



Clinical trial results:

A Phase 2b, Open-label, Single-arm Study of Zanidatamab (ZW25) Monotherapy in Participants with Advanced or Metastatic HER2-amplified Biliary Tract Cancers

Summary

EudraCT number	2020-000459-11
Trial protocol	FR GB IT
Global end of trial date	11 July 2024

Results information

Result version number	v2 (current)
This version publication date	23 October 2025
First version publication date	27 July 2025
Version creation reason	<ul style="list-style-type: none">Correction of full data set Outcome measure timeframes were updated.

Trial information

Trial identification

Sponsor protocol code	ZWI-ZW25-203
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04466891
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Jazz Pharmaceuticals, Inc.
Sponsor organisation address	3170 Porter Drive, Palo Alto, United States, 94304
Public contact	Director Clinical Trial Disclosure & Transparency, Jazz Pharmaceuticals, Inc., +1 2158323750, ClinicalTrialDisclosure@JazzPharma.com
Scientific contact	Director Clinical Trial Disclosure & Transparency, Jazz Pharmaceuticals, Inc., +1 2158323750, ClinicalTrialDisclosure@JazzPharma.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	11 July 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	11 July 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the trial was to evaluate the anti-tumor activity of zanidatamab monotherapy in participants with advanced or metastatic HER2-amplified biliary tract cancers (BTC) by evaluating the confirmed ORR by RECIST v1.1, assessed by Independent Central Review.

Protection of trial subjects:

This trial was conducted in compliance with the protocol, ICH GCP guidelines, the ethical principles of the Declaration of Helsinki, and applicable local laws and regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 September 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	China: 24
Country: Number of subjects enrolled	Korea, Republic of: 31
Country: Number of subjects enrolled	Canada: 1
Country: Number of subjects enrolled	United States: 17
Country: Number of subjects enrolled	Chile: 1
Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	United Kingdom: 2
Country: Number of subjects enrolled	Italy: 3
Country: Number of subjects enrolled	Spain: 4
Worldwide total number of subjects	87
EEA total number of subjects	11

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)	45
From 65 to 84 years	42
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 87 participants who met all eligibility criteria were enrolled and received treatment.

Pre-assignment

Screening details:

Participants must have received at least 1 prior gemcitabine-containing systemic chemotherapy regimen for advanced disease and experienced disease progression after or developed intolerance to the most recent prior therapy.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort I

Arm description:

Participants with advanced or metastatic biliary tract cancer with HER2 amplification by in situ hybridization (ISH) and HER2 overexpression by immunohistochemistry (IHC) which includes IHC 2+ or 3+

Arm type	Experimental
Investigational medicinal product name	Zanidatamab
Investigational medicinal product code	
Other name	ZIIHERA®, ZW25, JZP598
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered at 20 mg/kg on Days 1 and 15 of each 28-day cycle

Arm title	Cohort II
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Arm description:

Participants with advanced or metastatic biliary tract cancer with HER2 amplification by ISH and HER2 IHC 0 or 1+.

Arm type	Experimental
Investigational medicinal product name	Zanidatamab
Investigational medicinal product code	
Other name	ZIIHERA®, ZW25, JZP598
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered at 20 mg/kg on Days 1 and 15 of each 28-day cycle

Number of subjects in period 1	Cohort I	Cohort II
Started	80	7
Completed	0	0
Not completed	80	7
Adverse event, serious fatal	60	6
Transitioned to Named Patient Supply (NPS) program	5	-
Study terminated by sponsor	5	-
Withdrawal of consent	8	1
Lost to follow-up	2	-

Baseline characteristics

Subject analysis sets

Subject analysis set title	Cohort I
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants with advanced or metastatic biliary tract cancer with HER2 amplification by in situ hybridization (ISH) and HER2 overexpression by immunohistochemistry (IHC) which includes IHC 2+ or 3+

Subject analysis set title	Cohort II
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants with advanced or metastatic biliary tract cancer with HER2 amplification by ISH and HER2 IHC 0 or 1+.

Reporting group values	Cohort I	Cohort II	
Number of subjects	80	7	
Age categorical			
Units: Subjects			
In Utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days - 23 months)	0	0	
Children (2 - 11 years)	0	0	
12 - 17 years	0	0	
Adults (18 - 64 years)	41	4	
From 65 - 84 years	39	3	
85 years and over	0	0	
Gender categorical			
Units: Subjects			
Male	35	5	
Female	45	2	

End points

End points reporting groups

Reporting group title	Cohort I
Reporting group description: Participants with advanced or metastatic biliary tract cancer with HER2 amplification by in situ hybridization (ISH) and HER2 overexpression by immunohistochemistry (IHC) which includes IHC 2+ or 3+	
Reporting group title	Cohort II
Reporting group description: Participants with advanced or metastatic biliary tract cancer with HER2 amplification by ISH and HER2 IHC 0 or 1+.	
Subject analysis set title	Cohort I
Subject analysis set type	Safety analysis
Subject analysis set description: Participants with advanced or metastatic biliary tract cancer with HER2 amplification by in situ hybridization (ISH) and HER2 overexpression by immunohistochemistry (IHC) which includes IHC 2+ or 3+	
Subject analysis set title	Cohort II
Subject analysis set type	Safety analysis
Subject analysis set description: Participants with advanced or metastatic biliary tract cancer with HER2 amplification by ISH and HER2 IHC 0 or 1+.	

Primary: Confirmed Objective Response Rate (ORR) by Independent Central Review (ICR)

End point title	Confirmed Objective Response Rate (ORR) by Independent Central Review (ICR) ^[1]
End point description: Number of participants who achieved a confirmed best overall response (BOR) of either complete response (CR) or partial response (PR) during treatment per Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1. Complete response (CR) is defined as a disappearance of all target and non-target lesions and partial response (PR) is defined as at least a 30% decrease in the sum of diameters of all target lesions.	
End point type	Primary
End point timeframe: Up to 34 months	
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: This outcome was assessed using descriptive statistics.	

End point values	Cohort I	Cohort II		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	80	7		
Units: Participants				
number (not applicable)	33	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR) by ICR

End point title	Duration of Response (DOR) by ICR
End point description: The time from the first confirmed objective response (CR or PR) to documented progressive disease (PD) per RECIST 1.1 or death from any cause.	
End point type	Secondary
End point timeframe: Up to 45 months	

End point values	Cohort I	Cohort II		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	33	0 ^[2]		
Units: months				
median (confidence interval 95%)	14.92 (7.39 to 23.98)	(to)		

Notes:

[2] - Participant data were not available for assessment in this cohort.

Statistical analyses

No statistical analyses for this end point

Secondary: DOR ≥ 16 weeks by ICR

End point title	DOR ≥ 16 weeks by ICR
End point description: Proportion of subjects with a DOR ≥ 16 weeks per RECIST 1.1	
End point type	Secondary
End point timeframe: 24 weeks, up to 45 months	

End point values	Cohort I	Cohort II		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	33	0 ^[3]		
Units: participants				
number (not applicable)	28			

Notes:

[3] - Participant data were not available for assessment in this cohort.

Statistical analyses

No statistical analyses for this end point

Secondary: Disease control rate (DCR) by ICR

End point title	Disease control rate (DCR) by ICR
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End point description:

Number of subjects who achieved a best overall response of stable disease (SD), non-CR/non-PD, or confirmed CR or PR per RECIST 1.1

End point type	Secondary
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End point timeframe:

Up to 45 months

End point values	Cohort I	Cohort II		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	80	7		
Units: participants				
number (not applicable)	55	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free survival (PFS) by ICR

End point title	Progression-free survival (PFS) by ICR
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End point description:

The time from the first dose of study treatment to the date of documented disease progression (per RECIST 1.1) or death from any cause.

End point type	Secondary
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End point timeframe:

Up to 45 months

End point values	Cohort I	Cohort II		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	80	7		
Units: months				
median (confidence interval 95%)	5.49 (3.65 to 7.29)	1.87 (1.22 to 1.87)		

Statistical analyses

No statistical analyses for this end point

Secondary: ORR by Investigator Assessment

End point title	ORR by Investigator Assessment
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End point description:

Number of subjects who achieved a confirmed BOR of either CR or PR during treatment per RECIST 1.1

End point type	Secondary
End point timeframe:	
Up to 45 months	

End point values	Cohort I	Cohort II		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	80	7		
Units: participants				
number (not applicable)	34	0		

Statistical analyses

No statistical analyses for this end point

Secondary: DOR by Investigator Assessment

End point title	DOR by Investigator Assessment
End point description:	
The time from the first confirmed objective response (CR or PR) to documented PD per RECIST 1.1 or death from any cause.	
End point type	Secondary
End point timeframe:	
Up to 45 months	

End point values	Cohort I	Cohort II		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	34	0 ^[4]		
Units: months				
median (confidence interval 95%)	11.10 (7.46 to 14.06)	(to)		

Notes:

[4] - Participant data were not available for assessment in this cohort.

Statistical analyses

No statistical analyses for this end point

Secondary: DOR ≥ 16 Weeks by Investigator Assessment

End point title	DOR ≥ 16 Weeks by Investigator Assessment
End point description:	
Proportion of subjects with a DOR ≥ 16 weeks per RECIST 1.1	
End point type	Secondary
End point timeframe:	
24 weeks, up to 45 months	

End point values	Cohort I	Cohort II		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	34	0 ^[5]		
Units: participants				
number (not applicable)	31			

Notes:

[5] - Participant data were not available for assessment in this cohort.

Statistical analyses

No statistical analyses for this end point

Secondary: DCR by Investigator Assessment

End point title	DCR by Investigator Assessment
End point description: Number of subjects who achieved a best overall response of stable disease (SD), non-CR/non-PD, or confirmed CR or PR per RECIST 1.1	
End point type	Secondary
End point timeframe: Up to 45 months	

End point values	Cohort I	Cohort II		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	80	7		
Units: participants				
number (not applicable)	54	1		

Statistical analyses

No statistical analyses for this end point

Secondary: PFS by Investigator Assessment

End point title	PFS by Investigator Assessment
End point description: The time from the first dose of study treatment to the date of documented disease progression (per RECIST 1.1) or death from any cause.	
End point type	Secondary
End point timeframe: Up to 45 months	

End point values	Cohort I	Cohort II		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	80	7		
Units: months				
median (confidence interval 95%)	5.37 (3.55 to 7.29)	1.77 (0.79 to 1.94)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

End point title	Overall Survival
End point description:	The time from the first dose of study treatment until the date of death from any cause
End point type	Secondary
End point timeframe:	Up to 45 months

End point values	Cohort I	Cohort II		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	80	7		
Units: months				
median (confidence interval 95%)	15.54 (10.38 to 18.66)	5.52 (1.22 to 5.52)		

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of Adverse Events (AEs)

End point title	Incidence of Adverse Events (AEs)
End point description:	Number of subjects who experienced AEs or serious adverse events
End point type	Secondary
End point timeframe:	Up to 45 months

End point values	Cohort I	Cohort II		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	80	7		
Units: participants				
number (not applicable)				
Any Treatment Emergent Adverse Events (TEAEs)	78	6		
Zanidatamab related TEAE	61	2		
Any Treatment Emergent Serious Adverse Event (SAE)	43	3		
Zanidatamab related serious TEAE	8	0		
Zanidatamab related TEAE led to discontinuation	2	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of Laboratory Abnormalities

End point title	Incidence of Laboratory Abnormalities
End point description: Number of subjects who experienced a maximum severity of Grade 3 or higher post-baseline laboratory abnormality, including either hematology or chemistry. Grades are defined using National Cancer Institute's Common Terminology Criteria for Adverse Events (CTCAE), version 5.0	
End point type	Secondary
End point timeframe: Up to 45 months	

End point values	Cohort I	Cohort II		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	80	7		
Units: participants				
number (not applicable)	37	7		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Serum Concentration of ZW25

End point title	Maximum Serum Concentration of ZW25
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End point description:

End point type	Secondary
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End point timeframe:

Pre-dose, end of infusion, 2, 4, 8, 24 and 96 hours post dose

End point values	Cohort I	Cohort II		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	3		
Units: microgram per milliliter				
geometric mean (geometric coefficient of variation)	457.6 (\pm 15.44)	443.6 (\pm 24.10)		

Statistical analyses

No statistical analyses for this end point

Secondary: Trough concentration of ZW25

End point title	Trough concentration of ZW25
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End point description:

Minimum observed serum concentration (trough)

End point type	Secondary
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End point timeframe:

Pre-dose, end of infusion, 2, 4, 8, 24 and 96 hours post dose

End point values	Cohort I	Cohort II		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	3		
Units: microgram per milliliter				
geometric mean (geometric coefficient of variation)	73.4 (\pm 42.10)	46.5 (\pm 18.66)		

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of Anti-drug Antibodies (ADAs)

End point title	Incidence of Anti-drug Antibodies (ADAs)
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End point description:

Number of subjects who develop ADAs

End point type	Secondary
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End point timeframe:

Up to 45 months

End point values	Cohort I	Cohort II		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	78	7		
Units: participants				
number (not applicable)	1	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected from the start of dosing of any study drug up until 30 days after last study dose, up to approximately 3 years 10 months (46 months).

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	25
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Reporting groups

Reporting group title	Cohort I
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Reporting group description:

Participants with advanced or metastatic biliary tract cancer with HER2 amplification by in situ hybridization (ISH) and HER2 overexpression by immunohistochemistry (IHC) which includes IHC 2+ or 3+

Reporting group title	Cohort II
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Reporting group description:

Participants with advanced or metastatic biliary tract cancer with HER2 amplification by ISH and HER2 IHC 0 or 1+.

Serious adverse events	Cohort I	Cohort II	
Total subjects affected by serious adverse events			
subjects affected / exposed	43 / 80 (53.75%)	3 / 7 (42.86%)	
number of deaths (all causes)	60	6	
number of deaths resulting from adverse events	2	2	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cholangiocarcinoma			
subjects affected / exposed	1 / 80 (1.25%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Haemangioma			
subjects affected / exposed	1 / 80 (1.25%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraneoplastic syndrome			
subjects affected / exposed	1 / 80 (1.25%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			

Aortic aneurysm			
subjects affected / exposed	1 / 80 (1.25%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 80 (2.50%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 80 (0.00%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pyrexia			
subjects affected / exposed	1 / 80 (1.25%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	1 / 80 (1.25%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	1 / 80 (1.25%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	1 / 80 (1.25%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Aspartate aminotransferase increased			

subjects affected / exposed	1 / 80 (1.25%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alanine aminotransferase increased			
subjects affected / exposed	2 / 80 (2.50%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bilirubin conjugated increased			
subjects affected / exposed	1 / 80 (1.25%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ejection fraction decreased			
subjects affected / exposed	1 / 80 (1.25%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	1 / 80 (1.25%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Supraventricular tachycardia			
subjects affected / exposed	1 / 80 (1.25%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 80 (1.25%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	1 / 80 (1.25%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Blood and lymphatic system disorders			
Abdominal lymphadenopathy			
subjects affected / exposed	1 / 80 (1.25%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia			
subjects affected / exposed	1 / 80 (1.25%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Obstruction gastric			
subjects affected / exposed	3 / 80 (3.75%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	2 / 80 (2.50%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	1 / 80 (1.25%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematemesis			
subjects affected / exposed	1 / 80 (1.25%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Duodenal obstruction			
subjects affected / exposed	1 / 80 (1.25%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			
subjects affected / exposed	1 / 80 (1.25%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Dyspepsia			
subjects affected / exposed	0 / 80 (0.00%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal stenosis			
subjects affected / exposed	1 / 80 (1.25%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Faeces discoloured			
subjects affected / exposed	1 / 80 (1.25%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer			
subjects affected / exposed	1 / 80 (1.25%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	1 / 80 (1.25%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestinal obstruction			
subjects affected / exposed	1 / 80 (1.25%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	1 / 80 (1.25%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 80 (1.25%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			

subjects affected / exposed	1 / 80 (1.25%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	3 / 80 (3.75%)	2 / 7 (28.57%)	
occurrences causally related to treatment / all	0 / 6	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary obstruction			
subjects affected / exposed	4 / 80 (5.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice			
subjects affected / exposed	2 / 80 (2.50%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice cholestatic			
subjects affected / exposed	5 / 80 (6.25%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bile duct stenosis			
subjects affected / exposed	1 / 80 (1.25%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	1 / 80 (1.25%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic failure			
subjects affected / exposed	1 / 80 (1.25%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hepatitis cholestatic			

subjects affected / exposed	0 / 80 (0.00%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematochezia			
subjects affected / exposed	1 / 80 (1.25%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 80 (1.25%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	4 / 80 (5.00%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	4 / 80 (5.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary tract infection			
subjects affected / exposed	1 / 80 (1.25%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary sepsis			
subjects affected / exposed	0 / 80 (0.00%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
subjects affected / exposed	2 / 80 (2.50%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			

subjects affected / exposed	1 / 80 (1.25%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis infective			
subjects affected / exposed	1 / 80 (1.25%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral candidiasis			
subjects affected / exposed	1 / 80 (1.25%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver abscess			
subjects affected / exposed	1 / 80 (1.25%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	1 / 80 (1.25%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 80 (0.00%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudomembranous colitis			
subjects affected / exposed	1 / 80 (1.25%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 80 (1.25%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gamma-glutamyltransferase increased			

subjects affected / exposed	1 / 80 (1.25%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Malnutrition			
subjects affected / exposed	1 / 80 (1.25%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Cohort I	Cohort II	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	78 / 80 (97.50%)	5 / 7 (71.43%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	10 / 80 (12.50%)	0 / 7 (0.00%)	
occurrences (all)	16	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	6 / 80 (7.50%)	1 / 7 (14.29%)	
occurrences (all)	7	1	
Fatigue			
subjects affected / exposed	11 / 80 (13.75%)	0 / 7 (0.00%)	
occurrences (all)	15	0	
Odema peripheral			
subjects affected / exposed	5 / 80 (6.25%)	0 / 7 (0.00%)	
occurrences (all)	5	0	
Pyrexia			
subjects affected / exposed	14 / 80 (17.50%)	0 / 7 (0.00%)	
occurrences (all)	23	0	
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	3 / 80 (3.75%)	1 / 7 (14.29%)	
occurrences (all)	3	1	
Reproductive system and breast			

disorders			
Pelvic pain			
subjects affected / exposed	0 / 80 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	2	
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	2 / 80 (2.50%)	1 / 7 (14.29%)	
occurrences (all)	2	2	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	6 / 80 (7.50%)	0 / 7 (0.00%)	
occurrences (all)	6	0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	16 / 80 (20.00%)	1 / 7 (14.29%)	
occurrences (all)	28	1	
Aspartate aminotransferase increased			
subjects affected / exposed	15 / 80 (18.75%)	1 / 7 (14.29%)	
occurrences (all)	30	1	
Blood bilirubin increased			
subjects affected / exposed	10 / 80 (12.50%)	0 / 7 (0.00%)	
occurrences (all)	12	0	
Blood alkaline phosphatase increased			
subjects affected / exposed	7 / 80 (8.75%)	2 / 7 (28.57%)	
occurrences (all)	10	2	
Gamma-glutamyltransferase increased			
subjects affected / exposed	6 / 80 (7.50%)	1 / 7 (14.29%)	
occurrences (all)	8	1	
Ejection fraction decreased			
subjects affected / exposed	11 / 80 (13.75%)	0 / 7 (0.00%)	
occurrences (all)	12	0	
Blood creatinine increased			
subjects affected / exposed	6 / 80 (7.50%)	1 / 7 (14.29%)	
occurrences (all)	10	1	
Neutrophil count increased			

subjects affected / exposed occurrences (all)	0 / 80 (0.00%) 0	1 / 7 (14.29%) 1	
Platelet count decreased subjects affected / exposed occurrences (all)	3 / 80 (3.75%) 3	1 / 7 (14.29%) 1	
Weight decreased subjects affected / exposed occurrences (all)	11 / 80 (13.75%) 13	1 / 7 (14.29%) 1	
Injury, poisoning and procedural complications Procedural pain subjects affected / exposed occurrences (all)	1 / 80 (1.25%) 1	1 / 7 (14.29%) 1	
Infusion related reaction subjects affected / exposed occurrences (all)	27 / 80 (33.75%) 30	1 / 7 (14.29%) 1	
Fall subjects affected / exposed occurrences (all)	0 / 80 (0.00%) 0	1 / 7 (14.29%) 1	
Cardiac disorders Palpitations subjects affected / exposed occurrences (all)	0 / 80 (0.00%) 0	1 / 7 (14.29%) 1	
Nervous system disorders Peripheral sensory neuropathy subjects affected / exposed occurrences (all)	6 / 80 (7.50%) 6	0 / 7 (0.00%) 0	
Dizziness subjects affected / exposed occurrences (all)	7 / 80 (8.75%) 8	0 / 7 (0.00%) 0	
Blood and lymphatic system disorders Anemia subjects affected / exposed occurrences (all)	18 / 80 (22.50%) 25	3 / 7 (42.86%) 4	
Leukocytosis subjects affected / exposed occurrences (all)	0 / 80 (0.00%) 0	1 / 7 (14.29%) 1	

Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	16 / 80 (20.00%)	0 / 7 (0.00%)	
occurrences (all)	21	0	
Abdominal pain upper			
subjects affected / exposed	7 / 80 (8.75%)	0 / 7 (0.00%)	
occurrences (all)	8	0	
Duodenal ulcer			
subjects affected / exposed	1 / 80 (1.25%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Diarrhoea			
subjects affected / exposed	39 / 80 (48.75%)	0 / 7 (0.00%)	
occurrences (all)	106	0	
Constipation			
subjects affected / exposed	5 / 80 (6.25%)	0 / 7 (0.00%)	
occurrences (all)	5	0	
Ascites			
subjects affected / exposed	4 / 80 (5.00%)	1 / 7 (14.29%)	
occurrences (all)	4	1	
Dyspepsia			
subjects affected / exposed	5 / 80 (6.25%)	0 / 7 (0.00%)	
occurrences (all)	6	0	
Vomiting			
subjects affected / exposed	13 / 80 (16.25%)	1 / 7 (14.29%)	
occurrences (all)	20	1	
Nausea			
subjects affected / exposed	14 / 80 (17.50%)	0 / 7 (0.00%)	
occurrences (all)	20	0	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	11 / 80 (13.75%)	0 / 7 (0.00%)	
occurrences (all)	13	0	
Rash			
subjects affected / exposed	7 / 80 (8.75%)	0 / 7 (0.00%)	
occurrences (all)	7	0	
Renal and urinary disorders			

Pollakiuria			
subjects affected / exposed	1 / 80 (1.25%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Renal failure			
subjects affected / exposed	0 / 80 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	0 / 80 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
COVID-19			
subjects affected / exposed	5 / 80 (6.25%)	1 / 7 (14.29%)	
occurrences (all)	5	1	
Urinary tract infection			
subjects affected / exposed	6 / 80 (7.50%)	0 / 7 (0.00%)	
occurrences (all)	8	0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	13 / 80 (16.25%)	0 / 7 (0.00%)	
occurrences (all)	14	0	
Hypoalbuminaemia			
subjects affected / exposed	6 / 80 (7.50%)	0 / 7 (0.00%)	
occurrences (all)	11	0	
Hypomagnesaemia			
subjects affected / exposed	5 / 80 (6.25%)	0 / 7 (0.00%)	
occurrences (all)	8	0	
Hypokalaemia			
subjects affected / exposed	11 / 80 (13.75%)	0 / 7 (0.00%)	
occurrences (all)	15	0	
Hypochloraemia			
subjects affected / exposed	1 / 80 (1.25%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Hyponatraemia			
subjects affected / exposed	3 / 80 (3.75%)	1 / 7 (14.29%)	
occurrences (all)	3	1	
Hypoproteinaemia			

subjects affected / exposed	1 / 80 (1.25%)	1 / 7 (14.29%)	
occurrences (all)	1	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 April 2020	Updated pain assessment questionnaires, removed quality of life questionnaires, and clarified administration procedures
21 April 2021	Clarified and revised eligibility criteria, added clarification on assessments and procedures, and updated safety reporting procedures.
08 September 2023	Administrative changes were incorporated.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported