Clinical trial results:
A Phase IIa, Multicenter, Randomized, Double-Blind, Parallel- Group, Placebo-Controlled, Proof of Concept Study to Evaluate the Efficacy and Safety of Orally Administered TU2670 in Subjects with Moderate to Severe Endometriosis-Associated Pain

Summary

EudraCT number	2020-000090-25
Trial protocol	IT
Global end of trial date	08 August 2024

Results information

Result version number	v1 (current)
This version publication date	07 February 2025
First version publication date	07 February 2025

Trial information

Trial identification

Sponsor protocol code	TUC3PII-01

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05138562
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	TiumBio Co., Ltd.
Sponsor organisation address	6F, Pangyo IT Center, 30 Changup-ro 40 beon-gil, Sujeong-gu, Seongnam-si, Gyeonggi-do, Korea, Republic of, 13449
Public contact	TiumBio General Inquiry, TiumBio, tiumbio@tiumbio.com
Scientific contact	TiumBio General Inquiry, TiumBio, tiumbio@tiumbio.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	23 January 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	08 August 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy and safety of orally administered TU2670 in the reduction of endometriosis-associated pain compared with placebo after 12 weeks of treatment.

Protection of trial subjects:

The study was conducted in accordance with the protocol, the ethical principles derived from international guidelines including the Declaration of Helsinki and Council for International Organizations of Medical Sciences, International Ethical Guidelines, applicable International Council for Harmonization Good Clinical Practice and other guidelines, and applicable laws and regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 August 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Czechia: 14
Country: Number of subjects enrolled	Italy: 2
Country: Number of subjects enrolled	Poland: 53
Country: Number of subjects enrolled	Russian Federation: 7
Country: Number of subjects enrolled	Ukraine: 10
Worldwide total number of subjects	86
EEA total number of subjects	69

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)	86
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This Phase IIa, randomized, placebo-controlled study was conducted in subjects with moderate to severe endometriosis-associated pain at 27 study centers.

Pre-assignment

Screening details:

This study consists of a washout period (up to 12 weeks), screening period (up to 12 weeks), randomized treatment period (12 weeks) and follow-up period (12 weeks). Subjects were randomly assigned to receive either TU2670 120 milligram (mg), TU2670 240 mg, TU2670 320 mg, or matching placebo. A total of 86 subjects were enrolled in the study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	TU2670 120 mg

Arm description:

Subjects received TU2670 120 mg capsule orally once daily for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	TU2670
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Hard gelatin capsule of TU2670 was administered once daily in the morning after an overnight fast, preferably around the same time every day.

Arm title	TU2670 240 mg

Arm description:

Subjects received TU2670 240 mg capsule orally once daily for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	TU2670
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Hard gelatin capsule of TU2670 was administered once daily in the morning after an overnight fast, preferably around the same time every day.

Arm title	TU2670 320 mg

Arm description:

Subjects received TU2670 320 mg capsule orally once daily for 12 weeks.

Arm type	Experimental

Investigational medicinal product name	TU2670
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Hard gelatin capsule of TU2670 was administered once daily in the morning after an overnight fast, preferably around the same time every day.

Arm title	Placebo

Arm description:

Subjects received placebo matching with TU2670 capsule orally once daily for 12 weeks.

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

Dosage and administration details:

Hard gelatin capsule of placebo matching with TU2670 was administered once daily in the morning after an overnight fast, preferably around the same time every day.

Number of subjects in period 1	TU2670 120 mg	TU2670 240 mg	TU2670 320 mg
Started	20	21	22
Completed	20	19	20
Not completed	0	2	2
Consent withdrawn by subject	-	1	-
Adverse event, non-fatal	-	1	1
Lost to follow-up	-	-	1
Protocol deviation	-	-	-

Number of subjects in period 1	Placebo
Started	23
Completed	20
Not completed	3
Consent withdrawn by subject	2
Adverse event, non-fatal	-
Lost to follow-up	-
Protocol deviation	1

Baseline characteristics

Reporting groups	
Reporting group title	TU2670 120 mg
Reporting group description:	
Subjects received TU2670 120 mg capsule orally once daily for 12 weeks.	
Reporting group title	TU2670 240 mg
Reporting group description:	
Subjects received TU2670 240 mg capsule orally once daily for 12 weeks.	
Reporting group title	TU2670 320 mg
Reporting group description:	
Subjects received TU2670 320 mg capsule orally once daily for 12 weeks.	
Reporting group title	Placebo
Reporting group description:	
Subjects received placebo matching with TU2670 capsule orally once daily for 12 weeks.	

Reporting group values	TU2670 120 mg	TU2670 240 mg	TU2670 320 mg
Number of subjects	20	21	22
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	33.5	36.0	33.5
standard deviation	± 6.02	± 7.25	± 5.69
Gender categorical Units: Subjects			
Female	20	21	22
Male	0	0	0
Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Black or African American	0	0	0
Native Hawaiian or Other Pacific Islanders	0	0	0
White	20	21	22
Other	0	0	0
Not Reported	0	0	0
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	20	20	22
Not Reported	0	1	0
Unknown	0	0	0

Reporting group values	Placebo	Total	
Number of subjects	23	86	

Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean	33.8		
standard deviation	± 6.29	-	
Gender categorical Units: Subjects			
Female	23	86	
Male	0	0	
Race Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	0	0	
Black or African American	0	0	
Native Hawaiian or Other Pacific Islanders	0	0	
White	23	86	
Other	0	0	
Not Reported	0	0	
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	22	84	
Not Reported	1	2	
Unknown	0	0	

End points

End points reporting groups

Reporting group title	TU2670 120 mg
Reporting group description:	
Subjects received TU2670 120 mg capsule orally once daily for 12 weeks.	
Reporting group title	TU2670 240 mg
Reporting group description:	
Subjects received TU2670 240 mg capsule orally once daily for 12 weeks.	
Reporting group title	TU2670 320 mg
Reporting group description:	
Subjects received TU2670 320 mg capsule orally once daily for 12 weeks.	
Reporting group title	Placebo
Reporting group description:	
Subjects received placebo matching with TU2670 capsule orally once daily for 12 weeks.	

Primary: Change From Baseline in Mean Dysmenorrhea Score at Week 12

End point title	Change From Baseline in Mean Dysmenorrhea Score at Week 12

End point description:

Mean Dysmenorrhea Score was defined as mean overall pelvic pain (OPP) score on menstrual bleeding days as measured by the Numeric Rating Scale (NRS) over the past month. The electronic NRS was self-completed by subjects in the electronic (e)-diary daily for the duration of the study. The total score on NRS range from 0 to 10 where 0= no pain and 10= worst pain imaginable. Higher scores indicate worse outcome. Baseline cycle was defined as cycle which started within Day -84 and ended at 1 day before next menstrual cycle. If multiple cycles were there, then last complete cycle prior to Visit 2 was considered. The full analysis set (FAS) included all subjects randomly assigned to study treatment and who took at least 1 dose of study treatment and had at least 1 post-baseline assessment available.

End point type	Primary

End point timeframe:

Baseline and Week 12

End point values	TU2670 120 mg	TU2670 240 mg	TU2670 320 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	18	19	21
Units: score on a scale				
arithmetic mean (standard deviation)	-4.8 (± 3.22)	-5.3 (± 2.39)	-5.9 (± 2.21)	-2.5 (± 2.78)

Statistical analyses

Statistical analysis title	Treatment difference in Mean Dysmenorrhea Score

Statistical analysis description:

Analysis was performed on the data in which the missing mean monthly NRS pain scores at Week 12 were imputed by having the previous visit value carried forward using last observation carried forward (LOCF).

Comparison groups	TU2670 120 mg v Placebo
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.044 [1]
Method	ANCOVA
Parameter estimate	Least Square (LS) Mean Difference
Point estimate	-1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3
upper limit	0
Variability estimate	Standard error of the mean
Dispersion value	0.75

Notes:

[1] - Estimates, 2-sided 95% confidence intervals and p-values were obtained using an analysis of covariance (ANCOVA) model with dose group as a fixed factor and baseline mean dysmenorrhea score as covariate at 5% significance level.

Statistical analysis title	Treatment difference in Mean Dysmenorrhea Score

Statistical analysis description:

Analysis was performed on the data in which the missing mean monthly NRS pain scores at Week 12 were imputed by having the previous visit value carried forward using LOCF.

Comparison groups	TU2670 240 mg v Placebo
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001 [2]
Method	ANCOVA
Parameter estimate	Least Square (LS) Mean Difference
Point estimate	-2.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.2
upper limit	-1.2
Variability estimate	Standard error of the mean
Dispersion value	0.76

Notes:

[2] - Estimates, 2-sided 95% confidence intervals and p-values were obtained using an ANCOVA model with dose group as a fixed factor and baseline mean dysmenorrhea score as covariate at 5% significance level.

Statistical analysis title	Treatment difference in Mean Dysmenorrhea Score

Statistical analysis description:

Analysis was performed on the data in which the missing mean monthly NRS pain scores at Week 12 were imputed by having the previous visit value carried forward using LOCF.

Comparison groups	TU2670 320 mg v Placebo

Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [3]
Method	ANCOVA
Parameter estimate	Least Square (LS) Mean Difference
Point estimate	-3.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.9
upper limit	-1.9
Variability estimate	Standard error of the mean
Dispersion value	0.75

Notes:

[3] - Estimates, 2-sided 95% confidence intervals and p-values were obtained using an ANCOVA model with dose group as a fixed factor and baseline mean dysmenorrhea score as covariate at 5% significance level.

Secondary: Change From Baseline in Mean Numeric Rating Scale Pain Score for Non-Menstrual Pelvic Pain (NMPP) at Week 12

End point title	Change From Baseline in Mean Numeric Rating Scale Pain Score for Non-Menstrual Pelvic Pain (NMPP) at Week 12

End point description:

Mean NRS pain score for NMPP was the mean NRS pain score on non-menstrual bleeding days. The mean NMPP (non-menstrual days) was calculated for each cycle as the total of daily NMPP scores reported during the cycle divided by the number of days during the cycle when a NMPP score was reported. The electronic NRS was self-completed by subjects in the e-diary daily for the duration of the study. The total score on NRS range from 0 to 10 where 0=no pain and 10=worst pain imaginable. Higher scores indicate worse outcome. Baseline Cycle was defined as cycle which started within day -84 and ended at 1 day before next menstrual cycle. If multiple cycles were there, then last complete cycle prior to Visit 2 was considered. The FAS included all subjects randomly assigned to study treatment and who took at least 1 dose of study treatment and had at least 1 post-baseline assessment available. Only subjects with data collected at Baseline and Week 12 are reported.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	TU2670 120 mg	TU2670 240 mg	TU2670 320 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	19	19	19
Units: score on a scale				
arithmetic mean (standard deviation)	-2.6 (± 1.95)	-2.3 (± 2.13)	-2.8 (± 2.13)	-1.4 (± 1.55)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Mean Overall Pelvic Pain Numeric Rating Scale Pain Score at Week 12

End point title	Change From Baseline in Mean Overall Pelvic Pain Numeric Rating Scale Pain Score at Week 12

End point description:

Mean OPP NRS pain was the mean NRS pain score over all 28 days. The mean OPP (including menstrual and non-menstrual bleeding days) was calculated for each cycle as the total of daily OPP scores reported during the cycle divided by the number of days during the cycle when an OPP score was reported. The electronic NRS was self-completed by subjects in the e-diary daily for the duration of the study. The total score on NRS range from 0 to 10 where 0=no pain and 10=worst pain imaginable. Higher scores indicate worse outcome. Baseline Cycle was defined as cycle which started within day -84 and ended at 1 day before next menstrual cycle. If multiple cycles were there, then last complete cycle prior to Visit 2 was considered. The FAS included all subjects randomly assigned to study treatment and who took at least 1 dose of study treatment and had at least 1 post-baseline assessment available. Only subjects with data collected at Baseline and Week 12 are reported.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	TU2670 120 mg	TU2670 240 mg	TU2670 320 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	19	19	19
Units: score on a scale				
arithmetic mean (standard deviation)	-2.8 (± 2.01)	-2.6 (± 2.18)	-3.2 (± 1.98)	-1.6 (± 1.55)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Mean Numeric Rating Scale Dyspareunia Score at Week 12

End point title	Change From Baseline in Mean Numeric Rating Scale Dyspareunia Score at Week 12

End point description:

Mean dyspareunia was based upon response information collected from diary for question 'Did you have sexual intercourse including penetration over the past 24 hours?' as 'Yes'. Electronic NRS was self-completed by subjects in e-diary daily. Total score: ranged from 0 to 10 where 0=no pain and 10=worst pain imaginable. Higher scores: worse outcome. Mean dyspareunia score was calculated for each cycle as total of dyspareunia scores divided by number of days when subjects engaged in any sexual activity that involved full vaginal penetration. Baseline Cycle was defined as cycle which started within day -84 and ended at 1 day before next menstrual cycle. If multiple cycles were there, then last complete cycle prior to Visit 2 was considered. FAS: all subjects randomly assigned to study treatment and who took at least 1 dose of study treatment and had at least 1 post-baseline assessment available. Only subjects with data collected at Baseline and Week 12 are reported.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	TU2670 120 mg	TU2670 240 mg	TU2670 320 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	15	15	13
Units: score on a scale				
arithmetic mean (standard deviation)	-2.4 (± 2.24)	-2.7 (± 2.10)	-3.3 (± 2.54)	-1.4 (± 2.04)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the use of Protocol-Defined Rescue Medication at Week 12

End point title	Change From Baseline in the use of Protocol-Defined Rescue Medication at Week 12

End point description:

A responder was defined as a subject with a decrease in average daily rescue medication (ibuprofen) compared with baseline or who did not take rescue medication post-baseline. Baseline was defined as the last non-missing measurement taken prior to reference start date (-35 till Day 1), that is (i.e.), before first dose of study treatment. The FAS included all subjects randomly assigned to study treatment and who took at least 1 dose of study treatment and had at least 1 post-baseline assessment available. Only responders with data collected at Baseline and Week 12 are reported.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	TU2670 120 mg	TU2670 240 mg	TU2670 320 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	10	6	11
Units: Milligram (mg)				
arithmetic mean (standard deviation)	-1.3 (± 1.85)	-0.3 (± 0.43)	-1.2 (± 0.85)	-0.5 (± 0.69)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Responders who Used Protocol-Defined Rescue Medication at Week 12

End point title	Percentage of Responders who Used Protocol-Defined Rescue Medication at Week 12

End point description:

A responder was defined as a subject with a decrease in average daily rescue medication (ibuprofen) compared with baseline or who did not take rescue medication post-baseline. Baseline was defined as the last non-missing measurement taken prior to reference start date (-35 till day 1), i.e., before first dose of study treatment. The FAS included all subjects randomly assigned to study treatment and who took at least 1 dose of study treatment and had at least 1 post-baseline assessment available. Only subjects with data collected at Week 12 are reported.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	TU2670 120 mg	TU2670 240 mg	TU2670 320 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	19	18	21
Units: Percentage of responders				
number (not applicable)	95.0	89.5	100.0	90.5

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Modified Biberoglu and Behrman (MB&B) Sign and Symptom Scores at Week 12

End point title	Change From Baseline in Modified Biberoglu and Behrman (MB&B) Sign and Symptom Scores at Week 12

End point description:

MB&B scale consists of 2 parts. First part evaluates symptoms of endometriosis. There are 3 subscales: pelvic pain (A: 0=none and 3=severe), dysmenorrhea (B: 0=none and 3=severe), and deep dyspareunia (C: 0=none and 3=severe). Total pelvic pain score is sum of 3 scores (A+B+C) and ranges from 0 to 9;higher scores indicate worse outcome. Second part evaluates signs of endometriosis. There are 2 subscales pelvic tenderness (D: 0=none and 3=severe) and induration (E: 0=none and 3=severe). Total physical sign score is sum of two scores (D+E) and ranged from 0 to 6;higher scores indicate worse outcome. Total symptom and sign severity score is sum of all 5 scores (A+B+C+D+E) and ranges from 0 to 15;higher scores indicate worse outcome. Baseline: last non-missing measurement taken prior to reference start date (including unscheduled assessments), i.e., before first dose of study treatment. Analysis was performed on FAS. Only subjects with data collected at Baseline and Week 12 are reported

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	TU2670 120 mg	TU2670 240 mg	TU2670 320 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	18	18	19
Units: score on a scale				
arithmetic mean (standard deviation)	-5.9 (± 3.77)	-6.8 (± 3.43)	-6.7 (± 2.35)	-4.1 (± 3.65)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Patient Global Impression of Change (PGIC) Score at Week 12

End point title	Number of Subjects With Patient Global Impression of Change (PGIC) Score at Week 12

End point description:

PGIC score is recorded 4 weeks after initial treatment completion. The PGIC asks the subject to "check the box that best describes how your urinary and/or vaginal symptoms are now, compared with how your symptoms were before you began this study." It is measured using a 7-item scale, where 1: "Very Much Better", 2: "Much Better, 3: "A Little Better", 4: "No Change", 5: "A Little Worse", 6: "Much Worse", and 7: "Very Much Worse". The score ranges from 1-7; higher scores indicate worse outcome. The FAS included all subjects randomly assigned to study treatment and who took at least 1 dose of study treatment and had at least 1 post-baseline assessment available.

End point type	Secondary

End point timeframe:

Week 12

End point values	TU2670 120 mg	TU2670 240 mg	TU2670 320 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	20	21	22
Units: Participants				
Very much better	4	5	8	4
Much better	8	8	9	4
A little better	5	4	1	5
No change	1	1	1	5
A little worse	0	0	0	1
Much worse	0	0	0	1
Very much worse	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Endometriosis Health Profile (EHP)-5 Score at Week 12

End point title	Change From Baseline in Endometriosis Health Profile (EHP)-5 Score at Week 12

End point description:

EHP-5 is a valid short-form patient-reported outcome measure that was developed to measure health-related quality of life (QoL) in subjects with endometriosis. EHP consists of a core instrument which has 30 items divided into 5 different dimensions: pain (11 items), control and powerlessness (6 items), emotional well-being (6 items), lack of social support (4 items) and self-image (3 items). Items are answered on a 5-point Likert scale (0=never, 1=rarely, 2=sometimes, 3=often, 4=always). Scores in each dimension generate a sum score ranging from 0 (best possible health status) to 100 (worst possible health status); higher score indicates a worse QoL. Baseline: last non-missing measurement taken prior to reference start date (including unscheduled assessments), i.e., before first dose of study treatment. Analysis was performed on FAS. Only subjects with data collected at Baseline and Week 12 are reported.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	TU2670 120 mg	TU2670 240 mg	TU2670 320 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18	18	19	20
Units: score on a scale				
arithmetic mean (standard deviation)				
Pain	-0.9 (± 1.45)	-1.4 (± 1.20)	-1.6 (± 1.12)	-0.8 (± 0.77)
Control and powerlessness	-1.7 (± 0.91)	-1.7 (± 1.18)	-1.7 (± 1.19)	-0.9 (± 0.88)
Emotional well-being	-0.5 (± 1.15)	-1.3 (± 1.24)	-1.2 (± 1.38)	-1.5 (± 0.83)
Lack of social support	-1.0 (± 1.03)	-1.7 (± 1.19)	-1.3 (± 1.20)	-1.3 (± 0.92)
Self-image	-0.8 (± 0.81)	-1.0 (± 1.19)	-1.4 (± 1.38)	-0.8 (± 1.62)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in 36-Item Short Form Health Survey (SF-36) at Week 12

End point title	Change From Baseline in 36-Item Short Form Health Survey (SF-36) at Week 12

End point description:

SF-36 is a 36-item patient-reported scale which consists of 8 scaled scores: physical functioning scale (10 items), role physical scale (4 items), bodily pain scale (2 items), general health scale (5 items), vitality scale (4 items), social functioning scale (2 items), role emotional scale (4 items) and mental health scale (5 items). The score for a section is an average of the individual question scores, which are scaled 0-100; higher scores indicate better outcome. The summary score is comprised of a physical component summary (PCS) score and a mental component summary (MCS) score. The score ranges from 0 to 100; higher scores indicated better outcomes. Baseline was defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments), i.e., before first dose of study treatment. Analysis was performed on FAS. Only subjects with data collected at Baseline and Week 12 are reported.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	TU2670 120 mg	TU2670 240 mg	TU2670 320 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18	18	19	20
Units: score on a scale				
arithmetic mean (standard deviation)				
Physical functioning scale	20.0 (± 22.94)	19.7 (± 21.25)	20.5 (± 23.68)	15.8 (± 20.54)
Role physical scale	17.0 (± 17.26)	25.3 (± 19.93)	28.3 (± 27.51)	21.3 (± 21.50)
Bodily pain scale	30.0 (± 19.93)	34.8 (± 25.19)	43.7 (± 23.22)	17.5 (± 17.52)
General health scale	8.5 (± 15.34)	8.4 (± 17.94)	15.8 (± 17.24)	8.2 (± 17.36)
Vitality scale	16.7 (± 18.81)	16.0 (± 19.56)	17.8 (± 25.37)	14.4 (± 20.79)

Social functioning scale	18.1 (± 19.28)	21.5 (± 23.41)	23.0 (± 32.08)	20.0 (± 29.08)
Role emotional scale	12.5 (± 17.45)	15.3 (± 19.65)	16.7 (± 33.68)	19.6 (± 23.92)
Mental health scale	11.4 (± 19.01)	14.4 (± 16.88)	15.8 (± 24.05)	15.3 (± 19.83)
PCS score	8.1 (± 6.69)	9.1 (± 8.01)	11.4 (± 7.23)	5.2 (± 5.55)
MCS score	5.2 (± 8.75)	6.3 (± 8.42)	6.6 (± 13.62)	8.1 (± 10.87)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Work Productivity and Activity Impairment Questionnaire: General Health (WPAI:GH) at Week 12

End point title	Change From Baseline in Work Productivity and Activity Impairment Questionnaire: General Health (WPAI:GH) at Week 12

End point description:

WPAI:GH measures the effect of health and symptom severity on work productivity and non-work activities by assessing absenteeism, presenteeism, and impairment of daily activities. It consists of 6-questions each with unique answers and yields 4 sub-scores: work time missed (absenteeism), impairment while working (presenteeism or reduced on-the-job effectiveness), overall work impairment (work productivity loss or absenteeism plus presenteeism) and activity impairment (daily activity impairment). These sub-scores are transformed to impairment percentages (range from 0 to 100), with higher numbers indicating greater impairment and less productivity. Baseline was defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments), i.e., before first dose of study treatment. Analysis was performed on FAS. Here, n= number of subjects with data collected at specified timepoints for each specified category.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	TU2670 120 mg	TU2670 240 mg	TU2670 320 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	14	17	16
Units: score on a scale				
arithmetic mean (standard deviation)				
Work time missed (n=15,13,16,15)	2.6 (± 27.77)	-0.6 (± 19.42)	3.7 (± 33.02)	1.1 (± 24.13)
Impairment while working (n=14,13,15,14)	-27.9 (± 30.17)	-19.2 (± 13.82)	-28.7 (± 22.64)	-16.4 (± 25.30)
Overall work impairment (n=14,13,15,14)	-28.3 (± 29.52)	-19.2 (± 20.30)	-27.6 (± 26.04)	-17.4 (± 25.63)
Activity impairment (n=15,14,17,16)	-21.3 (± 41.90)	-23.6 (± 25.90)	-34.7 (± 24.01)	-23.8 (± 30.08)

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma concentration of TU2670

End point title	Plasma concentration of TU2670[4]

End point description:

Blood samples were collected at specified timepoints to determine plasma concentration of TU2670. Pharmacokinetic (PK) analysis set was a subset of the safety analysis set and included all subjects who received at least 1 dose of TU2670 and had at least 1 post-dose quantifiable TU2670 concentration without protocol deviations or events affecting the PK results. Only subjects with data collected at each specified timepoints are reported. Here, n=number of subjects with data collected for each specified category. 99999 denotes that mean was not computable as the values were below the lower limit of quantification (LLOQ), LLOQ value was 0.1 nanogram per milliliter (ng/mL). 55555 denotes that standard deviation was not computable as the mean was below LLOQ.

End point type	Secondary

End point timeframe:

Pre-dose, 1 hour and 2 hours post-dose on Days 1, 8, 29, 57 and 85

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The PK parameters were evaluated for TU2670 arms.

End point values	TU2670 120 mg	TU2670 240 mg	TU2670 320 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	16	16	15	
Units: nanogram per mililiter (ng/mL)				
arithmetic mean (standard deviation)				
Day 1: Pre-dose (n=10, 12, 11)	99999 (± 55555)	99999 (± 55555)	99999 (± 55555)	
Day 1: 1 hour post-dose (n=15,16,15)	89.97 (± 52.65)	195.0 (± 150.4)	254.5 (± 190.4)	
Day 1: 2 hours post-dose (n=12,12,14)	75.90 (± 73.68)	206.1 (± 112.8)	273.5 (± 166.0)	
Day 8: Pre-dose (n=13,15,7)	1.173 (± 3.578)	0.9720 (± 0.9557)	1.441 (± 0.3866)	
Day 8: 1 hour post-dose (n=16,16,12)	83.44 (± 55.76)	200.5 (± 101.0)	278.4 (± 146.7)	
Day 8: 2 hours post-dose (n=13,14,11)	71.23 (± 48.37)	184.4 (± 64.33)	247.5 (± 187.0)	
Day 29: Pre-dose (n=11,14,10)	0.4627 (± 0.7996)	0.5629 (± 0.8671)	1.781 (± 2.574)	
Day 29: 1 hour post-dose (n=16,15,14)	74.54 (± 48.34)	204.3 (± 110.3)	253.3 (± 178.1)	
Day 29: 2 hours post-dose (n=15,10,12)	63.42 (± 54.73)	153.1 (± 86.88)	191.8 (± 82.78)	
Day 57: Pre-dose (n=15,11,11)	0.6889 (± 1.508)	1.071 (± 1.321)	2.994 (± 6.419)	
Day 57: 1 hour post-dose (n=14,13,13)	69.11 (± 54.62)	161.8 (± 121.1)	264.8 (± 180.6)	
Day 57: 2 hours post-dose (n=12,10,11)	54.28 (± 29.99)	157.4 (± 103.5)	205.5 (± 168.2)	
Day 85: Pre-dose (n=12,10,10)	1.733 (± 6.004)	0.5740 (± 0.6109)	2.225 (± 2.626)	
Day 85: 1 hour post-dose (n=14,12,12)	60.26 (± 35.63)	145.1 (± 107.8)	199.0 (± 190.7)	
Day 85: 2 hours post-dose (n=13,8,10)	43.87 (± 38.25)	151.9 (± 93.67)	163.0 (± 110.9)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent adverse events were collected from the first administration of study treatment up to 30 days after the last administration of study treatment, approximately 248 days.

Adverse event reporting additional description:

The Safety analysis set included all subjects randomly assigned to study treatment and who took at least 1 dose of study treatment. Subjects were analyzed according to the treatment they actually received.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups

Reporting group title	TU2670 120 mg

Reporting group description:

Subjects received TU2670 120 mg capsule orally once daily for 12 weeks.

Reporting group title	TU2670 240 mg

Reporting group description:

Subjects received TU2670 240 mg capsule orally once daily for 12 weeks.

Reporting group title	TU2670 320 mg

Reporting group description:

Subjects received TU2670 320 mg capsule orally once daily for 12 weeks.

Reporting group title	Placebo

Reporting group description:

Subjects received placebo matching with TU2670 capsule orally once daily for 12 weeks.

Serious adverse events	TU2670 120 mg	TU2670 240 mg	TU2670 320 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)	2 / 21 (9.52%)	0 / 22 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Reproductive system and breast disorders			
Endometriosis			
subjects affected / exposed	0 / 20 (0.00%)	2 / 21 (9.52%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 23 (0.00%)		
number of deaths (all causes)	0		

number of deaths resulting from adverse events	0		
Reproductive system and breast disorders			
Endometriosis			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	TU2670 120 mg	TU2670 240 mg	TU2670 320 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 20 (60.00%)	14 / 21 (66.67%)	19 / 22 (86.36%)
Injury, poisoning and procedural complications			
Arthropod sting			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			
Hot flush			
subjects affected / exposed	3 / 20 (15.00%)	2 / 21 (9.52%)	6 / 22 (27.27%)
occurrences (all)	3	2	6
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 20 (5.00%)	2 / 21 (9.52%)	2 / 22 (9.09%)
occurrences (all)	1	2	2
Migraine			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Syncope			
subjects affected / exposed	1 / 20 (5.00%)	1 / 21 (4.76%)	0 / 22 (0.00%)
occurrences (all)	1	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 20 (5.00%)	1 / 21 (4.76%)	0 / 22 (0.00%)
occurrences (all)	1	1	0
Gastrointestinal disorders			

Nausea			
subjects affected / exposed	1 / 20 (5.00%)	2 / 21 (9.52%)	2 / 22 (9.09%)
occurrences (all)	1	2	2
Diarrhoea			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	3 / 22 (13.64%)
occurrences (all)	0	0	3
Abdominal pain			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	2 / 20 (10.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	2	0	0
Vomiting			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Flatulence			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	2 / 20 (10.00%)	2 / 21 (9.52%)	2 / 22 (9.09%)
occurrences (all)	2	2	2
Amenorrhoea			
subjects affected / exposed	1 / 20 (5.00%)	1 / 21 (4.76%)	1 / 22 (4.55%)
occurrences (all)	1	1	1
Intermenstrual bleeding			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Breast pain			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Respiratory tract inflammation			

subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Libido decreased			
subjects affected / exposed	0 / 20 (0.00%)	1 / 21 (4.76%)	2 / 22 (9.09%)
occurrences (all)	0	1	2
Depressed mood			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
occurrences (all)	1	0	1
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	0 / 20 (0.00%)	2 / 21 (9.52%)	1 / 22 (4.55%)
occurrences (all)	0	2	1
Spinal pain			
subjects affected / exposed	2 / 20 (10.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	2	0	0
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 20 (0.00%)	1 / 21 (4.76%)	2 / 22 (9.09%)
occurrences (all)	0	1	2
Cystitis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	2 / 22 (9.09%)
occurrences (all)	1	0	2
Upper respiratory tract infection			
subjects affected / exposed	1 / 20 (5.00%)	1 / 21 (4.76%)	1 / 22 (4.55%)
occurrences (all)	1	1	1
Rhinitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0

Nasopharyngitis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Placebo		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 23 (52.17%)		
Injury, poisoning and procedural complications			
Arthropod sting			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	2		
Migraine			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Syncope			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	2		
Diarrhoea			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Abdominal pain			

subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all) Flatulence subjects affected / exposed occurrences (all)	2 / 23 (8.70%) 2 0 / 23 (0.00%) 0 1 / 23 (4.35%) 1 0 / 23 (0.00%) 0		
Reproductive system and breast disorders Vaginal haemorrhage subjects affected / exposed occurrences (all) Amenorrhoea subjects affected / exposed occurrences (all) Intermenstrual bleeding subjects affected / exposed occurrences (all) Breast pain subjects affected / exposed occurrences (all)	 0 / 23 (0.00%) 0 0 / 23 (0.00%) 0 1 / 23 (4.35%) 1 0 / 23 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Respiratory tract inflammation subjects affected / exposed occurrences (all)	 2 / 23 (8.70%) 2 0 / 23 (0.00%) 0		
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all)	 2 / 23 (8.70%) 2		
Psychiatric disorders			

Libido decreased subjects affected / exposed occurrences (all) Depressed mood subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0 0 / 23 (0.00%) 0		
Musculoskeletal and connective tissue disorders Myalgia subjects affected / exposed occurrences (all) Spinal pain subjects affected / exposed occurrences (all)	 0 / 23 (0.00%) 0 0 / 23 (0.00%) 0		
Infections and infestations COVID-19 subjects affected / exposed occurrences (all) Cystitis subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all) Rhinitis subjects affected / exposed occurrences (all) Bronchitis subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all)	 1 / 23 (4.35%) 1 0 / 23 (0.00%) 0 0 / 23 (0.00%) 0 2 / 23 (8.70%) 2 0 / 23 (0.00%) 0 0 / 23 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 December 2021	The protocol was amended to remove the sample-rich PK subset population from the study; instead, pre-dose and postdose sampling was to be done for all study subjects. In addition, changes were made throughout to clarify that the Investigator was empowered to make determinations of clinical significance of laboratory results and appropriate treatment of possible overdose without having to contact the study Medical Monitor beforehand (but that they were to contact the Medical Monitor at any time for consultation if they deemed it necessary).
14 March 2024	The protocol was amended to modify the imputation methods for missing data pertaining to primary and key secondary efficacy variables. Medical management of endometriosis included analgesics and treatments aimed at decidualization followed by atrophy of endometrial tissue with reduction or antagonism of estrogen production and induction of amenorrhea. The subjects had consistently completed the NRS pain score and experienced no menstrual bleeding days during both of Week 8 and Week 12 study period, the bias introduced by relying solely on LOCF for the imputation methods of missing data may be supplemented.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported