Clinical trial results:
A Phase 2 trial of Nirogacestat in Patients with Recurrent Ovarian Granulosa Cell Tumors

Summary

EudraCT number	2022-001816-25
Trial protocol	PL
Global end of trial date	14 July 2025

Results information

Result version number	v1 (current)
This version publication date	18 July 2026
First version publication date	18 July 2026

Trial information

Trial identification

Sponsor protocol code	NIR-OGT-201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05348356
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	SpringWorks Therapeutics, Inc.
Sponsor organisation address	100 Washington Blvd, Stamford, United States, 06902
Public contact	Communication Center, Merck Healthcare KGaA, Darmstadt, Germany, an affiliate of Merck KGaA, Darmstadt, Germany, +49 6151725200, service@emdgroup.com
Scientific contact	Communication Center, Merck Healthcare KGaA, Darmstadt, Germany, an affiliate of Merck KGaA, Darmstadt, Germany, +49 6151725200, service@emdgroup.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	28 August 2025
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 July 2025
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the anti-tumor activity of nirogacestat in adult participants with relapsed/refractory ovarian granulosa cell tumors (OvGCT)

Protection of trial subjects:

This study was conducted in accordance with the protocol and the consensus 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 Harmonisation (ICH) Good Clinical Practice (GCP) guidelines, and applicable laws and regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 September 2022
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	United States: 50
Country: Number of subjects enrolled	Poland: 3
Worldwide total number of subjects	53
EEA total number of subjects	3

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)	42
From 65 to 84 years	10
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 79 participants were screened, with 53 participants who enrolled and received study treatment (nirogacestat).

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Nirogacestat Open-Label

Arm description:

Nirogacestat 150 mg, by mouth, twice daily.

Arm type	Experimental
Investigational medicinal product name	Nirogacestat
Investigational medicinal product code	
Other name	PF-03084014, Ogsiveo
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Nirogacestat 150 mg, by mouth, twice daily.

Number of subjects in period 1	Nirogacestat Open-Label
Started	53
Completed	1
Not completed	52
Adverse event, serious fatal	1
Consent withdrawn by subject	4
Physician decision	8
Disease progression	38
Clinical Progression	1

Baseline characteristics

Reporting groups	
Reporting group title	Nirogacestat Open-Label
Reporting group description:	
Nirogacestat 150 mg, by mouth, twice daily.	

Reporting group values	Nirogacestat Open-Label	Total	
Number of subjects	53	53	
Age Categorical Units: participants			
<45 years	13	13	
>=45 years	40	40	
Age Continuous Units: years			
arithmetic mean	55.1		
standard deviation	± 12.85	-	
Sex: Female, Male			
Sex/Gender at birth (Customized)			
Units: participants			
Female	53	53	
Male	0	0	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	6	6	
Not Hispanic or Latino	43	43	
Unknown or Not Reported	4	4	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	3	3	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	4	4	
White	37	37	
More than one race	2	2	
Unknown or Not Reported	7	7	
Region of Enrollment Units: Subjects			
United States	50	50	
Poland	3	3	
Baseline Height Units: meter			
arithmetic mean	1.632		
standard deviation	± 0.0611	-	
Baseline Weight Units: kilogram			
arithmetic mean	82.48		
standard deviation	± 19.672	-	

End points

End points reporting groups

Reporting group title	Nirogacestat Open-Label
Reporting group description:	
Nirogacestat 150 mg, by mouth, twice daily.	

Primary: Objective Response Rate (ORR)

End point title	Objective Response Rate (ORR)[1]
End point description:	
The percentage of participants with complete response (CR) + partial response (PR) assessed using Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 criteria. Full Analysis Set which consisted of all participants who received at least 1 dose of nirogacestat.	
End point type	Primary
End point timeframe:	
2.5 years	

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: Statistical analyses were not planned for this endpoint.

End point values	Nirogacestat Open-Label			
Subject group type	Reporting group			
Number of subjects analysed	53			
Units: percentage of participants	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival at 6 months (PFS-6)

End point title	Progression Free Survival at 6 months (PFS-6)
End point description:	
The number of participants without progression according to RECIST v1.1 or death at 6 months. Full Analysis Set which consisted of all participants who received at least 1 dose of nirogacestat.	
End point type	Secondary
End point timeframe:	
First day of cycle 7 (approximately 6 months after the first dose of study treatment). Each cycle is 28 days.	

End point values	Nirogacestat Open-Label			
Subject group type	Reporting group			
Number of subjects analysed	53			
Units: participants	22			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival at Year 2

End point title	Overall Survival at Year 2

End point description:

The number of participants who have not died of any cause by Year 2. Full Analysis Set which consisted of all participants who received at least 1 dose of nirogacestat.

End point type	Secondary

End point timeframe:

2 years after first dose of study treatment

End point values	Nirogacestat Open-Label			
Subject group type	Reporting group			
Number of subjects analysed	53			
Units: participants	47			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline at Cycle 2 Day 1 in the Functional Assessment of Cancer Therapy - Ovarian Symptom Index (FOSI) Score.

End point title	Change from baseline at Cycle 2 Day 1 in the Functional Assessment of Cancer Therapy - Ovarian Symptom Index (FOSI) Score.

End point description:

Participant reported ovarian cancer symptoms as measured by Functional Assessment of Cancer Therapy - Ovarian Symptom Index (FOSI). The FOSI is an 8-question evaluation scored on a Likert scale of 0-4 from not at all to very much. Metrics assessed include lack of energy, vomiting, pain, nausea, swelling in stomach area, concern condition will get worse, quality of life assessment and stomach cramps. Higher score means worse outcome. The responses to the statements except for statement 7 (I am content with the quality of my life right now) were reversed and the sum of non-missing responses is calculated. The FOSI score is the sum multiplied by 8, then divided by the number of responded statements. The FOSI score was missing if a participants had 5 or more missing values in the 8 individual symptom scores at a visit. Participants evaluable for outcome of change from baseline at Cycle 2 Day 1 in the FOSI score.

End point type	Secondary

End point timeframe:

Baseline and at Cycle 2 Day 1 (cycle length is 28 days).

End point values	Nirogacestat Open-Label			
Subject group type	Reporting group			
Number of subjects analysed	49			
Units: score on a scale				
arithmetic mean (standard deviation)	-1.1 (± 3.86)			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response

End point title	Duration of Response

End point description:

The time from response (Complete Response [CR] + Partial Response [PR] using RECIST v.1.) to disease progression and/or death, in participants with CR or PR.

End point type	Secondary

End point timeframe:

First day of every other cycle (each cycle is 28 days) for the first year, and then every 3 cycles thereafter until study completion (estimated to be an average of 2.5 years).

End point values	Nirogacestat Open-Label			
Subject group type	Reporting group			
Number of subjects analysed	0[2]			
Units: months				

Notes:

[2] - Participants who had CR or PR.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline at Cycle 4 Day 1 in the Functional Assessment of Cancer Therapy - Ovarian Symptom Index (FOSI) Score

End point title	Change From Baseline at Cycle 4 Day 1 in the Functional Assessment of Cancer Therapy - Ovarian Symptom Index (FOSI) Score

End point description:

Participant reported ovarian cancer symptoms as measured by Functional Assessment of Cancer Therapy - Ovarian Symptom Index (FOSI). The FOSI is an 8-question evaluation scored on a Likert scale of 0-4 from not at all to very much. Metrics assessed include lack of energy, vomiting, pain, nausea, swelling in stomach area, concern condition will get worse, quality of life assessment and stomach cramps. Higher score means worse outcome. The responses to the statements except for statement 7 (I am content with the quality of my life right now) were reversed and the sum of non-missing responses is calculated. The FOSI score is the sum multiplied by 8, then divided by the number of responded

statements. The FOSI score was missing if a participants had 5 or more missing values in the 8 individual symptom scores at a visit. Participants evaluable for the outcome of change from baseline at Cycle 4 Day 1 in the FOSI score.

End point type	Secondary

End point timeframe:

Baseline and at Cycle 4 Day 1 (cycle length is 28 days).

End point values	Nirogacestat Open-Label			
Subject group type	Reporting group			
Number of subjects analysed	33			
Units: score on a scale				
arithmetic mean (standard deviation)	-1.5 (± 3.08)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline at Cycle 3 Day 1 Treatment in the Functional Assessment of Cancer Therapy - Ovarian Symptom Index (FOSI) Score

End point title	Change From Baseline at Cycle 3 Day 1 Treatment in the Functional Assessment of Cancer Therapy - Ovarian Symptom Index (FOSI) Score

End point description:

Participant reported ovarian cancer symptoms as measured by Functional Assessment of Cancer Therapy - Ovarian Symptom Index (FOSI). The FOSI is an 8-question evaluation scored on a Likert scale of 0-4 from not at all to very much. Metrics assessed include lack of energy, vomiting, pain, nausea, swelling in stomach area, concern condition will get worse, quality of life assessment and stomach cramps. Higher score means worse outcome. The responses to the statements except for statement 7 (I am content with the quality of my life right now) were reversed and the sum of non-missing responses is calculated. The FOSI score is the sum multiplied by 8, then divided by the number of responded statements. The FOSI score was missing if a participants had 5 or more missing values in the 8 individual symptom scores at a visit. Participants evaluable for outcome of change from baseline at Cycle 3 Day 1 in the FOSI score.

End point type	Secondary

End point timeframe:

Baseline and at Cycle 3 Day 1 (cycle length is 28 days).

End point values	Nirogacestat Open-Label			
Subject group type	Reporting group			
Number of subjects analysed	36			
Units: score on a scale				
arithmetic mean (standard deviation)	-1.2 (± 4.00)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline at Cycle 5 Day 1 in the Functional Assessment of Cancer Therapy - Ovarian Symptom Index (FOSI) Score

End point title	Change From Baseline at Cycle 5 Day 1 in the Functional Assessment of Cancer Therapy - Ovarian Symptom Index (FOSI) Score

End point description:

Participant reported ovarian cancer symptoms as measured by Functional Assessment of Cancer Therapy - Ovarian Symptom Index (FOSI). The FOSI is an 8-question evaluation scored on a Likert scale of 0-4 from not at all to very much. Metrics assessed include lack of energy, vomiting, pain, nausea, swelling in stomach area, concern condition will get worse, quality of life assessment and stomach cramps. Higher score means worse outcome. The responses to the statements except for statement 7 (I am content with the quality of my life right now) were reversed and the sum of non-missing responses is calculated. The FOSI score is the sum multiplied by 8, then divided by the number of responded statements. The FOSI score was missing if a participants had 5 or more missing values in the 8 individual symptom scores at a visit. Participants evaluable for the outcome of change from baseline at Cycle 5 Day 1 in the FOSI score.

End point type	Secondary

End point timeframe:

Baseline and at Cycle 5 Day 1 (cycle length is 28 days).

End point values	Nirogacestat Open-Label			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: score on a scale				
arithmetic mean (standard deviation)	-1.3 (± 3.36)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline at End of Treatment in the Functional Assessment of Cancer Therapy - Ovarian Symptom Index (FOSI) Score

End point title	Change From Baseline at End of Treatment in the Functional Assessment of Cancer Therapy - Ovarian Symptom Index (FOSI) Score

End point description:

Participant reported ovarian cancer symptoms as measured by Functional Assessment of Cancer Therapy - Ovarian Symptom Index (FOSI). The FOSI is an 8-question evaluation scored on a Likert scale of 0-4 from not at all to very much. Metrics assessed include lack of energy, vomiting, pain, nausea, swelling in stomach area, concern condition will get worse, quality of life assessment and stomach cramps. Higher score means worse outcome. The responses to the statements except for statement 7 (I am content with the quality of my life right now) were reversed and the sum of non-missing responses is calculated. The FOSI score is the sum multiplied by 8, then divided by the number of responded statements. The FOSI score was missing if a participants had 5 or more missing values in the 8 individual symptom scores at a visit. Participants evaluable for the outcome of change from baseline in the FOSI score at end of treatment.

End point type	Secondary

End point timeframe:

Baseline and at end of treatment (estimated to be an average of 5.5 months [minimum of 0 month and maximum of 33 months]).

End point values	Nirogacestat Open-Label			
Subject group type	Reporting group			
Number of subjects analysed	48			
Units: score on a scale				
arithmetic mean (standard deviation)	-2.2 (± 4.48)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline at Safety Follow-up in the Functional Assessment of Cancer Therapy - Ovarian Symptom Index (FOSI) Score

End point title	Change From Baseline at Safety Follow-up in the Functional Assessment of Cancer Therapy - Ovarian Symptom Index (FOSI) Score

End point description:

Participant reported ovarian cancer symptoms as measured by Functional Assessment of Cancer Therapy - Ovarian Symptom Index (FOSI). The FOSI is an 8-question evaluation scored on a Likert scale of 0-4 from not at all to very much. Metrics assessed include lack of energy, vomiting, pain, nausea, swelling in stomach area, concern condition will get worse, quality of life assessment and stomach cramps. Higher score means worse outcome. The responses to the statements except for statement 7 (I am content with the quality of my life right now) were reversed and the sum of non-missing responses is calculated. The FOSI score is the sum multiplied by 8, then divided by the number of responded statements. The FOSI score was missing if a participants had 5 or more missing values in the 8 individual symptom scores at a visit. Participants evaluable for the outcome of change from baseline in the FOSI score at safety follow-up.

End point type	Secondary

End point timeframe:

Baseline and at safety follow-up (up to a maximum of 34 months).

End point values	Nirogacestat Open-Label			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: score on a scale				
arithmetic mean (standard deviation)	-0.8 (± 3.75)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All SAEs and AEs were collected from the time of signing ICF until 30 days after the last dose of study treatment (an average of 5.5 months [minimum of 0 month and maximum of 33 months] and up to 34 months).

Adverse event reporting additional description:

All SAEs and AEs were collected from the time of signing ICF until 30 days after the last dose of study treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups

Reporting group title	Nirogacestat Open-Label

Reporting group description:

Nirogacestat 150 mg, by mouth, twice daily.

Serious adverse events	Nirogacestat Open-Label		
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 53 (22.64%)		
number of deaths (all causes)	7		
number of deaths resulting from adverse events			
Investigations			
Electrocardiogram QT prolonged			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardio-respiratory arrest			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	1 / 1		
Angina pectoris			
alternative dictionary used: MedDRA 27.1			

subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Acute myocardial infarction			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Encephalopathy			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Influenza like illness			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Leukocytosis			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	4 / 53 (7.55%)		
occurrences causally related to treatment / all	1 / 4		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
alternative dictionary used: MedDRA 27.1			

subjects affected / exposed	2 / 53 (3.77%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Colitis				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	1 / 53 (1.89%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Nausea				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	1 / 53 (1.89%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pancreatitis				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	1 / 53 (1.89%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Small intestinal obstruction				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	2 / 53 (3.77%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Dyspnoea				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	1 / 53 (1.89%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary oedema				
alternative dictionary used: MedDRA 27.1				

subjects affected / exposed	1 / 53 (1.89%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Hidradenitis				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	1 / 53 (1.89%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Acute kidney injury				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	2 / 53 (3.77%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Gastroenteritis astroviral				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	1 / 53 (1.89%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sepsis				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	1 / 53 (1.89%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Dehydration				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	2 / 53 (3.77%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Hypomagnesaemia				
alternative dictionary used: MedDRA 27.1				

subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hypophagia			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hypokalaemia			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	2 / 53 (3.77%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Hypophosphataemia			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Nirogacestat Open-Label		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	52 / 53 (98.11%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	3 / 53 (5.66%)		
occurrences (all)	3		
Vascular disorders			
Hypertension			
subjects affected / exposed	5 / 53 (9.43%)		
occurrences (all)	5		
General disorders and administration site conditions			

Influenza like illness subjects affected / exposed occurrences (all)	3 / 53 (5.66%) 3		
Fatigue subjects affected / exposed occurrences (all)	21 / 53 (39.62%) 30		
Pyrexia subjects affected / exposed occurrences (all)	5 / 53 (9.43%) 5		
Oedema peripheral subjects affected / exposed occurrences (all)	4 / 53 (7.55%) 4		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea subjects affected / exposed occurrences (all)	4 / 53 (7.55%) 5		
Cough subjects affected / exposed occurrences (all)	17 / 53 (32.08%) 25		
Epistaxis subjects affected / exposed occurrences (all)	8 / 53 (15.09%) 8		
Nasal congestion subjects affected / exposed occurrences (all)	5 / 53 (9.43%) 6		
Oropharyngeal pain subjects affected / exposed occurrences (all)	4 / 53 (7.55%) 6		
Psychiatric disorders			
Insomnia subjects affected / exposed occurrences (all)	6 / 53 (11.32%) 8		
Anxiety subjects affected / exposed occurrences (all)	5 / 53 (9.43%) 6		
Investigations			

Blood alkaline phosphatase increased subjects affected / exposed occurrences (all)	3 / 53 (5.66%) 6		
Neutrophil count decreased subjects affected / exposed occurrences (all)	3 / 53 (5.66%) 4		
Weight decreased subjects affected / exposed occurrences (all)	3 / 53 (5.66%) 4		
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	4 / 53 (7.55%) 4		
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	7 / 53 (13.21%) 7		
Cardiac disorders Sinus tachycardia subjects affected / exposed occurrences (all)	3 / 53 (5.66%) 3		
Nervous system disorders Dysgeusia subjects affected / exposed occurrences (all)	3 / 53 (5.66%) 3		
Headache subjects affected / exposed occurrences (all)	5 / 53 (9.43%) 9		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	5 / 53 (9.43%) 11		
Eye disorders Photopsia subjects affected / exposed occurrences (all)	3 / 53 (5.66%) 3		
Gastrointestinal disorders			

Gastrooesophageal reflux disease subjects affected / exposed occurrences (all)	3 / 53 (5.66%) 3			
Dry mouth subjects affected / exposed occurrences (all)	4 / 53 (7.55%) 4			
Dyspepsia subjects affected / exposed occurrences (all)	4 / 53 (7.55%) 7			
Flatulence subjects affected / exposed occurrences (all)	4 / 53 (7.55%) 4			
Constipation subjects affected / exposed occurrences (all)	4 / 53 (7.55%) 5			
Nausea subjects affected / exposed occurrences (all)	30 / 53 (56.60%) 42			
Vomiting subjects affected / exposed occurrences (all)	20 / 53 (37.74%) 28			
Abdominal pain subjects affected / exposed occurrences (all)	11 / 53 (20.75%) 12			
Abdominal distension subjects affected / exposed occurrences (all)	6 / 53 (11.32%) 6			
Stomatitis subjects affected / exposed occurrences (all)	5 / 53 (9.43%) 6			
Diarrhoea subjects affected / exposed occurrences (all)	38 / 53 (71.70%) 68			
Skin and subcutaneous tissue disorders Dry skin				

subjects affected / exposed	3 / 53 (5.66%)		
occurrences (all)	3		
Rash			
subjects affected / exposed	3 / 53 (5.66%)		
occurrences (all)	4		
Dermatitis acneiform			
subjects affected / exposed	4 / 53 (7.55%)		
occurrences (all)	4		
Rash maculo-papular			
subjects affected / exposed	17 / 53 (32.08%)		
occurrences (all)	23		
Pruritus			
subjects affected / exposed	6 / 53 (11.32%)		
occurrences (all)	6		
Alopecia			
subjects affected / exposed	6 / 53 (11.32%)		
occurrences (all)	7		
Renal and urinary disorders			
Glycosuria			
subjects affected / exposed	3 / 53 (5.66%)		
occurrences (all)	5		
Proteinuria			
subjects affected / exposed	4 / 53 (7.55%)		
occurrences (all)	11		
Musculoskeletal and connective tissue disorders			
Flank pain			
subjects affected / exposed	3 / 53 (5.66%)		
occurrences (all)	9		
Myalgia			
subjects affected / exposed	3 / 53 (5.66%)		
occurrences (all)	3		
Arthralgia			
subjects affected / exposed	7 / 53 (13.21%)		
occurrences (all)	11		
Back pain			

subjects affected / exposed	6 / 53 (11.32%)		
occurrences (all)	8		
Pain in extremity			
subjects affected / exposed	4 / 53 (7.55%)		
occurrences (all)	4		
Infections and infestations			
Bronchitis			
subjects affected / exposed	3 / 53 (5.66%)		
occurrences (all)	3		
COVID-19			
subjects affected / exposed	3 / 53 (5.66%)		
occurrences (all)	3		
Sinusitis			
subjects affected / exposed	3 / 53 (5.66%)		
occurrences (all)	3		
Skin infection			
subjects affected / exposed	3 / 53 (5.66%)		
occurrences (all)	3		
Fungal infection			
subjects affected / exposed	4 / 53 (7.55%)		
occurrences (all)	4		
Urinary tract infection			
subjects affected / exposed	4 / 53 (7.55%)		
occurrences (all)	5		
Metabolism and nutrition disorders			
Hypermagnesaemia			
subjects affected / exposed	3 / 53 (5.66%)		
occurrences (all)	7		
Hypoalbuminaemia			
subjects affected / exposed	3 / 53 (5.66%)		
occurrences (all)	5		
Hypomagnesaemia			
subjects affected / exposed	3 / 53 (5.66%)		
occurrences (all)	7		
Hypophosphataemia			

subjects affected / exposed	15 / 53 (28.30%)		
occurrences (all)	32		
Hypokalaemia			
subjects affected / exposed	10 / 53 (18.87%)		
occurrences (all)	25		
Hyperglycaemia			
subjects affected / exposed	6 / 53 (11.32%)		
occurrences (all)	7		
Decreased appetite			
subjects affected / exposed	6 / 53 (11.32%)		
occurrences (all)	11		
Hypocalcaemia			
subjects affected / exposed	5 / 53 (9.43%)		
occurrences (all)	8		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 December 2021	Protocol Amendment 1: • Added a safety electrocardiogram (ECG) assessment 1-hour post dose at Cycle 1 Day 1 (C1D1) • Updated Gastric Acid Reducing Agents administration guidelines • Updated preferred terms for Reproductive System Disorders in the adverse events of special interest (AESI) table - Updated inclusion/exclusion criteria: Specified that participant must have had radiological evidence of relapse, and removed clinical relapse and increasing tumor markers as evidence of relapse - Added further detail regarding prior therapy - Removed life expectancy from inclusion criteria - Removed anticipated need for major surgical procedure from exclusion criteria - Removed placement of vascular access device from an exclusion criterion - Removed positive human immunodeficiency virus (HIV) infection and Hepatitis C infection as exclusion criteria - Removed Hepatitis B surface antigen at Screening from an exclusion criterion - Added duration of contraceptive use for women of childbearing potential (WOCBP)
18 July 2022	Protocol Amendment 2: • Changed serum creatinine (using the Cockcroft-Gault equation) to estimated glomerular filtration rate (eGFR) to better measure steady-state renal function
31 January 2023	Protocol Amendment 3: • Updated language regarding risks based on new information from Phase 3 study • Updated inclusion/exclusion criteria: - Reworded 2 inclusion criteria for accuracy – Revised exclusion criterion 11 regarding previous or current treatment for OvGCT to clarify use of bevacizumab or other monoclonal antibody therapy • Added guidance for selected toxicities not considered treatment-related and updated the list of selected toxicities • Updated duration of study to state the minimum duration • Updated laboratory assessments • Revised pregnancy information collection
04 June 2023	Protocol Amendment 4: • Added exploratory objective and endpoint • Updated estimated duration of the study • Updated study treatment duration parameters • Added scientific rationale and new guidance for continuation of treatment beyond initial evidence of disease progression • Added updated guidance for timing of co-administrating of acid reducing agents • Updated AESIs
19 March 2024	Protocol Amendment 5: • Added in assessment for continued use of nirogacestat following first disease progression • Added in analysis for progression free survival 2 (PFS2) • Additional text added to 2-year survival check-in to explain process for collection of PFS2 data • Duration of contraception and egg donation/harvesting shorted from 6 months to at least 1 week after the last dose of study treatment • Updated AESI table • Added additional text regarding reporting Suspected Unexpected Serious Adverse Reactions, data protection, and publication policy aligned with EU CTR requirements

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported