Clinical trial results:
A MULTICENTER, PHASE I/II STUDY OF SEQUENTIAL EPIGENETIC AND IMMUNE TARGETING IN COMBINATION WITH NAB-PACLITAXEL/GEMCITABINE IN PATIENTS WITH ADVANCED PANCREATIC DUCTAL ADENOCARCINOMA

Summary

EudraCT number	2017-001625-40
Trial protocol	DE
Global end of trial date	02 July 2024

Results information

Result version number	v1 (current)
This version publication date	28 February 2026
First version publication date	28 February 2026

Trial information

Trial identification

Sponsor protocol code	AX-CL-PANC-PI-008619

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04257448
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GWT-TUD GmbH
Sponsor organisation address	Freiberger Str. 33, Dresden, Germany, 01067
Public contact	FB MEDIZIN, GWT-TUD GmbH, +49 35125933100, medical.consulting@g-wt.de
Scientific contact	FB MEDIZIN, GWT-TUD GmbH, +49 35125933100, medical.consulting@g-wt.de

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	17 July 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 July 2024
Global end of trial reached?	Yes
Global end of trial date	02 July 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study, including the dose escalating part (Part 1a), the dose expansion part (Part 1b) as well as the consolidation part (Part 2), is to determine the safety and tolerability of Azacitidine and/or Romidepsin in combination with nab-Paclitaxel/Gemcitabine, followed by sequential immune targeting with PD-L1 blockade in combination with low-dose Lenalidomide in patients with advanced PDAC (Part 1 and 2).
Moreover, in the dose escalating part of the study (Part 1a), the recommended dose for expansion and dose-limiting toxicity of Azacitidine and/or Romidepsin in combination with nab-Paclitaxel/Gemcitabine will be identified.

Protection of trial subjects:

An independent data safety monitoring board was established to supervise the conduct of this trial. The DMC issued recommendations for early termination, modifications or continuation of the trial according to the DMC Operating Procedure. Based on the novel combination regimen applied in this study, the DMC monitored safety and efficacy data every 3 to 6 months (at least twice a year) throughout the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 May 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	Germany: 73
Worldwide total number of subjects	73
EEA total number of subjects	73

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	33
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Clinical conduct of the study was between 25 May 2020 (date of first informed consent) and 02 Jul 2024 (LPLV). Overall, 85 patients were screened at 9 participating sites across Germany.

Pre-assignment

Screening details:

75 out of 85 patients were assigned to treatment: 19 patients in Part 1a of the study, with 6 continuing to Part 1b, additional 33 patients in Part 1b and 23 patients were assigned to the standard arm. In total, 39 patients were treated with RDE (Recommended Dose for Expansion).

Period 1

Period 1 title	Part 1
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	No
Arm title	Arm A (dose escalation)

Arm description:

Part 1a employed a standard 3 + 3 design to test safety and tolerability. Study treatment was given until intolerable toxicity. Treatment was escalated until the recommended dose was identified.

Arm type	Experimental
Investigational medicinal product name	Romidepsin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Romidepsin (dose range: 2 - 7 mg/m²) was administered on Day 1, Day 8 and Day 15 (every 28 days) of each treatment cycle. Study treatment was given for a maximum of 3 cycles.

Investigational medicinal product name	nab-Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for suspension for injection
Routes of administration	Intravenous use

Dosage and administration details:

nab-Paclitaxel was given on Day 1, Day 8 and Day 15 at a dose of 125 mg/m² (every 28 days) of each treatment cycle. nab-Paclitaxel was administered sequentially with Gemcitabine. Study treatment was given for a maximum of 3 cycles.

Investigational medicinal product name	Gemcitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Gemcitabine was given on Day 1, Day 8 and Day 15 at a dose of 1000 mg/m² (every 28 days) of each treatment cycle. Study treatment was given for a maximum of 3 cycles.

Arm title	Arm B (dose escalation)

Arm description:

Part 1a employed a standard 3 + 3 design to test safety and tolerability. Study treatment was given

until intolerable toxicity. Treatment was escalated until the recommended dose was identified.

Arm type	Experimental
Investigational medicinal product name	Azacitidine
Investigational medicinal product code	
Other name	Vidaza®
Pharmaceutical forms	Powder for suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Azacitidine(dose range: 20- 40 mg/m²) was administered on Day -7 to Day -3 (every 28 days) of each treatment cycle. Study treatment was given for a maximum of 3 cycles.

Investigational medicinal product name	nab-Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for suspension for injection
Routes of administration	Intravenous use

Dosage and administration details:

nab-Paclitaxel was given on Day 1, Day 8 and Day 15 at a dose of 125 mg/m² (every 28 days) of each treatment cycle. nab-Paclitaxel was administered sequentially with Gemcitabine. Study treatment was given for a maximum of 3 cycles.

Investigational medicinal product name	Gemcitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Gemcitabine was given on Day 1, Day 8 and Day 15 at a dose of 1000 mg/m² (every 28 days) of each treatment cycle. Study treatment was given for a maximum of 3 cycles.

Arm title	Arm C (dose escalation)

Arm description:

Part 1a employed a standard 3 + 3 design to test safety and tolerability. Study treatment was given until intolerable toxicity. Treatment was escalated until the recommended dose was identified.

Arm type	Experimental
Investigational medicinal product name	Romidepsin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Romidepsin was given on Day 1, Day 8 and Day 15 at a dose of 2 mg/m² (every 28 days) of each treatment cycle. Study treatment was given for a maximum of 3 cycles.

Investigational medicinal product name	Azacitidine
Investigational medicinal product code	
Other name	Vidaza®
Pharmaceutical forms	Powder for suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Azacitidine was given on Day -7 to Day -3 at a dose of 30 mg/m² (every 28 days) of each treatment cycle. Study treatment was given for a maximum of 3 cycles.

Investigational medicinal product name	nab-Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for suspension for injection
Routes of administration	Intravenous use

Dosage and administration details:

nab-Paclitaxel was given on Day 1, Day 8 and Day 15 at a dose of 125 mg/m² (every 28 days) of each treatment cycle. nab-Paclitaxel was administered sequentially with Gemcitabine. Study treatment was given for a maximum of 3 cycles.

Investigational medicinal product name	Gemcitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Gemcitabine was given on Day 1, Day 8 and Day 15 at a dose of 1000 mg/m² (every 28 days) of each treatment cycle. Study treatment was given for a maximum of 3 cycles.

Arm title	Standard arm

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	nab-Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for suspension for injection
Routes of administration	Intravenous use

Dosage and administration details:

nab-Paclitaxel was given on Day 1, Day 8 and Day 15 at a dose of 125 mg/m² (every 28 days) of each treatment cycle. nab-Paclitaxel was administered sequentially with Gemcitabine. Study treatment was given for a maximum of 3 cycles.

Investigational medicinal product name	Gemcitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Gemcitabine was given on Day 1, Day 8 and Day 15 at a dose of 1000 mg/m² (every 28 days) of each treatment cycle. Study treatment was given for a maximum of 3 cycles.

Arm title	Arm B (dose expansion)

Arm description:

One of the treatment arms (Arm C over Arm B over Arm A) was planned to be continued and additional patients were recruited. Selection of the expansion arm was as follows in case of successful determination of the RDE: Arm C preferred over Arm B over Arm A. For Part 1b the treatment regimen of Arm B dose level L1 (30 mg/m² azacitidine sc on day -7 to day -3) in combination with nab-paclitaxel/gemcitabine (day 1, day 8 and day 15 at a dose of 125 mg/m² iv and 1000 mg/m², respectively) was selected.

Arm type	Experimental
Investigational medicinal product name	Azacitidine
Investigational medicinal product code	
Other name	Vidaza®
Pharmaceutical forms	Powder for suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Azacitidine was given on Day -7 to Day -3 at a dose of 30 mg/m² (every 28 days) of each treatment cycle. Study treatment was given for a maximum of 3 cycles.

Investigational medicinal product name	nab-Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for suspension for injection
Routes of administration	Intravenous use

Dosage and administration details:

nab-Paclitaxel was given on Day 1, Day 8 and Day 15 at a dose of 125 mg/m² (every 28 days) of each treatment cycle. nab-Paclitaxel was administered sequentially with Gemcitabine. Study treatment was given for a maximum of 3 cycles.

Investigational medicinal product name	Gemcitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Gemcitabine was given on Day 1, Day 8 and Day 15 at a dose of 1000 mg/m² (every 28 days) of each treatment cycle. Study treatment was given for a maximum of 3 cycles.

Number of subjects in period 1	Arm A (dose escalation)	Arm B (dose escalation)	Arm C (dose escalation)
Started	6	10	3
Completed	6	10	3
Not completed	0	0	0
Consent withdrawn by subject	-	-	-
Physician decision	-	-	-
Adverse event, non-fatal	-	-	-
Lost to follow-up	-	-	-
Reason missing	-	-	-
Lack of efficacy	-	-	-
Protocol deviation	-	-	-

Number of subjects in period 1	Standard arm	Arm B (dose expansion)
Started	23	39
Completed	15	27
Not completed	8	12
Consent withdrawn by subject	2	-
Physician decision	1	-
Adverse event, non-fatal	1	1
Lost to follow-up	-	1
Reason missing	1	1
Lack of efficacy	3	8
Protocol deviation	-	1

Period 2

Period 2 title	Part 2
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Consolidation therapy

Arm description:

All patients from Part 1 (dose escalation and expansion cohorts from experimental arms and standard arm) who did not progress after three cycles of gemcitabine/nab-paclitaxel/ (GnP) with or without additional epigenetic treatment received sequential immune targeting with PD-L1 blockade (standard fixed dose of durvalumab 1500 mg/kg q4w iv) in combination with low-dose lenalidomide (10 mg d1-21 q4w po) until documented disease progression.

Arm type	Experimental
Investigational medicinal product name	Durvalumab
Investigational medicinal product code	
Other name	Imfinzi®
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Standard fixed dose of durvalumab 1500 mg/kg q4w iv in combination with low-dose lenalidomide until documented disease progression

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

Dosage and administration details:

10 mg d1-21 q4w po until documented disease progression

Number of subjects in period 2	Consolidation therapy
Started	46
Completed	12
Not completed	34
Consent withdrawn by subject	1
Lack of efficacy	33

Baseline characteristics

Reporting groups	
Reporting group title	Part 1

Reporting group description: -

Reporting group values	Part 1	Total	
Number of subjects	73	73	
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			
log mean	62.6		
standard deviation	± 9.7	-	
Gender categorical Units: Subjects			
Female	35	35	
Male	38	38	

End points

End points reporting groups

Reporting group title	Arm A (dose escalation)
Reporting group description:	
Part 1a employed a standard 3 + 3 design to test safety and tolerability. Study treatment was given until intolerable toxicity. Treatment was escalated until the recommended dose was identified.	
Reporting group title	Arm B (dose escalation)
Reporting group description:	
Part 1a employed a standard 3 + 3 design to test safety and tolerability. Study treatment was given until intolerable toxicity. Treatment was escalated until the recommended dose was identified.	
Reporting group title	Arm C (dose escalation)
Reporting group description:	
Part 1a employed a standard 3 + 3 design to test safety and tolerability. Study treatment was given until intolerable toxicity. Treatment was escalated until the recommended dose was identified.	
Reporting group title	Standard arm
Reporting group description: -	
Reporting group title	Arm B (dose expansion)
Reporting group description:	
One of the treatment arms (Arm C over Arm B over Arm A) was planned to be continued and additional patients were recruited. Selection of the expansion arm was as follows in case of successful determination of the RDE: Arm C preferred over Arm B over Arm A. For Part 1b the treatment regimen of Arm B dose level L1 (30 mg/m² azacitidine sc on day -7 to day -3) in combination with nab-paclitaxel/gemcitabine (day 1, day 8 and day 15 at a dose of 125 mg/m² iv and 1000 mg/m², respectively) was selected.	
Reporting group title	Consolidation therapy
Reporting group description:	
All patients from Part 1 (dose escalation and expansion cohorts from experimental arms and standard arm) who did not progress after three cycles of gemcitabine/nab-paclitaxel/ (GnP) with or without additional epigenetic treatment received sequential immune targeting with PD-L1 blockade (standard fixed dose of durvalumab 1500 mg/kg q4w iv) in combination with low-dose lenalidomide (10 mg d1-21 q4w po) until documented disease progression.	

Primary: Adverse Events

End point title	Adverse Events[1]
End point description:	
End point type	Primary
End point timeframe:	
3 cycles	

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: There were no statistical hypotheses. The emphasis of the analyses was on estimation of key summary statistics.

End point values	Arm A (dose escalation)	Arm B (dose escalation)	Arm C (dose escalation)	Standard arm
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	10	3	23
Units: subjects with at least one event				
number (not applicable)				
AE unrelated	6	10	3	22

AE related to Azacitidine	0	4	3	0
AE related to Romidepsin	5	0	3	0
AE related to nab-Paclitaxel	5	4	3	22
AE related to Gemcitabine	5	4	3	21
AE related, but relation unknown	1	0	0	0
SAE unrelated	3	1	1	7
SAE related to Azacitidine	0	0	0	0
SAE related to Romidepsin	2	0	1	0
SAE related to nab-Paclitaxel	1	0	2	5
SAE related to Gemcitabine	1	0	2	5
Fatal event	1	1	0	3

End point values	Arm B (dose expansion)			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: subjects with at least one event				
number (not applicable)				
AE unrelated	33			
AE related to Azacitidine	28			
AE related to Romidepsin	5			
AE related to nab-Paclitaxel	33			
AE related to Gemcitabine	33			
AE related, but relation unknown	0			
SAE unrelated	13			
SAE related to Azacitidine	5			
SAE related to Romidepsin	0			
SAE related to nab-Paclitaxel	7			
SAE related to Gemcitabine	7			
Fatal event	1			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

18 month

Adverse event reporting additional description:

AE and SAE collection and reporting continued for further 90 days after a patient’s last use of IMP within the study.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups

Reporting group title	Safety Analysis Set

Reporting group description:

In Part 1 of the study, 73 patients received treatment with study medication and were included in the FAS which corresponds to the safety analysis set (SAF).

Serious adverse events	Safety Analysis Set		
Total subjects affected by serious adverse events			
subjects affected / exposed	25 / 73 (34.25%)		
number of deaths (all causes)	6		
number of deaths resulting from adverse events	6		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tumour associated fever			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			

Thrombosis				
subjects affected / exposed	1 / 73 (1.37%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Cerebral ischaemia				
subjects affected / exposed	1 / 73 (1.37%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
General disorders and administration site conditions				
Pyrexia				
subjects affected / exposed	1 / 73 (1.37%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
General physical health deterioration				
subjects affected / exposed	1 / 73 (1.37%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Duodenal stenosis				
subjects affected / exposed	2 / 73 (2.74%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Gastric disorder				
subjects affected / exposed	1 / 73 (1.37%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Ileus				
subjects affected / exposed	1 / 73 (1.37%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nausea/Vomiting				

subjects affected / exposed	1 / 73 (1.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ileus paralytic			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholestasis			
subjects affected / exposed	3 / 73 (4.11%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Cholangitis			
subjects affected / exposed	3 / 73 (4.11%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 0		
Acute hepatic failure			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	1 / 1		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 73 (2.74%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	1 / 2		
Infections and infestations			
Pneumonia			

subjects affected / exposed	2 / 73 (2.74%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Catheter site infection				
subjects affected / exposed	1 / 73 (1.37%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Biliary sepsis				
subjects affected / exposed	1 / 73 (1.37%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Urinary tract infection				
subjects affected / exposed	1 / 73 (1.37%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Anal abscess				
subjects affected / exposed	1 / 73 (1.37%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infection				
subjects affected / exposed	1 / 73 (1.37%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Cachexia				
subjects affected / exposed	1 / 73 (1.37%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Dehydration				
subjects affected / exposed	1 / 73 (1.37%)			
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	Safety Analysis Set		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	68 / 73 (93.15%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	8 / 73 (10.96%)		
occurrences (all)	15		
Cancer fatigue			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Breast cancer			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Tumour associated fever			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	2		
Vascular disorders			
Hypertension			
subjects affected / exposed	6 / 73 (8.22%)		
occurrences (all)	7		
Thrombosis			
subjects affected / exposed	4 / 73 (5.48%)		
occurrences (all)	5		
Hypotension			
subjects affected / exposed	2 / 73 (2.74%)		
occurrences (all)	2		
Thrombophlebitis			
subjects affected / exposed	2 / 73 (2.74%)		
occurrences (all)	2		
Venous thrombosis			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Embolism			

subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Venous thrombosis limb			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Embolism arterial			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	8 / 73 (10.96%)		
occurrences (all)	15		
Pyrexia			
subjects affected / exposed	7 / 73 (9.59%)		
occurrences (all)	11		
Oedema peripheral			
subjects affected / exposed	6 / 73 (8.22%)		
occurrences (all)	10		
General physical health deterioration			
subjects affected / exposed	3 / 73 (4.11%)		
occurrences (all)	3		
Chills			
subjects affected / exposed	2 / 73 (2.74%)		
occurrences (all)	2		
Oedema			
subjects affected / exposed	2 / 73 (2.74%)		
occurrences (all)	2		
Pain			
subjects affected / exposed	2 / 73 (2.74%)		
occurrences (all)	4		
Injection site reaction			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Adverse drug reaction			

subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Catheter site thrombosis			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Peripheral swelling			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Extravasation			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Inflammation			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Malaise			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Amenorrhoea			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	4 / 73 (5.48%)		
occurrences (all)	4		
Pulmonary embolism			
subjects affected / exposed	3 / 73 (4.11%)		
occurrences (all)	4		
Dyspnoea exertional			

subjects affected / exposed	2 / 73 (2.74%)		
occurrences (all)	2		
Dyspnoea			
subjects affected / exposed	2 / 73 (2.74%)		
occurrences (all)	2		
Epistaxis			
subjects affected / exposed	2 / 73 (2.74%)		
occurrences (all)	3		
Pleural effusion			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	2 / 73 (2.74%)		
occurrences (all)	3		
Sleep disorder			
subjects affected / exposed	2 / 73 (2.74%)		
occurrences (all)	2		
Depression			
subjects affected / exposed	2 / 73 (2.74%)		
occurrences (all)	2		
Agitation			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	2		
Adjustment disorder			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Mental disorder			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	2		
Product issues			
Stent malfunction			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Device malfunction			

subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	22 / 73 (30.14%)		
occurrences (all)	40		
Aspartate aminotransferase increased			
subjects affected / exposed	20 / 73 (27.40%)		
occurrences (all)	34		
C-reactive protein increased			
subjects affected / exposed	10 / 73 (13.70%)		
occurrences (all)	18		
Blood alkaline phosphatase increased			
subjects affected / exposed	8 / 73 (10.96%)		
occurrences (all)	11		
Blood bilirubin increased			
subjects affected / exposed	8 / 73 (10.96%)		
occurrences (all)	13		
Gamma-glutamyltransferase increased			
subjects affected / exposed	5 / 73 (6.85%)		
occurrences (all)	5		
Weight decreased			
subjects affected / exposed	4 / 73 (5.48%)		
occurrences (all)	4		
Lipase increased			
subjects affected / exposed	4 / 73 (5.48%)		
occurrences (all)	6		
Haemoglobin increased			
subjects affected / exposed	2 / 73 (2.74%)		
occurrences (all)	4		
White blood cell count decreased			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	2		
Platelet count increased			

subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Blood calcium decreased			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Blood sodium increased			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Blood alkaline phosphatase			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Blood thyroid stimulating hormone decreased			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Platelet count decreased			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Mycobacterium tuberculosis complex test			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Amylase increased			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Neutrophil count decreased			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Nutritional condition abnormal			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			

Fall			
subjects affected / exposed	2 / 73 (2.74%)		
occurrences (all)	2		
Upper limb fracture			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Post procedural haemorrhage			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Cardiac disorders			
Angina unstable			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Diastolic dysfunction			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Nervous system disorders			
Taste disorder			
subjects affected / exposed	3 / 73 (4.11%)		
occurrences (all)	3		
Headache			
subjects affected / exposed	2 / 73 (2.74%)		
occurrences (all)	3		
Dizziness			
subjects affected / exposed	2 / 73 (2.74%)		
occurrences (all)	2		
Cerebral ischaemia			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Hypotonia			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Dysaesthesia			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Peripheral sensory neuropathy			

subjects affected / exposed occurrences (all)	1 / 73 (1.37%) 2		
Orthostatic intolerance subjects affected / exposed occurrences (all)	1 / 73 (1.37%) 1		
Polyneuropathy subjects affected / exposed occurrences (all)	1 / 73 (1.37%) 1		
Syncope subjects affected / exposed occurrences (all)	1 / 73 (1.37%) 1		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	7 / 73 (9.59%) 9		
Thrombocytopenia subjects affected / exposed occurrences (all)	3 / 73 (4.11%) 3		
Leukocytosis subjects affected / exposed occurrences (all)	1 / 73 (1.37%) 1		
Neutropenia subjects affected / exposed occurrences (all)	1 / 73 (1.37%) 1		
Ear and labyrinth disorders Deafness subjects affected / exposed occurrences (all)	1 / 73 (1.37%) 1		
Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all)	24 / 73 (32.88%) 29		
Abdominal pain subjects affected / exposed occurrences (all)	15 / 73 (20.55%) 26		
Nausea/Vomiting			

subjects affected / exposed	11 / 73 (15.07%)			
occurrences (all)	15			
Diarrhoea				
subjects affected / exposed	11 / 73 (15.07%)			
occurrences (all)	13			
Abdominal pain upper				
subjects affected / exposed	6 / 73 (8.22%)			
occurrences (all)	6			
Flatulence				
subjects affected / exposed	4 / 73 (5.48%)			
occurrences (all)	4			
Ascites				
subjects affected / exposed	2 / 73 (2.74%)			
occurrences (all)	2			
Dyspepsia				
subjects affected / exposed	2 / 73 (2.74%)			
occurrences (all)	2			
Duodenal stenosis				
subjects affected / exposed	2 / 73 (2.74%)			
occurrences (all)	2			
Haemorrhoids thrombosed				
subjects affected / exposed	2 / 73 (2.74%)			
occurrences (all)	3			
Colitis				
subjects affected / exposed	1 / 73 (1.37%)			
occurrences (all)	1			
Dysphagia				
subjects affected / exposed	1 / 73 (1.37%)			
occurrences (all)	1			
Abdominal distension				
subjects affected / exposed	1 / 73 (1.37%)			
occurrences (all)	2			
Ileus paralytic				
subjects affected / exposed	1 / 73 (1.37%)			
occurrences (all)	1			
Impaired gastric emptying				

subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Enteritis			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Gastrointestinal disorder			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Gastric disorder			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	3		
Stomatitis			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Ileus			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Abdominal discomfort			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Hiatus hernia			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	5 / 73 (6.85%)		
occurrences (all)	13		
Cholestasis			
subjects affected / exposed	4 / 73 (5.48%)		
occurrences (all)	5		
Acute hepatic failure			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		

Bile duct stenosis subjects affected / exposed occurrences (all)	1 / 73 (1.37%) 2		
Hepatic function abnormal subjects affected / exposed occurrences (all)	1 / 73 (1.37%) 1		
Skin and subcutaneous tissue disorders			
Pruritus subjects affected / exposed occurrences (all)	2 / 73 (2.74%) 4		
Rash subjects affected / exposed occurrences (all)	2 / 73 (2.74%) 2		
Dry skin subjects affected / exposed occurrences (all)	1 / 73 (1.37%) 11		
Night sweats subjects affected / exposed occurrences (all)	1 / 73 (1.37%) 1		
Erythema subjects affected / exposed occurrences (all)	1 / 73 (1.37%) 2		
Renal and urinary disorders			
Acute kidney injury subjects affected / exposed occurrences (all)	2 / 73 (2.74%) 2		
Dysuria subjects affected / exposed occurrences (all)	1 / 73 (1.37%) 1		
Urinary retention subjects affected / exposed occurrences (all)	1 / 73 (1.37%) 1		
Endocrine disorders			
Hypothyroidism subjects affected / exposed occurrences (all)	4 / 73 (5.48%) 4		
Hyperthyroidism			

subjects affected / exposed	2 / 73 (2.74%)		
occurrences (all)	2		
Thyroid mass			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	4 / 73 (5.48%)		
occurrences (all)	8		
Muscle spasms			
subjects affected / exposed	2 / 73 (2.74%)		
occurrences (all)	2		
Bone pain			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Muscular weakness			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Arthritis			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	5 / 73 (6.85%)		
occurrences (all)	5		
Pneumonia			
subjects affected / exposed	2 / 73 (2.74%)		
occurrences (all)	3		
Infection			
subjects affected / exposed	2 / 73 (2.74%)		
occurrences (all)	2		
Respiratory tract infection			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Bronchitis			

subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Tonsillitis			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Conjunctivitis			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Biliary sepsis			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Anal abscess			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Catheter site infection			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	2		
Cystitis			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Urogenital infection fungal			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	4 / 73 (5.48%)		
occurrences (all)	5		
Decreased appetite			
subjects affected / exposed	3 / 73 (4.11%)		
occurrences (all)	3		
Hyperuricaemia			
subjects affected / exposed	2 / 73 (2.74%)		
occurrences (all)	2		

Hypoalbuminaemia subjects affected / exposed occurrences (all)	2 / 73 (2.74%) 2		
Vitamin D deficiency subjects affected / exposed occurrences (all)	1 / 73 (1.37%) 1		
Hyperphosphataemia subjects affected / exposed occurrences (all)	1 / 73 (1.37%) 1		
Hyperglycaemia subjects affected / exposed occurrences (all)	1 / 73 (1.37%) 1		
Cachexia subjects affected / exposed occurrences (all)	1 / 73 (1.37%) 1		
Dehydration subjects affected / exposed occurrences (all)	1 / 73 (1.37%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 March 2020	Protocol V4.0
06 May 2021	Protocol V5.0
28 June 2022	Protocol V6.0

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported