Clinical trial results:
A Phase Ib/II, Open-label, Multicenter Study of Novel Oncology Therapies in Combination with Chemotherapy and Bevacizumab as First-line Therapy in Metastatic Microsatellite-stable Colorectal Cancer (COLUMBIA-1)

Summary

EudraCT number	2019-000974-44
Trial protocol	ES
Global end of trial date	10 October 2022

Results information

Result version number	v1 (current)
This version publication date	22 October 2023
First version publication date	22 October 2023

Trial information

Trial identification

Sponsor protocol code	D910CC00001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04068610
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca Clinical study Information Center
Sponsor organisation address	One MedImmune Way, Gaithersburg, Maryland, United States, 20878
Public contact	Global Clinical Lead, AstraZeneca Clinical study Information Center, +1 8772409479, information.center@astrazeneca.com
Scientific contact	Global Clinical Lead, AstraZeneca Clinical study Information Center, +1 8772409479, information.center@astrazeneca.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	19 May 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	10 October 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of the study are:
1. Part 1: To evaluate the safety and tolerability profile of FOLFOX (oxaliplatin, folinic acid, fluorouracil [5-FU]) + bevacizumab + novel oncology therapy combinations.
2. Part 2: To compare the efficacy of FOLFOX + bevacizumab + novel oncology therapy combinations versus FOLFOX + bevacizumab.

Protection of trial subjects:

The conduct of this clinical study met all local and regulatory requirements. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and are consistent with International Conference on Harmonization guideline: Good Clinical Practice, and applicable regulatory requirements. Participants signed an informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 September 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 6
Country: Number of subjects enrolled	Canada: 3
Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	Spain: 7
Country: Number of subjects enrolled	United States: 39
Worldwide total number of subjects	59
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)	37
From 65 to 84 years	22
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at study sites located in Australia, Canada, France, Spain, and United States.

Pre-assignment

Screening details:

A total of 61 participants were randomized in this study of which 59 participants received treatment.

Period 1

Period 1 title	Overall 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	Part 1 (S1): FOLFOX + Bevacizumab + Durvalumab + Oleclumab

Arm description:

Participants in Part 1 safety run-in arm (S1) received intravenous (IV) infusions of FOLFOX (5-fluorouracil [5-FU]: 2400 mg/m^2 over 46-48 hours [Day 1 and 2 of every 14-day Cycle], oxaliplatin: 85 mg/m^2, folinic acid: 400 mg/m^2,) and bevacizumab 5 mg/kg on Day 1 of every Cycle (14-day cycle) in combination with IV durvalumab 1500 mg every 4 weeks (Q4W) and IV oleclumab 3000 mg every 2 weeks (Q2W) till 4 doses (Cycle 4) then Q4W starting on Cycle 5 Day 1 until disease progression, unacceptable toxicity, withdrawal of participant consent, or another discontinuation criterion was met.

Arm type	Experimental
Investigational medicinal product name	Durvalumab
Investigational medicinal product code	MEDI4736
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous infusion of durvalumab 1500 mg Q4W until disease progression, unacceptable toxicity, withdrawal of participant consent, or another discontinuation criterion was met.

Investigational medicinal product name	Bevacizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous infusion of bevacizumab 5 mg/kg on Day 1 of every Cycle (14-day cycle) until disease progression, unacceptable toxicity, withdrawal of participant consent, or another discontinuation criterion was met.

Investigational medicinal product name	FOLFOX
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous infusion of FOLFOX (5-FU: 2400 mg/m^2 over 46-48 hours [Day 1 and 2 of every 14-day Cycle], oxaliplatin: 85 mg/m^2, folinic acid: 400 mg/m^2 on Day 1 of every Cycle [14-day cycle]) until disease progression, unacceptable toxicity, withdrawal of participant consent, or another discontinuation criterion was met.

Investigational medicinal product name	Oleclumab
Investigational medicinal product code	MEDI9447
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous infusion of oleclumab 3000 mg Q2W till 4 doses (Cycle 4) then Q4W starting on Cycle 5 Day 1 until disease progression, unacceptable toxicity, withdrawal of participant consent, or another discontinuation criterion was met.

Arm title	Part 2 (C1): FOLFOX + Bevacizumab

Arm description:

Participants in Part 2 control 1 arm (C1) received IV infusions of FOLFOX (5-FU: 2400 mg/m^2 over 46-48 hours [Day 1 and 2 of every 14-day Cycle], oxaliplatin: 85 mg/m^2, folinic acid: 400 mg/m^2) in combination with IV bevacizumab 5 mg/kg on Day 1 of every Cycle (14-day cycle) until disease progression, unacceptable toxicity, withdrawal of participant consent, or another discontinuation criterion was met.

Arm type	Experimental
Investigational medicinal product name	Bevacizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous infusion of bevacizumab 5 mg/kg on Day 1 of every Cycle (14-day cycle) until disease progression, unacceptable toxicity, withdrawal of participant consent, or another discontinuation criterion was met.

Investigational medicinal product name	FOLFOX
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous infusion of FOLFOX (5-FU: 2400 mg/m^2 over 46-48 hours [Day 1 and 2 of every 14-day Cycle], oxaliplatin: 85 mg/m^2, folinic acid: 400 mg/m^2 on Day 1 of every Cycle [14-day cycle]) until disease progression, unacceptable toxicity, withdrawal of participant consent, or another discontinuation criterion was met.

Arm title	Part 2 (E1): FOLFOX + Bevacizumab + Durvalumab + Oleclumab

Arm description:

Participants in Part 2 experimental 1 arm (E1) received IV infusions of FOLFOX (5-FU: 2400 mg/m^2 over 46-48 hours [Day 1 and 2 of every 14-day Cycle], oxaliplatin: 85 mg/m^2, folinic acid: 400 mg/m^2) and bevacizumab 5 mg/kg on Day 1 of every Cycle (14-day cycle) in combination with IV durvalumab 1500 mg Q4W and IV oleclumab 3000 mg Q2W till 4 doses (Cycle 4) then Q4W starting on Cycle 5 Day 1 until disease progression, unacceptable toxicity, withdrawal of participant consent, or another discontinuation criterion was met.

Arm type	Experimental
Investigational medicinal product name	Durvalumab
Investigational medicinal product code	MEDI4736
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous infusion of durvalumab 1500 mg Q4W until disease progression, unacceptable toxicity, withdrawal of participant consent, or another discontinuation criterion was met.

Investigational medicinal product name	Bevacizumab
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous infusion of bevacizumab 5 mg/kg on Day 1 of every Cycle (14-day cycle) until disease progression, unacceptable toxicity, withdrawal of participant consent, or another discontinuation criterion was met.

Investigational medicinal product name	FOLFOX
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous infusion of FOLFOX (5-FU: 2400 mg/m^2 over 46-48 hours [Day 1 and 2 of every 14-day Cycle], oxaliplatin: 85 mg/m^2, folinic acid: 400 mg/m^2 on Day 1 of every Cycle [14-day cycle]) until disease progression, unacceptable toxicity, withdrawal of participant consent, or another discontinuation criterion was met.

Investigational medicinal product name	Oleclumab
Investigational medicinal product code	MEDI9447
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous infusion of oleclumab 3000 mg Q2W till 4 doses (Cycle 4) then Q4W starting on Cycle 5 Day 1 until disease progression, unacceptable toxicity, withdrawal of participant consent, or another discontinuation criterion was met.

Number of subjects in period 1	Part 1 (S1): FOLFOX + Bevacizumab + Durvalumab + Oleclumab	Part 2 (C1): FOLFOX + Bevacizumab	Part 2 (E1): FOLFOX + Bevacizumab + Durvalumab + Oleclumab
Started	7	26	26
Completed	0	0	0
Not completed	7	26	26
Adverse event, serious fatal	-	1	3
Consent withdrawn by subject	-	4	2
Death	4	7	10
Unspecified	3	12	11
Lost to follow-up	-	2	-

Baseline characteristics

Reporting groups	
Reporting group title	Part 1 (S1): FOLFOX + Bevacizumab + Durvalumab + Oleclumab

Reporting group description:

Participants in Part 1 safety run-in arm (S1) received intravenous (IV) infusions of FOLFOX (5-fluorouracil [5-FU]: 2400 mg/m^2 over 46-48 hours [Day 1 and 2 of every 14-day Cycle], oxaliplatin: 85 mg/m^2, folinic acid: 400 mg/m^2,) and bevacizumab 5 mg/kg on Day 1 of every Cycle (14-day cycle) in combination with IV durvalumab 1500 mg every 4 weeks (Q4W) and IV oleclumab 3000 mg every 2 weeks (Q2W) till 4 doses (Cycle 4) then Q4W starting on Cycle 5 Day 1 until disease progression, unacceptable toxicity, withdrawal of participant consent, or another discontinuation criterion was met.

Reporting group title	Part 2 (C1): FOLFOX + Bevacizumab

Reporting group description:

Participants in Part 2 control 1 arm (C1) received IV infusions of FOLFOX (5-FU: 2400 mg/m^2 over 46-48 hours [Day 1 and 2 of every 14-day Cycle], oxaliplatin: 85 mg/m^2, folinic acid: 400 mg/m^2) in combination with IV bevacizumab 5 mg/kg on Day 1 of every Cycle (14-day cycle) until disease progression, unacceptable toxicity, withdrawal of participant consent, or another discontinuation criterion was met.

Reporting group title	Part 2 (E1): FOLFOX + Bevacizumab + Durvalumab + Oleclumab

Reporting group description:

Participants in Part 2 experimental 1 arm (E1) received IV infusions of FOLFOX (5-FU: 2400 mg/m^2 over 46-48 hours [Day 1 and 2 of every 14-day Cycle], oxaliplatin: 85 mg/m^2, folinic acid: 400 mg/m^2) and bevacizumab 5 mg/kg on Day 1 of every Cycle (14-day cycle) in combination with IV durvalumab 1500 mg Q4W and IV oleclumab 3000 mg Q2W till 4 doses (Cycle 4) then Q4W starting on Cycle 5 Day 1 until disease progression, unacceptable toxicity, withdrawal of participant consent, or another discontinuation criterion was met.

Reporting group values	Part 1 (S1): FOLFOX + Bevacizumab + Durvalumab + Oleclumab	Part 2 (C1): FOLFOX + Bevacizumab	Part 2 (E1): FOLFOX + Bevacizumab + Durvalumab + Oleclumab
Number of subjects	7	26	26
Age categorical Units: Participants			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	4	18	15
From 65-84 years	3	8	11
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	59.4	55.5	59.8
standard deviation	± 12.4	± 13.5	± 12.5
Sex: Female, Male Units: Participants			
Female	3	7	11
Male	4	19	15

Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	1	2
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	1	0
White	7	20	23
More than one race	0	0	0
Unknown or Not Reported	0	4	1
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	4	1
Not Hispanic or Latino	7	19	23
Unknown or Not Reported	0	3	2

Reporting group values	Total		
Number of subjects	59		
Age categorical Units: Participants			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	37		
From 65-84 years	22		
85 years and over	0		
Age Continuous Units: Years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male Units: Participants			
Female	21		
Male	38		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0		
Asian	3		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	1		
White	50		
More than one race	0		
Unknown or Not Reported	5		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	5		
Not Hispanic or Latino	49		

Unknown or Not Reported	5		

End points

End points reporting groups

Reporting group title	Part 1 (S1): FOLFOX + Bevacizumab + Durvalumab + Oleclumab

Reporting group description:

Participants in Part 1 safety run-in arm (S1) received intravenous (IV) infusions of FOLFOX (5-fluorouracil [5-FU]: 2400 mg/m^2 over 46-48 hours [Day 1 and 2 of every 14-day Cycle], oxaliplatin: 85 mg/m^2, folinic acid: 400 mg/m^2,) and bevacizumab 5 mg/kg on Day 1 of every Cycle (14-day cycle) in combination with IV durvalumab 1500 mg every 4 weeks (Q4W) and IV oleclumab 3000 mg every 2 weeks (Q2W) till 4 doses (Cycle 4) then Q4W starting on Cycle 5 Day 1 until disease progression, unacceptable toxicity, withdrawal of participant consent, or another discontinuation criterion was met.

Reporting group title	Part 2 (C1): FOLFOX + Bevacizumab

Reporting group description:

Participants in Part 2 control 1 arm (C1) received IV infusions of FOLFOX (5-FU: 2400 mg/m^2 over 46-48 hours [Day 1 and 2 of every 14-day Cycle], oxaliplatin: 85 mg/m^2, folinic acid: 400 mg/m^2) in combination with IV bevacizumab 5 mg/kg on Day 1 of every Cycle (14-day cycle) until disease progression, unacceptable toxicity, withdrawal of participant consent, or another discontinuation criterion was met.

Reporting group title	Part 2 (E1): FOLFOX + Bevacizumab + Durvalumab + Oleclumab

Reporting group description:

Participants in Part 2 experimental 1 arm (E1) received IV infusions of FOLFOX (5-FU: 2400 mg/m^2 over 46-48 hours [Day 1 and 2 of every 14-day Cycle], oxaliplatin: 85 mg/m^2, folinic acid: 400 mg/m^2) and bevacizumab 5 mg/kg on Day 1 of every Cycle (14-day cycle) in combination with IV durvalumab 1500 mg Q4W and IV oleclumab 3000 mg Q2W till 4 doses (Cycle 4) then Q4W starting on Cycle 5 Day 1 until disease progression, unacceptable toxicity, withdrawal of participant consent, or another discontinuation criterion was met.

Primary: Number of Participants With Treatment Emergent Adverse Events (TEAEs) and Treatment Emergent Serious Adverse Events (TESAEs) in Part 1

End point title	Number of Participants With Treatment Emergent Adverse Events (TEAEs) and Treatment Emergent Serious Adverse Events (TESAEs) in Part 1[1][2]

End point description:

An adverse event (AE) is any untoward medical occurrence in a participant who received study drug without regard to possibility of causal relationship. A serious adverse event (SAE) is an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. The TEAEs are defined as events present at baseline that worsened in intensity after administration of study drug or events absent at baseline that emerged after administration of study drug. As-treated population included all participants who received any study drugs and were analyzed according to the treatment they actually received.

End point type	Primary

End point timeframe:

Day 1 through 90 days after the last dose of study drug (approximately 2.8 years)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: 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.
[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

End point values	Part 1 (S1): FOLFOX + Bevacizumab + Durvalumab + Oleclumab			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: Participants				
Any TEAE	7			
Any TESAE	1			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Dose Limiting Toxicities (DLTs) in Part 1

End point title	Number of Participants With Dose Limiting Toxicities (DLTs) in Part 1[3][4]

End point description:

DLT:Any study drug related Grade (G)3/higher toxicity including: G3/G4 immune-mediated AE, G3/4 noninfectious pneumonitis/colitis, transaminase elevation (TE) >8x upper limit of normal (ULN)/total bilirubin (TBL) >5xULN, increase in AST/ALT >=3xULN plus TBL >=2xULN, isolated liver TE >5 but =<8xULN/isolated TBL >3 but =<5xULN not downgrading to <=G1 within 14 days (D) of onset, G3 nausea/vomiting/diarrhea not resolving to <=G2 within 3D of supportive care, G3/4 febrile neutropenia, G3/4 neutropenia not associated with fever/systemic infection, anemia (G4,G3 with clinical sequelae/requires >2 units of RBC transfusion, thrombocytopenia (G4, G3 that did not improve by at least 1 G within 7D, G3/4 associated with >=G3 hemorrhage). DLT evaluable population: participants in Part 1 safety run-in who received full dose of durvalumab and ≥75% of number of doses of FOLFOX+bevacizumab+other novel oncology therapy and completed safety follow-up through DLT evaluation period/experienced any DLT.

End point type	Primary

End point timeframe:

From Day 1 to 28 days after the first dose of novel oncology therapy (durvalumab and oleclumab)

Notes:

[3] - 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: 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.
[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

End point values	Part 1 (S1): FOLFOX + Bevacizumab + Durvalumab + Oleclumab			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: Participants	0			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With at Least 2-Grade Shift From Baseline to Worst Toxicity Grade in Clinical Laboratory Parameters in Part 1

End point title	Number of Participants With at Least 2-Grade Shift From Baseline to Worst Toxicity Grade in Clinical Laboratory Parameters in Part 1[5][6]

End point description:

Number of participants with at least common terminology criteria for adverse events (CTCAE v5.0) 2-grade shift from baseline (last assessment prior to first dose) to worst toxicity grade in clinical laboratory parameters are reported. Clinical laboratory parameter analysis included hematology, clinical chemistry, coagulation, and urinalysis. As-treated population included all participants who received any study drugs and were analyzed according to the treatment they actually received.

End point type	Primary

End point timeframe:

Baseline (Day 1) through 90 days after the last dose of study drug (approximately 2.8 years)

Notes:

[5] - 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: 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.
[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

End point values	Part 1 (S1): FOLFOX + Bevacizumab + Durvalumab + Oleclumab			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: Participants				
Hemoglobin (Hypo)	1			
Lymphocytes (Hypo)	2			
Neutrophils	4			
Leukocytes (Hypo)	3			
Activated partial thromboplastin time	1			
Albumin	1			
Amylase	2			
Bilirubin	1			
Calcium corrected (Hypo)	1			
Creatine kinase	2			
Creatinine	1			
Gamma glutamyl transferase	1			
Glucose	1			
Lipase	5			
Magnesium (Hyper)	1			
Magnesium (Hypo)	1			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Abnormal Vital Signs Reported as TEAEs in Part 1

End point title	Number of Participants With Abnormal Vital Signs Reported as TEAEs in Part 1[7][8]

End point description:

Number of participants with abnormal vital signs reported as TEAEs are reported. Abnormal vital signs are defined as any abnormal finding in the vital sign parameters (body temperature, blood pressure, and pulse rate). As-treated population included all participants who received any study drugs and were analyzed according to the treatment they actually received.

End point type	Primary

End point timeframe:

Day 1 through 90 days after the last dose of study drug (approximately 2.8 years)

Notes:

[7] - 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: 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.
[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

End point values	Part 1 (S1): FOLFOX + Bevacizumab + Durvalumab + Oleclumab			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: Participants				
Pyrexia	2			
Temperature intolerance	1			
Hypertension	3			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants With Objective Response (OR) per Response Evaluation Criteria in Solid Tumours Version 1.1 (RECIST v1.1) in Part 2

End point title	Percentage of Participants With Objective Response (OR) per Response Evaluation Criteria in Solid Tumours Version 1.1 (RECIST v1.1) in Part 2[9]

End point description:

The OR is defined as best overall response (BOR) of confirmed complete response (CR) or confirmed partial response (PR) based on RECIST v1.1 criteria. The CR is defined as disappearance of all target lesions (TLs) and non-target lesions (NTLs), normalization of tumor marker level, any pathological lymph nodes (target and non-target) must have reduction in short axis < 10 mm, and no new lesion. The PR is defined as at least a 30% decrease in the sum of the diameters (SoD) of TLs (compared to baseline) and no new lesions. Confirmation of CR and PR is required by a repeat, consecutive assessment no less than 4 weeks from the date of first documentation. Intent-to-treat (ITT) population

included participants who received any study drug and were analyzed according to the treatment group they were randomized to. In Part 2, randomization occurred between Day -8 and the same date as dosing.

End point type	Primary

End point timeframe:

Randomization through end of study (approximately 2.6 years)

Notes:

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

End point values	Part 2 (C1): FOLFOX + Bevacizumab	Part 2 (E1): FOLFOX + Bevacizumab + Durvalumab + Oleclumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	26		
Units: Percentage of Participants				
number (confidence interval 95%)	46.2 (26.6 to 66.6)	61.5 (40.6 to 79.8)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Part 2 (C1): FOLFOX + Bevacizumab v Part 2 (E1): FOLFOX + Bevacizumab + Durvalumab + Oleclumab
Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3173
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	5.6

Secondary: Percentage of Participants With OR per RECIST v1.1 in Part 1

End point title	Percentage of Participants With OR per RECIST v1.1 in Part

End point description:

The OR is defined as BOR of confirmed CR or confirmed PR based on RECIST v1.1 criteria. The CR is defined as disappearance of all TLs and NTLs, normalization of tumor marker level, any pathological lymph nodes (target and non-target) must have reduction in short axis < 10 mm, and no new lesions. The PR is defined as at least a 30% decrease in the SoD of TLs (compared to baseline) and no new lesions. Confirmation of CR and PR is required by a repeat, consecutive assessment no less than 4 weeks from the date of first documentation. As-treated population included all participants who received

any study drugs and were analyzed according to the treatment they actually received.

End point type	Secondary

End point timeframe:

First dose (Day 1) through end of study (approximately 2.8 years)

Notes:

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

End point values	Part 1 (S1): FOLFOX + Bevacizumab + Durvalumab + Oleclumab			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: Percentage of Participants				
number (confidence interval 95%)	71.4 (29.0 to 96.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Best Overall Response (BOR) per RECIST v1.1 in Part 1

End point title	Best Overall Response (BOR) per RECIST v1.1 in Part 1[11]

End point description:

BOR: best response including CR, PR, stable disease (SD), progressive disease (PD), and non-evaluable (NE) among all overall responses per RECIST v1.1 application to investigator assessments. CR: disappearance of all TLs and NTLs, any pathological lymph nodes (target, non-target) must have reduction in short axis <10mm, and no new lesions. PR: at least 30% decrease in SoD of TL (compared to baseline) and no new NTL. Confirmation of CR and PR is required after 4 weeks. PD: at least 20% increase in SoDs of TLs, or unequivocal progression of existing NTL, or new lesions. SD: neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD in at least 8 weeks from first dose of study drug. NE: either when no or only subset of lesion measurements are made at an assessment. Number of participants with BOR are reported. As-treated population: participants who received any study drugs and were analyzed according to the treatment they actually received.

End point type	Secondary

End point timeframe:

First dose (Day 1) through end of study (approximately 2.8 years)

Notes:

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

End point values	Part 1 (S1): FOLFOX + Bevacizumab + Durvalumab + Oleclumab			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: Participants				
CR	0			
PR	5			
SD >=8 weeks	2			
PD	0			
NE	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Disease Control (DC) per RECIST v1.1 in Part 1

End point title	Percentage of Participants with Disease Control (DC) per RECIST v1.1 in Part 1[12]

End point description:

The DC is defined as BOR of confirmed CR, confirmed PR, or stable disease (SD; maintained for ≥ 16 weeks) per RECIST v1.1. The CR is defined as disappearance of all TLs and NTLs, normalization of tumor marker level, any pathological lymph nodes (target and non-target) must have reduction in short axis < 10 mm, and no new lesions. The PR is defined as at least a 30% decrease in the SoD of TLs (compared to baseline) and no new lesion. Confirmation of CR and PR is required by a repeat, consecutive assessment no less than 4 weeks from the date of first documentation. The SD is defined as neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD. Participants with SD will be included in the DC if they maintain SD for >= 16 weeks from start of treatment. As-treated population included all participants who received any study drugs and were analyzed according to the treatment they actually received.

End point type	Secondary

End point timeframe:

First dose (Day 1) through end of study (approximately 2.8 years)

Notes:

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

End point values	Part 1 (S1): FOLFOX + Bevacizumab + Durvalumab + Oleclumab			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: Percentage of Participants				
number (confidence interval 95%)	100 (59.0 to 100)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with PFS at 12 months (PFS-12) per RECIST v1.1 in Part 1

End point title	Percentage of Participants with PFS at 12 months (PFS-12) per RECIST v1.1 in Part 1[13]

End point description:

The PFS is defined as the time from assignment until the first documentation of PD or death due to any cause, whichever occurs first, regardless of whether the participant received subsequent anticancer therapy prior to progression. The PD is defined as at least a 20% increase in the SoDs of TLs, taking as reference the smallest sum on study, and an absolute increase of at least 5 mm, or unequivocal progression of existing NTL, or new lesions. The PFS was analyzed using Kaplan-Meier method based on application of RECIST v1.1 to investigator assessments. The percentage of participants progression free and alive at 12 months (PFS-12) are reported. As-treated population included all participants who received any study drugs and were analyzed according to the treatment they actually received. Assignment occurred between Day -3 and -1.

End point type	Secondary

End point timeframe:

Assignment through 12 months

Notes:

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

End point values	Part 1 (S1): FOLFOX + Bevacizumab + Durvalumab + Oleclumab			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: Percentage of Participants				
number (confidence interval 95%)	28.6 (4.1 to 61.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS) per RECIST v1.1 in Part 1

End point title	Overall Survival (OS) per RECIST v1.1 in Part 1[14]

End point description:

The OS is defined as the time from first dose until death due to any cause. The overall survival was

analyzed using the Kaplan-Meier method based on application of RECIST v1.1 to investigator assessments. As-treated population included all participants who received any study drugs and were analyzed according to the treatment they actually received. The arbitrary number 99999 signified the data for upper limit of CI could not be derived due to insufficient events being observed.

End point type	Secondary

End point timeframe:

First dose (Day 1) through end of study (approximately 2.8 years)

Notes:

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

End point values	Part 1 (S1): FOLFOX + Bevacizumab + Durvalumab + Oleclumab			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: Months				
median (confidence interval 95%)	30.1 (11.9 to 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival (PFS) per RECIST v1.1 in Part 1

End point title	Progression-Free Survival (PFS) per RECIST v1.1 in Part 1[15]

End point description:

The PFS is defined as the time from assignment until the first documentation of PD or death due to any cause, whichever occurs first, regardless of whether the participant received subsequent anticancer therapy prior to progression. The PD is defined as at least a 20% increase in the SoDs of TLs, taking as reference the smallest sum on study, and an absolute increase of at least 5 mm, or unequivocal progression of existing NTL, or new lesions. The PFS was analyzed using the Kaplan-Meier method based on application of RECIST v1.1 to investigator assessments. As-treated population included all participants who received any study drugs and were analyzed according to the treatment they actually received. Assignment occurred between Day -3 and -1.

End point type	Secondary

End point timeframe:

Assignment through end of study (approximately 2.8 years)

Notes:

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

End point values	Part 1 (S1): FOLFOX + Bevacizumab + Durvalumab + Oleclumab			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: Months				
median (confidence interval 95%)	9.5 (7.8 to 18.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DoR) per RECIST v1.1 in Part 1

End point title	Duration of Response (DoR) per RECIST v1.1 in Part 1[16]

End point description:

DoR: time from the first documentation of a confirmed response (CR/PR) until first documentation of PD/death due to any cause, whichever occurs first. CR: disappearance of all TLs and NTLs, normalization of tumor marker level, any pathological lymph nodes (target and non-target) must have reduction in short axis <10mm, and no new lesions. PR: at least 30% decrease in the SoD of TLs (compared to baseline) and no new lesion. Confirmation of CR and PR is required after 4 weeks. PD: at least 20% increase in SoDs of TLs (reference the smallest sum on study and increase of at least 5mm), or unequivocal progression of existing NTL/new lesions. The DoR was analyzed using Kaplan-Meier method and was assessed for those participants who had OR. As-treated population: participants who received any study drugs and were analyzed according to received treatment. Arbitrary number 99999 signified upper limit confidence interval (CI) could not be derived as insufficient number of participants had DoR.

End point type	Secondary

End point timeframe:

First dose (Day 1) through end of study (approximately 2.8 years)

Notes:

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

End point values	Part 1 (S1): FOLFOX + Bevacizumab + Durvalumab + Oleclumab			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: Months				
median (confidence interval 95%)	6.0 (5.5 to 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With TEAEs and TESAEs in Part 2

End point title	Number of Participants With TEAEs and TESAEs in Part 2[17]

End point description:

An AE is any untoward medical occurrence in a participant who received study drug without regard to possibility of causal relationship. A SAE is an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. The TEAEs are defined as events present at baseline that worsened in intensity after administration of study drug or events absent at baseline that emerged after administration of study drug. As-treated population included all participants who received any study drugs and were analyzed according to the treatment they actually received.

End point type	Secondary

End point timeframe:

Day 1 through 90 days after the last dose of study drug (approximately 2.6 years)

Notes:

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

End point values	Part 2 (C1): FOLFOX + Bevacizumab	Part 2 (E1): FOLFOX + Bevacizumab + Durvalumab + Oleclumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	26		
Units: Participants				
Any TEAE	26	26		
Any TESAE	7	12		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With at Least 2-Grade Shift From Baseline to Worst Toxicity Grade in Clinical Laboratory Parameters in Part 2

End point title	Number of Participants With at Least 2-Grade Shift From Baseline to Worst Toxicity Grade in Clinical Laboratory Parameters in Part 2[18]

End point description:

Number of participants with at least CTCAE v5.0 2-grade shift from baseline (last assessment prior to first dose) to worst toxicity grade in clinical laboratory parameters are reported. Clinical laboratory parameter analysis included hematology, clinical chemistry, coagulation, and urinalysis. As-treated population included all participants who received any study drugs and were analyzed according to the treatment they actually received. Here, number analyzed (n) denotes number of participants analyzed for the specified parameter.

End point type	Secondary

End point timeframe:

Baseline (Day 1) through 90 days after the last dose of study drug (approximately 2.6 years)

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

End point values	Part 2 (C1): FOLFOX + Bevacizumab	Part 2 (E1): FOLFOX + Bevacizumab + Durvalumab + Oleclumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	26		
Units: Participants				
Hemoglobin (Hypo)	0	1		
Lymphocytes (Hyper)	0	2		
Lymphocytes (Hypo)	3	6		
Neutrophils	7	8		
Platelets	3	2		
Leukocytes (Hypo)	2	4		
Activated partial thromboplastin time	5	5		
Albumin	0	3		
Alkaline phosphatase	1	1		
Alanine aminotransferase	2	1		
Amylase	7	3		
Aspartate aminotransferase	1	0		
Bilirubin	1	1		
Calcium corrected (Hypo)	0	1		
Creatine kinase (n=25, 26)	2	3		
Creatinine	2	2		
Gamma glutamyl transferase (n=26,25)	5	4		
Potassium (Hyper)	0	2		
Potassium (Hypo)	0	2		
Lipase	12	15		
Magnesium (Hypo)	0	1		
Sodium (Hypo)	2	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Abnormal Vital Signs Reported as TEAEs in Part 2

End point title	Number of Participants With Abnormal Vital Signs Reported as TEAEs in Part 2[19]

End point description:

Number of participants with abnormal vital signs reported as TEAEs are reported. Abnormal vital signs are defined as any abnormal finding in the vital sign parameters (body temperature, blood pressure, and pulse rate). As-treated population included all participants who received any study drugs and were analyzed according to the treatment they actually received.

End point type	Secondary

End point timeframe:

Day 1 through 90 days after the last dose of study drug (approximately 2.6 years)

Notes:

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

End point values	Part 2 (C1): FOLFOX + Bevacizumab	Part 2 (E1): FOLFOX + Bevacizumab + Durvalumab + Oleclumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	26		
Units: Participants				
Pyrexia	3	5		
Temperature intolerance	5	5		
Hypertension	4	4		
Hypotension	1	1		
Supraventricular tachycardia	1	0		
Ventricular tachycardia	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: BOR per RECIST v1.1 in Part 2

End point title	BOR per RECIST v1.1 in Part 2[20]

End point description:

BOR: best response including CR, PR, SD, PD, NE among all overall responses per RECIST v1.1 application to investigator assessments. CR: disappearance of all TLs and NTLs, any pathological lymph nodes (target, non-target) must have reduction in short axis <10mm, no new lesions. PR: at least 30% decrease in SoD of TL, no new NTL. Confirmation of CR, PR is required after 4 weeks. PD: at least 20% increase in SoDs of TLs (reference the smallest sum on study and increase of at least 5mm), or unequivocal progression of existing NTL, or new lesions. SD: neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD in at least 8 weeks from first dose of study drug. NE: either when no or only subset of lesion measurements are made at an assessment. Number of participants with BOR are reported. ITT population: participants who received any study drug and were analyzed according randomized treatment. Randomization occurred between Day -8 and the same date as dosing.

End point type	Secondary

End point timeframe:

Randomization through end of study (approximately 2.6 years)

Notes:

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

End point values	Part 2 (C1): FOLFOX + Bevacizumab	Part 2 (E1): FOLFOX + Bevacizumab + Durvalumab + Oleclumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	26		
Units: Participants				
CR	0	1		
PR	12	15		
SD >=8 weeks	11	6		
PD	1	3		
NE	2	1		

Statistical analyses

No statistical analyses for this end point

Secondary: PFS per RECIST v1.1 in Part 2

End point title	PFS per RECIST v1.1 in Part 2[21]

End point description:

The PFS is defined as the time from randomization until the first documentation of PD or death due to any cause, whichever occurs first, regardless of whether the participant received subsequent anticancer therapy prior to progression. The PD is defined as at least a 20% increase in the SoDs of TLs, taking as reference the smallest sum on study, and an absolute increase of at least 5 mm, or unequivocal progression of existing NTL, or new lesions. The PFS was analyzed using the Kaplan-Meier method based on application of RECIST v1.1 to investigator assessments. The ITT population included participants who received any study drug and were analyzed according to the treatment group they were randomized to. In Part 2, randomization occurred between Day -8 and the same date as dosing.

End point type	Secondary

End point timeframe:

Randomization through end of study (approximately 2.6 years)

Notes:

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

End point values	Part 2 (C1): FOLFOX + Bevacizumab	Part 2 (E1): FOLFOX + Bevacizumab + Durvalumab + Oleclumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	26		
Units: Months				
median (confidence interval 95%)	11.1 (7.3 to 16.2)	10.9 (6.9 to 15.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with DC per RECIST v1.1 in Part 2

End point title	Percentage of Participants with DC per RECIST v1.1 in Part 2[22]

End point description:

The DC is defined as BOR of confirmed CR, confirmed PR, or SD (maintained for ≥ 16 weeks) per RECIST v1.1. The CR is defined as disappearance of all TLs and NTLs, normalization of tumor marker level, any pathological lymph nodes (target and non-target) must have reduction in short axis < 10 mm, and no new lesions. The PR is defined as at least a 30% decrease in the SoD of TLs (compared to baseline) and no new lesion. Confirmation of CR and PR is required by a repeat, consecutive assessment no less than 4 weeks from the date of first documentation. The SD is defined as neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD. Participants with SD will be included in the DC if they maintain SD for >= 16 weeks from start of treatment. The ITT population included participants who received any study drug and were analyzed according to the treatment group they were randomized to. In Part 2, randomization occurred between Day -8 and the same date as dosing.

End point type	Secondary

End point timeframe:

Randomization through end of study (approximately 2.6 years)

Notes:

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

End point values	Part 2 (C1): FOLFOX + Bevacizumab	Part 2 (E1): FOLFOX + Bevacizumab + Durvalumab + Oleclumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	26		
Units: Percentage of Participants				
number (confidence interval 95%)	88.5 (69.8 to 97.6)	84.6 (65.1 to 95.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: DoR per RECIST v1.1 in Part 2

End point title	DoR per RECIST v1.1 in Part 2[23]

End point description:

DoR: time from first documentation of confirmed response (CR/PR) until first documentation of PD/death due to any cause, whichever occurs first. CR: disappearance of all TLs, NTLs, normalization of tumor marker level, any pathological lymph nodes (target, non-target) must have reduction in short axis <10mm, no new lesions. PR: at least 30% decrease in the SoD of TLs, no new lesion. Confirmation of CR and PR is required after 4 weeks. PD: at least 20% increase in SoDs of TLs (reference smallest sum on study and increase of at least 5mm), or unequivocal progression of existing NTL, or new lesions. The DoR was analyzed using Kaplan-Meier method. ITT population: participants who received any study drug and were analyzed according to randomized treatment. DoR was assessed for only those participants who had OR. Arbitrary number 99999 signified upper limit CI could not be derived due to insufficient events being observed. Randomization occurred between Day -8 and the same date as dosing.

End point type	Secondary

End point timeframe:

Randomization through end of study (approximately 2.6 years)

Notes:

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

End point values	Part 2 (C1): FOLFOX + Bevacizumab	Part 2 (E1): FOLFOX + Bevacizumab + Durvalumab + Oleclumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	16		
Units: Months				
median (confidence interval 95%)	7.7 (4.6 to 15.4)	10.3 (5.8 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Concentrations of Durvalumab in Part 1 (S1) and Part 2 (E1)

End point title	Serum Concentrations of Durvalumab in Part 1 (S1) and Part 2 (E1)[24]

End point description:

Serum concentrations of durvalumab collected over time in Part 1 and Part 2 (E1) are reported. The lower limit of quantification (LLOQ) for durvalumab was considered to be 50 ng/mL. Pharmacokinetic (PK) evaluable population included participants who received at least 1 dose of any study drug with at least 1 reportable PK concentration. Here, number of subjects analyzed denotes those participants who were analyzed for this endpoint. Number analyzed (n) denotes those participants who had adequate serum samples. The arbitrary numbers 999.99 and 99.999 signified geometric mean and geometric CV%, respectively, were not reported as the concentration was below the LLOQ. The arbitrary number 9999999 denotes data was not reported as no participants were analyzed for the specified time point.

End point type	Secondary

End point timeframe:

Part 1: Pre-dose on Day 1 of Cycle 1, 3, 7, 13; Part 2 (E1): Pre-dose on Day 1 of Cycle 1, 3, 7, 13, and 27

Notes:

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

End point values	Part 1 (S1): FOLFOX + Bevacizumab + Durvalumab + Oleclumab	Part 2 (E1): FOLFOX + Bevacizumab + Durvalumab + Oleclumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	21		
Units: ng/mL				

geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1 (n=4,21)	999.99 (± 99.999)	999.99 (± 99.999)		
Cycle 3 Day 1 (n=6,18)	67980 (± 20.31)	48600 (± 39.67)		
Cycle 7 Day 1 (n=7,18)	112500 (± 28.63)	97610 (± 46.56)		
Cycle 13 Day 1 (n=4,14)	101500 (± 30.22)	147000 (± 30.57)		
Cycle 27 Day 1 (n=0,5)	9999999 (± 9999999)	120700 (± 29.83)		

Statistical analyses

No statistical analyses for this end point

Secondary: OS per RECIST v1.1 in Part 2

End point title	OS per RECIST v1.1 in Part 2[25]

End point description:

The OS is defined as the time from randomization until death due to any cause. The overall survival was analyzed using the Kaplan-Meier method based on application of RECIST v1.1 to investigator assessments. The ITT population included participants who received any study drug and were analyzed according to the treatment group they were randomized to. The arbitrary number 99999 and 99.999 signified the data for upper limit of CI and median could not be derived because an insufficient number of participants had event. In Part 2, randomization occurred between Day -8 and the same date as dosing.

End point type	Secondary

End point timeframe:

Randomization through end of study (approximately 2.6 years)

Notes:

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

End point values	Part 2 (C1): FOLFOX + Bevacizumab	Part 2 (E1): FOLFOX + Bevacizumab + Durvalumab + Oleclumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	26		
Units: Months				
median (confidence interval 95%)	99.999 (20.6 to 99999)	22.4 (10.6 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with PFS at 12 months (PFS-12) per RECIST v1.1 in Part 2

End point title	Percentage of Participants with PFS at 12 months (PFS-12) per RECIST v1.1 in Part 2[26]

End point description:

The PFS is defined as the time from randomization until the first documentation of PD or death due to any cause, whichever occurs first, regardless of whether the participant received subsequent anticancer therapy prior to progression. The PD is defined as at least a 20% increase in the SoDs of TLs, taking as reference the smallest sum on study, and an absolute increase of at least 5 mm, or unequivocal progression of existing NTL, or new lesions. The PFS was analyzed using Kaplan-Meier method based on application of RECIST v1.1 to investigator assessments. The percentage of participants progression free and alive at 12 months (PFS-12) are reported. The ITT population included participants who received any study drug and were analyzed according to the treatment group they were randomized to. In Part 2, randomization occurred between Day -8 and the same date as dosing.

End point type	Secondary

End point timeframe:

Randomization through 12 months

Notes:

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

End point values	Part 2 (C1): FOLFOX + Bevacizumab	Part 2 (E1): FOLFOX + Bevacizumab + Durvalumab + Oleclumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	26		
Units: Percentage of Participants				
number (confidence interval 95%)	38.6 (18.6 to 58.3)	36.1 (17.1 to 55.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Concentrations of Oleclumab in Part 1 (S1) and Part 2 (E1)

End point title	Serum Concentrations of Oleclumab in Part 1 (S1) and Part 2 (E1)[27]

End point description:

Serum concentrations of oleclumab collected over time in Part 1 and Part 2 (E1) are reported. The LLOQ for oleclumab was considered to be 1 µg/mL. The PK evaluable population included participants who received at least 1 dose of any study drug with at least 1 reportable PK concentration. Here, number of subjects analyzed denotes those participants who were analyzed for this endpoint. Number analyzed (n) denotes those participants who had adequate serum samples. The arbitrary numbers 999.99 and 99.999 signified geometric mean and geometric CV%, respectively, were not reported as the concentration was below the LLOQ. The arbitrary number 9999 denotes data was not reported as no participants were analyzed for the specified time point.

End point type	Secondary

End point timeframe:

Part 1: Pre-dose on Day 1 of Cycle 1, 2, 7, and 13; Part 2 (E1): Pre-dose on Day 1 of Cycle 1, 2, 7, 13, and 27

Notes:

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

End point values	Part 1 (S1): FOLFOX + Bevacizumab + Durvalumab + Oleclumab	Part 2 (E1): FOLFOX + Bevacizumab + Durvalumab + Oleclumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	22		
Units: µg/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1 (n=7,22)	999.99 (± 99.999)	999.99 (± 99.999)		
Cycle 2 Day 1 (n=6,19)	111.2 (± 25.38)	69.81 (± 199.1)		
Cycle 7 Day 1 (n=7,19)	186.5 (± 53.45)	159.8 (± 81.62)		
Cycle 13 Day 1 (n=4,14)	146.7 (± 24.43)	170.1 (± 35.77)		
Cycle 27 Day 1 (n=0,5)	9999 (± 9999)	107.9 (± 30.42)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Positive Anti-Drug Antibodies (ADA) to Durvalumab in Part 1 (S1) and Part 2 (E1)

End point title	Number of Participants With Positive Anti-Drug Antibodies (ADA) to Durvalumab in Part 1 (S1) and Part 2 (E1)[28]

End point description:

Number of participants with positive ADA to durvalumab in Part 1 (S1) and Part 2 (E1) are reported. The ADA evaluable population included all participants who received at least 1 dose of any study drug, who have a non-missing baseline ADA result and at least 1 non-missing post-baseline ADA result. Number of subjects analyzed denotes the number of participants analyzed for this endpoint. Number analyzed (n) denotes those participants who had adequate ADA sample. The arbitrary number 9999 denotes data was not reported as no participants were analyzed for the specified time point.

End point type	Secondary

End point timeframe:

Part 1: Pre-dose on Day(D)1 of Cycles(C)1 (baseline [BL]), 3, 7, 13, and 90 days post last dose of study drug (approximately 2.8 years); Part 2(E1):Pre-dose on D1 of C1 (BL), 3, 7, 13, 27, and 90 days post last dose of study drug (approximately 2.6 years)

Notes:

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

End point values	Part 1 (S1): FOLFOX + Bevacizumab + Durvalumab + Oleclumab	Part 2 (E1): FOLFOX + Bevacizumab + Durvalumab + Oleclumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	20		
Units: Participants				
ADA positive at baseline (n=7,20)	0	2		
ADA positive at Cycle 3 Day 1 (n=7,16)	0	1		
ADA positive at Cycle 7 Day 1 (n=7,18)	0	0		
ADA positive at Cycle 13 Day 1 (n=4,13)	0	0		
ADA positive at Cycle 27 Day 1 (n=0,5)	9999	0		
ADA positive at 90 days post last dose (n=4,7)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Concentrations of Bevacizumab in Part 1 (S1)

End point title	Serum Concentrations of Bevacizumab in Part 1 (S1)[29]

End point description:

Serum concentrations of bevacizumab collected over time in Part 1 are reported. The LLOQ for bevacizumab was considered to be 500 ng/mL. The PK evaluable population included participants who received at least 1 dose of any study drug with at least 1 reportable PK concentration. Here, number analyzed denotes those participants who had adequate serum samples. The arbitrary numbers 999.99 and 99.999 signified geometric mean and geometric CV%, respectively were not reported as the concentration was below the LLOQ.

End point type	Secondary

End point timeframe:

Pre-dose on Day 1 of Cycle 1, 2, 7, 13, and 27

Notes:

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

End point values	Part 1 (S1): FOLFOX + Bevacizumab + Durvalumab + Oleclumab			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1 (n=7)	999.99 (± 99.999)			
Cycle 2 Day 1 (n=6)	36090 (± 16.55)			

Cycle 7 Day 1 (n=7)	73350 (± 39.94)			
Cycle 13 Day 1 (n=5)	70370 (± 30.52)			
Cycle 27 Day 1 (n=1)	999.99 (± 99.999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Positive ADA to Oleclumab in Part 1 (S1) and Part 2 (E1)

End point title	Number of Participants With Positive ADA to Oleclumab in Part 1 (S1) and Part 2 (E1)[30]

End point description:

Number of participants with positive ADA to oleclumab in Part 1 (S1) and Part 2 (E1) are reported. The ADA evaluable population included all participants who received at least 1 dose of any study drug, who have a non-missing baseline ADA result and at least 1 non-missing post-baseline ADA result. Number of subjects analyzed denotes the number of participants analyzed for this endpoint. Number analyzed (n) denotes those participants who had adequate ADA sample. The arbitrary number 9999 denotes data was not reported as no participants were analyzed for the specified time point.

End point type	Secondary

End point timeframe:

Part 1: Pre-dose on D1 of C1 (BL), 2, 7, 13, and 90 days post last dose of study drug (approximately 2.8 years); Part 2 (E1): Pre-dose on D1 of C1 (BL), 2, 7, 13, 27, and 90 days post last dose of study drug (approximately 2.6 years)

Notes:

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

End point values	Part 1 (S1): FOLFOX + Bevacizumab + Durvalumab + Oleclumab	Part 2 (E1): FOLFOX + Bevacizumab + Durvalumab + Oleclumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	21		
Units: Participants				
ADA positive at baseline (n=7,21)	0	0		
ADA positive at Cycle 2 Day 1 (n=6,17)	0	2		
ADA positive at Cycle 7 Day 1 (n=7,18)	0	0		
ADA positive at Cycle 13 Day 1 (n=4,13)	0	0		
ADA positive at Cycle 27 Day 1 (n=0,5)	9999	0		
ADA positive at 90 days post last dose (n=4,7)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Positive ADA to Bevacizumab in Part 1 (S1)

End point title	Number of Participants With Positive ADA to Bevacizumab in Part 1 (S1)[31]

End point description:

Number of participants with positive ADA to bevacizumab in Part 1 (S1) are reported. The ADA evaluable population included all participants who received at least 1 dose of any study drug, who have a non-missing baseline ADA result and at least 1 non-missing post-baseline ADA result. Here, number analyzed (n) denotes those participants who had adequate ADA sample. Number of subjects analyzed denotes the number of participants analyzed for this endpoint. Number analyzed (n) denotes those participants who had adequate ADA sample.

End point type	Secondary

End point timeframe:

Pre-dose on D1 of C1 (BL), 2, 7, 13, 27, and 90 days post last dose of study drug (approximately 2.8 years)

Notes:

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

End point values	Part 1 (S1): FOLFOX + Bevacizumab + Durvalumab + Oleclumab			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: Participants				
ADA positive at baseline (n=7)	0			
ADA positive at Cycle 2 Day 1 (n=6)	5			
ADA positive at Cycle 7 Day 1 (n=7)	7			
ADA positive at Cycle 13 Day 1 (n=5)	5			
ADA positive at Cycle 27 Day 1 (n=1)	1			
ADA positive at 90 days post last dose (n=4)	4			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Part 1: Day 1 through 90 days after the last dose of study drug (approximately 2.8 years); Part 2: Day 1 through 90 days after the last dose of study drug (approximately 2.6 years)

Adverse event reporting additional description:

As-treated population included all participants who received any study drugs and were analyzed according to the treatment they actually received.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	Part 1 - S1 - FOLFOX + Bevacizumab + Durvalumab + Oleclumab

Reporting group description: -

Reporting group title	Part 2 - E1 - FOLFOX + Bevacizumab + Durvalumab + Oleclumab

Reporting group description: -

Reporting group title	Part 2 - C1 - FOLFOX + Bevacizumab

Reporting group description: -

Serious adverse events	Part 1 - S1 - FOLFOX + Bevacizumab + Durvalumab + Oleclumab	Part 2 - E1 - FOLFOX + Bevacizumab + Durvalumab + Oleclumab	Part 2 - C1 - FOLFOX + Bevacizumab
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 7 (14.29%)	12 / 26 (46.15%)	7 / 26 (26.92%)
number of deaths (all causes)	4	13	8
number of deaths resulting from adverse events	0	3	1
Investigations			
Blood bilirubin increased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (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
Injury, poisoning and procedural complications			
Stoma complication			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (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
Cardiac disorders			

Ventricular tachycardia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Lumbar radiculopathy			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (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
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Large intestinal obstruction			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine perforation			
subjects affected / exposed	1 / 7 (14.29%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal perforation			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	2 / 26 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			

subjects affected / exposed	1 / 7 (14.29%)	0 / 26 (0.00%)	0 / 26 (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
Ascites			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (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
Epistaxis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (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
Renal and urinary disorders			
Pyelocaliectasis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (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
Renal failure			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (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

Musculoskeletal and connective tissue disorders			
Bursitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Rectal abscess			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (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
COVID-19			
subjects affected / exposed	0 / 7 (0.00%)	2 / 26 (7.69%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Sepsis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (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
Metabolism and nutrition disorders			
Dehydration			

subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (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

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Part 1 - S1 - FOLFOX + Bevacizumab + Durvalumab + Oleclumab	Part 2 - E1 - FOLFOX + Bevacizumab + Durvalumab + Oleclumab	Part 2 - C1 - FOLFOX + Bevacizumab
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 7 (100.00%)	26 / 26 (100.00%)	25 / 26 (96.15%)
Vascular disorders			
Hot flush			
subjects affected / exposed	1 / 7 (14.29%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	2	0	1
Embolism			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Hypertension			
subjects affected / exposed	3 / 7 (42.86%)	4 / 26 (15.38%)	4 / 26 (15.38%)
occurrences (all)	5	4	4
Hypotension			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	1 / 26 (3.85%)
occurrences (all)	0	1	1
Phlebitis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Venous thrombosis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Pain			
subjects affected / exposed	0 / 7 (0.00%)	2 / 26 (7.69%)	0 / 26 (0.00%)
occurrences (all)	0	2	0
Oedema peripheral			

subjects affected / exposed	1 / 7 (14.29%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	1	1	0
Mucosal inflammation			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	3 / 26 (11.54%)
occurrences (all)	0	3	3
Malaise			
subjects affected / exposed	1 / 7 (14.29%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	0
Localised oedema			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Influenza like illness			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Feeling cold			
subjects affected / exposed	1 / 7 (14.29%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	0
Fatigue			
subjects affected / exposed	5 / 7 (71.43%)	11 / 26 (42.31%)	10 / 26 (38.46%)
occurrences (all)	7	12	16
Crepitations			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Chills			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	2 / 26 (7.69%)
occurrences (all)	0	0	2
Asthenia			
subjects affected / exposed	0 / 7 (0.00%)	4 / 26 (15.38%)	2 / 26 (7.69%)
occurrences (all)	0	7	3
Temperature intolerance			
subjects affected / exposed	1 / 7 (14.29%)	5 / 26 (19.23%)	5 / 26 (19.23%)
occurrences (all)	1	5	5
Pyrexia			
subjects affected / exposed	2 / 7 (28.57%)	5 / 26 (19.23%)	3 / 26 (11.54%)
occurrences (all)	4	11	3
Peripheral swelling			

subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Nasal dryness			
subjects affected / exposed	1 / 7 (14.29%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	0
Aphonia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Cough			
subjects affected / exposed	0 / 7 (0.00%)	3 / 26 (11.54%)	1 / 26 (3.85%)
occurrences (all)	0	4	1
Dysphonia			
subjects affected / exposed	0 / 7 (0.00%)	2 / 26 (7.69%)	2 / 26 (7.69%)
occurrences (all)	0	2	2
Dyspnoea			
subjects affected / exposed	1 / 7 (14.29%)	2 / 26 (7.69%)	6 / 26 (23.08%)
occurrences (all)	1	3	6
Epistaxis			
subjects affected / exposed	0 / 7 (0.00%)	3 / 26 (11.54%)	5 / 26 (19.23%)
occurrences (all)	0	4	5
Hiccups			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Laryngospasm			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Pneumonitis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	0
Pulmonary embolism			

subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Rhinorrhoea			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	2 / 26 (7.69%)
occurrences (all)	0	1	2
Throat irritation			
subjects affected / exposed	1 / 7 (14.29%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	0
Pulmonary congestion			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Psychiatric disorders			
Irritability			
subjects affected / exposed	1 / 7 (14.29%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	2	1	0
Insomnia			
subjects affected / exposed	1 / 7 (14.29%)	4 / 26 (15.38%)	2 / 26 (7.69%)
occurrences (all)	1	4	2
Depression			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	1 / 26 (3.85%)
occurrences (all)	0	1	1
Anxiety			
subjects affected / exposed	0 / 7 (0.00%)	3 / 26 (11.54%)	1 / 26 (3.85%)
occurrences (all)	0	3	1
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 7 (14.29%)	2 / 26 (7.69%)	4 / 26 (15.38%)
occurrences (all)	1	2	4
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 7 (28.57%)	2 / 26 (7.69%)	5 / 26 (19.23%)
occurrences (all)	3	2	5
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 7 (14.29%)	2 / 26 (7.69%)	3 / 26 (11.54%)
occurrences (all)	2	2	3
Blood creatine phosphokinase increased			

subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Blood creatinine increased			
subjects affected / exposed	1 / 7 (14.29%)	1 / 26 (3.85%)	2 / 26 (7.69%)
occurrences (all)	2	1	2
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	4 / 26 (15.38%)
occurrences (all)	0	1	6
International normalised ratio increased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Lipase increased			
subjects affected / exposed	1 / 7 (14.29%)	4 / 26 (15.38%)	3 / 26 (11.54%)
occurrences (all)	1	4	4
Neutrophil count decreased			
subjects affected / exposed	4 / 7 (57.14%)	4 / 26 (15.38%)	4 / 26 (15.38%)
occurrences (all)	6	5	6
Platelet count decreased			
subjects affected / exposed	1 / 7 (14.29%)	3 / 26 (11.54%)	4 / 26 (15.38%)
occurrences (all)	1	5	7
Weight decreased			
subjects affected / exposed	2 / 7 (28.57%)	2 / 26 (7.69%)	2 / 26 (7.69%)
occurrences (all)	2	2	2
Weight increased			
subjects affected / exposed	2 / 7 (28.57%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences (all)	2	0	0
White blood cell count decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	2 / 26 (7.69%)
occurrences (all)	0	0	3
Amylase increased			
subjects affected / exposed	1 / 7 (14.29%)	2 / 26 (7.69%)	5 / 26 (19.23%)
occurrences (all)	1	2	8
Injury, poisoning and procedural complications			

Muscle strain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Contusion			
subjects affected / exposed	1 / 7 (14.29%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	1	0	1
Fall			
subjects affected / exposed	1 / 7 (14.29%)	0 / 26 (0.00%)	2 / 26 (7.69%)
occurrences (all)	1	0	3
Infusion related reaction			
subjects affected / exposed	0 / 7 (0.00%)	3 / 26 (11.54%)	3 / 26 (11.54%)
occurrences (all)	0	4	5
Wound complication			
subjects affected / exposed	1 / 7 (14.29%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	0
Tooth fracture			
subjects affected / exposed	1 / 7 (14.29%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	0
Rib fracture			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	4
Atrial fibrillation			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	1 / 26 (3.85%)
occurrences (all)	0	1	1
Supraventricular tachycardia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Palpitations			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Nervous system disorders			

Peripheral sensory neuropathy			
subjects affected / exposed	5 / 7 (71.43%)	10 / 26 (38.46%)	11 / 26 (42.31%)
occurrences (all)	6	10	18
Amnesia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Cognitive disorder			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Dizziness			
subjects affected / exposed	1 / 7 (14.29%)	2 / 26 (7.69%)	2 / 26 (7.69%)
occurrences (all)	1	2	2
Dysaesthesia			
subjects affected / exposed	1 / 7 (14.29%)	1 / 26 (3.85%)	1 / 26 (3.85%)
occurrences (all)	1	1	2
Dysgeusia			
subjects affected / exposed	2 / 7 (28.57%)	4 / 26 (15.38%)	8 / 26 (30.77%)
occurrences (all)	4	4	8
Headache			
subjects affected / exposed	1 / 7 (14.29%)	3 / 26 (11.54%)	5 / 26 (19.23%)
occurrences (all)	2	3	5
Hypoaesthesia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Memory impairment			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Neuropathy peripheral			
subjects affected / exposed	0 / 7 (0.00%)	5 / 26 (19.23%)	3 / 26 (11.54%)
occurrences (all)	0	7	3
Neurotoxicity			
subjects affected / exposed	0 / 7 (0.00%)	3 / 26 (11.54%)	2 / 26 (7.69%)
occurrences (all)	0	6	4
Paraesthesia			
subjects affected / exposed	5 / 7 (71.43%)	5 / 26 (19.23%)	7 / 26 (26.92%)
occurrences (all)	6	7	7

Peripheral motor neuropathy			
subjects affected / exposed	1 / 7 (14.29%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	0
Presyncope			
subjects affected / exposed	1 / 7 (14.29%)	0 / 26 (0.00%)	2 / 26 (7.69%)
occurrences (all)	1	0	2
Taste disorder			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Tremor			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Syncope			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 7 (14.29%)	2 / 26 (7.69%)	4 / 26 (15.38%)
occurrences (all)	1	3	4
Iron deficiency anaemia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Neutropenia			
subjects affected / exposed	0 / 7 (0.00%)	3 / 26 (11.54%)	2 / 26 (7.69%)
occurrences (all)	0	5	4
Thrombocytopenia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	10
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Vertigo			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Eye disorders			

Vision blurred			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	2 / 26 (7.69%)
occurrences (all)	0	0	2
Visual acuity reduced			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	1 / 26 (3.85%)
occurrences (all)	0	1	1
Vitreous floaters			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Haemorrhoids			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Abdominal hernia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	2 / 26 (7.69%)
occurrences (all)	0	0	2
Abdominal pain			
subjects affected / exposed	1 / 7 (14.29%)	3 / 26 (11.54%)	5 / 26 (19.23%)
occurrences (all)	1	4	6
Abdominal pain upper			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	2 / 26 (7.69%)
occurrences (all)	0	0	3
Ascites			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Constipation			
subjects affected / exposed	3 / 7 (42.86%)	12 / 26 (46.15%)	9 / 26 (34.62%)
occurrences (all)	4	13	11
Diarrhoea			
subjects affected / exposed	5 / 7 (71.43%)	14 / 26 (53.85%)	12 / 26 (46.15%)
occurrences (all)	7	19	16
Dry mouth			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	2 / 26 (7.69%)
occurrences (all)	0	0	2
Dyspepsia			

subjects affected / exposed	0 / 7 (0.00%)	2 / 26 (7.69%)	1 / 26 (3.85%)
occurrences (all)	0	2	1
Dysphagia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Flatulence			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 7 (14.29%)	4 / 26 (15.38%)	2 / 26 (7.69%)
occurrences (all)	3	4	2
Hypoaesthesia oral			
subjects affected / exposed	1 / 7 (14.29%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	2 / 7 (28.57%)	12 / 26 (46.15%)	13 / 26 (50.00%)
occurrences (all)	2	12	16
Oral dysaesthesia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	0
Oral pain			
subjects affected / exposed	1 / 7 (14.29%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	1	0	1
Proctalgia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	0
Rectal haemorrhage			
subjects affected / exposed	2 / 7 (28.57%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	2	0	1
Rectal obstruction			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	2
Retching			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Stomatitis			

subjects affected / exposed	3 / 7 (42.86%)	8 / 26 (30.77%)	5 / 26 (19.23%)
occurrences (all)	4	9	5
Vomiting			
subjects affected / exposed	0 / 7 (0.00%)	6 / 26 (23.08%)	4 / 26 (15.38%)
occurrences (all)	0	13	4
Mouth ulceration			
subjects affected / exposed	1 / 7 (14.29%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	1	1	0
Hepatobiliary disorders			
Hepatic steatosis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Cholelithiasis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Alopecia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	1 / 26 (3.85%)
occurrences (all)	0	1	1
Angioedema			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Blister			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Cold sweat			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Dermatitis acneiform			
subjects affected / exposed	0 / 7 (0.00%)	2 / 26 (7.69%)	0 / 26 (0.00%)
occurrences (all)	0	2	0
Dry skin			

subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	2 / 26 (7.69%)
occurrences (all)	0	1	3
Eczema			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Erythema			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Hyperhidrosis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Miliaria			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Night sweats			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Onychoclasis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	2 / 26 (7.69%)
occurrences (all)	0	0	2
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 7 (0.00%)	3 / 26 (11.54%)	0 / 26 (0.00%)
occurrences (all)	0	5	0
Photosensitivity reaction			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Rash			
subjects affected / exposed	1 / 7 (14.29%)	3 / 26 (11.54%)	0 / 26 (0.00%)
occurrences (all)	1	4	0
Rash macular			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Rash maculo-papular			
subjects affected / exposed	0 / 7 (0.00%)	2 / 26 (7.69%)	1 / 26 (3.85%)
occurrences (all)	0	2	1

Skin discolouration			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Urticaria			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 7 (14.29%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	1	0	1
Dysuria			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	1 / 26 (3.85%)
occurrences (all)	0	1	1
Haematuria			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Pollakiuria			
subjects affected / exposed	0 / 7 (0.00%)	2 / 26 (7.69%)	0 / 26 (0.00%)
occurrences (all)	0	2	0
Proteinuria			
subjects affected / exposed	2 / 7 (28.57%)	1 / 26 (3.85%)	4 / 26 (15.38%)
occurrences (all)	2	1	6
Urinary hesitation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Urinary incontinence			
subjects affected / exposed	0 / 7 (0.00%)	2 / 26 (7.69%)	0 / 26 (0.00%)
occurrences (all)	0	2	0
Urinary retention			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	1 / 7 (14.29%)	2 / 26 (7.69%)	0 / 26 (0.00%)
occurrences (all)	1	2	0
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	0 / 7 (0.00%)	3 / 26 (11.54%)	2 / 26 (7.69%)
occurrences (all)	0	3	3
Arthritis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Back pain			
subjects affected / exposed	1 / 7 (14.29%)	3 / 26 (11.54%)	1 / 26 (3.85%)
occurrences (all)	1	3	1
Pain in jaw			
subjects affected / exposed	1 / 7 (14.29%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	0
Pain in extremity			
subjects affected / exposed	0 / 7 (0.00%)	2 / 26 (7.69%)	0 / 26 (0.00%)
occurrences (all)	0	3	0
Osteoarthritis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences (all)	2	0	0
Neck pain			
subjects affected / exposed	0 / 7 (0.00%)	2 / 26 (7.69%)	1 / 26 (3.85%)
occurrences (all)	0	2	1
Myalgia			
subjects affected / exposed	1 / 7 (14.29%)	1 / 26 (3.85%)	2 / 26 (7.69%)
occurrences (all)	1	1	2
Musculoskeletal chest pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Muscular weakness			
subjects affected / exposed	1 / 7 (14.29%)	1 / 26 (3.85%)	1 / 26 (3.85%)
occurrences (all)	1	1	1
Muscle spasms			
subjects affected / exposed	1 / 7 (14.29%)	1 / 26 (3.85%)	2 / 26 (7.69%)
occurrences (all)	1	1	2
Joint range of motion decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1

Bone pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Infections and infestations			
Eye infection			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Folliculitis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Conjunctivitis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Cellulitis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Candida infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Bronchitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Anorectal infection			
subjects affected / exposed	1 / 7 (14.29%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences (all)	2	0	0
Diarrhoea infectious			
subjects affected / exposed	1 / 7 (14.29%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	0
Pharyngitis streptococcal			
subjects affected / exposed	1 / 7 (14.29%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	0
Hordeolum			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Gastroenteritis viral			

subjects affected / exposed	1 / 7 (14.29%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	0
Fungal skin infection			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Pneumonia			
subjects affected / exposed	1 / 7 (14.29%)	1 / 26 (3.85%)	2 / 26 (7.69%)
occurrences (all)	1	1	2
Rash pustular			
subjects affected / exposed	0 / 7 (0.00%)	2 / 26 (7.69%)	0 / 26 (0.00%)
occurrences (all)	0	2	0
Rhinitis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Sinusitis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	0
Tooth abscess			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Tooth infection			
subjects affected / exposed	1 / 7 (14.29%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	1	0	1
Upper respiratory tract infection			
subjects affected / exposed	1 / 7 (14.29%)	2 / 26 (7.69%)	0 / 26 (0.00%)
occurrences (all)	1	2	0
Urinary tract infection			
subjects affected / exposed	0 / 7 (0.00%)	4 / 26 (15.38%)	1 / 26 (3.85%)
occurrences (all)	0	5	1
Vaginal infection			
subjects affected / exposed	1 / 7 (14.29%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	1	1	0
Wound infection			
subjects affected / exposed	1 / 7 (14.29%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	0
Medical device site infection			

subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
COVID-19			
subjects affected / exposed	0 / 7 (0.00%)	4 / 26 (15.38%)	0 / 26 (0.00%)
occurrences (all)	0	4	0
Metabolism and nutrition disorders			
Hyperlipidaemia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Hyperlipasaemia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Hyperkalaemia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	0
Hyperglycaemia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	0
Hyperamylasaemia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Dehydration			
subjects affected / exposed	2 / 7 (28.57%)	5 / 26 (19.23%)	3 / 26 (11.54%)
occurrences (all)	4	5	5
Decreased appetite			
subjects affected / exposed	1 / 7 (14.29%)	8 / 26 (30.77%)	5 / 26 (19.23%)
occurrences (all)	2	9	6
Tumour lysis syndrome			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Increased appetite			
subjects affected / exposed	1 / 7 (14.29%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences (all)	2	0	0
Hypophosphataemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	3 / 26 (11.54%)
occurrences (all)	0	0	3

Hyponatraemia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	1 / 26 (3.85%)
occurrences (all)	0	1	1
Hypomagnesaemia			
subjects affected / exposed	1 / 7 (14.29%)	2 / 26 (7.69%)	0 / 26 (0.00%)
occurrences (all)	1	2	0
Hypokalaemia			
subjects affected / exposed	0 / 7 (0.00%)	2 / 26 (7.69%)	1 / 26 (3.85%)
occurrences (all)	0	3	1
Hypocalcaemia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Hyperuricaemia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Hyperphosphataemia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Hypermagnesaemia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 May 2019	Section 3.1.3 (Safety Run-in [Part 1]): Revised to further clarify that Part 1 will not involve dose escalation. Section 3.1.5.2 (Safety Review Committee [SRC] [Part 2]): Clarified that the SRC will also be responsible for making recommendations for investigational product dose selection to ensure participants maintain adequate exposure to standard of care treatment. Section 3.1.6 (Management of Study Medication Related Toxicities): Clarified that the toxicity management guidelines provided via the website and Annex to Protocol are applicable to oleclumab. Clarified that guidelines regarding treatment modification and toxicity management for standard of care therapies are provided in Appendix H.
12 June 2020	Section (S) 1.6.2.1, 5.3.2: Updated per durvalumab IB edition 15.0. S 1.6.3: Added language to discuss participants with active SARS CoV 2 infection. S 2.2, 2.3: PK, immunogenicity of bevacizumab when used with FOLFOX+novel oncology therapy (Part 2) moved from Secondary Objectives to Exploratory Objectives. S 3.1.2: Specified if leucovorin is not available, use of levoleucovorin at an equivalent dose is acceptable. S 3.1.5, 4.6.1: Clarified that allocation ratio to different arms may be adjusted via protocol amendment after 50 participants are randomized to control arm and the control arm will continue to enroll participants although 50 participants have been enrolled. S 3.1.6.1: Revised language for toxicity management guidelines per sponsor guidelines, added statement to clarify that participants receiving oleclumab + durvalumab should follow durvalumab toxicity management guidelines. S 4.3.2; Table 10, S 4.3.2.2: Clarified requirements for archival and fresh tumor samples. Specified that mandatory biopsies can be waived during SARS-CoV2 pandemic. S 5.3.1: Added this section to indicate that it applies to all biological products used in the study. S 5.3.3: Added section on immune complex disease to align with the potential risks of oleclumab. S 5.5: Updated it to ensure that country-specific regulatory reporting requirements for SAEs are met according to updated sponsor guidelines. Appendix I: Added text to address site and study closure as required in ICH GCP. S 4.1.2: Added statement to inclusion criteria 9, 10 "(except in countries where spermicides are not approved)". S 4.1.3: Revised Criterion 6 to specify that ECGs will be obtained in triplicate within a 5-minute period at least 1min apart. Revised footnote for ECG in Table 6 to reflect the same. S 4.5.2: Clarified that the use of bevacizumab biosimilars is acceptable in regions/countries where their use is approved. S 4.8.8: Updated to clarify that randomization may be paused during the interim analysis.

11 May 2022	S 2.2: Removed text specifying the PK of bevacizumab will be described only when used in combination with FOLFOX + novel therapy. S 2.2: Clarified that PK for novel agents and bevacizumab are endpoints in Part 1, 2, and Part 1, respectively. S 2.2: Separated statement on immunogenicity objectives into Part 1 and 2, and Part 1. S 2.2: Clarified that the incidence of ADA to novel agents is an endpoint in Part 1 and 2, and ADA to bevacizumab is an endpoint in Part 1. S 2.3: Removed text specifying the PK of bevacizumab/novel agents will be described only when in combination with FOLFOX and clarified that the PK of bevacizumab will be described. Added that immunogenicity of bevacizumab and novel agents will be evaluated in Part 1. Clarified that the immunogenicity of bevacizumab and novel agents will be evaluated in Part 1 and 2, and immunogenicity of bevacizumab will be described in Part 2, and removed text specifying this is only when used in combination with FOLFOX + novel therapy. Separated statement on endpoints into Part 1 and 2, and Part 1. Clarified that an evaluation of ADA will be carried out in Part 1 and 2 as an endpoint. Clarified that the incidence of ADA to bevacizumab in Part 2 is an endpoint. Added table footnote stating that summaries and analyses for exploratory endpoints may be reported outside the CSR in a separate report. S 3.1.7: Clarified that any participants still receiving investigational product (IP) at the time of the data cutoff (DCO) will be able to continue to receive IP. Specified that the DCO refers to the final analysis in the CSR. S 3.2.3: Added endpoints (best overall response, disease control), clarified which endpoints are defined as primary or secondary. S 6.3: Added that participants still receiving IP at the time of "study completion" may be able to continue to receive IP, if, in the investigator's opinion, the participant is deriving clinical benefit and has not fulfilled any discontinuation criteria.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

On 17 February 2022, the decision was made to terminate the clinical study because superior efficacy was not observed for the novel study drug combinations under investigation.

Notes: