Clinical trial results:
A Phase 2b/3 Multi-Center, Randomized, Double-Blind, Multi-Dose, Placebo-Controlled, Parallel-Group Set of Studies to Evaluate the Efficacy and Safety of Induction and Maintenance Therapy With TD-1473 in Subjects With Moderately-to-Severely Active Ulcerative Colitis

Summary

EudraCT number	2018-002136-24
Trial protocol	FR DE SK PT BG PL GR HU ES IT RO
Global end of trial date	20 October 2021

Results information

Result version number	v1 (current)
This version publication date	06 November 2022
First version publication date	06 November 2022

Trial information

Trial identification

Sponsor protocol code	0157

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03758443
WHO universal trial number (UTN)	-
Other trial identifiers	US IND: 128299

Notes:

Sponsors

Sponsor organisation name	Theravance Biopharma Ireland Limited
Sponsor organisation address	Ten Earlsfort Terrace, Dublin, Ireland, D02 T380
Public contact	Medical Monitor , Theravance Biopharma Ireland Limited, +1 855 633 8479, medinfo@theravance.com
Scientific contact	Medical Monitor , Theravance Biopharma Ireland Limited, +1 855 633 8479, medinfo@theravance.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	20 October 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 October 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of this study were as follows:
Phase 2b Dose-Finding Induction Study
-Assess the effect of TD-1473 taken daily for 8 weeks at daily doses of 20 mg, 80 mg, and 200 mg on the change from baseline in the total Mayo score
-Assess the effect of TD-1473 on rates of clinical remission, endoscopic healing, clinical response, and mucosal healing
-Select dose(s) of TD-1473 for evaluation in the Phase 3 dose-confirming Induction Study and the Phase 3 Maintenance Study

Phase 3 Dose-Confirming Induction Study
-Establish the clinical remission rate associated with TD-1473 compared to placebo treatment at Week 8
-To assess the safety and tolerability of TD-1473 when taken for up to 16 weeks

Phase 3 Maintenance Study
-Establish the clinical remission rate associated with TD-1473 compared to placebo treatment at Maintenance Week 44
-Establish the safety and tolerability of TD-1473 with up to 44 additional weeks of treatment

Protection of trial subjects:

This trial was conducted in accordance with the ethical principles of Good Clinical Practice, according to the International Council for Harmonisation (ICH) Harmonised Tripartite Guideline.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 March 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 53
Country: Number of subjects enrolled	Ukraine: 29
Country: Number of subjects enrolled	Bulgaria: 13
Country: Number of subjects enrolled	Serbia: 10
Country: Number of subjects enrolled	Slovakia: 5
Country: Number of subjects enrolled	Georgia: 4
Country: Number of subjects enrolled	Hungary: 4
Country: Number of subjects enrolled	Romania: 2
Country: Number of subjects enrolled	France: 16
Country: Number of subjects enrolled	Italy: 12

Country: Number of subjects enrolled	Portugal: 6
Country: Number of subjects enrolled	Spain: 5
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	Greece: 2
Country: Number of subjects enrolled	Japan: 25
Country: Number of subjects enrolled	Australia: 9
Country: Number of subjects enrolled	Korea, Republic of: 4
Country: Number of subjects enrolled	Taiwan: 2
Country: Number of subjects enrolled	United States: 26
Country: Number of subjects enrolled	Israel: 9
Country: Number of subjects enrolled	South Africa: 1
Worldwide total number of subjects	239
EEA total number of subjects	120

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	221
From 65 to 84 years	18
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 239 participants were enrolled at sites in Europe, Asia/Pacific, the United States, Israel, Australia, and South Africa between 11 March 2019 and 20 October 2021.

Pre-assignment

Screening details:

Participants were screened for eligibility over a 4-week period prior to randomization.

Period 1

Period 1 title	Induction Period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants were randomized to receive once-daily administrations of placebo for 8 weeks during the Induction Period.

Participants who achieved clinical response by adapted Mayo Score at Week 8 continued to receive blinded placebo in the Maintenance Period. Participants who did not achieve clinical response at Week 8 received 80 mg TD-1473 for 8 weeks in the Extended Induction Period.

Participants who achieved clinical response to a total of 8 weeks of TD-1473 induction therapy, either at Week 8 or Week 16, were re-randomized to received placebo; 20 mg, 80 mg, or 200 mg TD-1473 for 44 weeks in the Maintenance Period. Participants who did not achieve clinical response to a total of 8 weeks of TD-1473 induction therapy underwent study exit procedures.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Received orally.

Arm title	TD-1473 20 mg

Arm description:

Participants were randomized to receive once-daily administrations of 20 mg TD-1473 for 8 weeks during the Induction Period.

Participants who achieved clinical response by adapted Mayo Score at Week 8 continued to receive 20 mg TD-1473 in the Maintenance Period. Participants who did not achieve clinical response at Week 8 continued to receive 20 mg TD-1473 for 8 weeks in the Extended Induction Period.

Participants who achieved clinical response to a total of 16 weeks of TD-1473 induction therapy continued to receive 20 mg TD-1473 for 44 weeks in the Maintenance Period. Participants who did not achieve clinical response to a total of 16 weeks of TD-1473 induction therapy underwent study exit procedures.

Arm type	Experimental

Investigational medicinal product name	TD-1473
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Received orally.

Arm title	TD-1473 80 mg

Arm description:

Participants were randomized to receive once-daily administrations of 80 mg TD-1473 for 8 weeks during the Induction Period.

Participants who achieved clinical response by adapted Mayo Score at Week 8 continued to receive 80 mg TD-1473 in the Maintenance Period. Participants who did not achieve clinical response at Week 8 continued to receive 80 mg TD-1473 for 8 weeks in the Extended Induction Period.

Participants who achieved clinical response to a total of 16 weeks of TD-1473 induction therapy continued to receive 80 mg TD-1473 for 44 weeks in the Maintenance Period. Participants who did not achieve clinical response to a total of 16 weeks of TD-1473 induction therapy underwent study exit procedures.

Arm type	Experimental
Investigational medicinal product name	TD-1473
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Received orally.

Arm title	TD-1473 200 mg

Arm description:

Participants were randomized to receive once-daily administrations of 200 mg TD-1473 for 8 weeks during the Induction Period.

Participants who achieved clinical response by adapted Mayo Score at Week 8 continued to receive 200 mg TD-1473 in the Maintenance Period. Participants who did not achieve clinical response at Week 8 continued to receive 200 mg TD-1473 for 8 weeks in the Extended Induction Period.

Participants who achieved clinical response to a total of 16 weeks of TD-1473 induction therapy continued to receive 200 mg TD-1473 for 44 weeks in the Maintenance Period. Participants who did not achieve clinical response to a total of 16 weeks of TD-1473 induction therapy underwent study exit procedures.

Arm type	Experimental
Investigational medicinal product name	TD-1473
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Received orally.

Number of subjects in period 1	Placebo	TD-1473 20 mg	TD-1473 80 mg
Started	61	61	59
Completed	55	54	52
Not completed	6	7	7
Physician decision	1	1	3
Consent withdrawn by subject	3	2	2
Adverse event, non-fatal	2	4	2
Protocol deviation	-	-	-

Number of subjects in period 1	TD-1473 200 mg
Started	58
Completed	50
Not completed	8
Physician decision	-
Consent withdrawn by subject	4
Adverse event, non-fatal	3
Protocol deviation	1

Period 2	
Period 2 title	Extended Induction Period
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants were randomized to receive once-daily administrations of placebo for 8 weeks during the Induction Period.

Participants who achieved clinical response by adapted Mayo Score at Week 8 continued to receive blinded placebo in the Maintenance Period. Participants who did not achieve clinical response at Week 8 received 80 mg TD-1473 for 8 weeks in the Extended Induction Period.

Participants who achieved clinical response to a total of 8 weeks of TD-1473 induction therapy, either at Week 8 or Week 16, were re-randomized to received placebo; 20 mg, 80 mg, or 200 mg TD-1473 for 44 weeks in the Maintenance Period. Participants who did not achieve clinical response to a total of 8 weeks of TD-1473 induction therapy underwent study exit procedures.

Arm type	Placebo

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Received orally.

Arm title	TD-1473 20 mg

Arm description:

Participants were randomized to receive once-daily administrations of 20 mg TD-1473 for 8 weeks during the Induction Period.

Participants who achieved clinical response by adapted Mayo Score at Week 8 continued to receive 20 mg TD-1473 in the Maintenance Period. Participants who did not achieve clinical response at Week 8 continued to receive 20 mg TD-1473 for 8 weeks in the Extended Induction Period.

Participants who achieved clinical response to a total of 16 weeks of TD-1473 induction therapy continued to receive 20 mg TD-1473 for 44 weeks in the Maintenance Period. Participants who did not achieve clinical response to a total of 16 weeks of TD-1473 induction therapy underwent study exit procedures.

Arm type	Experimental
Investigational medicinal product name	TD-1473
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Received orally.

Arm title	TD-1473 80 mg

Arm description:

Participants were randomized to receive once-daily administrations of 80 mg TD-1473 for 8 weeks during the Induction Period.

Participants who achieved clinical response by adapted Mayo Score at Week 8 continued to receive 80 mg TD-1473 in the Maintenance Period. Participants who did not achieve clinical response at Week 8 continued to receive 80 mg TD-1473 for 8 weeks in the Extended Induction Period.

Participants who achieved clinical response to a total of 16 weeks of TD-1473 induction therapy continued to receive 80 mg TD-1473 for 44 weeks in the Maintenance Period. Participants who did not achieve clinical response to a total of 16 weeks of TD-1473 induction therapy underwent study exit procedures.

Arm type	Experimental
Investigational medicinal product name	TD-1473
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Received orally.

Arm title	TD-1473 200 mg

Arm description:

Participants were randomized to receive once-daily administrations of 200 mg TD-1473 for 8 weeks during the Induction Period.

Participants who achieved clinical response by adapted Mayo Score at Week 8 continued to receive 200 mg TD-1473 in the Maintenance Period. Participants who did not achieve clinical response at Week 8 continued to receive 200 mg TD-1473 for 8 weeks in the Extended Induction Period.

Participants who achieved clinical response to a total of 16 weeks of TD-1473 induction therapy continued to receive 200 mg TD-1473 for 44 weeks in the Maintenance Period. Participants who did not achieve clinical response to a total of 16 weeks of TD-1473 induction therapy underwent study exit procedures.

Arm type	Experimental
Investigational medicinal product name	TD-1473
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Received orally.

Number of subjects in period 2[1]	Placebo	TD-1473 20 mg	TD-1473 80 mg
Started	42	32	32
Completed	29	29	23
Not completed	13	3	9
Physician decision	2	1	2
Consent withdrawn by subject	8	1	7
Adverse event, non-fatal	1	1	-
Miscellaneous	1	-	-
Lost to follow-up	1	-	-
Protocol deviation	-	-	-

Number of subjects in period 2[1]	TD-1473 200 mg
Started	29
Completed	22
Not completed	7
Physician decision	2
Consent withdrawn by subject	3
Adverse event, non-fatal	1
Miscellaneous	-
Lost to follow-up	-
Protocol deviation	1

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: The extended induction period included only participants who did not achieve clinical response at Week 8.

Period 3

Period 3 title	Maintenance Period
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	No
Arm title	Placebo

Arm description:

Participants were randomized to receive once-daily administrations of placebo for 8 weeks during the Induction Period.

Participants who achieved clinical response by adapted Mayo Score at Week 8 continued to receive blinded placebo in the Maintenance Period. Participants who did not achieve clinical response at Week 8 received 80 mg TD-1473 for 8 weeks in the Extended Induction Period.

Participants who achieved clinical response to a total of 8 weeks of TD-1473 induction therapy, either at Week 8 or Week 16, were re-randomized to received placebo; 20 mg, 80 mg, or 200 mg TD-1473 for 44 weeks in the Maintenance Period. Participants who did not achieve clinical response to a total of 8 weeks of TD-1473 induction therapy underwent study exit procedures.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Received orally.

Arm title	TD-1473 20 mg

Arm description:

Participants were randomized to receive once-daily administrations of 20 mg TD-1473 for 8 weeks during the Induction Period.

Participants who achieved clinical response by adapted Mayo Score at Week 8 continued to receive 20 mg TD-1473 in the Maintenance Period. Participants who did not achieve clinical response at Week 8 continued to receive 20 mg TD-1473 for 8 weeks in the Extended Induction Period.

Participants who achieved clinical response to a total of 16 weeks of TD-1473 induction therapy continued to receive 20 mg TD-1473 for 44 weeks in the Maintenance Period. Participants who did not achieve clinical response to a total of 16 weeks of TD-1473 induction therapy underwent study exit procedures.

Arm type	Experimental
Investigational medicinal product name	TD-1473
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Received orally.

Arm title	TD-1473 80 mg

Arm description:

Participants were randomized to receive once-daily administrations of 80 mg TD-1473 for 8 weeks during the Induction Period.

Participants who achieved clinical response by adapted Mayo Score at Week 8 continued to receive 80 mg TD-1473 in the Maintenance Period. Participants who did not achieve clinical response at Week 8

continued to receive 80 mg TD-1473 for 8 weeks in the Extended Induction Period.

Participants who achieved clinical response to a total of 16 weeks of TD-1473 induction therapy continued to receive 80 mg TD-1473 for 44 weeks in the Maintenance Period. Participants who did not achieve clinical response to a total of 16 weeks of TD-1473 induction therapy underwent study exit procedures.

Arm type	Experimental
Investigational medicinal product name	TD-1473
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Received orally.

Arm title	TD-1473 200 mg

Arm description:

Participants were randomized to receive once-daily administrations of 200 mg TD-1473 for 8 weeks during the Induction Period.

Participants who achieved clinical response by adapted Mayo Score at Week 8 continued to receive 200 mg TD-1473 in the Maintenance Period. Participants who did not achieve clinical response at Week 8 continued to receive 200 mg TD-1473 for 8 weeks in the Extended Induction Period.

Participants who achieved clinical response to a total of 16 weeks of TD-1473 induction therapy continued to receive 200 mg TD-1473 for 44 weeks in the Maintenance Period. Participants who did not achieve clinical response to a total of 16 weeks of TD-1473 induction therapy underwent study exit procedures.

Arm type	Experimental
Investigational medicinal product name	TD-1473
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Received orally.

Number of subjects in period 3	Placebo	TD-1473 20 mg	TD-1473 80 mg
Started	29	31	25
Completed	13	11	12
Not completed	16	20	13
Consent withdrawn by subject	1	-	1
Adverse event, non-fatal	1	2	-
Persistent Loss of Response During Maintenance	3	1	2
Miscellaneous	-	-	1
Study Terminated by Sponsor	11	16	9
Lost to follow-up	-	-	-
Protocol deviation	-	1	-

Number of subjects in period 3	TD-1473 200 mg
Started	22
Completed	9
Not completed	13
Consent withdrawn by subject	1
Adverse event, non-fatal	-
Persistent Loss of Response During Maintenance	-
Miscellaneous	-
Study Terminated by Sponsor	11
Lost to follow-up	1
Protocol deviation	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo

Reporting group description:

Participants were randomized to receive once-daily administrations of placebo for 8 weeks during the Induction Period.

Participants who achieved clinical response by adapted Mayo Score at Week 8 continued to receive blinded placebo in the Maintenance Period. Participants who did not achieve clinical response at Week 8 received 80 mg TD-1473 for 8 weeks in the Extended Induction Period.

Participants who achieved clinical response to a total of 8 weeks of TD-1473 induction therapy, either at Week 8 or Week 16, were re-randomized to received placebo; 20 mg, 80 mg, or 200 mg TD-1473 for 44 weeks in the Maintenance Period. Participants who did not achieve clinical response to a total of 8 weeks of TD-1473 induction therapy underwent study exit procedures.

Reporting group title	TD-1473 20 mg

Reporting group description:

Participants were randomized to receive once-daily administrations of 20 mg TD-1473 for 8 weeks during the Induction Period.

Participants who achieved clinical response by adapted Mayo Score at Week 8 continued to receive 20 mg TD-1473 in the Maintenance Period. Participants who did not achieve clinical response at Week 8 continued to receive 20 mg TD-1473 for 8 weeks in the Extended Induction Period.

Participants who achieved clinical response to a total of 16 weeks of TD-1473 induction therapy continued to receive 20 mg TD-1473 for 44 weeks in the Maintenance Period. Participants who did not achieve clinical response to a total of 16 weeks of TD-1473 induction therapy underwent study exit procedures.

Reporting group title	TD-1473 80 mg

Reporting group description:

Participants were randomized to receive once-daily administrations of 80 mg TD-1473 for 8 weeks during the Induction Period.

Participants who achieved clinical response by adapted Mayo Score at Week 8 continued to receive 80 mg TD-1473 in the Maintenance Period. Participants who did not achieve clinical response at Week 8 continued to receive 80 mg TD-1473 for 8 weeks in the Extended Induction Period.

Participants who achieved clinical response to a total of 16 weeks of TD-1473 induction therapy continued to receive 80 mg TD-1473 for 44 weeks in the Maintenance Period. Participants who did not achieve clinical response to a total of 16 weeks of TD-1473 induction therapy underwent study exit procedures.

Reporting group title	TD-1473 200 mg

Reporting group description:

Participants were randomized to receive once-daily administrations of 200 mg TD-1473 for 8 weeks during the Induction Period.

Participants who achieved clinical response by adapted Mayo Score at Week 8 continued to receive 200 mg TD-1473 in the Maintenance Period. Participants who did not achieve clinical response at Week 8 continued to receive 200 mg TD-1473 for 8 weeks in the Extended Induction Period.

Participants who achieved clinical response to a total of 16 weeks of TD-1473 induction therapy continued to receive 200 mg TD-1473 for 44 weeks in the Maintenance Period. Participants who did not achieve clinical response to a total of 16 weeks of TD-1473 induction therapy underwent study exit procedures.

Reporting group values	Placebo	TD-1473 20 mg	TD-1473 80 mg
Number of subjects	61	61	59

Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous Units: years			
arithmetic mean	40.92	38.87	42.02
standard deviation	± 15.390	± 14.576	± 15.317
Gender categorical Units: Subjects			
Female	27	17	20
Male	34	44	39
Ethnicity Units: Subjects			
Hispanic or Latino	3	2	1
Not Hispanic or Latino	54	59	56
Unknown or Not Reported	4	0	2
Race Units: Subjects			
White	48	50	51
Black or African American	1	0	0
Asian	9	11	6
Other	3	0	2

Reporting group values	TD-1473 200 mg	Total	
Number of subjects	58	239	
Age categorical Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		0	
Newborns (0-27 days)		0	
Infants and toddlers (28 days-23 months)		0	
Children (2-11 years)		0	
Adolescents (12-17 years)		0	
Adults (18-64 years)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous Units: years			
arithmetic mean	44.38		
standard deviation	± 14.122	-	

Gender categorical Units: Subjects			
Female	29	93	
Male	29	146	
Ethnicity Units: Subjects			
Hispanic or Latino	1	7	
Not Hispanic or Latino	55	224	
Unknown or Not Reported	2	8	
Race Units: Subjects			
White	51	200	
Black or African American	0	1	
Asian	6	32	
Other	1	6	

End points

End points reporting groups

Reporting group title	Placebo

Reporting group description:

Participants were randomized to receive once-daily administrations of placebo for 8 weeks during the Induction Period.

Participants who achieved clinical response by adapted Mayo Score at Week 8 continued to receive blinded placebo in the Maintenance Period. Participants who did not achieve clinical response at Week 8 received 80 mg TD-1473 for 8 weeks in the Extended Induction Period.

Participants who achieved clinical response to a total of 8 weeks of TD-1473 induction therapy, either at Week 8 or Week 16, were re-randomized to received placebo; 20 mg, 80 mg, or 200 mg TD-1473 for 44 weeks in the Maintenance Period. Participants who did not achieve clinical response to a total of 8 weeks of TD-1473 induction therapy underwent study exit procedures.

Reporting group title	TD-1473 20 mg

Reporting group description:

Participants were randomized to receive once-daily administrations of 20 mg TD-1473 for 8 weeks during the Induction Period.

Participants who achieved clinical response by adapted Mayo Score at Week 8 continued to receive 20 mg TD-1473 in the Maintenance Period. Participants who did not achieve clinical response at Week 8 continued to receive 20 mg TD-1473 for 8 weeks in the Extended Induction Period.

Participants who achieved clinical response to a total of 16 weeks of TD-1473 induction therapy continued to receive 20 mg TD-1473 for 44 weeks in the Maintenance Period. Participants who did not achieve clinical response to a total of 16 weeks of TD-1473 induction therapy underwent study exit procedures.

Reporting group title	TD-1473 80 mg

Reporting group description:

Participants were randomized to receive once-daily administrations of 80 mg TD-1473 for 8 weeks during the Induction Period.

Participants who achieved clinical response by adapted Mayo Score at Week 8 continued to receive 80 mg TD-1473 in the Maintenance Period. Participants who did not achieve clinical response at Week 8 continued to receive 80 mg TD-1473 for 8 weeks in the Extended Induction Period.

Participants who achieved clinical response to a total of 16 weeks of TD-1473 induction therapy continued to receive 80 mg TD-1473 for 44 weeks in the Maintenance Period. Participants who did not achieve clinical response to a total of 16 weeks of TD-1473 induction therapy underwent study exit procedures.

Reporting group title	TD-1473 200 mg

Reporting group description:

Participants were randomized to receive once-daily administrations of 200 mg TD-1473 for 8 weeks during the Induction Period.

Participants who achieved clinical response by adapted Mayo Score at Week 8 continued to receive 200 mg TD-1473 in the Maintenance Period. Participants who did not achieve clinical response at Week 8 continued to receive 200 mg TD-1473 for 8 weeks in the Extended Induction Period.

Participants who achieved clinical response to a total of 16 weeks of TD-1473 induction therapy continued to receive 200 mg TD-1473 for 44 weeks in the Maintenance Period. Participants who did not achieve clinical response to a total of 16 weeks of TD-1473 induction therapy underwent study exit procedures.

Reporting group title	Placebo

Reporting group description:

Participants were randomized to receive once-daily administrations of placebo for 8 weeks during the Induction Period.

Participants who achieved clinical response by adapted Mayo Score at Week 8 continued to receive blinded placebo in the Maintenance Period. Participants who did not achieve clinical response at Week 8 received 80 mg TD-1473 for 8 weeks in the Extended Induction Period.

Participants who achieved clinical response to a total of 8 weeks of TD-1473 induction therapy, either at Week 8 or Week 16, were re-randomized to received placebo; 20 mg, 80 mg, or 200 mg TD-1473 for 44 weeks in the Maintenance Period. Participants who did not achieve clinical response to a total of 8 weeks of TD-1473 induction therapy underwent study exit procedures.

Reporting group title	TD-1473 20 mg

Reporting group description:

Participants were randomized to receive once-daily administrations of 20 mg TD-1473 for 8 weeks during the Induction Period.

Participants who achieved clinical response by adapted Mayo Score at Week 8 continued to receive 20 mg TD-1473 in the Maintenance Period. Participants who did not achieve clinical response at Week 8 continued to receive 20 mg TD-1473 for 8 weeks in the Extended Induction Period.

Participants who achieved clinical response to a total of 16 weeks of TD-1473 induction therapy continued to receive 20 mg TD-1473 for 44 weeks in the Maintenance Period. Participants who did not achieve clinical response to a total of 16 weeks of TD-1473 induction therapy underwent study exit procedures.

Reporting group title	TD-1473 80 mg

Reporting group description:

Participants were randomized to receive once-daily administrations of 80 mg TD-1473 for 8 weeks during the Induction Period.

Participants who achieved clinical response by adapted Mayo Score at Week 8 continued to receive 80 mg TD-1473 in the Maintenance Period. Participants who did not achieve clinical response at Week 8 continued to receive 80 mg TD-1473 for 8 weeks in the Extended Induction Period.

Participants who achieved clinical response to a total of 16 weeks of TD-1473 induction therapy continued to receive 80 mg TD-1473 for 44 weeks in the Maintenance Period. Participants who did not achieve clinical response to a total of 16 weeks of TD-1473 induction therapy underwent study exit procedures.

Reporting group title	TD-1473 200 mg

Reporting group description:

Participants were randomized to receive once-daily administrations of 200 mg TD-1473 for 8 weeks during the Induction Period.

Participants who achieved clinical response by adapted Mayo Score at Week 8 continued to receive 200 mg TD-1473 in the Maintenance Period. Participants who did not achieve clinical response at Week 8 continued to receive 200 mg TD-1473 for 8 weeks in the Extended Induction Period.

Participants who achieved clinical response to a total of 16 weeks of TD-1473 induction therapy continued to receive 200 mg TD-1473 for 44 weeks in the Maintenance Period. Participants who did not achieve clinical response to a total of 16 weeks of TD-1473 induction therapy underwent study exit procedures.

Reporting group title	Placebo

Reporting group description:

Participants were randomized to receive once-daily administrations of placebo for 8 weeks during the Induction Period.

Participants who achieved clinical response by adapted Mayo Score at Week 8 continued to receive blinded placebo in the Maintenance Period. Participants who did not achieve clinical response at Week 8 received 80 mg TD-1473 for 8 weeks in the Extended Induction Period.

Participants who achieved clinical response to a total of 8 weeks of TD-1473 induction therapy, either at Week 8 or Week 16, were re-randomized to received placebo; 20 mg, 80 mg, or 200 mg TD-1473 for 44 weeks in the Maintenance Period. Participants who did not achieve clinical response to a total of 8 weeks of TD-1473 induction therapy underwent study exit procedures.

Reporting group title	TD-1473 20 mg

Reporting group description:

Participants were randomized to receive once-daily administrations of 20 mg TD-1473 for 8 weeks during the Induction Period.

Participants who achieved clinical response by adapted Mayo Score at Week 8 continued to receive 20 mg TD-1473 in the Maintenance Period. Participants who did not achieve clinical response at Week 8 continued to receive 20 mg TD-1473 for 8 weeks in the Extended Induction Period.

Participants who achieved clinical response to a total of 16 weeks of TD-1473 induction therapy continued to receive 20 mg TD-1473 for 44 weeks in the Maintenance Period. Participants who did not achieve clinical response to a total of 16 weeks of TD-1473 induction therapy underwent study exit procedures.

Reporting group title	TD-1473 80 mg

Reporting group description:

Participants were randomized to receive once-daily administrations of 80 mg TD-1473 for 8 weeks during the Induction Period.

Participants who achieved clinical response by adapted Mayo Score at Week 8 continued to receive 80 mg TD-1473 in the Maintenance Period. Participants who did not achieve clinical response at Week 8 continued to receive 80 mg TD-1473 for 8 weeks in the Extended Induction Period.

Participants who achieved clinical response to a total of 16 weeks of TD-1473 induction therapy continued to receive 80 mg TD-1473 for 44 weeks in the Maintenance Period. Participants who did not achieve clinical response to a total of 16 weeks of TD-1473 induction therapy underwent study exit procedures.

Reporting group title	TD-1473 200 mg

Reporting group description:

Participants were randomized to receive once-daily administrations of 200 mg TD-1473 for 8 weeks during the Induction Period.

Participants who achieved clinical response by adapted Mayo Score at Week 8 continued to receive 200 mg TD-1473 in the Maintenance Period. Participants who did not achieve clinical response at Week 8 continued to receive 200 mg TD-1473 for 8 weeks in the Extended Induction Period.

Participants who achieved clinical response to a total of 16 weeks of TD-1473 induction therapy continued to receive 200 mg TD-1473 for 44 weeks in the Maintenance Period. Participants who did not achieve clinical response to a total of 16 weeks of TD-1473 induction therapy underwent study exit procedures.

Subject analysis set title	Induction Period: Placebo
Subject analysis set type	Full analysis

Subject analysis set description:

Participants were randomized to receive once-daily administrations of placebo for 8 weeks during the Induction Period.

Subject analysis set title	Induction Period: TD-1473 20 mg
Subject analysis set type	Full analysis

Subject analysis set description:

Participants were randomized to receive once-daily administrations of 20 mg TD-1473 for 8 weeks during the Induction Period.

Subject analysis set title	Induction Period: TD-1473 80 mg
Subject analysis set type	Full analysis

Subject analysis set description:

Participants were randomized to receive once-daily administrations of 80 mg TD-1473 for 8 weeks during the Induction Period.

Subject analysis set title	Induction Period: TD-1473 200 mg
Subject analysis set type	Full analysis

Subject analysis set description:

Participants were randomized to receive once-daily administrations of 200 mg TD-1473 for 8 weeks during the Induction Period.

Subject analysis set title	Maintenance Period: Placebo
Subject analysis set type	Full analysis

Subject analysis set description:

Participants who were randomized to receive once-daily administrations of placebo for 8 weeks during the Induction Period and achieved clinical response by adapted Mayo Score at Week 8 of the Induction Period continued to receive blinded placebo for 44 weeks in the Maintenance Period.

Subject analysis set title	Maintenance Period: TD-1473 20 mg
Subject analysis set type	Full analysis

Subject analysis set description:

Participants who achieved clinical response to a total of 8 weeks of TD-1473 induction therapy, either at Week 8 or Week 16, and continued to receive 20 mg TD-1473 for 44 weeks in the Maintenance Period.

Subject analysis set title	Maintenance Period: TD-1473 80 mg
Subject analysis set type	Full analysis

Subject analysis set description:

Participants who achieved clinical response to a total of 8 weeks of TD-1473 induction therapy, either at Week 8 or Week 16, and continued to receive 80 mg TD-1473 for 44 weeks in the Maintenance Period.

Subject analysis set title	Maintenance Period: TD-1473 200 mg
Subject analysis set type	Full analysis

Subject analysis set description:

Participants who achieved clinical response to a total of 8 weeks of TD-1473 induction therapy, either at Week 8 or Week 16, and continued to receive 200 mg TD-1473 for 44 weeks in the Maintenance Period.

Primary: Change From Baseline in Total Mayo Score (tMS) at Week 8

End point title	Change From Baseline in Total Mayo Score (tMS) at Week 8

End point description:

Total Mayo Score (tMS) was calculated as the sum of four components: rectal bleeding (0-3), stool frequency (0-3), physician's global assessment (0-3) and Mayo endoscopic subscore (0-3). tMS was reported as a 0-12 point score with 12 reflecting the highest severity.

Modified Intent-to-Treat (mITT) Analysis Set (Induction Period): Comprised all randomized participants who received at least one dose of study drug.

End point type	Primary

End point timeframe:

Baseline to Week 8

End point values	Induction Period: Placebo	Induction Period: TD-1473 20 mg	Induction Period: TD-1473 80 mg	Induction Period: TD-1473 200 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	56	54	53	55
Units: score on a scale				
least squares mean (standard error)	-1.75 (± 0.341)	-2.02 (± 0.350)	-2.12 (± 0.351)	-2.40 (± 0.346)

Statistical analyses

Statistical analysis title	Placebo v TD-1473 20 mg

Statistical analysis description:

Least square estimates, 95% CI, and p-values were obtained by fitting an ANCOVA model with terms for treatment, steroid use at baseline (yes, no) and prior biologic failure (yes, no), and baseline total Mayo score as covariate.

Comparison groups	Induction Period: TD-1473 20 mg v Induction Period: Placebo

Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5809
Method	ANCOVA
Parameter estimate	Least Square Mean Difference
Point estimate	-0.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.22
upper limit	0.69

Statistical analysis title	Placebo v TD-1473 80 mg

Statistical analysis description:

Least square estimates, 95% CI, and p-values were obtained by fitting an ANCOVA model with terms for treatment, steroid use at baseline (yes, no) and prior biologic failure (yes, no), and baseline total Mayo score as covariate.

Comparison groups	Induction Period: Placebo v Induction Period: TD-1473 80 mg
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4501
Method	ANCOVA
Parameter estimate	Least Square Mean Difference
Point estimate	-0.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.33
upper limit	0.59

Statistical analysis title	Placebo v TD-1473 200 mg

Statistical analysis description:

Least square estimates, 95% CI, and p-values were obtained by fitting an ANCOVA model with terms for treatment, steroid use at baseline (yes, no) and prior biologic failure (yes, no), and baseline total Mayo score as covariate.

Comparison groups	Induction Period: Placebo v Induction Period: TD-1473 200 mg
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1809
Method	ANCOVA
Parameter estimate	Least Square Mean Difference
Point estimate	-0.65

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	0.3

Primary: Phase 3 Maintenance: Number of Participants Who Demonstrated Clinical Remission by Adapted Mayo Score Components at Maintenance Week (mWeek) 44

End point title	Phase 3 Maintenance: Number of Participants Who Demonstrated Clinical Remission by Adapted Mayo Score Components at Maintenance Week (mWeek) 44

End point description:

Clinical remission by Adapted Mayo score was defined based on Adapted Mayo score components within specific ranges: stool frequency score of 0 or 1, a rectal bleeding subscore of 0 and a Mayo endoscopy subscore of 0 or 1.

The Adapted Mayo score was the sum of three components: rectal bleeding, stool frequency, and Mayo endoscopic subscore, each measured on a scale of 0-3 with higher scores reflecting higher severity.

Participants with missing Week 44 values were imputed as non-responders.

mITT Analysis Set (Maintenance Period): All participants randomized into the Phase 3 Maintenance Study who were also treated. Only participants randomized at least 44 weeks prior to database lock were included.

End point type	Primary

End point timeframe:

mWeek 44

End point values	Maintenance Period: Placebo	Maintenance Period: TD-1473 20 mg	Maintenance Period: TD-1473 80 mg	Maintenance Period: TD-1473 200 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	13	11	8
Units: participants	4	3	5	3

Statistical analyses

Statistical analysis title	Placebo v TD-1473 20 mg
Comparison groups	Maintenance Period: Placebo v Maintenance Period: TD-1473 20 mg
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3762
Method	Fisher exact

Statistical analysis title	Placebo v TD-1473 80 mg
Comparison groups	Maintenance Period: TD-1473 80 mg v Maintenance Period: Placebo
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 1
Method	Fisher exact

Statistical analysis title	Placebo v TD-1473 200 mg
Comparison groups	Maintenance Period: Placebo v Maintenance Period: TD-1473 200 mg
Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 1
Method	Fisher exact

Secondary: Number of Participants Who Demonstrated Clinical Remission by Adapted Mayo Score Components at Week 8

End point title	Number of Participants Who Demonstrated Clinical Remission by Adapted Mayo Score Components at Week 8

End point description:

Clinical remission by Adapted Mayo score was defined based on Adapted Mayo score components within specific ranges: stool frequency score of 0 or 1, a rectal bleeding subscore of 0 and a Mayo endoscopy subscore of 0 or 1.

The Adapted Mayo score was the sum of three components: rectal bleeding, stool frequency, and Mayo endoscopic subscore, each measured on a scale of 0-3 with higher scores reflecting higher severity.

mITT Analysis Set (Induction Period): Comprised all randomized participants who received at least one dose of study drug.

End point type	Secondary

End point timeframe:

Week 8

End point values	Induction Period: Placebo	Induction Period: TD-1473 20 mg	Induction Period: TD-1473 80 mg	Induction Period: TD-1473 200 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	61	61	59	58
Units: participants	6	6	4	4

Statistical analyses

Statistical analysis title	Placebo v TD-1473 20 mg
Statistical analysis description:	
Difference in proportion estimates used Mantel-Haenszel stratum weights.	
Comparison groups	Induction Period: Placebo v Induction Period: TD-1473 20 mg
Number of subjects included in analysis	122
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9542 [1]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in Proportion
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.104
upper limit	0.11

Notes:

[1] - P-value is shown for Cochran-Mantel Haenszel tests stratified by prior biologic failure and steroid use at baseline.

Statistical analysis title	Placebo v TD-1473 80 mg
Statistical analysis description:	
Difference in proportion estimates used Mantel-Haenszel stratum weights.	
Comparison groups	Induction Period: Placebo v Induction Period: TD-1473 80 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5863 [2]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in Proportion
Point estimate	-0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.126
upper limit	0.071

Notes:

[2] - P-value is shown for Cochran-Mantel Haenszel tests stratified by prior biologic failure and steroid use at baseline.

Statistical analysis title	Placebo v TD-1473 200 mg
Statistical analysis description:	
Difference in proportion estimates used Mantel-Haenszel stratum weights.	
Comparison groups	Induction Period: Placebo v Induction Period: TD-1473 200 mg
Number of subjects included in analysis	119
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5408 [3]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in Proportion
Point estimate	-0.03

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.131
upper limit	0.069

Notes:

[3] - P-value is shown for Conhran-Mantel Haenszel tests stratified by prior biologic failure and steroid use at baseline.

Secondary: Phase 3 Maintenance: Number of Participants Who Demonstrated a Clinical Response by Adapted Mayo Score Components at mWeek 44

End point title	Phase 3 Maintenance: Number of Participants Who Demonstrated a Clinical Response by Adapted Mayo Score Components at mWeek 44

End point description:

Clinical response was defined as a reduction from baseline in adapted Mayo score of ≥ 2 points and ≥ 30% relative to baseline. It also required ≥ 1 reduction in the rectal bleeding subscore or an absolute subscore ≤ 1.

The Adapted Mayo score was the sum of three components: rectal bleeding, stool frequency, and Mayo endoscopic subscore, each measured on a scale of 0-3 with higher scores reflecting higher severity.

Participants with missing Week 44 values were imputed as non-responders.

mITT Analysis Set (Maintenance Period): All participants randomized into the Phase 3 Maintenance Study who were also treated. Only participants randomized at least 44 weeks prior to database lock were included.

End point type	Secondary

End point timeframe:

Baseline to mWeek 44

End point values	Maintenance Period: Placebo	Maintenance Period: TD-1473 20 mg	Maintenance Period: TD-1473 80 mg	Maintenance Period: TD-1473 200 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	8	13	11	8
Units: participants	5	5	8	6

Statistical analyses

Statistical analysis title	Placebo v TD-1473 20 mg
Comparison groups	Maintenance Period: Placebo v Maintenance Period: TD-1473 20 mg
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6656
Method	Fisher exact

Statistical analysis title	Placebo v TD-1473 80 mg
Comparison groups	Maintenance Period: Placebo v Maintenance Period: TD-1473 80 mg
Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6424
Method	Fisher exact

Statistical analysis title	Placebo v TD-1473 200 mg
Comparison groups	Maintenance Period: Placebo v Maintenance Period: TD-1473 200 mg
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6199
Method	Fisher exact

Secondary: Phase 3 Maintenance: Number of Participants Who Demonstrated Endoscopic Remission by Adapted Mayo Score Components at mWeek 44

End point title	Phase 3 Maintenance: Number of Participants Who Demonstrated Endoscopic Remission by Adapted Mayo Score Components at mWeek 44

End point description:

Endoscopic remission was defined as an endoscopic subscore ≤ 1.

Endoscopic subscore was measured using scale of 0-3, where higher numbers reflected greater severity.

mITT Analysis Set (Maintenance Period): All participants randomized into the Phase 3 Maintenance Study who were also treated. Only participants randomized at least 44 weeks prior to database lock were included.

End point type	Secondary

End point timeframe:

mWeek 44

End point values	Maintenance Period: Placebo	Maintenance Period: TD-1473 20 mg	Maintenance Period: TD-1473 80 mg	Maintenance Period: TD-1473 200 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	13	11	8
Units: participants	3	1	3	2

Statistical analyses

Statistical analysis title	Placebo v TD-1473 20 mg
Comparison groups	Maintenance Period: Placebo v Maintenance Period: TD-1473 20 mg
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2643
Method	Fisher exact

Statistical analysis title	Placebo v TD-1473 80 mg
Comparison groups	Maintenance Period: Placebo v Maintenance Period: TD-1473 80 mg
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 1
Method	Fisher exact

Statistical analysis title	Placebo v TD-1473 200 mg
Comparison groups	Maintenance Period: Placebo v Maintenance Period: TD-1473 200 mg
Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 1
Method	Fisher exact

Secondary: Phase 3 Maintenance: Number of Participants Who Demonstrated Symptomatic Remission by Adapted Mayo Score Components at mWeek 44

End point title	Phase 3 Maintenance: Number of Participants Who Demonstrated Symptomatic Remission by Adapted Mayo Score Components at mWeek 44

End point description:

Symptomatic remission was defined as a stool frequency score ≤ 1 and a rectal bleeding subscore of 0.

Stool frequency score and rectal bleeding score were each measured using scale of 0-3, where higher numbers reflected greater severity.

Participants with missing Week 44 values were imputed as non-responders.

mITT Analysis Set (Maintenance Period): All participants randomized into the Phase 3 Maintenance Study who were also treated. Only participants randomized at least 44 weeks prior to database lock were included.

End point type	Secondary

End point timeframe:

mWeek 44

End point values	Maintenance Period: Placebo	Maintenance Period: TD-1473 20 mg	Maintenance Period: TD-1473 80 mg	Maintenance Period: TD-1473 200 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	13	11	8
Units: participants	5	7	7	5

Statistical analyses

Statistical analysis title	Placebo v TD-1473 20 mg
Comparison groups	Maintenance Period: Placebo v Maintenance Period: TD-1473 20 mg
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 1
Method	Fisher exact

Statistical analysis title	Placebo v TD-1473 80 mg
Comparison groups	Maintenance Period: Placebo v Maintenance Period: TD-1473 80 mg
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 1
Method	Fisher exact

Statistical analysis title	Placebo v TD-1473 200 mg
Comparison groups	Maintenance Period: Placebo v Maintenance Period: TD-1473 200 mg
Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 1
Method	Fisher exact

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Induction Period: Up to Week 20 Maintenance Period: Up to Week 48

Adverse event reporting additional description:

The Safety analysis set included all participants who received at least one dose of study drug (TD-1473 or placebo).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups

Reporting group title	Induction Period: Placebo

Reporting group description:

Participants who were randomized to receive once-daily administrations of placebo for 8 weeks during the Induction Period.

Reporting group title	Induction Period: TD-1473 20 mg

Reporting group description:

Participants who were randomized to receive once-daily administrations of 20 mg TD-1473 for 8 weeks during the Induction Period.

Participants who did not achieve clinical response at Week 8 continued to receive 20 mg TD-1473 for 8 weeks in the Extended Induction Period.

Reporting group title	Induction Period: TD-1473 80 mg

Reporting group description:

Participants who were randomized to receive once-daily administrations of 80 mg TD-1473 for 8 weeks during the Induction Period.

Participants who did not achieve clinical response at Week 8 continued to receive 80 mg TD-1473 for 8 weeks in the Extended Induction Period.

Reporting group title	Induction Period: Placebo to TD-1473 80 mg

Reporting group description:

Participants who were randomized to receive once-daily administrations of placebo for 8 weeks during the Induction Period.

Participants who did not achieve clinical response at Week 8 received 80 mg TD-1473 for 8 weeks in the Extended Induction Period.

Reporting group title	Induction Period: TD-1473 200 mg

Reporting group description:

Participants who were randomized to receive once-daily administrations of 200 mg TD-1473 for 8 weeks during the Induction Period.

Participants who did not achieve clinical response at Week 8 continued to receive 200 mg TD-1473 for 8 weeks in the Extended Induction Period.

Reporting group title	Maintenance Period: Placebo

Reporting group description:

Participants who were randomized to receive once-daily administrations of placebo for 8 weeks during the Induction Period and achieved clinical response by adapted Mayo Score at Week 8 of the Induction Period continued to receive blinded placebo for 44 weeks in the Maintenance Period.

Reporting group title	Maintenance Period: TD-1473 20 mg

Reporting group description:

Participants who achieved clinical response to a total of 8 weeks of TD-1473 induction therapy, either at Week 8 or Week 16, and were re-randomized to 20 mg TD-1473 for 44 weeks in the Maintenance Period.

Reporting group title	Maintenance Period: TD-1473 80 mg

Reporting group description:

Participants who achieved clinical response to a total of 8 weeks of TD-1473 induction therapy, either at Week 8 or Week 16, and were re-randomized to 80 mg TD-1473 for 44 weeks in the Maintenance Period.

Reporting group title	Maintenance Period: TD-1473 200 mg

Reporting group description:

Participants who achieved clinical response to a total of 8 weeks of TD-1473 induction therapy, either at Week 8 or Week 16, and were re-randomized to 200 mg TD-1473 for 44 weeks in the Maintenance Period.

Serious adverse events	Induction Period: Placebo	Induction Period: TD-1473 20 mg	Induction Period: TD-1473 80 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 61 (6.56%)	4 / 61 (6.56%)	2 / 59 (3.39%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	0 / 61 (0.00%)	1 / 61 (1.64%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine leiomyoma			
subjects affected / exposed	0 / 61 (0.00%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Joint injury			
subjects affected / exposed	0 / 61 (0.00%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 61 (0.00%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			

subjects affected / exposed	0 / 61 (0.00%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Large intestine operation			
subjects affected / exposed	0 / 61 (0.00%)	0 / 61 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed	2 / 61 (3.28%)	3 / 61 (4.92%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Tubulointerstitial nephritis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urethral stenosis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 61 (0.00%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rhabdomyolysis			

subjects affected / exposed	1 / 61 (1.64%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cytomegalovirus colitis			
subjects affected / exposed	1 / 61 (1.64%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver abscess			
subjects affected / exposed	0 / 61 (0.00%)	1 / 61 (1.64%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Induction Period: Placebo to TD-1473 80 mg	Induction Period: TD-1473 200 mg	Maintenance Period: Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 42 (7.14%)	4 / 58 (6.90%)	1 / 29 (3.45%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	0 / 42 (0.00%)	0 / 58 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine leiomyoma			
subjects affected / exposed	0 / 42 (0.00%)	0 / 58 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Joint injury			
subjects affected / exposed	0 / 42 (0.00%)	0 / 58 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			

subjects affected / exposed	1 / 42 (2.38%)	0 / 58 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	0 / 42 (0.00%)	1 / 58 (1.72%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Large intestine operation			
subjects affected / exposed	0 / 42 (0.00%)	0 / 58 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 42 (0.00%)	1 / 58 (1.72%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed	1 / 42 (2.38%)	2 / 58 (3.45%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Tubulointerstitial nephritis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 58 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urethral stenosis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 58 (0.00%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			

subjects affected / exposed	1 / 42 (2.38%)	0 / 58 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rhabdomyolysis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 58 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cytomegalovirus colitis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 58 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver abscess			
subjects affected / exposed	0 / 42 (0.00%)	0 / 58 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Maintenance Period: TD-1473 20 mg	Maintenance Period: TD-1473 80 mg	Maintenance Period: TD-1473 200 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 31 (6.45%)	2 / 25 (8.00%)	1 / 22 (4.55%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	0 / 31 (0.00%)	0 / 25 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine leiomyoma			
subjects affected / exposed	0 / 31 (0.00%)	1 / 25 (4.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Joint injury			

subjects affected / exposed	1 / 31 (3.23%)	0 / 25 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 31 (0.00%)	0 / 25 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	0 / 31 (0.00%)	0 / 25 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Large intestine operation			
subjects affected / exposed	0 / 31 (0.00%)	0 / 25 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 31 (0.00%)	0 / 25 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed	0 / 31 (0.00%)	1 / 25 (4.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Tubulointerstitial nephritis			
subjects affected / exposed	1 / 31 (3.23%)	0 / 25 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urethral stenosis			

subjects affected / exposed	0 / 31 (0.00%)	0 / 25 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 31 (0.00%)	0 / 25 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rhabdomyolysis			
subjects affected / exposed	0 / 31 (0.00%)	0 / 25 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cytomegalovirus colitis			
subjects affected / exposed	0 / 31 (0.00%)	0 / 25 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver abscess			
subjects affected / exposed	0 / 31 (0.00%)	0 / 25 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	Induction Period: Placebo	Induction Period: TD-1473 20 mg	Induction Period: TD-1473 80 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 61 (11.48%)	11 / 61 (18.03%)	9 / 59 (15.25%)
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 61 (3.28%)	0 / 61 (0.00%)	2 / 59 (3.39%)
occurrences (all)	3	0	2
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	1 / 61 (1.64%)	2 / 61 (3.28%)	2 / 59 (3.39%)
occurrences (all)	1	4	2
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	2 / 61 (3.28%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences (all)	2	0	0
Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed	1 / 61 (1.64%)	3 / 61 (4.92%)	5 / 59 (8.47%)
occurrences (all)	1	4	7
Haemorrhoids			
subjects affected / exposed	0 / 61 (0.00%)	0 / 61 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 61 (1.64%)	6 / 61 (9.84%)	0 / 59 (0.00%)
occurrences (all)	1	6	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 61 (1.64%)	1 / 61 (1.64%)	1 / 59 (1.69%)
occurrences (all)	1	1	1

Non-serious adverse events	Induction Period: Placebo to TD-1473 80 mg	Induction Period: TD-1473 200 mg	Maintenance Period: Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 42 (9.52%)	14 / 58 (24.14%)	6 / 29 (20.69%)
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 42 (2.38%)	2 / 58 (3.45%)	1 / 29 (3.45%)
occurrences (all)	1	2	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 42 (2.38%)	2 / 58 (3.45%)	1 / 29 (3.45%)
occurrences (all)	1	2	1
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 42 (0.00%)	0 / 58 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0

Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed	1 / 42 (2.38%)	7 / 58 (12.07%)	4 / 29 (13.79%)
occurrences (all)	1	7	4
Haemorrhoids			
subjects affected / exposed	0 / 42 (0.00%)	0 / 58 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 42 (0.00%)	4 / 58 (6.90%)	0 / 29 (0.00%)
occurrences (all)	0	4	0
Upper respiratory tract infection			
subjects affected / exposed	2 / 42 (4.76%)	0 / 58 (0.00%)	2 / 29 (6.90%)
occurrences (all)	2	0	2

Non-serious adverse events	Maintenance Period: TD-1473 20 mg	Maintenance Period: TD-1473 80 mg	Maintenance Period: TD-1473 200 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 31 (45.16%)	5 / 25 (20.00%)	1 / 22 (4.55%)
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 31 (6.45%)	1 / 25 (4.00%)	0 / 22 (0.00%)
occurrences (all)	2	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 31 (9.68%)	0 / 25 (0.00%)	1 / 22 (4.55%)
occurrences (all)	5	0	1
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	2 / 31 (6.45%)	0 / 25 (0.00%)	0 / 22 (0.00%)
occurrences (all)	2	0	0
Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed	6 / 31 (19.35%)	3 / 25 (12.00%)	0 / 22 (0.00%)
occurrences (all)	6	3	0
Haemorrhoids			
subjects affected / exposed	2 / 31 (6.45%)	0 / 25 (0.00%)	0 / 22 (0.00%)
occurrences (all)	2	0	0
Infections and infestations			

Nasopharyngitis			
subjects affected / exposed	0 / 31 (0.00%)	1 / 25 (4.00%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 31 (0.00%)	0 / 25 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 October 2018	Changes were made to the following protocol sections: • Eligibility criteria • Study drugs • Study procedures • Statistical considerations
09 January 2020	Changes were made to the following protocol sections: • Objectives and endpoints • Eligibility criteria • Schedule of study procedures • Study procedures • Adverse events • Statistical considerations • Appendices
29 May 2020	Changes were made to the following protocol sections: • Study design • Eligibility criteria • Schedule of study procedures • Study drugs • Study procedures • Adverse events • Statistical considerations • Appendices

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Stopped early due to company decision. Company decision based on interim analysis results in TD-1473-0157

Notes: