Clinical trial results:
A 3-Year, Multi-Center, Long-Term Safety (LTS) Study to Evaluate the Safety and Tolerability of TD-1473 in Subjects with Ulcerative Colitis (UC)

Summary

EudraCT number	2018-002135-19
Trial protocol	HU DE PT SK FR PL ES GR BG IT RO
Global end of trial date	27 October 2021

Results information

Result version number	v1 (current)
This version publication date	26 October 2022
First version publication date	26 October 2022

Trial information

Trial identification

Sponsor protocol code	0164

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03920254
WHO universal trial number (UTN)	-
Other trial identifiers	US IND Number: 128299

Notes:

Sponsors

Sponsor organisation name	Theravance Biopharma Ireland Limited
Sponsor organisation address	10 Earlsfort Terrace, Dublin, Ireland, D04 C5Y6
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	27 October 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 October 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To assess the safety and tolerability of TD-1473 administered up to 3 years in participants with moderate to severe UC after participation in the Maintenance Study of Protocol 0157 (EudraCT number: 2018-002136-24).

Protection of trial subjects:

This trial was conducted in accordance with the ethical principles of Good Clinical Practice, according to the International Conference on Harmonization Harmonised Tripartite Guideline.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 July 2020
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: 9
Country: Number of subjects enrolled	Portugal: 2
Country: Number of subjects enrolled	Slovakia: 1
Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	Bulgaria: 5
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	Italy: 1
Country: Number of subjects enrolled	Ukraine: 8
Country: Number of subjects enrolled	Japan: 5
Country: Number of subjects enrolled	Serbia: 5
Country: Number of subjects enrolled	United States: 4
Country: Number of subjects enrolled	Australia: 2
Country: Number of subjects enrolled	Georgia: 1
Worldwide total number of subjects	46
EEA total number of subjects	21

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)	40
From 65 to 84 years	6
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 46 out of the planned 500 participants were enrolled and received study drug between 23 July 2020 and 27 October 2021.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	TD-1473 20mg

Arm description:

Participants received TD-1473 orally at a dose of 20mg once daily.

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 80mg

Arm description:

Participants received TD-1473 orally at a dose of 80mg once daily.

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 200mg

Arm description:

Participants received TD-1473 orally at a dose of 200mg once daily.

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	TD-1473 20mg	TD-1473 80mg	TD-1473 200mg
Started	13	18	15
Completed	0	0	0
Not completed	13	18	15
Physician decision	-	1	2
Consent withdrawn by subject	-	-	1
Adverse event, non-fatal	1	-	-
Study Terminated By Sponsor	12	17	12

Baseline characteristics

Reporting groups	
Reporting group title	TD-1473 20mg
Reporting group description:	
Participants received TD-1473 orally at a dose of 20mg once daily.	
Reporting group title	TD-1473 80mg
Reporting group description:	
Participants received TD-1473 orally at a dose of 80mg once daily.	
Reporting group title	TD-1473 200mg
Reporting group description:	
Participants received TD-1473 orally at a dose of 200mg once daily.	

Reporting group values	TD-1473 20mg	TD-1473 80mg	TD-1473 200mg
Number of subjects	13	18	15
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	46.31	43.22	46.13
standard deviation	± 17.375	± 15.869	± 13.432
Gender categorical Units: Subjects			
Female	8	7	7
Male	5	11	8
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1	1	0
Not Hispanic or Latino	12	17	15
Unknown or Not Reported	0	0	0
Race (NIH/OMB) Units: Subjects			
Asian	1	3	1
White	12	15	13
Unknown or Not Reported	0	0	1

Reporting group values	Total		
Number of subjects	46		
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean			
standard deviation	-		

Gender categorical Units: Subjects			
Female	22		
Male	24		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	2		
Not Hispanic or Latino	44		
Unknown or Not Reported	0		
Race (NIH/OMB) Units: Subjects			
Asian	5		
White	40		
Unknown or Not Reported	1		

End points

End points reporting groups

Reporting group title	TD-1473 20mg
Reporting group description:	
Participants received TD-1473 orally at a dose of 20mg once daily.	
Reporting group title	TD-1473 80mg
Reporting group description:	
Participants received TD-1473 orally at a dose of 80mg once daily.	
Reporting group title	TD-1473 200mg
Reporting group description:	
Participants received TD-1473 orally at a dose of 200mg once daily.	

Primary: Number of Participants Who Experienced a Treatment-emergent Adverse Event (TEAE)

End point title	Number of Participants Who Experienced a Treatment-emergent Adverse Event (TEAE)[1]
End point description:	
A TEAE was defined as any AE with a recorded start date on or after the date of the first dose of study drug up through 4 weeks after the last dose of study drug. Any clinically significant changes in laboratory safety tests, electrocardiograms (ECGs) and vital signs, were also recorded as TEAEs. Includes all participants from the Safety Analysis Set.	
End point type	Primary
End point timeframe:	
Day 1 up to 4 weeks after last dose of study drug (median treatment duration was: TD-1473 20 mg - 142 days; TD-1473 80 mg - 180 days; TD-1473 200 mg - 158 days)	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No additional statistical analyses were pre-specified for this endpoint.

End point values	TD-1473 20mg	TD-1473 80mg	TD-1473 200mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	18	15	
Units: participants	4	5	6	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Day 1 up to 4 weeks after last dose of study drug (median treatment duration was: TD-1473 20 mg - 142 days; TD-1473 80 mg - 180 days; TD-1473 200 mg - 158 days)	
Adverse event reporting additional description:	
Includes all participants from the Safety Analysis Set.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups	
Reporting group title	TD-1473 20mg
Reporting group description:	
Participants received TD-1473 orally at a dose of 20mg once daily.	
Reporting group title	TD-1473 80mg
Reporting group description:	
Participants received TD-1473 orally at a dose of 80mg once daily.	
Reporting group title	TD-1473 200mg
Reporting group description:	
Participants received TD-1473 orally at a dose of 200mg once daily.	

Serious adverse events	TD-1473 20mg	TD-1473 80mg	TD-1473 200mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 13 (0.00%)	0 / 18 (0.00%)	1 / 15 (6.67%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Blood and lymphatic system disorders			
Anaemia of chronic disease			
subjects affected / exposed	0 / 13 (0.00%)	0 / 18 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	TD-1473 20mg	TD-1473 80mg	TD-1473 200mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 13 (30.77%)	5 / 18 (27.78%)	5 / 15 (33.33%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Skin papilloma			
subjects affected / exposed	0 / 13 (0.00%)	1 / 18 (5.56%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 13 (7.69%)	0 / 18 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	2 / 13 (15.38%)	0 / 18 (0.00%)	0 / 15 (0.00%)
occurrences (all)	2	0	0
Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed	1 / 13 (7.69%)	3 / 18 (16.67%)	1 / 15 (6.67%)
occurrences (all)	1	3	1
Diarrhoea			
subjects affected / exposed	1 / 13 (7.69%)	0 / 18 (0.00%)	0 / 15 (0.00%)
occurrences (all)	2	0	0
Reproductive system and breast disorders			
Endometriosis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 18 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 13 (7.69%)	0 / 18 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Rhinorrhoea			
subjects affected / exposed	1 / 13 (7.69%)	0 / 18 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Eczema asteatotic			
subjects affected / exposed	0 / 13 (0.00%)	1 / 18 (5.56%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Depression			

subjects affected / exposed	0 / 13 (0.00%)	1 / 18 (5.56%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 18 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 13 (0.00%)	0 / 18 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Chlamydial infection			
subjects affected / exposed	0 / 13 (0.00%)	0 / 18 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Clostridium difficile infection			
subjects affected / exposed	1 / 13 (7.69%)	0 / 18 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Tinea pedis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 18 (5.56%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 13 (0.00%)	1 / 18 (5.56%)	0 / 15 (0.00%)
occurrences (all)	0	2	0
Urinary tract infection			
subjects affected / exposed	0 / 13 (0.00%)	0 / 18 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 13 (0.00%)	0 / 18 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 November 2018	This protocol was amended to correct incorrect formatting , correct incorrect spelling, correct incorrect references to sections within the protocol, delete duplicated information, add updated information throughout, clarify wording, add updated results of a completed study, include minor administration changes.
15 February 2021	This protocol was amended to clarify some key points related to the inclusion and exclusion criteria. Additionally, some administrative updates were made along with some additional clarifications to provide operational guidance to sites on the appropriate implementation of key study activities. Lastly, typographical errors were corrected.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
18 March 2020	The Sponsor notified all global clinical research sites in writing that screening of new participants was suspended initially for a period of 4 weeks (18 March 2020 to 17 April 2020) with planned reassessment thereafter. Participants already enrolled in the study screening period at the time of this notification could progress to randomization if they met safety criteria as specified by the Medical Director or per the study-specific COVID-19 mitigation plan.	17 April 2020

Notes:

Limitations and caveats

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

Study 0164 was terminated early because Study 0157 was terminated early and participation in Study 0164 was predicated on participation in Study 0157.

Notes: