CLINICAL UPDATE

Brand Name	Rinvoq®
Generic Name	upadacitinib
Drug Manufacturer	AbbVie Inc

Clinical Update

TYPE OF CLINICAL UPDATE

New Strength

FDA APPROVAL DATE

March 16, 2022

LAUNCH DATE

March 3, 2022

REVIEW DESIGNATION

Priority

TYPE OF REVIEW

Type 1 - New Molecular Entity; New Drug Application (NDA): 211675

DISPENSING RESTRICTIONS

N/A

Overview

INDICATION(S) FOR USE

Rinvoq® is a Janus kinase (JAK) inhibitor indicated for the treatment of

- Adults with moderately to severely active rheumatoid arthritis who have had an inadequate response or intolerance to one or more TNF blockers.
- Adults with active psoriatic arthritis who have had an inadequate response or intolerance to one or more TNF blockers.

  Limitations of Use

  Pyrexia, increased weight, herpes zoster, influenza, fatigue, neutropenia, myalgia, and influenza like illness.

Ulcerative colitis: Adverse reactions (≥ 5%) reported during induction or maintenance are: upper respiratory tract infections, increased blood creatine phosphokinase, acne, neutropenia, elevated liver enzymes, and rash.
Use of Rinvoq® in combination with other JAK inhibitors, biologic DMARDs, or with potent immunosuppressants such as azathioprine and cyclosporine is not recommended.

- Adults and pediatric patients 12 years of age and older with refractory, moderate to severe atopic dermatitis whose disease is not adequately controlled with other systemic drug products, including biologics, or when use of those therapies is inadvisable.

  Limitations of Use

  Rinvoq® is not recommended for use in combination with other JAK inhibitors, biologic immunomodulators, or with other immunosuppressants.

- Adults with moderately to severely active ulcerative colitis who have had an inadequate response or intolerance to one or more TNF blockers.

  Limitations of Use

  Rinvoq®is not recommended for use in combination with other JAK inhibitors, biological therapies for ulcerative colitis, or with other potent immunosuppressants such as azathioprine and cyclosporine.

MECHANISMS OF ACTION

Upadacitinib is a Janus kinase (JAK) inhibitor. JAKs are intracellular enzymes which transmit signals arising from cytokine or growth factor-receptor interactions on the cellular membrane to influence cellular processes of hematopoiesis and immune cell function. Within the signaling pathway, JAKs phosphorylate and activate signal transducers and activators of transcription (STATs) which modulate intracellular activity including gene expression. Upadacitinib modulates the signaling pathway at the point of JAKs, preventing the phosphorylation and activation of STATs. JAK enzymes transmit cytokine signaling through their pairing (e.g., JAK1/JAK2, JAK1/JAK3, JAK1/TYK2, JAK2/JAK2, JAK2/TYK2). In a cell-free isolated enzyme assay, upadacitinib had greater inhibitory potency at JAK1 and JAK2 relative to JAK3 and TYK2. In human leukocyte cellular assays, upadacitinib inhibited cytokine-induced STAT phosphorylation mediated by JAK1 and JAK1/JAK3 more potently than JAK2/JAK2 mediated STAT phosphorylation. The relevance of inhibition of specific JAK enzymes to therapeutic effectiveness is not currently known.

DOSAGE FORM(S) AND STRENGTH(S)

Extended-release tablets: 15 mg, 30 mg, and 45 mg

DOSE & ADMINISTRATION

- Prior to treatment update immunizations and consider evaluating for active and latent tuberculosis, viral hepatitis, hepatic function, and pregnancy status.
- Avoid initiation or interrupt Rinvoq® if absolute lymphocyte count is less than 500 cells/mm3 absolute neutrophil count is less than 1000 cells/mm3, or haemoglobin level is less than 8 g/dL.

Rheumatoid Arthritis and Psoriatic Arthritis:

The recommended dosage is 15 mg once daily.

Atopic Dermatitis

- Pediatric Patients 12 Years of Age and Older Weighing at Least 40 kg and Adults Less Than 65 Years of Age: Initiate treatment with 15 mg orally once daily. If an adequate response is not achieved, consider increasing the dosage to 30 mg orally once daily.
- Adults 65 Years of Age and Older: Recommended dosage is 15 mg once daily.
- Severe Renal Impairment: Recommended dosage is 15 mg once daily.

Ulcerative Colitis

- Adults: The recommended induction dosage is 45 mg once daily for 8 weeks. The recommended maintenance dosage is 15 mg once daily. A maintenance dosage of 30 mg once daily may be considered for patients with refractory, severe, or extensive disease.
- Discontinue Rinvoq® if adequate therapeutic response is not achieved with the 30 mg dosage. Use the lowest effective dosage needed to maintain response.

EFFICACY

Rheumatoid Arthritis

CLINICAL UPDATE

The efficacy and safety of Rinvoq® 15 mg once daily were assessed in five Phase 3 randomized, double-blind, multicentre trials in patients with moderately to severely active rheumatoid arthritis and fulfilling the ACR/EULAR 2010 classification criteria. Patients 18 years of age and older were eligible to participate. The presence of at least 6 tender and 6 swollen joints and evidence of systemic inflammation based on elevation of hsCRP was required at baseline. Although other doses have been studied, the recommended dosage of Rinvoq® is 15 mg once daily.

Trial RA-I (NCT02706873) was a 24-week monotherapy trial in 947 patients with moderately to severely active rheumatoid arthritis who were naïve to methotrexate (MTX). Patients received Rinvoq®15 mg or upadacitinib 30 mg orally once daily or MTX as monotherapy. At Week 26, non-responding patients on upadacitinib could be rescued with the addition of MTX, while patients on MTX could be rescued with the addition of blinded Rinvoq® 15 mg or upadacitinib 30 mg once daily. The primary endpoint was the proportion of patients who achieved an ACR50 response at Week 12. Key secondary endpoints included disease activity score (DAS28-CRP) ≤3.2 at Week 12, DAS28-CRP.

Trial RA-II (NCT02706951) was a 14-week monotherapy trial in 648 patients with moderately to severely active rheumatoid arthritis who had an inadequate response to MTX. Patients received Rinvoq®15 mg or upadacitinib 30 mg once daily monotherapy or continued their stable dose of MTX monotherapy. At Week 14, patients who were randomized to MTX were advanced to Rinvoq® 15 mg or upadacitinib 30 mg once daily monotherapy in a blinded manner based on pre-determined assignment at baseline. The primary endpoint was the proportion of patients who achieved an ACR20 response at Week 14. Key secondary endpoints included DAS28-CRP ≤3.2, DAS28-CRP.

Trial RA-III (NCT02675426) was a 12-week trial in 661 patients with moderately to severely active rheumatoid arthritis who had an inadequate response to conventional disease modifying anti-rheumatic drugs (cDMARDs). Patients received Rinvoq® 15 mg or upadacitinib 30 mg once daily or placebo added to background cDMARD therapy. At Week 12, patients who were randomized to placebo were advanced to Rinvoq® 15 mg or upadacitinib 30 mg once daily in a blinded manner based on pre-determined assignment at baseline. The primary endpoint was the proportion of patients who achieved an ACR20 response at Week 12. Key secondary endpoints included DAS28-CRP ≤3.2, DAS28-CRP.

Trial RA-IV (NCT02629159) was a 48-week trial in 1629 patients with moderately to severely active rheumatoid arthritis who had an inadequate response to MTX. Patients received Rinvoq® 15 mg once daily, active comparator, or placebo added to background MTX. From Week 14, non-responding patients on Rinvoq® 15 mg could be rescued to active comparator in a blinded manner, and non-responding patients on active comparator or placebo could be rescued to Rinvoq® 15 mg in a blinded manner. At Week 26, all patients randomized to placebo were switched to Rinvoq® 15 mg once daily in a blinded manner. The primary endpoint was the proportion of patients who achieved an ACR20 response at Week 12 versus placebo. Key secondary endpoints versus placebo included DAS28-CRP ≤3.2, DAS28-CRP.

Trial RA-V (NCT02706847) was a 12-week trial in 499 patients with moderately to severely active rheumatoid arthritis who had an inadequate response or intolerance to biologic DMARDs. Patients received Rinvoq®15 mg or upadacitinib 30 mg once daily or placebo added to background cDMARD therapy. At Week 12, patients who were randomized to placebo were advanced to Rinvoq® 15 mg or upadacitinib 30 mg once daily in a blinded manner based on pre-determined assignment at baseline. The primary endpoint was the proportion of patients who achieved an ACR20 response at Week 12. Key secondary endpoints included DAS28-CRP ≤3.2 and change from baseline in HAQ-DI at Week 12.

Clinical Response The percentages of Rinvoq® -treated patients achieving ACR20, ACR50, and ACR70 responses, and DAS28(CRP) < 2.6 in all trials are shown in Table 1.

Patients treated with Rinvoq® 15 mg, alone or in combination with cDMARDs, achieved higher ACR response rates compared to MTX monotherapy or placebo, respectively, at the primary efficacy timepoint (Table 8). In Trial IV, the percent of patients achieving ACR20 response by visit is shown in Figure 1. In Trials RA-III and RA-V, higher

ACR20 response rates were observed at 1 week with Rinvoq® 15 mg versus placebo. Treatment with Rinvoq® 15 mg, alone or in combination with cDMARDs, resulted in greater improvements in the ACR components compared to MTX or placebo at the primary efficacy timepoint. (Table 2)

Table 1: Clinical Response in RA Patients in Trials RA-I, RA-II, RA-III, RA-IV and RA V

	Trial RA-I MTX-Naïve		Trial RA-II MTX-IR		Trial RA-III cDMARD-IR		Trial RA-IV MTX-IR		Trial RA-V bDMARD-IR	
	Monotherapy		Monotherapy		Background cDMARDs		Background MTX		Background cDMARDs	
	MTX	RINVOQ 15 mg % Δ (95% CI)	MTX	RINVOQ 15 mg % Δ (95% CI)	PBO	RINVOQ 15 mg % Δ (95% CI)	PBO	RINVOQ 15 mg % Δ (95% CI)	PBO	RINVOQ 15 mg % Δ (95% CI)
N	314	317	216	217	221	221	651	651	169	164
Week										
ACR20										
12[a]/14[b]	54	76 22 (14, 29)	41	68 26 (17, 36)	36	64 28 (19, 37)	36	71 34 (29, 39)	28	65 36 (26, 46)
24[c]/26[d]	59	79 20 (13, 27)					36	67 32 (27, 37)		
ACR50										
12[a]/14[b]	28	52 24 (16, 31)	15	42 27 (18, 35)	15	38 23 (15, 31)	15	45 30 (26, 35)	12	34 22 (14, 31)
24[c]/26[d]	33	60 27 (19, 34)					21	54 33 (28, 38)		
ACR70										
12[a]/14[b]	14	32 18 (12, 25)	3	23 20 (14, 26)	6	21 15 (9, 21)	5	25 20 (16, 24)	7	12 5 (-1, 11)
24[c]/26[d]	18	44 26 (19, 33)					10	35 25 (21, 29)		
DAS28-CRP <2.6										
12[a]/14[b]	14	36 22 (15, 28)	8	28 20 (13, 27)	10	31 21 (14, 28)	6	29 23 (19, 27)	9	29 19 (11, 27)
24[c]/26[d]	18	48 30 (23, 37)					9	41 32 (27, 36)		

Abbreviations: ACR20 (or 50 or 70) = American College of Rheumatology ≥20% (or ≥50% or ≥70%) improvement; bDMARD = biologic disease-modifying anti-rheumatic drug; CRP = c-reactive protein; DAS28 = Disease Activity Score 28 joints; cDMARDs = conventional disease-modifying anti-rheumatic drugs; MTX = methotrexate; PBO = placebo; IR = inadequate responder

Patients who discontinued randomized treatment, or had cross-over between randomized treatments, or were missing data at week of evaluation were imputed as non-responders in the analyses.

[a] Trial RA-I, Trial RA-III, Trial RA-IV, Trial RA-V

[b] Trial RA-II

[c] Trial RA-I

[d] Trial RA-IV

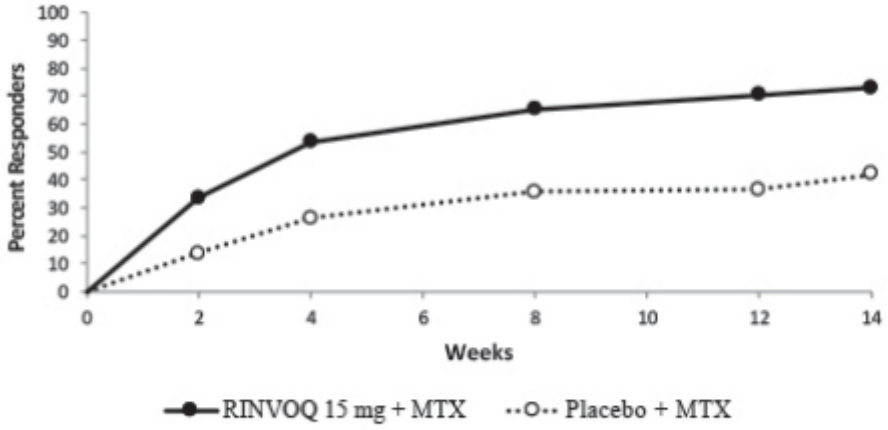
Table 2: Components of ACR Response at Primary Efficacy Timepoint[a]

	Trial RA-I MTX-Naïve		Trial RA-II[b] MTX-IR		Trial RA-III cDMARD-IR		Trial RA-IV MTX-IR		Trial RA-V bDMARD-IR	
	Monotherapy		Monotherapy		Background cDMARDs		Background MTX		Background cDMARDs	
	MTX	RINVOQ 15 mg	MTX	RINVOQ 15 mg	PBO	RINVOQ 15 mg	PBO	RINVOQ 15 mg	PBO	RINVOQ 15 mg
N	314	317	216	217	221	221	651	651	169	164
Number of tender joints (0-68)										
Baseline	26 (16)	25 (14)	25 (16)	24 (15)	25 (15)	25 (14)	26 (14)	26 (15)	28 (15)	28 (16)
Week 12/14	13 (15)	9 (12)	15 (16)	10 (13)	16 (17)	12 (14)	16 (15)	10 (13)	18 (17)	11 (14)
Number of swollen joints (0-66)										
Baseline	17 (11)	17 (10)	17 (12)	16 (11)	15 (9)	16 (10)	16 (9)	17 (10)	16 (10)	17 (11)
Week 12/14	6 (8)	5 (7)	9 (11)	6 (9)	9 (10)	7 (10)	9 (9)	5 (7)	9 (10)	6 (8)
Pain[c]										
Baseline	66 (21)	68 (21)	63 (21)	62 (23)	62 (21)	64 (19)	65 (21)	66 (21)	69 (21)	68 (20)
Week 12/14	41 (25)	31 (25)	49 (25)	36 (27)	51 (26)	33 (24)	49 (25)	33 (24)	55 (28)	41 (28)
Patient global assessment[c]										
Baseline	66 (21)	67 (22)	60 (22)	62 (22)	60 (20)	63 (22)	64 (21)	64 (22)	66 (23)	67 (20)
Week 12/14	42 (25)	31 (24)	48 (26)	37 (27)	50 (26)	32 (24)	48 (24)	33 (24)	54 (28)	40 (26)
Disability Index (HAQ-DI)[d]										
Baseline	1.60 (0.67)	1.60 (0.67)	1.47 (0.66)	1.47 (0.66)	1.42 (0.63)	1.48 (0.61)	1.61 (0.61)	1.63 (0.64)	1.56 (0.60)	1.67 (0.64)
Week 12/14	1.08 (0.72)	0.76 (0.69)	1.19 (0.69)	0.86 (0.67)	1.13 (0.70)	0.85 (0.66)	1.28 (0.67)	0.98 (0.68)	1.33 (0.66)	1.24 (0.77)
Physician global assessment[c]										
Baseline	69 (16)	67 (17)	62 (17)	66 (18)	64 (18)	64 (16)	66 (18)	66 (17)	67 (17)	69 (17)
Week 12/14	32 (22)	22 (19)	37 (24)	26 (21)	41 (24)	26 (21)	41 (25)	27 (21)	39 (25)	29 (22)
CRP (mg/L)										
Baseline	21.2 (22.1)	23.0 (27.4)	14.5 (17.3)	14.0 (16.5)	12.6 (14.0)	16.6 (19.2)	18.0 (21.5)	17.9 (22.5)	16.3 (21.1)	16.3 (18.6)
Week 12/14	10.9 (14.9)	4.2 (8.8)	12.8 (21.4)	3.7 (7.8)	13.1 (15.5)	4.6 (9.6)	16.2 (19.8)	5.5 (10.9)	13.9 (17.3)	5.0 (14.0)

Abbreviations: ACR = American College of Rheumatology; bDMARD = biologic disease-modifying anti-rheumatic drug; CRP = c-reactive protein; cDMARDs = conventional disease-modifying anti-rheumatic drugs; HAQ-DI = Health Assessment Questionnaire Disability Index; IR = inadequate responder; MTX = methotrexate; PBO = placebo

[a] Data shown are mean (standard deviation).
[b] Primary efficacy timepoint is at Week 14.
[c] Visual analog scale: 0 = best, 100 = worst.
[d] Health Assessment Questionnaire-Disability Index: 0=best, 3=worst; 20 questions; 8 categories: dressing and grooming, arising, eating, walking, hygiene, reach, grip, and activities.

Figure 1. Percent of Patients Achieving ACR20 in Trial RA-IV



Abbreviations: ACR20 = American College of Rheumatology ≥20% improvement; MTX = methotrexate
Patients who discontinued randomized treatment, or were missing ACR20 results, or were lost-to-follow-up or withdrawn from the trial were imputed as non-responders.

In RA-I and RA-IV, a higher proportion of patients treated with Rinvoq® 15 mg alone or in combination with MTX, achieved DAS28-CRP < 2.6 compared to MTX or placebo at the primary efficacy timepoint (Table 3).

Table 3: Proportion of Patients with DAS28-CRP Less Than 2.6 with Number of Residual Active Joints at Primary Efficacy Timepoint

	Trial RA-I MTX-Naive	
	Monotherapy	
DAS28-CRP Less Than 2.6	**MTX** N = 314	**RINVOQ 15 mg** N = 317
Proportion of responders at Week 12 (n)	14% (43)	36% (113)
Of responders, proportion with 0 active joints (n)	51% (22)	45% (51)
Of responders, proportion with 1 active joint (n)	35% (15)	23% (26)
Of responders, proportion with 2 active joints (n)	9% (4)	17% (19)
Of responders, proportion with 3 or more active joints (n)	5% (2)	15% (17)
	Trial RA-IV MTX-IR	
	Background MTX	
DAS28-CRP Less Than 2.6	**PBO** N = 651	**RINVOQ 15 mg** N = 651
Proportion of responders at Week 12 (n)	6% (40)	29% (187)
Of responders, proportion with 0 active joints (n)	60% (24)	48% (89)
Of responders, proportion with 1 active joint (n)	20% (8)	23% (43)
Of responders, proportion with 2 active joints (n)	15% (6)	13% (25)
Of responders, proportion with 3 or more active joints (n)	5% (2)	16% (30)
Abbreviations: CRP = c-reactive protein; DAS28 = Disease Activity Score 28 joints; MTX = methotrexate; PBO = placebo; IR = inadequate responder		

Radiographic response

Inhibition of progression of structural joint damage was assessed using the modified Total Sharp Score (mTSS) and its components, the erosion score and joint space narrowing score, at Week 26 in Trial RA-IV and Week 24 in Trial RA-I. The proportion of patients with no radiographic progression (mTSS change from baseline ≤ 0) was also assessed. In Trial RA-IV, treatment with Rinvoq® 15 mg inhibited the progression of structural joint damage compared to placebo in combination with cDMARDs at Week 26 (Table 4). Analyses of erosion and joint space narrowing scores were consistent with overall results. In the placebo plus MTX group, 76% of the patients

experienced no radiographic progression at Week 26 compared to 83% of the patients treated with Rinvoq® 15 mg. In Trial RA-I, treatment with Rinvoq®15 mg monotherapy inhibited the progression of structural joint damage compared to MTX monotherapy at Week 24 (Table 4). Analyses of erosion and joint space narrowing scores were consistent with overall results. Reference ID: 4953928 In the MTX monotherapy group, 78% of the patients experienced no radiographic progression at Week 24 compared to 87% of the patients treated with Rinvoq® 15 mg monotherapy.

Table 4: Radiographic Changes

	Trial RA-IV MTX-IR		
	Background MTX		
mTSS	PBO (N=651) Mean (SD)	RINVOQ 15 mg (N=651) Mean (SD)	Estimated Difference vs PBO at Week 26 (95% CI)[a]
Baseline	35.9 (52)	34.0 (50)	
Week 26[b]	0.78 (0.1)	0.15 (0.1)	-0.63 (-0.92, -0.34)
	Trial RA-I MTX-naïve		
	Monotherapy		
	MTX (N=309) Mean (SD)	RINVOQ 15 mg (N=309) Mean (SD)	Estimated Difference vs MTX at Week 24 (95% CI)[c]
Baseline	13.3 (31)	18.1 (38)	
Week 24[d]	0.67 (2.8)	0.14 (1.4)	-0.53 (-0.85, -0.20)

Abbreviations: mTSS = modified Total Sharp Score, MTX = methotrexate; PBO = placebo; SD = standard deviation; IR = inadequate responders; bDMARDs = biologic disease modifying anti-rheumatic drugs; LS = least squares; CI = confidence intervals

[a] LS means and 95% CI based on a random coefficient model fit to the mTSS value adjusting for time, treatment group, prior bDMARDs use, treatment group-by-time interaction, with random slopes and random intercept.

[b] Estimated linear rate of structural progression by Week 26 and standard errors are presented.

[c] LS means and 95% CI based on a linear regression model fit to change from baseline in mTSS adjusting for treatment group, baseline mTSS, and geographic region.

[d] Mean change from baseline and standard deviation are presented.

Physical Function Response Treatment with Rinvoq®15 mg, alone or in combination with cDMARDs, resulted in a greater improvement in physical function at Week 12/14 compared to all comparators as measured by HAQ-DI. Other Health-Related Outcomes In all trials except for Trial RA-V, patients receiving Rinvoq®15 mg had greater improvement from baseline in physical component summary (PCS) score, mental component summary (MCS) scores, and in all 8 domains of the Short Form Health Survey (SF-36) compared to placebo in combination with cDMARDs or MTX monotherapy at Week 12/14. Fatigue was assessed by the Functional Assessment of Chronic Illness Therapy-Fatigue score (FACIT-F) in Trials RA-I, RA-III, and RA-IV. Improvement in fatigue at Week 12 was observed in patients treated with Rinvoq® 15 mg compared to patients on placebo in combination with cDMARDs or MTX monotherapy.

Psoriatic Arthritis

The efficacy and safety of Rinvoq® 15 mg once daily were assessed in two Phase 3 randomized, double-blind, multicenter, placebo-controlled studies in patients 18 years of age or older with moderately to severely active psoriatic arthritis. All patients had active psoriatic arthritis for at least 6 months based upon the Classification Criteria for Psoriatic Arthritis (CASPAR), at least 3 tender joints and at least 3 swollen joints, and active plaque psoriasis or history of plaque psoriasis. Although another dose has been studied, the recommended dose of Rinvoq® is 15 mg once daily for psoriatic arthritis. Study PsA-I (NCT03104400) was a 24-week trial in 1705 patients with moderately to severely active psoriatic arthritis who had an inadequate response or intolerance to at least one nonbiologic DMARD. Patients received Rinvoq® 15 mg or upadacitinib 30 mg once daily, adalimumab, or placebo, alone or in combination with background non-biologic DMARDs. At Week 24, all patients randomized to placebo were switched to Rinvoq® 15 mg or upadacitinib 30 mg once daily in a blinded manner. The primary endpoint was the proportion of patients who achieved an ACR20 response at Week 12.

Study PsA-II (NCT03104374) was a 24-week trial in 642 patients with moderately to severely active psoriatic arthritis who had an inadequate response or intolerance to at least one biologic DMARD. Patients received Rinvoq® 15 mg or upadacitinib 30 mg once daily or placebo, alone or in combination with background non-biologic DMARDs. At Week 24, all patients randomized to placebo were switched to Rinvoq® 15 mg or upadacitinib 30 mg once daily in a blinded manner. The primary endpoint was the proportion of patients who achieved an ACR20 response at Week 12.

Clinical Response

In both studies, patients treated with Rinvoq® 15 mg achieved significantly higher ACR20 responses compared to placebo at Week 12 (Table 5, Figure 2). A higher proportion of patients treated with Rinvoq® 15 mg achieved ACR50 and ACR70 responses at Week 12 compared to placebo. Treatment with Rinvoq® 15 mg resulted in improvements in the ACR components compared to placebo at the primary efficacy timepoint. (Table 6)

Table 5: Clinical Response

Study	**Study PsA-I non-biologic DMARD-IR**		**Study PsA-II bDMARD-IR**	
Treatment Group	PBO % 	RINVOQ 15 mg % Δ (95% CI)	PBO % 	RINVOQ 15 mg % Δ (95% CI)
N	423	429	212	211
ACR20				
Week 12	36	71 35 (28, 41)	24	57 33 (24, 42)
ACR50				
Week 12	13	38 24 (19, 30)	5	32 27 (20, 34)
ACR70				
Week 12	2	16 13 (10, 17)	1	9 8 (4, 12)

Abbreviations: ACR20 (or 50 or 70) = American College of Rheumatology ≥20% (or ≥50% or ≥70%) improvement, bDMARD = biologic disease-modifying anti-rheumatic drug; IR = inadequate responder; PBO = placebo
Patients who discontinued randomized treatment or were missing data at week of evaluation were imputed as non-responders in the analyses.

Table 6: Components of ACR Response[a]

Study	Study PsA-I non-biologic DMARD-IR		Study PsA-II bDMARD-IR	
Treatment Group	PBO (N=423)	RINVOQ 15 mg (N=429)	PBO (N=212)	RINVOQ 15 mg (N=211)
Number of tender/painful joints (0-68)				
Baseline	20.0 (14.3)	20.4 (14.7)	25.3 (17.6)	24.9 (17.3)
Week 12	12.5 (13.3)	8.8 (12.5)	19.3 (18.5)	12.6 (15.6)
Number of swollen joints (0-66)				
Baseline	11.0 (8.2)	11.6 (9.3)	12.0 (8.9)	11.3 (8.2)
Week 12	5.6 (7.2)	3.5 (6.0)	7.3 (9.4)	4.4 (5.7)
Patient assessment of pain[b]				
Baseline	6.1 (2.1)	6.2 (2.1)	6.6 (2.1)	6.4 (2.1)
Week 12	5.1 (2.3)	3.8 (2.4)	5.9 (2.3)	4.4 (2.5)
Patient global assessment[b]				
Baseline	6.3 (2.0)	6.6 (2.0)	6.8 (2.0)	6.8 (1.9)
Week 12	5.2 (2.2)	3.8 (2.3)	6.1 (2.3)	4.5 (2.5)
Disability index (HAQ-DI)[c]				
Baseline	1.1 (0.6)	1.2 (0.7)	1.2 (0.7)	1.1 (0.6)
Week 12	1.0 (0.7)	0.7 (0.6)	1.1 (0.6)	0.8 (0.7)
Physician global assessment[b]				
Baseline	6.5 (1.6)	6.7 (1.6)	6.5 (1.8)	6.5 (1.8)
Week 12	4.3 (2.2)	3.1 (2.0)	5.0 (2.2)	3.4 (2.1)
hsCRP (mg/L)				
Baseline	11.5 (15.8)	11.0 (14.9)	10.4 (18.5)	11.2 (18.6)
Week 12	10.1 (15.2)	4.2 (9.9)	9.4 (13.4)	4.3 (7.9)

Abbreviations: ACR = American College of Rheumatology; hsCRP = high sensitivity c-reactive protein; HAQ-DI = Health Assessment Questionnaire-Disability Index; IR = inadequate responder; PBO = placebo

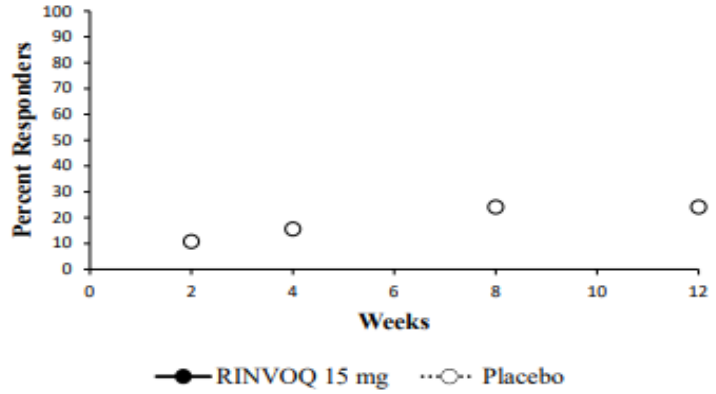
[a] Data shown are mean (standard deviation).

[b] Numeric rating scale (NRS): 0 = best, 10 = worst

[c] Health Assessment Questionnaire-Disability Index: 0=best, 3=worst; 20 questions; 8 categories: dressing and grooming, arising, eating, walking, hygiene, reach, grip, and activities.

The percentage of patients achieving ACR20 response by visit is shown in Figure 2.

Figure 2. Percent of Patients Achieving ACR20 in Study PsA-II



Abbreviations: ACR20 = American College of Rheumatology ≥20% improvement
Patients who discontinued randomized treatment, or were missing ACR20 results, or were lost-to-follow-up or withdrawn from the study were imputed as non-responders.

Treatment with Rinvoq® 15 mg resulted in improvement in dactylitis and enthesitis in patients with pre-existing dactylitis or enthesitis. Treatment with Rinvoq® 15 mg resulted in improvement in skin manifestations in patients with PsA. However, Rinvoq® has not been studied in and is not indicated for the treatment of plaque psoriasis.

Physical Function Response

In both studies, patients treated with Rinvoq® 15 mg showed significant improvement in physical function from baseline compared to placebo as assessed by HAQ-DI at Week 12 (Table 12). The mean difference (95% CI) from placebo in HAQ-DI change from baseline at Week 12 was -0.28 (-0.35, -0.22) in Study PsA-I and -0.21 (-0.30, -0.12) in Study PsA-II. The proportion of HAQ-DI responders (≥ 0.35 improvement from baseline in HAQ-DI score) at Week 12 in Study PsA-I and Study PsA-II was 58% and 45%, respectively, in patients receiving Rinvoq® 15 mg and 33% and 27%, respectively, in patients receiving placebo.

Radiographic Response

In Study PsA-I, inhibition of progression of structural damage was assessed radiographically and expressed as the change from baseline in modified Total Sharp Score (mTSS) and its components, the erosion score and the joint space narrowing score, at Week 24. Treatment with Rinvoq® 15 mg inhibited progression of structural joint damage compared to placebo at Week 24 (Table 7). Analyses of erosion and joint space narrowing scores were consistent with overall results. The proportion of patients with no radiographic progression (mTSS change ≤ 0) at Week 24 was 93% in patients receiving Rinvoq® 15 mg and 89% in patients receiving placebo.

Table 7: Radiographic Changes in Study PsA-I

	PBO (N=392) Mean (SD)	RINVOQ 15 mg (N=407) Mean (SD)	Estimated Difference vs PBO at Week 24 (95% CI)[a]
mTSS			
Baseline	13.32 (31.2)	13.14 (42.4)	
Week 24[b]	0.23 (0.07)	-0.02 (0.04)	-0.25 (-0.41, -0.09)

Abbreviations: CI = confidence intervals; LS = least squares; mTSS = modified Total Sharp Score; PBO = placebo; SD = standard deviation
[a] LS means and 95% CI based on a random coefficient model fit to the mTSS value adjusting for time, treatment group, current DMARD use (yes/no), treatment group-by-time interaction, with random slopes and random intercept.
[b] Estimated linear rate of structural progression by Week 24 and standard errors are presented.

Other Health-Related

Outcomes Health-related quality of life was assessed by SF-36. In both studies, patients receiving Rinvoq® 15 mg experienced significantly greater improvement from baseline in the Physical Component Summary score compared to placebo at Week 12. Greater improvement was also observed in the Mental Component Summary score and all 8 domains of SF-36 compared to placebo.

Patients receiving Rinvoq® 15 mg showed greater improvement from baseline in fatigue, as measured by FACIT-F score, at Week 12 compared to placebo in both studies.

Atopic Dermatitis

The efficacy of Rinvoq® 15 mg and 30 mg once daily, was assessed in three Phase 3 randomized, double-blind, multicenter trials (AD-1, AD-2, AD-3; NCT03569293, NCT03607422, and NCT03568318, respectively) in a total of 2584 patients (12 years of age and older). Rinvoq® was evaluated in 344 pediatric patients and 2240 adult patients with moderate to severe atopic dermatitis (AD) not adequately controlled by topical medication(s).

Disease severity at baseline was defined by a validated Investigator's Global Assessment (vIGAAD) score ≥3 in the overall assessment of AD on a severity scale of 0 to 4, an Eczema Area and Severity Index (EASI) score ≥16, a minimum body surface area (BSA) involvement of ≥10%, and weekly average Worst Pruritus Numerical Rating Scale (NRS) score ≥4. Overall, 57% of the patients were male and 69% were white. The mean age at baseline was 34 years (ranged from 12 to 75 years) and 13% of the patients were 12 to less than 18 years. At baseline, 49% of patients had a vIGA-AD score of 3 (moderate AD), and 51% of patients had a vIGA-AD score of 4 (severe AD). The baseline mean EASI score was 29 and the baseline weekly average Worst Pruritus NRS score was 7. Approximately 52% of the patients had prior exposure to systemic AD treatment.

In all three trials, patients received Rinvoq® once daily oral doses of 15 mg, 30 mg, or matching placebo for 16 weeks. In Trial AD-3, patients also received Rinvoq® or placebo with concomitant topical corticosteroids (TCS) for 16 weeks.

All three trials assessed the co-primary endpoints of the proportion of patients with a vIGA-AD score of 0 (clear) or 1 (almost clear) with at least a 2-point improvement and the proportion of patients with EASI-75 (improvement of at least 75% in EASI score from baseline) at Week 16. Secondary endpoints included EASI-90 and EASI-100 at Week 16, and the proportion of patients with reduction in itch (≥4-point improvement from baseline in the Worst Pruritus NRS) at Weeks 1, 4, and 16. In Trials AD-1 and AD-2, the proportion of patients with reduction in pain (≥4-point improvement in the Atopic Dermatitis Symptom Scale [ADerm-SS] Skin Pain NRS) from baseline to Week 16 was a secondary endpoint.

Clinical Response

Monotherapy Trials (AD-1 and AD-2) The results of Rinvoq® monotherapy trials (AD-1 and AD-2) are presented in Table 8. Figure 3 presents the proportion of patients with ≥ 4-point improvement in Worst Pruritus NRS at Weeks 1, 4, and 16 for Trials AD-1 and AD-2.

Table 8: Efficacy Results of Monotherapy Trials at Week 16 in Patients with Moderate to Severe AD

	Trial AD-1			Trial AD-2		
	PBO	RINVOQ 15 mg	RINVOQ 30 mg	PBO	RINVOQ 15 mg	RINVOQ 30 mg
Number of patients randomized	281	281	285	278	276	282
vIGA-AD 0/1[a,b]	8%	48%	62%	5%	39%	52%
Difference from PBO (95% CI)		40% (33%, 46%)	54% (47%, 60%)		34% (28%, 40%)	47% (41%, 54%)
EASI-75[a]	16%	70%	80%	13%	60%	73%
Difference from PBO (95% CI)		53% (46%, 60%)	63% (57%, 70%)		47% (40%, 54%)	60% (53%, 66%)
EASI-90[a]	8%	53%	66%	5%	42%	58%
Difference from PBO (95% CI)		45% (39%, 52%)	58% (51%, 64%)		37% (31%, 43%)	53% (47%, 59%)
EASI-100[a]	2%	17%	27%	1%	14%	19%
Difference from PBO (95% CI)		15% (10%, 20%)	25% (20%, 31%)		13% (9%, 18%)	18% (13%, 23%)
Number of patients with baseline Worst Pruritus NRS score ≥ 4	272	274	280	274	270	280
≥ 4-point improvement in Worst Pruritus NRS[c]	12%	52%	60%	9%	42%	60%
Difference from PBO (95% CI)		40% (33%, 48%)	48% (41%, 55%)		33% (26%, 39%)	50% (44%, 57%)
Number of patients with baseline ADerm-SS Skin Pain NRS score ≥ 4	233	237	249	247	237	238
≥ 4-point improvement in ADerm-SS Skin Pain NRS[d]	15%	54%	63%	13%	49%	65%
Difference from PBO (95% CI)		39% (31%, 47%)	49% (41%, 56%)		36% (28%, 43%)	52% (44%, 59%)

Abbreviations: ADerm-SS = Atopic Dermatitis Symptom Scale; PBO = placebo

[a] Based on number of patients randomized

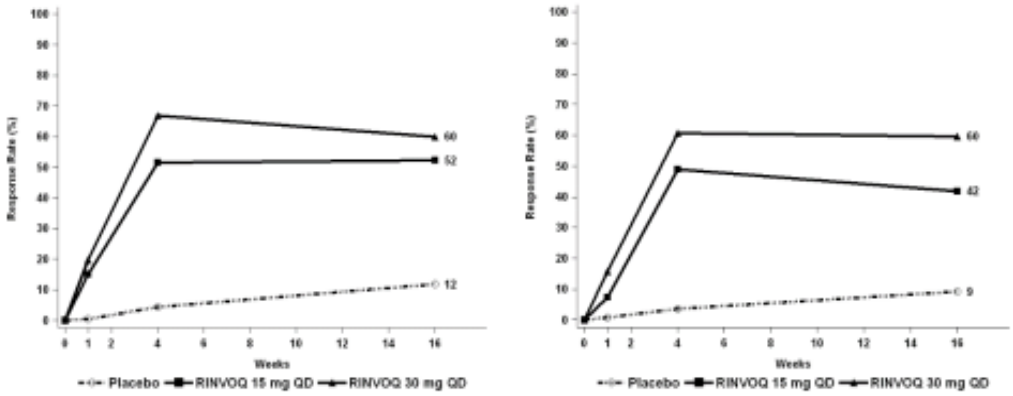
[b] Responder was defined as a patient with vIGA-AD 0 or 1 ("clear" or "almost clear") with a reduction of ≥ 2 points on a 0-4 ordinal scale

[c] Based on number of patients whose baseline Worst Pruritus NRS is ≥ 4

[d] Based on number of patients whose baseline ADerm-SS Skin Pain NRS is ≥ 4

Figure 3: Proportion of Patients with Moderate to Severe AD with ≥4-point Improvement in the Worst Pruritus NRS in Monotherapy Trials

Trial AD-1 **Trial AD-2**



Examination of age, gender, race, weight, and prior systemic treatment with immunosuppressants did not identify differences in response to RINVOQ among these subgroups in Trials AD-1 and AD-2.

Concomitant TCS Trial (AD-3)

Concomitant TCS Trial (AD-3)

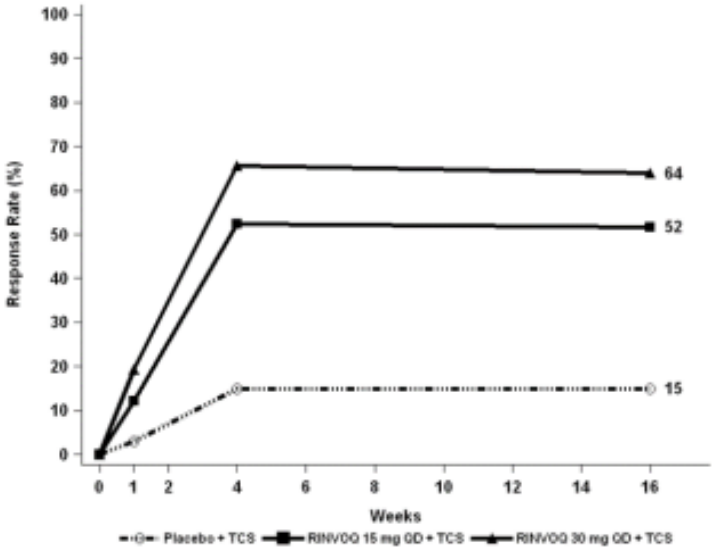
The results of the Rinvoq®with concomitant TCS trial (AD-3) are presented in Table 8. Figure 4 presents the proportion of patients with ≥ 4-point improvement in Worst Pruritus NRS at Weeks 1, 4, and 16 for Trial AD-3.

Table 9: Efficacy Results with Concomitant TCS at Week 16 in Patients with Moderate to Severe AD

	Trial AD-3		
	PBO + TCS	RINVOQ 15 mg + TCS	RINVOQ 30 mg + TCS
Number of patients randomized	304	300	297
vIGA-AD 0/1[a,b]	11%	40%	59%
Difference from PBO (95% CI)		29% (22%, 35%)	48% (41%, 54%)
EASI-75[a]	26%	65%	77%
Difference from PBO (95% CI)		38% (31%, 45%)	51% (44%, 57%)
EASI-90[a]	13%	43%	63%
Difference from PBO (95% CI)		30% (23%, 36%)	50% (43%, 56%)
EASI-100[a]	1%	12%	23%
Difference from PBO (95% CI)		11% (7%, 14%)	21% (16%, 26%)
Number of patients with baseline Worst Pruritus NRS score ≥ 4	294	288	291
≥ 4-point improvement in Worst Pruritus NRS[c]	15%	52%	64%
Difference from PBO (95% CI)		37% (30%, 44%)	49% (42%, 56%)

Abbreviations: PBO = placebo
[a] Based on number of patients randomized
[b] Responder was defined as a patient with vIGA-AD 0 or 1 ("clear" or "almost clear") with a reduction of ≥ 2 points on a 0-4 ordinal scale
[c] Based on number of patients whose baseline Worst Pruritus NRS is ≥ 4

Figure 4: Proportion of Patients with Moderate to Severe AD with ≥4-point Improvement in the Worst Pruritus NRS in Concomitant TCS Trial



Examination of age, gender, race, weight, and prior systemic treatment with immunosuppressants did not identify differences in response to RINVOQ among these subgroups in Trial AD-3.

Pediatric Patient Population The efficacy results of the Rinvoq® monotherapy trials (AD-1 and AD-2) and the Rinvoq® with concomitant TCS trial (AD-3) at Week 16 for pediatric patients 12 years of age and older are presented in Table 10 and Table 11, respectively.

Table 10: Efficacy Results of Monotherapy Trials for Pediatric Patients 12 Years of Age and Older with Moderate to Severe AD at Week 16

	Trial AD-1			Trial AD-2		
	PBO	RINVOQ 15 mg	RINVOQ 30 mg	PBO	RINVOQ 15 mg	RINVOQ 30 mg
Number of pediatric patients randomized	40	42	42	36	33	35
vIGA-AD 0/1[a,b]	8%	38%	69%	3%	42%	62%
Difference from PBO (95% CI)		31% (14%, 47%)	62% (45%, 78%)		40% (22%, 57%)	60% (42%, 77%)
EASI-75[a]	8%	71%	83%	14%	67%	74%
Difference from PBO (95% CI)		63% (47%, 79%)	75% (61%, 89%)		53% (33%, 72%)	61% (42%, 79%)
Number of pediatric patients with baseline Worst Pruritus NRS score ≥ 4	39	40	42	36	30	34
≥ 4-point improvement in Worst Pruritus NRS[c]	15%	45%	55%	3%	33%	50%
Difference from PBO (95% CI)		30% (10%, 49%)	39% (21%, 58%)		31% (13%, 48%)	47% (30%, 65%)

Abbreviations: PBO = placebo
[a] Based on number of pediatric patients randomized
[b] Responder was defined as a patient with vIGA-AD 0 or 1 ("clear" or "almost clear") with a reduction of ≥ 2 points on a 0-4 ordinal scale
[c] Based on number of pediatric patients whose baseline Worst Pruritus NRS is ≥ 4

Table 11: Efficacy Results with Concomitant TCS for Pediatric Patients 12 Years of Age and Older with Moderate to Severe AD at Week 16

	Trial AD-3		
	PBO + TCS	RINVOQ 15 mg + TCS	RINVOQ 30 mg + TCS
Number of pediatric patients randomized	40	39	37
vIGA-AD 0/1[a,b] Difference from PBO (95% CI)	8%	31% 23% (7%, 40%)	65% 57% (40%, 75%)
EASI-75[a] Difference from PBO (95% CI)	30%	56% 26% (5%, 47%)	76% 46% (26%, 65%)
Number of pediatric patients with baseline Worst Pruritus NRS score ≥ 4	38	36	33
≥ 4-point improvement in Worst Pruritus NRS[c] Difference from PBO (95% CI)	13%	42% 29% (9%, 48%)	55% 41% (21%, 61%)

Abbreviations: PBO = placebo
[a] Based on number of pediatric patients randomized
[b] Responder was defined as a patient with vIGA-AD 0 or 1 ("clear" or "almost clear") with a reduction of ≥ 2 points on a 0-4 ordinal scale
[c] Based on number of pediatric patients whose baseline Worst Pruritus NRS is ≥ 4

Ulcerative Colitis

Induction Trials (Study UC-1 and Study UC-2)

In two identical induction trials (UC-1; NCT02809635 and UC-2; NCT03653026), patients were randomized 2:1 to receive either Rinvoq® 45 mg once daily or placebo for 8 weeks. A total of 988 patients were analyzed across the two trials. These trials included adult patients with moderately to severely active ulcerative colitis who had an inadequate response, loss of response, or intolerance to oral aminosalicylates, corticosteroids, immunosuppressants, and/or biologic therapy. Enrolled patients were permitted to use stable doses of oral aminosalicylates, methotrexate, ulcerative colitis-related antibiotics, and/or oral corticosteroids (up to 30 mg/day prednisone or equivalent). At baseline, 38% of patients were receiving corticosteroids, and 68% of patients were receiving aminosalicylates. Concomitant biologic therapies, azathioprine, 6 mercaptopurine, intravenous or rectal corticosteroids were prohibited. A total of 51% of patients had previously failed treatment with or were intolerant to at least one biologic therapy. Rinvoq® is indicated for patients who have an inadequate response or intolerance to one or more TNF blockers.

Disease severity was assessed on the modified Mayo score (mMS), a 3-component Mayo score (0-9) which consists of the following subscores (0 to 3 for each subscore): stool frequency (SFS), rectal bleeding (RBS), and findings on centrally read endoscopy score (ES). An ES of 2 was defined by marked erythema, lack of vascular pattern, any friability, and/or erosions, and a score of 3 was defined by spontaneous bleeding and ulceration. Enrolled patients had a mMS between 5 to 9 with an ES of 2 or 3; at baseline the median mMS were 7, with 61% of patients having a baseline mMS of 5 to 7 and 39% having a mMS of 8 to 9.

At baseline, 39% and 37% of patients received corticosteroids, 1% and 1% of patients received methotrexate, and 68% and 69% of patients received aminosalicylates in UC-1 and UC-2, respectively. Patient disease severity was moderate (mMS ≤7) in 61% and 60% of patients and severe (mMS >7) in 39% and 40% of patients in UC-1 and UC-2, respectively.

The primary endpoint was clinical remission defined using the mMS at Week 8. Secondary endpoints included clinical response, endoscopic improvement, and histologic endoscopic mucosal improvement (see Table 12 and Table 13).

Table 12: Proportion of Patients Meeting Primary and Key Secondary Efficacy Endpoints at Week 8 - Study UC-1

Study UC-1			
Endpoint	**Placebo**	**RINVOQ 45 mg Once Daily**	**Treatment Difference vs Placebo (95% CI)**
Clinical Remission[a]			
Total Population	N=154 5%	N=319 26%	22%[b] (16, 27)
Prior biologic failure[c]	N=78 < 1%	N=168 18%	
Without prior biologic failure	N=76 9%	N=151 35%	
Clinical Response[d]			
Total Population	N=154 27%	N=319 73%	46%[b] (38, 54)
Prior biologic failure[c]	N=78 13%	N=168 64%	
Without prior biologic failure	N=76 42%	N=151 82%	
Endoscopic Improvement[e]			
Total Population	N=154 7%	N=319 36%	29%[b] (23, 36)
Prior biologic failure[c]	N=78 2%	N=168 27%	
Without prior biologic failure	N=76 13%	N=151 47%	
Histologic Endoscopic Mucosal Improvement[f]			
Total Population	N=154 7%	N=319 30%	24%[b] (17, 30)
Prior biologic failure[c]	N=78 1%	N=168 23%	
Without prior biologic failure	N=76 12%	N=151 38%	

[a] Per mMS: SFS ≤1 and not greater than baseline, RBS = 0, ES of ≤ 1 without friability
[b] p <0.001, adjusted treatment difference (95% CI) based on Cochran-Mantel-Haenszel method adjusted for randomization stratification factors
[c] Prior biologic failure includes inadequate response, loss of response, or intolerance to one or more biologic treatments for ulcerative colitis.
[d] Per mMS: decrease ≥ 2 points and ≥ 30% from baseline and a decrease in RBS ≥ 1 from baseline or an absolute RBS ≤1
[e] ES ≤ 1 without friability
[f] ES ≤1 without friability and Geboes score ≤ 3.1 (indicating neutrophil infiltration in <5% of crypts, no crypt destruction and no erosions, ulcerations or granulation tissue)

Table 13: Proportion of Patients Meeting Primary and Key Secondary Efficacy Endpoints at Week 8 - Study UC-2

Study UC-2			
Endpoint	**Placebo**	**RINVOQ 45 mg Once Daily**	**Treatment Difference vs Placebo (95% CI)**
Clinical Remission[a]			
Total Population	N=174 4%	N=341 33%	29%[b] (23, 35)
Prior biologic failure[c]	N=89 2%	N=173 30%	
Without prior biologic failure	N=85 6%	N=168 38%	
Clinical Response[d]			
Total Population	N=174 25%	N=341 74%	49%[b] (42, 57)
Prior biologic failure[c]	N=89 19%	N=173 69%	
Without prior biologic failure	N=85 32%	N=168 80%	
Endoscopic Improvement[e]			
Total Population	N=174 8%	N=341 44%	35%[b] (29, 42)
Prior biologic failure[c]	N=89 5%	N=173 37%	
Without prior biologic failure	N=85 12%	N=168 51%	
Histologic Endoscopic Mucosal Improvement[f]			
Total Population	N=174 6%	N=341 37%	30%[b] (24, 36)
Prior biologic failure[c]	N=89 5%	N=173 31%	
Without prior biologic failure	N=85 7%	N=168 43%	

[a] Per mMS: SFS ≤ 1 and not greater than baseline, RBS = 0, ES of ≤ 1 without friability
[b] p <0.001, adjusted treatment difference (95% CI) based on Cochran-Mantel-Haenszel method adjusted for randomization stratification factors
[c] Prior biologic failure includes inadequate response, loss of response, or intolerance to one or more biologic treatments for ulcerative colitis.
[d] Per mMS: decrease ≥ 2 points and ≥ 30% from baseline and a decrease in RBS ≥ 1 from baseline or an absolute RBS ≤1
[e] ES ≤ 1 without friability
[f] ES ≤1 without friability and Geboes score ≤ 3.1 (indicating neutrophil infiltration in <5% of crypts, no crypt destruction and no erosions, ulcerations or granulation tissue)

Studies UC-1 and UC-2 were not designed to evaluate the relationship of histologic endoscopic mucosal improvement at Week 8 to disease progression and long-term outcomes.

Rectal Bleeding and Stool Frequency Sub scores
Onset of clinical response was assessed using the SFS and RBS (partial modified Mayo Score [pmMS]). Initial response was defined as a decrease of ≥1 point and ≥30% from baseline in pmMS and a decrease in RBS ≥1 or an absolute RBS≤1. Onset of response occurred as early as Week 2 in a greater proportion of patients treated with Rinvoq® 45 mg once daily compared to placebo.

Endoscopic and Histologic Assessment
Normalization of the endoscopic appearance of the mucosa (endoscopic remission) was defined as ES of 0. At Week 8, a greater proportion of patients treated with Rinvoq® 45 mg once daily compared to placebo achieved endoscopic remission (UC-1: 14% vs 1%, UC-2: 18% vs 2%). Endoscopic remission with Geboes histologic score < 2.0 (indicating no neutrophils in crypts or lamina propria and no increase in eosinophil, no crypt destruction, and no erosions, ulcerations, or granulation tissue) was achieved by a greater proportion of patients treated with Rinvoq® 45 mg once daily compared to placebo at Week 8 (UC-1: 11% vs 1%, UC-2: 13% vs 2%). Abdominal Pain and Bowel Urgency A greater proportion of patients treated with Rinvoq® 45 mg once daily compared to placebo had no abdominal pain (UC-1: 47% vs 23%, UC-2: 54% vs 24%) and no bowel urgency (UC-1: 48% vs 21%, UC-2: 54% vs 26%) at Week 8.

Maintenance Study UC-3
In UC-3 (NCT02819635), a total of 451 patients who received Rinvoq® 45 mg once daily in either UC-1, UC-2 or UC-4 and achieved clinical response were re-randomized to receive Rinvoq® 15 mg, 30 mg or placebo once daily for up to 52 weeks.
The primary endpoint was clinical remission defined using mMS at Week 52. Secondary endpoints included corticosteroid-free clinical remission, endoscopic improvement, and histologic endoscopic mucosal improvement.

Table 14. Proportion of Patients Meeting Primary and Key Secondary Efficacy Endpoints at Week 52 in Maintenance Study UC-3

Endpoint	Placebo	RINVOQ 15 mg Once Daily	Treatment Difference 15 mg vs Placebo (95% CI)	RINVOQ 30 mg Once Daily	Treatment Difference 30 mg vs Placebo (95% CI)
Clinical remission[a]					
Total Population	N=149 12%	N=148 42%	31%[b] (22, 40)	N=154 52%	39%[b] (30, 48)
Prior biologic failure[c]	N=81 7%	N=71 41%		N=73 49%	
Without prior biologic failure	N=68 18%	N=77 44%		N=81 54%	
Corticosteroid-free clinical remission[d]					
Total Population	N=54 22%	N=47 57%	35%[b] (18, 53)	N=58 68%	45%[b] (29, 62)
Prior biologic failure[c]	N=22 14%	N=17 71%		N=20 73%	
Without prior biologic failure	N=32 28%	N=30 49%		N=38 65%	
Endoscopic Improvement[e]					
Total Population	N=149 14%	N=148 49%	34%[b] (25, 44)	N=154 62%	46%[b] (37, 56)
Prior biologic failure[c]	N=81 8%	N=71 43%		N=73 56%	
Without prior biologic failure	N=68 22%	N=77 54%		N=81 67%	
Histologic Endoscopic Mucosal Improvement[f]					
Total Population	N=149 12%	N=148 35%	24%[b] (15, 33)	N=154 50%	37%[b] (28, 47)
Prior biologic failure[c]	N=81 5%	N=71 33%		N=73 48%	
Without prior biologic failure	N=68 20%	N=77 37%		N=81 52%	

[a] Per mMS: SFS ≤1 and not greater than baseline, RBS = 0, ES ≤1 without friability
[b] p <0.001, adjusted treatment difference (95% CI) based on Cochran-Mantel-Haenszel method adjusted for randomization stratification factors
[c] Prior biologic failure includes inadequate response, loss of response, or intolerance to one or more biologic treatments for ulcerative colitis.
[d] Clinical remission per mMS at Week 52 and corticosteroid free for ≥90 days immediately preceding Week 52 among patients who achieved clinical remission at the end of the induction treatment
[e] ES ≤ 1 without friability
[f] ES ≤1 without friability and Geboes score ≤ 3.1 (indicating neutrophil infiltration in <5% of crypts, no crypt destruction and no erosions, ulcerations or granulation tissue)

The relationship between histologic endoscopic mucosal improvement at Week 52 and disease progression and longer-term outcomes after Week 52 was not evaluated in Study UC-3.

Endoscopic and Histologic Assessment

Normalization of the endoscopic appearance of the mucosa (endoscopic remission) was defined as ES of 0. In UC-3, a greater proportion of patients treated with Rinvoq® 15 mg and 30 mg once daily compared to placebo achieved endoscopic remission at Week 52 (24% and 26% vs 6%). Endoscopic remission with Geboes histologic score < 2.0 was achieved by a greater proportion of patients treated with Rinvoq® 15 mg and 30 mg once daily compared to placebo at Week 52 (18% and 19% vs 5%).

Abdominal Pain and Bowel Urgency

At Week 52, a greater proportion of patients treated with Rinvoq® 15 mg and 30 mg once daily compared to placebo had no abdominal pain (46%, 55% and 21%, respectively) and no bowel urgency (56%, 64% and 17%, respectively).