Clinical trial results:
A Phase Ib/II, Open-Label, Multicenter, Randomized Umbrella Study Evaluating the Efficacy and Safety of Multiple Immunotherapy-Based Treatment Combinations in Patients With Metastatic Colorectal Cancer (Morpheus-CRC)

Summary

EudraCT number	2017-004566-99
Trial protocol	GB ES
Global end of trial date	26 September 2022

Results information

Result version number	v1 (current)
This version publication date	08 October 2023
First version publication date	08 October 2023

Trial information

Trial identification

Sponsor protocol code	CO39612

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03555149
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
Public contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.com
Scientific contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.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	26 September 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 September 2022
Global end of trial reached?	Yes
Global end of trial date	26 September 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy, safety, and pharmacokinetics of multiple immunotherapy-based treatment combinations in patients with metastatic colorectal cancer (mCRC).

Protection of trial subjects:

All study subjects were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 September 2018
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy, Safety
Long term follow-up duration	4 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Switzerland: 2
Country: Number of subjects enrolled	France: 16
Country: Number of subjects enrolled	Korea, Republic of: 27
Country: Number of subjects enrolled	United States: 45
Country: Number of subjects enrolled	Australia: 6
Worldwide total number of subjects	96
EEA total number of subjects	16

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)	72
From 65 to 84 years	24
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 15 centers in 5 countries: United States, France, Republic of Korea, Australia, and Switzerland.

Pre-assignment

Screening details:

A total of 96 participants were enrolled.

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	Regorafenib (Control)

Arm description:

Participants will receive treatment until unacceptable toxicity or disease progression per Response Evaluation Criteria in Solid Tumors (RECIST) Version 1.1.

Arm type	Active comparator
Investigational medicinal product name	Regorafenib
Investigational medicinal product code	RO7069680
Other name	Stivarga
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

160 mg once daily on Days 1-21 of each cycle (21 day cycle)

Arm title	Atezolizumab + Imprime PGG + Bevacizumab

Arm description:

Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator.

Arm type	Experimental
Investigational medicinal product name	Atezolizumab
Investigational medicinal product code	RO5541267
Other name	Tecentriq
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1200 mg IV on Day 1 of each cycle (21 day cycle)

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

Dosage and administration details:

7.5 mg/kg on Day 1 of each cycle (21 day cycle)

Investigational medicinal product name	Imprime PGG
Investigational medicinal product code	RO7234832
Other name	PGG beta glucan
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

4 mg/kg on Days 1, 8 and 15 of each cycle (21 day cycle)

Arm title	Atezolizumab + Isatuximab

Arm description:

Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator.

Arm type	Experimental
Investigational medicinal product name	Isatuximab
Investigational medicinal product code	RO7268598
Other name	SAR650984
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

10 mg/kg on Days 1, 8, and 15 for Cycle 1 (21 day cycle)
10 mg/kg on Day 1 of each cycle Cycle 2+ (21 day cycle)

Investigational medicinal product name	Atezolizumab
Investigational medicinal product code	RO5541267
Other name	Tecentriq
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1200 mg on Day 1 of each cycle (21 day cycle)

Arm title	Atezolizumab + Selicrelumab + Bevacizumab

Arm description:

Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator.

Arm type	Experimental
Investigational medicinal product name	Atezolizumab
Investigational medicinal product code	RO5541267
Other name	Tecentriq
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

840 mg on Days 1 and 15 of each cycle (28 day cycle)

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

Dosage and administration details:

10 mg/kg on Days 1 and 15 of each cycle (28 day cycle)

Investigational medicinal product name	Selicrelumab
Investigational medicinal product code	RO7009789
Other name	CD40
Pharmaceutical forms	Concentrate for solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

16 mg SC on Day 1 of Cycles 1-4 and every third cycle there after (i.e., Cycles 7, 10, 13, etc.) (28 day cycle)

Arm title	Atezolizumab + Idasanutlin

Arm description:

Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator.

Arm type	Experimental
Investigational medicinal product name	Idasanutlin
Investigational medicinal product code	RO5503781/F33
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

150 mg once daily on Days 1-5 (28 day cycle)

Investigational medicinal product name	Atezolizumab
Investigational medicinal product code	RO5541267
Other name	Tecentriq
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

840 mg on Days 1 and 15 of each cycle (28 day cycle)

Arm title	Atezolizumab + Regorafenib

Arm description:

Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator.

Arm type	Experimental
Investigational medicinal product name	Regorafenib
Investigational medicinal product code	RO7069680
Other name	Stivarga
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

120 mg once daily on Days 1-21 of each cycle (28 day cycle)

Investigational medicinal product name	Atezolizumab
Investigational medicinal product code	RO5541267
Other name	Tecentriq
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

840 mg on Days 1 and 15 of each cycle (28 day cycle)

Arm title	Atezolizumab + Regorafenib + AB928

Arm description:

Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator.

Arm type	Experimental

Investigational medicinal product name	Atezolizumab
Investigational medicinal product code	RO5541267
Other name	Tecentriq
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Oral use

Dosage and administration details:

840 mg on Days 1 and 15 of each cycle (28 day cycle)

Investigational medicinal product name	Etrumadenant
Investigational medicinal product code	AB928
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

150 mg once daily on Days 1-28 of each cycle (28 day cycle)

Investigational medicinal product name	Regorafenib
Investigational medicinal product code	RO7069680
Other name	Stivarga
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

120 mg once daily on Days 1-21 of each cycle (28 day cycle)

Arm title	Atezolizumab + LOAd703

Arm description:

Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator.

Arm type	Experimental
Investigational medicinal product name	LOAd703
Investigational medicinal product code	
Other name	delolimogene mupadenorepvec
Pharmaceutical forms	Concentrate for solution for injection/infusion
Routes of administration	Intratumoral use

Dosage and administration details:

1 x 10^11 VP or 5 x 10^11 VP on Day 1 (21 day cycle)

Investigational medicinal product name	Atezolizumab
Investigational medicinal product code	RO5541267
Other name	Tecentriq
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1200 mg on Day 1 of each cycle (21 day cycle)

Number of subjects in period 1	Regorafenib (Control)	Atezolizumab + Imprime PGG + Bevacizumab	Atezolizumab + Isatuximab
Started	24	15	15
Received >/=1 Dose of Study Treatment	19	15	15
Completed	0	0	0
Not completed	24	15	15

Adverse event, serious fatal	18	15	15
Consent withdrawn by subject	3	-	-
Physician decision	1	-	-
Study Terminated By Sponsor	1	-	-
Lost to follow-up	1	-	-

Number of subjects in period 1	Atezolizumab + Selicrelumab + Bevacizumab	Atezolizumab + Idasanutlin	Atezolizumab + Regorafenib
Started	6	4	15
Received >/=1 Dose of Study Treatment	6	4	15
Completed	0	0	0
Not completed	6	4	15
Adverse event, serious fatal	4	4	11
Consent withdrawn by subject	2	-	1
Physician decision	-	-	-
Study Terminated By Sponsor	-	-	2
Lost to follow-up	-	-	1

Number of subjects in period 1	Atezolizumab + Regorafenib + AB928	Atezolizumab + LOAd703
Started	15	2
Received >/=1 Dose of Study Treatment	15	2
Completed	0	0
Not completed	15	2
Adverse event, serious fatal	12	1
Consent withdrawn by subject	-	-
Physician decision	-	-
Study Terminated By Sponsor	3	1
Lost to follow-up	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Regorafenib (Control)
Reporting group description:	
Participants will receive treatment until unacceptable toxicity or disease progression per Response Evaluation Criteria in Solid Tumors (RECIST) Version 1.1.	
Reporting group title	Atezolizumab + Imprime PGG + Bevacizumab
Reporting group description:	
Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator.	
Reporting group title	Atezolizumab + Isatuximab
Reporting group description:	
Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator.	
Reporting group title	Atezolizumab + Selicrelumab + Bevacizumab
Reporting group description:	
Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator.	
Reporting group title	Atezolizumab + Idasanutlin
Reporting group description:	
Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator.	
Reporting group title	Atezolizumab + Regorafenib
Reporting group description:	
Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator.	
Reporting group title	Atezolizumab + Regorafenib + AB928
Reporting group description:	
Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator.	
Reporting group title	Atezolizumab + LOAd703
Reporting group description:	
Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator.	

Reporting group values	Regorafenib (Control)	Atezolizumab + Imprime PGG + Bevacizumab	Atezolizumab + Isatuximab
Number of subjects	24	15	15
Age Categorical Units: Participants			
Preterm newborn (gestational age <37 weeks)	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
Adults (18-64 years)	17	13	12
From 65-84 years	7	2	3
85 years and over	0	0	0

Age Continuous Units: Years			
arithmetic mean	59.5	57.8	52.3
standard deviation	± 10.3	± 5.9	± 12.0
Sex: Female, Male Units:			
Female	12	7	6
Male	12	8	9
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	2	4	3
Not Hispanic or Latino	21	10	11
Unknown or Not Reported	1	1	1
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	1	0
Asian	7	6	4
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	0	0
White	15	7	10
More than one race	0	1	0
Unknown or Not Reported	1	0	1
ECOG score			
ECOG performance status scale. 0 - Fully active; able to carry on all predisease performance without restriction 1 - Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature			
Units: Subjects			
ECOG PS 0	11	8	5
ECOG PS 1	13	7	10
Number of Metastatic Sites at Enrollment Units: Subjects			
1 Site	3	1	0
2 Sites	4	5	3
3 Sites	9	5	8
>/=4 Sites	8	4	4

