Clinical trial results:
A Phase 2/3 Trial to Evaluate Margetuximab in Combination with INCMGA00012 and Chemotherapy or MGD013 and Chemotherapy in Patients with Metastatic or Locally Advanced, Treatment-naïve, HER2-Positive Gastric or Gastroesophageal Junction Cancer

Summary

EudraCT number	2019-004699-21
Trial protocol	DE GB PL IT
Global end of trial date	25 March 2025

Results information

Result version number	v1 (current)
This version publication date	13 June 2025
First version publication date	13 June 2025

Trial information

Trial identification

Sponsor protocol code	CP-MGAH22-06

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04082364
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	MacroGenics, Inc
Sponsor organisation address	9704 Medical Center Drive, Rockville, MD, United States, 20850
Public contact	Global Trial Manager, MacroGenics, Inc., 301 2515172, info@macrogenics.com
Scientific contact	Global Trial Manager, MacroGenics, Inc., 301 2515172, info@macrogenics.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	Interim
Date of interim/final analysis	26 September 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 January 2024
Global end of trial reached?	Yes
Global end of trial date	25 March 2025
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Cohort A:
To evaluate the safety and tolerability of margetuximab + retifanlimab in patients with untreated locally advanced or metastatic gastric cancer (GC) or gastroesophageal junction (GEJ) cancer that is human epidermal growth factor 2 (HER2) immunohistochemistry (IHC) 3+ and PD-L1+ by IHC staining.

To evaluate the ORR of margetuximab plus retifanlimab for non-MSI-H patients in the response evaluable population (REP) using Investigator-assessed radiology reviews.

Cohort B, Part 1:
To select the best margetuximab, chemotherapy and CPI-containing combination regimen for further evaluation in Part 2, based on evaluation of safety and ORR in the primary response evaluable population (PREP) of patients with GC or GEJ cancer, irrespective of PD-L1 status. Note: This objective was removed under Protocol Amendment 5.

Protection of trial subjects:

This study was conducted under United States Investigational New Drug application, in compliance with Good Clinical Practice, as well as all applicable local and national laws and regulations of countries in which the trial was performed. At each trial site, an institutional review board (IRB) or independent ethics committee (IEC) reviewed and approved the clinical trial protocol, the current and previous versions of the Investigator's Brochure, and informed consent form(s), as applicable. The IRB/IEC subsequently approved protocol amendments and revisions. Investigators were responsible for obtaining and documenting written informed consent from each participant or legal representative. Written informed consent was obtained for all participants before any protocol-specific procedures or interventions were performed.

Background therapy:

Part A contained no background therapy
Part B used a background chemotherapy combination of either modified fluorouracil, leucovorin, and oxaliplatin (mFOLFOX-6), or capecitabine and oxaliplatin (XELOX),commonly used regimens for first-line HER2 positive GC and GEJ cancer patients worldwide. The investigator selected the background therapy.

Evidence for comparator: -

Actual start date of recruitment	30 September 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 2
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	Italy: 1
Country: Number of subjects enrolled	Korea, Republic of: 19

Country: Number of subjects enrolled	Singapore: 1
Country: Number of subjects enrolled	United States: 24
Country: Number of subjects enrolled	China: 29
Country: Number of subjects enrolled	Taiwan: 5
Worldwide total number of subjects	82
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)	45
From 65 to 84 years	37
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants with untreated locally advanced unresectable or metastatic HER2+ gastric or gastroesophageal adenocarcinoma.

Period 1

Period 1 title	Entire study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort B: Control Arm

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Trastuzumab
Investigational medicinal product code	
Other name	Herceptin
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

8 mg/kg loading dose, then 6 mg/kg, every 3 weeks

Investigational medicinal product name	Background chemotherapy
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

One of two background chemotherapy regimens could be selected by the investigator;
1) modified FOLFOX-6: fluorouracil IV bolus (400 mg/m2), fluorouracil IV infusion (2400 mg/m2 over 48 hours), leucovorin IV (400 mg/m2) and oxaliplatin IV (85 mg/m2) (mFOLFOX-6), every 2 weeks
2) XELOX: capecitabine 1000 mg/m2 orally twice daily for 14/21 days, and oxaliplatin IV (130 mg/m2, every 3 weeks)

Arm title	Cohort B: Experimental Arm 1

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Margetuximab
Investigational medicinal product code	
Other name	MGAH22
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

15 mg/kg IV, every 3 weeks

Investigational medicinal product name	Background chemotherapy
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion

Routes of administration	Intravenous use

Dosage and administration details:

One of two background chemotherapy regimens could be selected by the investigator;
1) modified FOLFOX-6: fluorouracil IV bolus (400 mg/m2), fluorouracil IV infusion (2400 mg/m2 over 48 hours), leucovorin IV (400 mg/m2) and oxaliplatin IV (85 mg/m2) (mFOLFOX-6), every 2 weeks
2) XELOX: capecitabine 1000 mg/m2 orally twice daily for 14/21 days, and oxaliplatin IV (130 mg/m2, every 3 weeks)

Investigational medicinal product name	Retifanlimab
Investigational medicinal product code	
Other name	INCMAG00012, MGA012
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

375 mg IV, every 3 weeks

Arm title	Cohort B: Experimental Arm 2

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Margetuximab
Investigational medicinal product code	
Other name	MGAH22
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

15 mg/kg IV, every 3 weeks

Investigational medicinal product name	Tebotelimab
Investigational medicinal product code	
Other name	MGD013
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

600 mg IV, every 3 weeks

Investigational medicinal product name	Background chemotherapy
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

One of two background chemotherapy regimens could be selected by the investigator;
1) modified FOLFOX-6: fluorouracil IV bolus (400 mg/m2), fluorouracil IV infusion (2400 mg/m2 over 48 hours), leucovorin IV (400 mg/m2) and oxaliplatin IV (85 mg/m2) (mFOLFOX-6), every 2 weeks
2) XELOX: capecitabine 1000 mg/m2 orally twice daily for 14/21 days, and oxaliplatin IV (130 mg/m2, every 3 weeks)

Arm title	Cohort B: Experimental Arm 3

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Margetuximab
Investigational medicinal product code	
Other name	MGAH22
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

15 mg/kg IV, every 3 weeks

Investigational medicinal product name	Background chemotherapy
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

One of two background chemotherapy regimens could be selected by the investigator;
1) modified FOLFOX-6: fluorouracil IV bolus (400 mg/m2), fluorouracil IV infusion (2400 mg/m2 over 48 hours), leucovorin IV (400 mg/m2) and oxaliplatin IV (85 mg/m2) (mFOLFOX-6), every 2 weeks
2) XELOX: capecitabine 1000 mg/m2 orally twice daily for 14/21 days, and oxaliplatin IV (130 mg/m2, every 3 weeks)

Arm title	Cohort A: Chemotherapy-free Arm

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Margetuximab
Investigational medicinal product code	
Other name	MGAH22
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

15 mg/kg IV, every 3 weeks

Investigational medicinal product name	Retifanlimab
Investigational medicinal product code	
Other name	INCMAG00012, MGA012
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

375 mg IV, every 3 weeks

Number of subjects in period 1	Cohort B: Control Arm	Cohort B: Experimental Arm 1	Cohort B: Experimental Arm 2
Started	8	10	6
Completed	2	7	3
Not completed	6	3	3
Physician decision	1	1	-
Consent withdrawn by subject	1	1	-
Death	1	1	1
Study terminated by sponsor	2	-	2
Lost to follow-up	1	-	-
Progression of disease	-	-	-

Number of subjects in period 1	Cohort B: Experimental Arm 3	Cohort A: Chemotherapy-free Arm
Started	10	48
Completed	2	17
Not completed	8	31
Physician decision	2	1

Consent withdrawn by subject	-	1
Death	2	23
Study terminated by sponsor	3	5
Lost to follow-up	-	1
Progression of disease	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Cohort B: Control Arm
Reporting group description: -	
Reporting group title	Cohort B: Experimental Arm 1
Reporting group description: -	
Reporting group title	Cohort B: Experimental Arm 2
Reporting group description: -	
Reporting group title	Cohort B: Experimental Arm 3
Reporting group description: -	
Reporting group title	Cohort A: Chemotherapy-free Arm
Reporting group description: -	

Reporting group values	Cohort B: Control Arm	Cohort B: Experimental Arm 1	Cohort B: Experimental Arm 2
Number of subjects	8	10	6
Age categorical Units: Subjects			
Adults (18-64 years)	5	6	3
From 65-84 years	3	4	3
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	61.4	61.8	60.0
standard deviation	± 7.25	± 7.64	± 16.45
Gender categorical Units: Subjects			
Female	1	2	4
Male	7	8	2

Reporting group values	Cohort B: Experimental Arm 3	Cohort A: Chemotherapy-free Arm	Total
Number of subjects	10	48	82
Age categorical Units: Subjects			
Adults (18-64 years)	6	25	45
From 65-84 years	4	23	37
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	60.5	62.9	
standard deviation	± 19.70	± 12.25	-
Gender categorical Units: Subjects			
Female	1	6	14
Male	9	42	68

Subject analysis sets	
Subject analysis set title	Cohort A Response Evaluable Population
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

All patients who received at least one dose of study treatment and had baseline radiographic tumor assessment. This population will be used for objective response related efficacy analyses.

Subject analysis set title	Cohort B: Response Evaluable Population
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

All patients who were assigned to Cohort B, received at least one dose of study treatment, and had baseline radiographic tumor assessment. This population will be used for objective response related efficacy analyses

Subject analysis set title	ITT Population
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All patients who are assigned to treatment in Cohort A and all participants who are randomized into Cohort B of the study.

Subject analysis set title	Safety population
Subject analysis set type	Safety analysis

Subject analysis set description:

All patients who receive at least one dose of study drug.

Reporting group values	Cohort A Response Evaluable Population	Cohort B: Response Evaluable Population	ITT Population
Number of subjects	48	33	82
Age categorical Units: Subjects			
Adults (18-64 years)	25	20	20
From 65-84 years	23	13	14
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	62.9		62.5
standard deviation	± 12.25	±	± 10.30
Gender categorical Units: Subjects			
Female	6	8	14
Male	42	25	68

Reporting group values	Safety population		
Number of subjects	81		
Age categorical Units: Subjects			
Adults (18-64 years)	45		
From 65-84 years	36		
85 years and over	0		
Age continuous Units: years			
arithmetic mean			
standard deviation	±		
Gender categorical Units: Subjects			
Female	14		

Male	67		

End points

End points reporting groups

Reporting group title	Cohort B: Control Arm
Reporting group description: -	
Reporting group title	Cohort B: Experimental Arm 1
Reporting group description: -	
Reporting group title	Cohort B: Experimental Arm 2
Reporting group description: -	
Reporting group title	Cohort B: Experimental Arm 3
Reporting group description: -	
Reporting group title	Cohort A: Chemotherapy-free Arm
Reporting group description: -	
Subject analysis set title	Cohort A Response Evaluable Population
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
All patients who received at least one dose of study treatment and had baseline radiographic tumor assessment. This population will be used for objective response related efficacy analyses.	
Subject analysis set title	Cohort B: Response Evaluable Population
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
All patients who were assigned to Cohort B, received at least one dose of study treatment, and had baseline radiographic tumor assessment. This population will be used for objective response related efficacy analyses	
Subject analysis set title	ITT Population
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All patients who are assigned to treatment in Cohort A and all participants who are randomized into Cohort B of the study.	
Subject analysis set title	Safety population
Subject analysis set type	Safety analysis
Subject analysis set description:	
All patients who receive at least one dose of study drug.	

Primary: Type and number of adverse events in Cohort A

End point title	Type and number of adverse events in Cohort A[1]
End point description:	
End point type	Primary
End point timeframe:	
Adverse events are recorded from the time of informed consent signature through 30 days of the last dose of study treatment	

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: Data displays were summary tables with the number and percent of participants who experienced a given event. There is no active control or comparator to allow for statistical inferences.

End point values	Cohort B: Control Arm	Cohort B: Experimental Arm 1	Cohort B: Experimental Arm 2	Cohort B: Experimental Arm 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[2]	0[3]	0[4]	0[5]
Units: participants				
Study treatment related adverse event				
Severe adverse event				
Severe study treatment-related adverse event				
Study treatment-related serious adverse event				
Fatal adverse event				
Number not assigned to Part A				

Notes:

[2] - This is not an end point for Cohort B of the study.

[3] - This is not an end point for Cohort B of the study.

[4] - This is not an end point for Cohort B of the study.

[5] - This is not an end point for Cohort B of the study.

End point values	Cohort A: Chemotherapy-free Arm	Safety population		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	48	81		
Units: participants				
Study treatment related adverse event	38	38		
Severe adverse event	25	25		
Severe study treatment-related adverse event	12	12		
Study treatment-related serious adverse event	9	9		
Fatal adverse event	2	2		
Number not assigned to Part A	0	33		

Statistical analyses

No statistical analyses for this end point

Primary: Objective response rate in Cohort A

End point title	Objective response rate in Cohort A[6]

End point description:

The percentage of patients who have a complete or partial response to study treatment.

End point type	Primary

End point timeframe:

From the first dose of study treatment throughout the study

Notes:

[6] - 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 analysis is not indicated for single-arm evaluation of Objective Response Rate.

End point values	Cohort B: Control Arm	Cohort B: Experimental Arm 1	Cohort B: Experimental Arm 2	Cohort B: Experimental Arm 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[7]	0[8]	0[9]	0[10]
Units: percentage				
number (confidence interval 95%)	(to)	(to)	(to)	(to)

Notes:

[7] - This is not an end point for Cohort B of the study.

[8] - This is not an end point for Cohort B of the study.

[9] - This is not an end point for Cohort B of the study.

[10] - This is not an end point for Cohort B of the study.

End point values	Cohort A: Chemotherapy-free Arm	Cohort A Response Evaluable Population		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	48	48		
Units: percentage				
number (confidence interval 95%)	52.1 (37.2 to 66.7)	52.1 (37.2 to 66.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Median duration of Response in Cohort A

End point title	Median duration of Response in Cohort A

End point description:

End point type	Secondary

End point timeframe:

From the first date of complete or partial response to the date of first documented disease progression or death, whichever is first.

End point values	Cohort B: Control Arm	Cohort B: Experimental Arm 1	Cohort B: Experimental Arm 2	Cohort B: Experimental Arm 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[11]	0[12]	0[13]	0[14]
Units: Months				
median (confidence interval 95%)	(to)	(to)	(to)	(to)

Notes:

[11] - This is not an end point for Cohort B of the study.

[12] - This is not an end point for Cohort B of the study.

[13] - This is not an end point for Cohort B of the study.

[14] - This is not an end point for Cohort B of the study.

End point values	Cohort A: Chemotherapy-free Arm	Cohort A Response Evaluable Population		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	25[15]	25[16]		
Units: Months				
median (confidence interval 95%)	16.1 (9.00 to 21.91)	16.1 (9.00 to 21.91)		

Notes:

[15] - Only 25/48 participants responded to treatment and were assessed for duration of response.

[16] - Only 25/48 participants responded to treatment and were assessed for duration of response.

Statistical analyses

No statistical analyses for this end point

Secondary: Median progression-free survival in Cohort A

End point title	Median progression-free survival in Cohort A

End point description:

End point type	Secondary

End point timeframe:

Progression-free survival is assessed from the first dose of study treatment until documented disease progression or death, whichever comes first.

End point values	Cohort B: Control Arm	Cohort B: Experimental Arm 1	Cohort B: Experimental Arm 2	Cohort B: Experimental Arm 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[17]	0[18]	0[19]	0[20]
Units: Months				
median (confidence interval 95%)	(to)	(to)	(to)	(to)

Notes:

[17] - This is not an end point for Cohort B of the study.

[18] - This is not an end point for Cohort B of the study.

[19] - This is not an end point for Cohort B of the study.

[20] - This is not an end point for Cohort B of the study.

End point values	Cohort A: Chemotherapy-free Arm	Cohort A Response Evaluable Population		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	48	48		
Units: Months				
median (confidence interval 95%)	9.8 (4.60 to 14.75)	9.8 (4.60 to 14.75)		

Statistical analyses

No statistical analyses for this end point

Secondary: Objective response rate in Cohort B

End point title	Objective response rate in Cohort B

End point description:

End point type	Secondary

End point timeframe:

From the first dose of study treatment throughout the study

End point values	Cohort B: Control Arm	Cohort B: Experimental Arm 1	Cohort B: Experimental Arm 2	Cohort B: Experimental Arm 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	9	6	10
Units: percentage				
number (confidence interval 95%)	62.5 (24.5 to 91.5)	88.9 (51.8 to 99.7)	83.3 (35.9 to 99.6)	90.0 (55.5 to 99.7)

End point values	Cohort A: Chemotherapy-free Arm	Cohort B: Response Evaluable Population		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	0[21]	33		
Units: percentage				
number (confidence interval 95%)	(to)	81.8 (64.5 to 93.0)		

Notes:

[21] - This is not an end point for Cohort A of the study.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants who develop anti-drug antibodies to margetuximab

End point title	Number of participants who develop anti-drug antibodies to margetuximab

End point description:

End point type	Secondary

End point timeframe:

From the first dose of study treatment throughout the study treatment.

End point values	Cohort B: Control Arm	Cohort B: Experimental Arm 1	Cohort B: Experimental Arm 2	Cohort B: Experimental Arm 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[22]	9	6	10
Units: participants				
Negative at baseline, negative post-baseline		8	5	10
Negative at baseline, positive post-baseline		1	0	0
Positive at baseline, negative post-baseline		0	0	0
not done at baseline, negative post-baseline		0	1	0
Did not receive margetuximab		0	0	0

Notes:

[22] - Participants in this arm did not receive margetuximab.

End point values	Cohort A: Chemotherapy-free Arm	Safety population		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	48	81		
Units: participants				
Negative at baseline, negative post-baseline	40	63		
Negative at baseline, positive post-baseline	5	6		
Positive at baseline, negative post-baseline	2	2		
not done at baseline, negative post-baseline	1	2		
Did not receive margetuximab	0	8		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants who develop anti-drug antibodies to retifanlimab

End point title	Number of participants who develop anti-drug antibodies to retifanlimab

End point description:

End point type	Secondary

End point timeframe:

From the first dose of study treatment throughout study treatment.

End point values	Cohort B: Control Arm	Cohort B: Experimental Arm 1	Cohort B: Experimental Arm 2	Cohort B: Experimental Arm 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[23]	9	0[24]	0[25]
Units: participants				
Negative at baseline, negative post-baseline		9		
Negative at baseline, positive post - baseline		0		
Positive at baseline, negative post baseline		0		
Not done at baseline, negative post baseline		0		
Did not receive retifanlimab		0		

Notes:

[23] - This arm did not receive retifanlimab, and is not evaluable for retifanlimab ADA.

[24] - This arm did not receive retifanlimab, and is not evaluable for retifanlimab ADA.

[25] - This arm did not receive retifanlimab, and is not evaluable for retifanlimab ADA.

End point values	Cohort A: Chemotherapy-free Arm	Safety population		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	48	81		
Units: participants				
Negative at baseline, negative post-baseline	43	52		
Negative at baseline, positive post - baseline	3	3		
Positive at baseline, negative post baseline	1	1		
Not done at baseline, negative post baseline	1	1		
Did not receive retifanlimab	0	24		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants who develop anti-drug antibodies to tebotelimab

End point title	Number of participants who develop anti-drug antibodies to tebotelimab

End point description:

End point type	Secondary

End point timeframe:

y8b687

End point values	Cohort B: Control Arm	Cohort B: Experimental Arm 1	Cohort B: Experimental Arm 2	Cohort B: Experimental Arm 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[26]	0[27]	6	0[28]
Units: participants				
Negative at baseline, negative post-baseline			1	
Negative at baseline, positive post-baseline			4	
Negative at baseline, not done post-baseline			1	
Did not receive tebotelimab			0	

Notes:

[26] - This treatment group did not receive tebotelimab

[27] - This treatment group did not receive tebotelimab

[28] - This treatment group did not receive tebotelimab

End point values	Cohort A: Chemotherapy-free Arm	Safety population		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	0[29]	81		
Units: participants				
Negative at baseline, negative post-baseline		1		
Negative at baseline, positive post-baseline		4		
Negative at baseline, not done post-baseline		1		
Did not receive tebotelimab		75		

Notes:

[29] - This treatment group did not receive tebotelimab

Statistical analyses

No statistical analyses for this end point

Secondary: Disease control rate

End point title	Disease control rate

End point description:

End point type	Secondary

End point timeframe:

Disease control rate is measured from the randomization until 3 months after the first dose of study treatment for each participant.

End point values	Cohort B: Control Arm	Cohort B: Experimental Arm 1	Cohort B: Experimental Arm 2	Cohort B: Experimental Arm 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	9	6	10
Units: percentage				
number (confidence interval 95%)	87.5 (47.3 to 99.7)	100.0 (66.4 to 100.0)	100.0 (54.1 to 100.0)	100.0 (69.2 to 100.0)

End point values	Cohort A: Chemotherapy-free Arm	Cohort A Response Evaluable Population	Cohort B: Response Evaluable Population	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	48	48	33	
Units: percentage				
number (confidence interval 95%)	83.3 (69.8 to 92.5)	83.3 (69.8 to 92.5)	97.0 (84.2 to 99.9)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs were collected from the time of the first dose through 30 days after the last dose, average 6 month. All-cause mortality was collected from the first dose throughout the follow up period.

Adverse event reporting additional description:

AEs are based on physical exam, participant reports, and significant abnormal laboratory values. AEs were not collected in survival follow up. Only SAEs were collected in survival follow- if related to study treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups

Reporting group title	Cohort B: Control Arm
Reporting group description: -	
Reporting group title	Cohort B: Experimental Arm 1
Reporting group description: -	
Reporting group title	Cohort B: Experimental Arm 2
Reporting group description: -	
Reporting group title	Cohort B: Experimental Arm 3
Reporting group description: -	
Reporting group title	Cohort A: Chemotherapy-free Arm
Reporting group description: -	

Serious adverse events	Cohort B: Control Arm	Cohort B: Experimental Arm 1	Cohort B: Experimental Arm 2
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 8 (25.00%)	4 / 9 (44.44%)	5 / 6 (83.33%)
number of deaths (all causes)	1	1	1
number of deaths resulting from adverse events			
Investigations			
Platelet count decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant ovarian cyst			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pancreatic carcinoma			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 8 (0.00%)	2 / 9 (22.22%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest discomfort			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Dysphagia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			

subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric haemorrhage			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorder			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
oesophageal ulcer			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumatosis intestinalis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper gastrointestinal haemorrhage			

subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthenia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Biliary obstruction			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic function abnormal			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaundice cholestatic			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Combined pulmonary fibrosis and emphysema			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Immune-mediated lung disease			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash maculo-papular			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Immune-mediated renal disorder			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary incontinence			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Endocrine disorders			
Thyroiditis subacute			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
bacterial sepsis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza A			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Diabetic ketoacidosis			

subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Failure to thrive			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolic acidosis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Cohort B: Experimental Arm 3	Cohort A: Chemotherapy-free Arm	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 10 (40.00%)	20 / 48 (41.67%)	
number of deaths (all causes)	2	25	
number of deaths resulting from adverse events	1		
Investigations			
Platelet count decreased			
subjects affected / exposed	1 / 10 (10.00%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	3 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant ovarian cyst			
subjects affected / exposed	0 / 10 (0.00%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic carcinoma			

subjects affected / exposed	1 / 10 (10.00%)	0 / 48 (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			
Anaemia			
subjects affected / exposed	1 / 10 (10.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest discomfort			
subjects affected / exposed	0 / 10 (0.00%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Dysphagia			
subjects affected / exposed	0 / 10 (0.00%)	2 / 48 (4.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	0 / 10 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 10 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastric haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorder			
subjects affected / exposed	0 / 10 (0.00%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	0 / 10 (0.00%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
oesophageal ulcer			
subjects affected / exposed	0 / 10 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumatosis intestinalis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	0 / 10 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 10 (10.00%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthenia			

subjects affected / exposed	0 / 10 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Biliary obstruction			
subjects affected / exposed	0 / 10 (0.00%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic function abnormal			
subjects affected / exposed	0 / 10 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice cholestatic			
subjects affected / exposed	0 / 10 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Combined pulmonary fibrosis and emphysema			
subjects affected / exposed	0 / 10 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune-mediated lung disease			
subjects affected / exposed	0 / 10 (0.00%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pleural effusion			
subjects affected / exposed	0 / 10 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	0 / 10 (0.00%)	2 / 48 (4.17%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	0 / 10 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Rash maculo-papular			
subjects affected / exposed	0 / 10 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Immune-mediated renal disorder			
subjects affected / exposed	0 / 10 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	0 / 10 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary incontinence			
subjects affected / exposed	0 / 10 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Thyroiditis subacute			

subjects affected / exposed	0 / 10 (0.00%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
bacterial sepsis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 10 (10.00%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 10 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza A			
subjects affected / exposed	1 / 10 (10.00%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Metabolism and nutrition disorders			
Diabetic ketoacidosis			
subjects affected / exposed	0 / 10 (0.00%)	2 / 48 (4.17%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Failure to thrive			

subjects affected / exposed	0 / 10 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic acidosis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Cohort B: Control Arm	Cohort B: Experimental Arm 1	Cohort B: Experimental Arm 2
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 8 (87.50%)	9 / 9 (100.00%)	6 / 6 (100.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Fatigue			
subjects affected / exposed	1 / 8 (12.50%)	2 / 9 (22.22%)	1 / 6 (16.67%)
occurrences (all)	2	2	2
Oedema peripheral			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Pyrexia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	4
Respiratory, thoracic and mediastinal			

disorders			
Cough			
subjects affected / exposed	1 / 8 (12.50%)	3 / 9 (33.33%)	0 / 6 (0.00%)
occurrences (all)	1	4	0
Dyspnoea			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety disorder			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	1 / 8 (12.50%)	1 / 9 (11.11%)	1 / 6 (16.67%)
occurrences (all)	1	1	2
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	3 / 8 (37.50%)	5 / 9 (55.56%)	0 / 6 (0.00%)
occurrences (all)	3	6	0
Aspartate aminotransferase increased			
subjects affected / exposed	4 / 8 (50.00%)	6 / 9 (66.67%)	3 / 6 (50.00%)
occurrences (all)	6	10	6
Blood bilirubin increased			
subjects affected / exposed	3 / 8 (37.50%)	2 / 9 (22.22%)	1 / 6 (16.67%)
occurrences (all)	5	2	2
Blood creatine increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Ejection fraction decreased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	3 / 8 (37.50%)	0 / 9 (0.00%)	2 / 6 (33.33%)
occurrences (all)	5	0	2
Lymphocyte count decreased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	1 / 6 (16.67%)
occurrences (all)	5	0	4

Platelet count decreased			
subjects affected / exposed	7 / 8 (87.50%)	7 / 9 (77.78%)	6 / 6 (100.00%)
occurrences (all)	18	21	10
Weight decreased			
subjects affected / exposed	1 / 8 (12.50%)	1 / 9 (11.11%)	3 / 6 (50.00%)
occurrences (all)	1	1	6
White blood cell count decreased			
subjects affected / exposed	4 / 8 (50.00%)	7 / 9 (77.78%)	4 / 6 (66.67%)
occurrences (all)	12	22	9
Neutrophil count decreased			
subjects affected / exposed	5 / 8 (62.50%)	7 / 9 (77.78%)	6 / 6 (100.00%)
occurrences (all)	21	27	16
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	1 / 8 (12.50%)	3 / 9 (33.33%)	2 / 6 (33.33%)
occurrences (all)	1	6	4
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 8 (0.00%)	2 / 9 (22.22%)	1 / 6 (16.67%)
occurrences (all)	0	3	1
Headache			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Neurotoxicity			
subjects affected / exposed	1 / 8 (12.50%)	3 / 9 (33.33%)	1 / 6 (16.67%)
occurrences (all)	1	3	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 8 (25.00%)	3 / 9 (33.33%)	5 / 6 (83.33%)
occurrences (all)	9	6	8
Leukopenia			
subjects affected / exposed	1 / 8 (12.50%)	1 / 9 (11.11%)	2 / 6 (33.33%)
occurrences (all)	9	1	4
Gastrointestinal disorders			
Abdominal pain			

subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	2 / 8 (25.00%)	2 / 9 (22.22%)	0 / 6 (0.00%)
occurrences (all)	2	2	0
Diarrhoea			
subjects affected / exposed	2 / 8 (25.00%)	4 / 9 (44.44%)	2 / 6 (33.33%)
occurrences (all)	2	8	5
Dyspepsia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 6 (0.00%)
occurrences (all)	0	4	0
Nausea			
subjects affected / exposed	2 / 8 (25.00%)	4 / 9 (44.44%)	1 / 6 (16.67%)
occurrences (all)	3	10	1
Vomiting			
subjects affected / exposed	1 / 8 (12.50%)	1 / 9 (11.11%)	2 / 6 (33.33%)
occurrences (all)	1	3	2
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	1 / 8 (12.50%)	2 / 9 (22.22%)	1 / 6 (16.67%)
occurrences (all)	1	3	1
Rash			
subjects affected / exposed	1 / 8 (12.50%)	1 / 9 (11.11%)	0 / 6 (0.00%)
occurrences (all)	2	1	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	1 / 8 (12.50%)	2 / 9 (22.22%)	3 / 6 (50.00%)
occurrences (all)	1	2	3
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	0 / 8 (0.00%)	2 / 9 (22.22%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Infections and infestations			

COVID-19			
subjects affected / exposed	2 / 8 (25.00%)	1 / 9 (11.11%)	0 / 6 (0.00%)
occurrences (all)	3	1	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 8 (25.00%)	3 / 9 (33.33%)	2 / 6 (33.33%)
occurrences (all)	4	4	2
Hypoalbuminaemia			
subjects affected / exposed	1 / 8 (12.50%)	2 / 9 (22.22%)	4 / 6 (66.67%)
occurrences (all)	3	7	5
Hypocalcaemia			
subjects affected / exposed	2 / 8 (25.00%)	1 / 9 (11.11%)	2 / 6 (33.33%)
occurrences (all)	6	1	6
Hypokalaemia			
subjects affected / exposed	1 / 8 (12.50%)	1 / 9 (11.11%)	2 / 6 (33.33%)
occurrences (all)	1	1	2
Hyponatraemia			
subjects affected / exposed	0 / 8 (0.00%)	2 / 9 (22.22%)	3 / 6 (50.00%)
occurrences (all)	0	3	10

Non-serious adverse events	Cohort B: Experimental Arm 3	Cohort A: Chemotherapy-free Arm	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 10 (100.00%)	47 / 48 (97.92%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 10 (0.00%)	6 / 48 (12.50%)	
occurrences (all)	0	6	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 10 (20.00%)	3 / 48 (6.25%)	
occurrences (all)	2	4	
Fatigue			
subjects affected / exposed	0 / 10 (0.00%)	14 / 48 (29.17%)	
occurrences (all)	0	22	
Oedema peripheral			

subjects affected / exposed	1 / 10 (10.00%)	9 / 48 (18.75%)	
occurrences (all)	1	19	
Pyrexia			
subjects affected / exposed	2 / 10 (20.00%)	9 / 48 (18.75%)	
occurrences (all)	4	12	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 10 (0.00%)	7 / 48 (14.58%)	
occurrences (all)	0	9	
Dyspnoea			
subjects affected / exposed	0 / 10 (0.00%)	9 / 48 (18.75%)	
occurrences (all)	0	14	
Psychiatric disorders			
Anxiety disorder			
subjects affected / exposed	0 / 10 (0.00%)	5 / 48 (10.42%)	
occurrences (all)	0	7	
Insomnia			
subjects affected / exposed	0 / 10 (0.00%)	7 / 48 (14.58%)	
occurrences (all)	0	7	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	5 / 10 (50.00%)	2 / 48 (4.17%)	
occurrences (all)	17	2	
Aspartate aminotransferase increased			
subjects affected / exposed	3 / 10 (30.00%)	2 / 48 (4.17%)	
occurrences (all)	13	3	
Blood bilirubin increased			
subjects affected / exposed	4 / 10 (40.00%)	0 / 48 (0.00%)	
occurrences (all)	12	0	
Blood creatine increased			
subjects affected / exposed	0 / 10 (0.00%)	5 / 48 (10.42%)	
occurrences (all)	0	12	
Ejection fraction decreased			
subjects affected / exposed	2 / 10 (20.00%)	3 / 48 (6.25%)	
occurrences (all)	2	4	
Gamma-glutamyltransferase			

increased			
subjects affected / exposed	2 / 10 (20.00%)	0 / 48 (0.00%)	
occurrences (all)	2	0	
Lymphocyte count decreased			
subjects affected / exposed	3 / 10 (30.00%)	1 / 48 (2.08%)	
occurrences (all)	8	1	
Platelet count decreased			
subjects affected / exposed	7 / 10 (70.00%)	3 / 48 (6.25%)	
occurrences (all)	19	3	
Weight decreased			
subjects affected / exposed	1 / 10 (10.00%)	9 / 48 (18.75%)	
occurrences (all)	1	12	
White blood cell count decreased			
subjects affected / exposed	8 / 10 (80.00%)	1 / 48 (2.08%)	
occurrences (all)	15	1	
Neutrophil count decreased			
subjects affected / exposed	10 / 10 (100.00%)	1 / 48 (2.08%)	
occurrences (all)	28	1	
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	4 / 10 (40.00%)	12 / 48 (25.00%)	
occurrences (all)	5	16	
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 10 (0.00%)	6 / 48 (12.50%)	
occurrences (all)	0	7	
Headache			
subjects affected / exposed	0 / 10 (0.00%)	6 / 48 (12.50%)	
occurrences (all)	0	6	
Neurotoxicity			
subjects affected / exposed	4 / 10 (40.00%)	0 / 48 (0.00%)	
occurrences (all)	4	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	9 / 10 (90.00%)	14 / 48 (29.17%)	
occurrences (all)	28	23	

Leukopenia			
subjects affected / exposed	3 / 10 (30.00%)	0 / 48 (0.00%)	
occurrences (all)	16	0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 10 (0.00%)	10 / 48 (20.83%)	
occurrences (all)	0	12	
Constipation			
subjects affected / exposed	0 / 10 (0.00%)	8 / 48 (16.67%)	
occurrences (all)	0	8	
Diarrhoea			
subjects affected / exposed	4 / 10 (40.00%)	18 / 48 (37.50%)	
occurrences (all)	8	26	
Dyspepsia			
subjects affected / exposed	0 / 10 (0.00%)	7 / 48 (14.58%)	
occurrences (all)	0	9	
Nausea			
subjects affected / exposed	3 / 10 (30.00%)	16 / 48 (33.33%)	
occurrences (all)	7	24	
Vomiting			
subjects affected / exposed	3 / 10 (30.00%)	16 / 48 (33.33%)	
occurrences (all)	9	23	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 10 (0.00%)	10 / 48 (20.83%)	
occurrences (all)	0	16	
Rash			
subjects affected / exposed	1 / 10 (10.00%)	9 / 48 (18.75%)	
occurrences (all)	1	10	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 10 (0.00%)	5 / 48 (10.42%)	
occurrences (all)	0	6	
Musculoskeletal and connective tissue disorders			
Arthralgia			

subjects affected / exposed	0 / 10 (0.00%)	7 / 48 (14.58%)	
occurrences (all)	0	9	
Back pain			
subjects affected / exposed	0 / 10 (0.00%)	5 / 48 (10.42%)	
occurrences (all)	0	7	
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 10 (10.00%)	4 / 48 (8.33%)	
occurrences (all)	1	4	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 10 (10.00%)	13 / 48 (27.08%)	
occurrences (all)	1	16	
Hypoalbuminaemia			
subjects affected / exposed	6 / 10 (60.00%)	3 / 48 (6.25%)	
occurrences (all)	12	4	
Hypocalcaemia			
subjects affected / exposed	2 / 10 (20.00%)	2 / 48 (4.17%)	
occurrences (all)	5	3	
Hypokalaemia			
subjects affected / exposed	3 / 10 (30.00%)	8 / 48 (16.67%)	
occurrences (all)	10	8	
Hyponatraemia			
subjects affected / exposed	2 / 10 (20.00%)	4 / 48 (8.33%)	
occurrences (all)	2	5	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 June 2019	The criterion for defining uncontrolled hypertension in exclusion criterion 10(d) was reduced.
09 August 2019	The choice of backbone chemotherapy regimens was revised based on recommendation of the study steering committee Changes were made to the secondary objectives for Cohort B. The population of interest HER2+ /PD-1+ was more narrowly defined as also being non-MSI-high. Specific assays were specified for determining HER2 status Clarification to entry criterion 7: neoadjuvant and adjuvant immunotherapy is excluded. Cautionary statement related to the use of capecitabine or fluorouracil in combination with anticoagulants, phenytoin and CYP2C9 substrates was added. Cautionary statement related to the use of oxaliplatin and other potentially nephrotoxic compounds was added. Clarified that no pharmacokinetic or immunogenicity samples will be collect from participants in the control arm. Additional timepoints for collecting prothrombin time and international normalized ratio text were added.
26 January 2021	Cohort A was revised. MSI-high status is no longer required for study entry and the sample size was increased to 110. Fertility and contraception language was updated to be consistent with Clinical Trial Facilitation Group recommendations on contraception. Minor changes to the entry criteria were made for clarity. Stratification factors were revised from tumor location (stomach vs gastrointestinal junction) to HER2 testing (ICH2=/FISH+ vs ICH3+) The guidelines for premedication and prophylaxis was modified to allow substitution of equivalent medications based on local medical practice and availability. A typographical correction was made to correct 337 overall survival (OS) events in Cohort B to 377 OS events. Updated the number of sites and countries participating in the study. Updated clinical experience information for margetuximab + pembrolizumab, tebotelimab (MGD013), and shorter infusion durations for margetuximab. Clarified that the ORR in Cohort A will be based on independent radiology review. Added that interruption of all components of chemotherapy for toxicity is limited to 2 consecutive cycles (6 weeks).

06 June 2022	The study halted enrollment due to a business decision and not a safety concern. Many changes were made to the protocol study design and procedures to support a timely closeout of the study. The requirement for independent assessment of response to treatment in Cohort A was removed. Final analysis will be conducted on investigator-assessed response. No sensitivity analysis will be conducted. In Cohort A: Secondary objective related to efficacy and Fcγ receptor was removed. Secondary objective related to PK and exposure-response analysis was removed. In Cohort B, Part 1: Primary objective removed because enrollment was closed at 33 patients. Selection of the best treatment arm will not be made. Secondary objectives related to efficacy were hanged to ORR and DCR only for each treatment arm. Secondary objectives related efficacy in the double positive and MSI-high subgroups were removed. Secondary objective related to efficacy and Fcγ receptor was removed. Secondary objective related to PK and exposure-response analysis was removed. Cohort B, Part 2: Primary and secondary objectives were removed because no patients were enrolled. General guidance for dose reductions for chemotherapy agents were added. A clarification was made to the language on when to restart chemotherapy-related toxicity. The definition of the end of the study was changed to after the last patient completes the safety follow-up period. Patients in survival follow-up will be discontinued from the study. Revised the analysis to descriptive PK summaries. PPK, exposure-response modeling, and influence of intrinsic and extrinsic covariates will not be performed. Language to indicate that collection of PK, PD and ADA samples is no longer required was added. Removed the analysis of patient reported outcomes, as no questionnaires were completed.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported