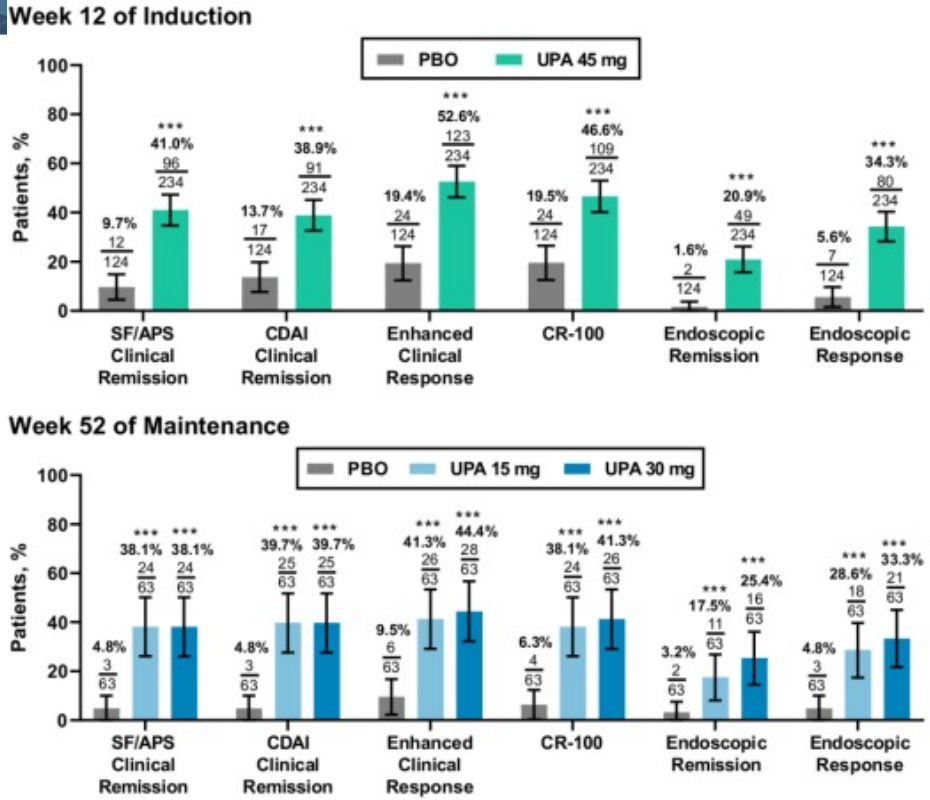
Figure 3. Corticosteroid Free and Achievement of Clinical and Endoscopic Endpoints at Week 12 and Week 52



Denominators represent the number of patients included in the intent-to-treat analysis who were taking corticosteroids at baseline of the induction studies or week 0 of maintenance

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Conclusion

- Patients with CD taking CS were able to taper and discontinue their CS regimen and experience clinical and endoscopic improvements with UPA treatment during the induction and maintenance periods.

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Upadacitinib Therapy Reduces Crohn's Disease Symptoms Within the First Week of Induction Therapy

Jean Frederic Colombel

Background

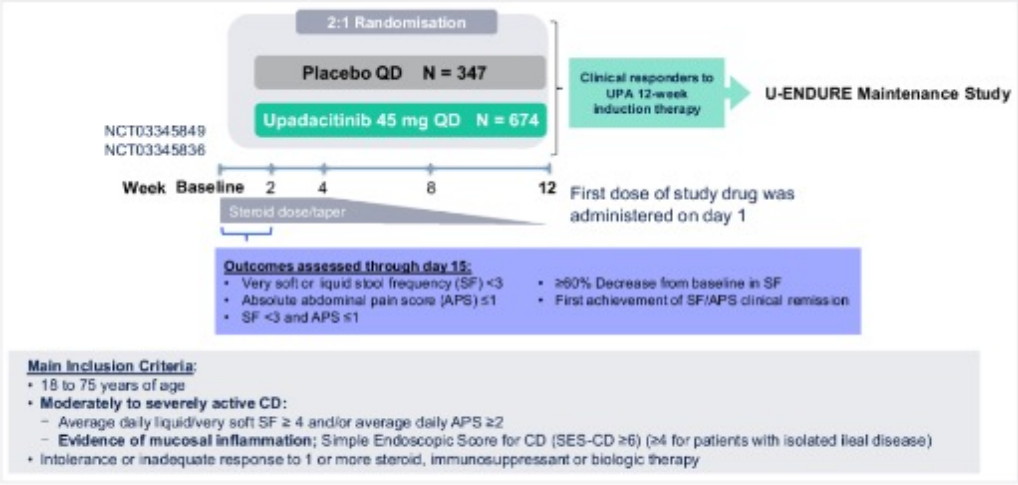
- Upadacitinib (UPA), an oral, selective JAK inhibitor demonstrated superior efficacy for clinical remission compared with placebo (PBO) and an acceptable safety profile in patients with moderately to severely active Crohn's disease (CD) in 2 phase 3 induction trials, U-EXCEL (NCT03345849) and U-EXCEED (NCT03345836).[1,2,3]
- There remains an unmet need for therapies that provide rapid symptom relief in ambulatory patients with moderate to severe CD experiencing disease flares. This sub-analysis evaluated the efficacy of UPA 45 mg once daily (UPA45) on early symptomatic improvement for the first 15 days of treatment, using pooled data from U-EXCEL and U-EXCEED.

Colombel JF et al. DDW Abstract. 2023.

Methods

This post-hoc analysis included patients with inadequate response or intolerance to conventional or biologic therapy from the phase 3 U-EXCEL and U-EXCEED induction studies (Figure 1)

Figure 1. U-EXCEL and U-EXCEED Were Multicentre, Double-blind, PBO-controlled Trials



SF/APS Clinical response: ≥30% decrease in average daily SF and/or in average daily APS and both not greater than baseline) at week 12 or 24 of UPA 45 mg QD induction treatment were randomised to the Maintenance Study.
SF/APS Clinical remission: Average daily very soft or liquid SF ≤2.8 and average daily abdominal pain score (APS) ≤1.0 and both not greater than baseline.

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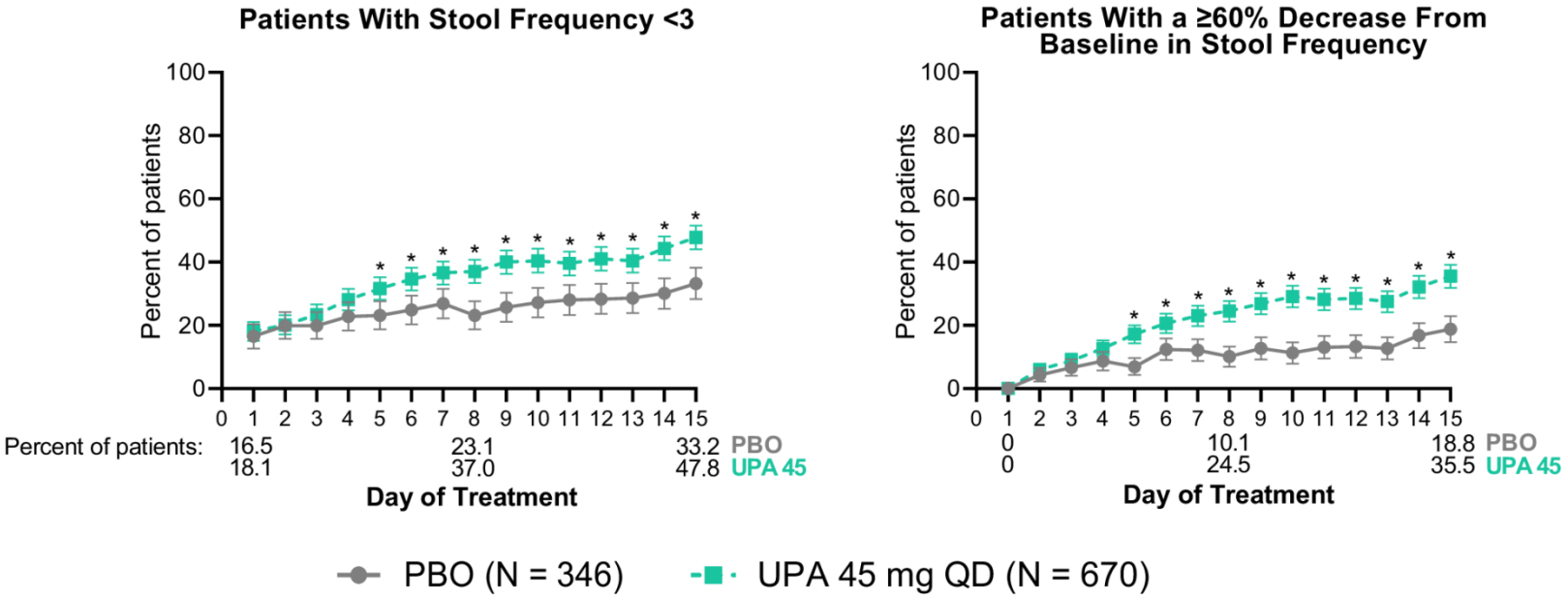
Figure 4. Stool Frequency Within the First 15 Days of Treatment



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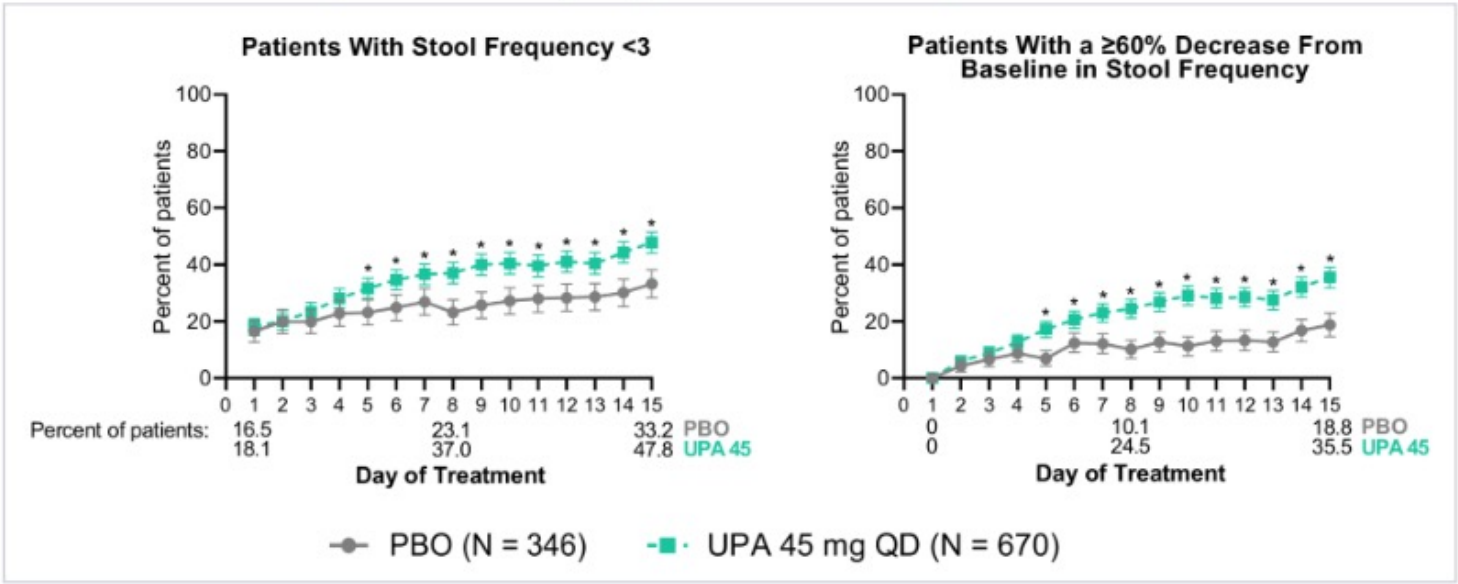
• Patients treated with UPA 45 mg QD achieved a significant reduction in daily stool frequency by day 5 compared to PBO **(Figure 4)**

Figure 4. Stool Frequency Within the First 15 Days of Treatment



PBO, Placebo; QD, once daily; UPA, upadacitinib.
Treatment groups were analysed using non-responder imputation with no special data handling for missing data due to COVID-19.
Error bars represent 95% confidence intervals, based on Wald limits without continuity correction.
Significance was determined using Pearson's Chi-Square test of association.
*P ≤ .05.

Colombel JF et al. DDW Abstract. 2023.

Conclusion

- Patients who received UPA 45 mg once daily significantly improved daily symptoms of diarrhea or abdominal pain within the first week of treatment and achieved daily clinical remission faster than PBO-treated patients, providing rapid symptom relief.

Colombel JF et al. DDW Abstract. 2023.

The Effects of Upadacitinib on Ulcerative Colitis Symptom Resolution and Fatigue Normalization in Patients With Moderately to Severely Active Ulcerative Colitis: Phase 3 U-Achieve and U-Accomplish Results

Dr. David Rubin

Background

- Abdominal pain (AP), bowel urgency (BU), stool frequency (SF), rectal bleeding (RB) and fatigue are debilitating symptoms that reduce quality of life in patients with ulcerative colitis (UC). Results from two Phase 3 induction trials and one maintenance trial (U-ACHIEVE [NCT02819635] and U-ACCOMPLISH [NCT03653026]) showed significant and clinically meaningful improvements in these symptoms following induction and maintenance treatment with upadacitinib (UPA) in patients with moderately to severely active UC. We evaluated the effects of 8-week UPA induction and 52-week UPA maintenance treatment on UC symptom resolution, defined as no BU, no AP, and symptomatic remission (no RB, SF≤1), and normalization of fatigue, defined as achievement of a Functional Assessment of Chronic Illness Therapy–Fatigue (FACIT–F) score ≥40.1.

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Results

- Approximately, half of the study participants had a history of failure to respond or an inadequate response to treatment with biologics **(Table 1)**
- A higher percentage of patients achieved symptom resolution during induction treatment, with some achieving symptom resolution as early as week 2, with UPA 45 mg vs placebo **(Figure 2)**
- Rates of symptom resolution observed during induction treatment were sustained during maintenance treatment with UPA 15 mg or 30 mg vs placebo **(Figure 3)**
- At week 8 of induction and week 52 of maintenance, the percentage of patients who achieved both complete symptom resolution and fatigue normalization was greater with UPA compared with placebo **(Figure 4)**

Table 1. Baseline Characteristics of the Induction Population

Variable	PBO (n = 328)	UPA 45 mg QD (n = 660)
Female, n (%)	124 (37.8)	248 (37.6)
White, n (%)	224 (68.3)	440 (66.7)
Age (y), median (range)	42.0 (17–76)	41.0 (17–76)
Disease duration (y), mean ± SD	8.2 ± 8.0	7.9 ± 6.8
Concomitant corticosteroid use, n (%)	133 (40.5)	244 (37.0)
Previous biologic treatment failure, n (%)	167 (50.9)	340 (51.5)
Abdominal pain score >0, n (%)	290 (89.2)	582 (90.0)
Presence of bowel urgency, n (%)	299 (92.0)	598 (92.4)
Stool frequency score >1, n (%)	313 (95.4)	619 (94.1)
Rectal bleeding score >0, n (%)	301 (91.8)	606 (92.1)
FACIT-F, mean ± SD	31.5 ± 11.8	30.1 ± 11.7

FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; PBO, placebo; SD, standard deviation; UPA, upadacitinib.
The induction population (PBO: n = 328; UPA: n = 660) includes all randomized subjects who received at least 2 dose of double-blinded study drug in the 8-week double-blinded induction period.

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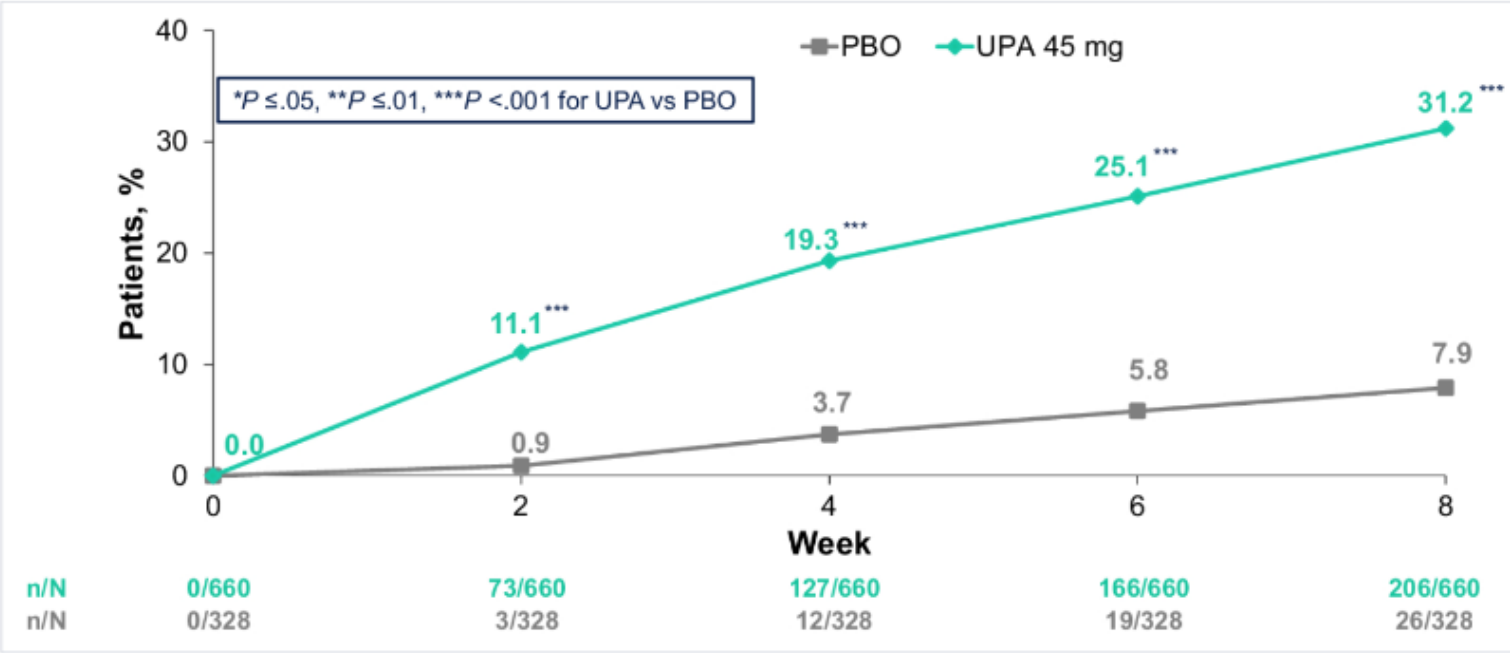
Figure 2. Patients With Complete Symptom Resolution During Induction Treatment: NRI-C



NRI-C, non-responder imputation incorporating multiple imputations to handle missing data because of COVID-19; PBO, placebo; UPA, upadacitinib.

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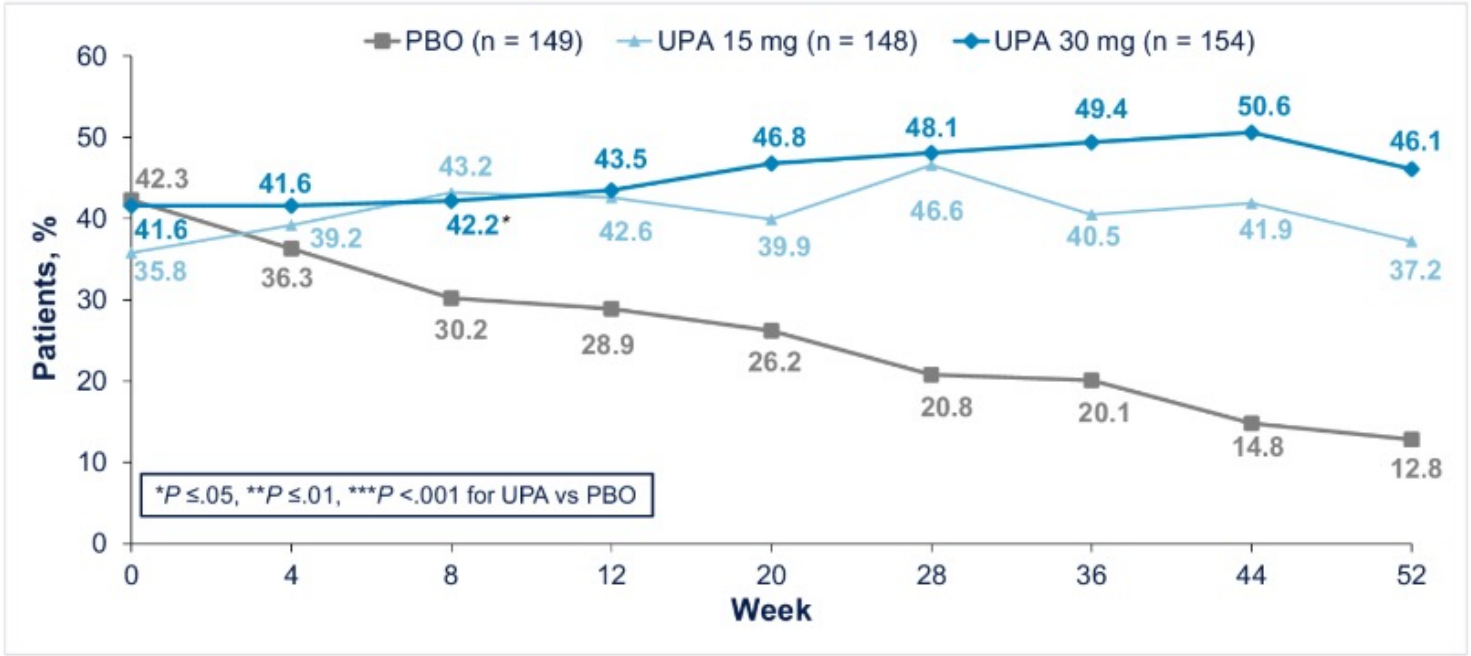
Figure 3. Patients With Complete Symptom Resolution During Maintenance Treatment Among UPA Induction Responders: NRI-C



NRI-C, non-responder imputation incorporating multiple imputations to handle missing data because of COVID-19; PBO, placebo; UPA, upadacitinib.

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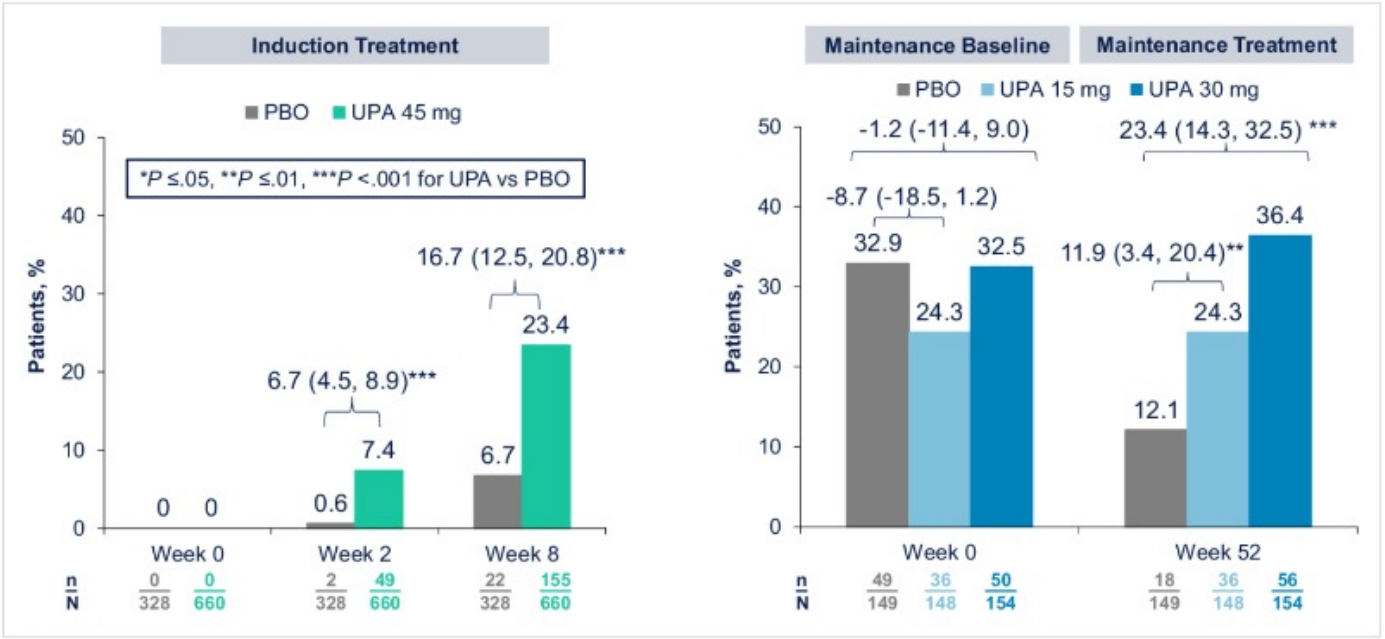
Figure 4. Patients Who Achieved Complete Symptom Resolution and FACIT-F Normalization During Induction and Maintenance: NRI-C



FACIT-F, Functional Assessment of Chronic Illness Therapy–Fatigue; NRI-C, non-responder imputation incorporating multiple imputations to handle missing data because of COVID-19; PBO, placebo; UPA, upadacitinib.
95% confidence intervals are shown in parentheses. Maintenance outcomes were based on UPA induction responders.

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Conclusion

- Patients with moderately to severely active UC were more likely to achieve symptom resolution and normalization of fatigue during induction treatment with UPA compared to PBO, and these benefits were sustained during maintenance therapy.

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Effects of Ozanimod on Histologic Remission and Mucosal Healing Over 3 Years of Continuous Treatment in Patients With Ulcerative Colitis

Maria Abreu

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Background

- Ozanimod is approved in the United States, European Union, and other countries for the treatment of moderately to severely active ulcerative colitis in adults (UC). The phase 3, randomized True North (TN) study demonstrated the efficacy and safety of ozanimod for up to 52 weeks in patients with moderately to severely active UC. The ongoing TN open-label extension (OLE) aims to assess the long-term efficacy and safety of ozanimod. This interim analysis of the TN OLE evaluated the efficacy of ozanimod on histologic remission (HR) and mucosal healing (MH) in patients who received approximately 3 years of continuous ozanimod treatment.

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Results

- Of the 131 total patients included in this analysis, 87% completed OLE Week 46 (98 weeks of continuous ozanimod) and 72% completed OLE Week 94 (146 weeks of continuous ozanimod).

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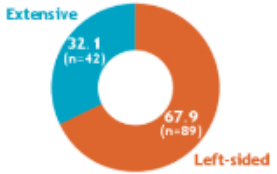
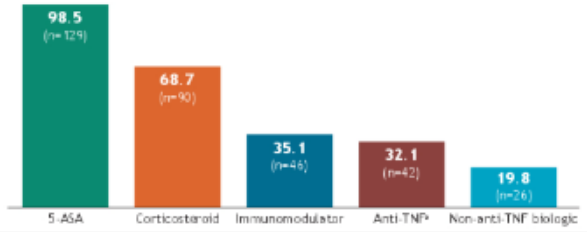
Baseline demographic and clinical characteristics in Week 52 clinical responders at OLE entry

Patient characteristics	Week 52 clinical responders at OLE entry (N=131)
Age, y, mean (SD)	44.3 (13.6)
Female, n (%)	68 (51.9)
BMI, kg/m², mean (SD)	25.9 (5.8)
Age at UC diagnosis, y, mean (SD)	36.1 (13.4)
Years since UC diagnosis, mean (SD)	8.5 (7.3)
Extent of UC disease, % (n)	
Corticosteroid use at screening for parent study[a] (True North), n (%)	31 (23.7)
Prior therapies, % (n)	

[a]Based on data from case report forms.
ASA, aminosalicylic acid; BMI, body mass index; OLE, open-label extension; TNF, tumor necrosis factor; UC, ulcerative colitis.

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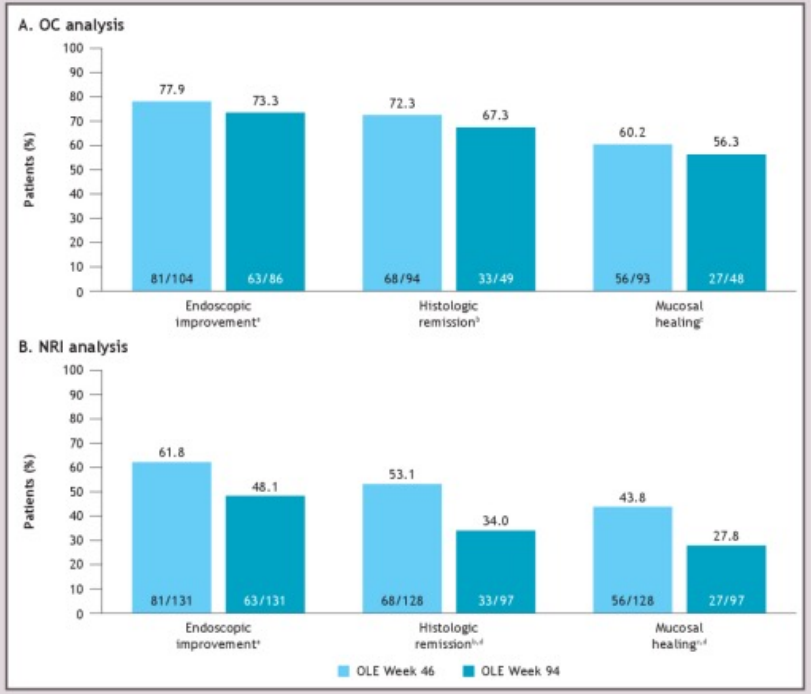
Most True North Week 52 clinical responders at OLE entry achieved endoscopic and histologic endpoints at OLE Weeks 46 and 94 (98 and 146 weeks of continuous treatment, respectively): (A) OC and (B) NRI analyses



Note: Denominators for the OC analyses were based on the numbers of patients who completed OLE Week 46 or OLE Week 94 and had data available for the endpoints in question. Denominators for the NRI analyses were based on the numbers of patients who completed OLE Week 46, completed OLE Week 94, or discontinued ozanimod treatment.

[a]Endoscopic improvement is defined as an endoscopy subscore of ≤1 point. [b]Histologic remission is defined as Geboes index score <2. [c]Mucosal healing is defined as an endoscopy subscore of ≤1 point and a Geboes index score <2. [d]3 patients at OLE Week 46 and 34 patients at OLE Week 94 did not have histology data available at the time of data cutoff and are therefore not included in the denominator for histologic remission and mucosal healing.

NRI, nonresponder imputation; OC, observed case; OLE, open-label extension.

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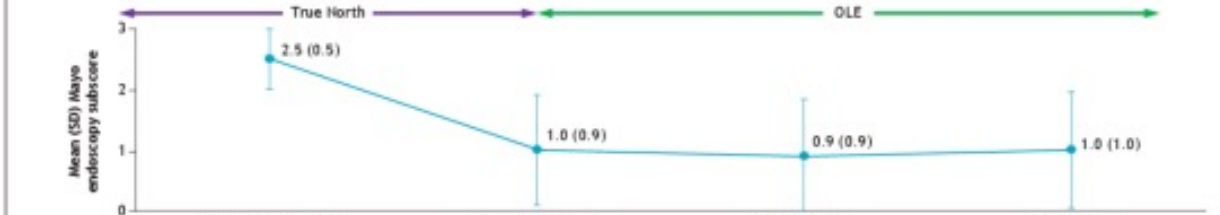
Ozanimod was associated with a reduction in mean Mayo endoscopy subscore to 1.0 at True North Week 52

- This was sustained through OLE Week 94 in True North Week 52 clinical responders at OLE entry



Mayo endoscopy subscore, n (%)	True North baseline (Week 0) (n=131)	True North Week 52 (OLE entry) (n=131)	OLE Week 46 (98 weeks of continuous ozanimod) (n=104)	OLE Week 94 (146 weeks of continuous ozanimod) (n=86)
0	0	50 (38.2)	45 (34.4)	32 (24.4)
1	0	43 (32.8)	36 (27.5)	31 (23.7)
2	64 (48.9)	31 (23.7)	15 (11.5)	15 (11.5)
3	67 (51.1)	7 (5.3)	8 (6.1)	8 (6.1)

OLE, open-label extension.

Conclusions

- Patients' mucosal healing was evaluated annually in the True North OLE
- In this interim analysis of the True North OLE, a large proportion of clinical responders after 1 year of ozanimod treatment achieved and maintained endoscopic improvement, histologic remission, and mucosal healing through 2 additional years of continuous ozanimod treatment
- Long-term ozanimod use is associated with sustained endoscopic and histologic benefits in patients with moderate to severe UC

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Conclusion

- In this interim analysis of the TN OLE, a large proportion of clinical responders after 1 year of ozanimod who remained on ozanimod for up to 2 years thereafter, achieved EI, HR, and MH after 2 and 3 years of continuous treatment. Long-term ozanimod use may be associated with sustained endoscopic and histologic benefits in patients with UC.

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