Reporting group values	Atezolizumab + Selicrelumab + Bevacizumab	Atezolizumab + Idasanutlin	Atezolizumab + Regorafenib
Number of subjects	6	4	15
Age Categorical Units: Participants			
Preterm newborn (gestational age <37 weeks)	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
Adults (18-64 years)	1	3	12
From 65-84 years	5	1	3
85 years and over	0	0	0

Age Continuous Units: Years			
arithmetic mean	66.8	56.3	56.4
standard deviation	± 10.0	± 6.8	± 8.2
Sex: Female, Male Units:			
Female	1	3	11
Male	5	1	4
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1	0	1
Not Hispanic or Latino	4	4	11
Unknown or Not Reported	1	0	3
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	1	5
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	1
White	5	3	7
More than one race	0	0	0
Unknown or Not Reported	1	0	2
ECOG score			
ECOG performance status scale. 0 - Fully active; able to carry on all predisease performance without restriction 1 - Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature			
Units: Subjects			
ECOG PS 0	5	1	7
ECOG PS 1	1	3	8
Number of Metastatic Sites at Enrollment Units: Subjects			
1 Site	0	0	1
2 Sites	3	3	7
3 Sites	0	0	2
>/=4 Sites	3	1	5

Reporting group values	Atezolizumab + Regorafenib + AB928	Atezolizumab + LOAd703	Total
Number of subjects	15	2	96
Age Categorical Units: Participants			
Preterm newborn (gestational age <37 weeks)	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
Adults (18-64 years)	13	1	72
From 65-84 years	2	1	24
85 years and over	0	0	0

Age Continuous Units: Years			
arithmetic mean	55.1	58.0	
standard deviation	± 9.2	± 11.3	-
Sex: Female, Male Units:			
Female	4	1	45
Male	11	1	51
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	1	12
Not Hispanic or Latino	14	1	76
Unknown or Not Reported	1	0	8
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	1
Asian	8	0	31
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	2
White	6	2	55
More than one race	0	0	1
Unknown or Not Reported	1	0	6
ECOG score			
ECOG performance status scale. 0 - Fully active; able to carry on all predisease performance without restriction 1 - Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature			
Units: Subjects			
ECOG PS 0	7	1	45
ECOG PS 1	8	1	51
Number of Metastatic Sites at Enrollment Units: Subjects			
1 Site	1	0	6
2 Sites	5	0	30
3 Sites	6	2	32
>/=4 Sites	3	0	28

End points

End points reporting groups

Reporting group title	Regorafenib (Control)
Reporting group description:	
Participants will receive treatment until unacceptable toxicity or disease progression per Response Evaluation Criteria in Solid Tumors (RECIST) Version 1.1.	
Reporting group title	Atezolizumab + Imprime PGG + Bevacizumab
Reporting group description:	
Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator.	
Reporting group title	Atezolizumab + Isatuximab
Reporting group description:	
Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator.	
Reporting group title	Atezolizumab + Selicrelumab + Bevacizumab
Reporting group description:	
Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator.	
Reporting group title	Atezolizumab + Idasanutlin
Reporting group description:	
Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator.	
Reporting group title	Atezolizumab + Regorafenib
Reporting group description:	
Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator.	
Reporting group title	Atezolizumab + Regorafenib + AB928
Reporting group description:	
Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator.	
Reporting group title	Atezolizumab + LOAd703
Reporting group description:	
Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator.	

Primary: Best Confirmed Overall Response Rate (ORR) as Determined by the Investigator According to Response Evaluation Criteria in Solid Tumors (RECIST) v1.1

End point title	Best Confirmed Overall Response Rate (ORR) as Determined by the Investigator According to Response Evaluation Criteria in Solid Tumors (RECIST) v1.1

End point description:

The best confirmed ORR is defined as the percentage of participants with a complete response or partial response on two consecutive occasions ≥4 weeks apart, as determined by the investigator according to RECIST v1.1. Participants could be classified as "Stable Disease" if the assessment was ≥6 weeks from randomization. They were classified as Missing if no post-baseline response assessments were available, or as Not Evaluable if all post-baseline response assessments were unevaluable. The differences in ORR between the experimental arms and the corresponding control arm were calculated, along with 95% confidence intervals (CIs), using normal approximation of the binomial distribution. The 95% CIs for ORRs were constructed using the Clopper-Pearson method, and 0 to 999999 indicates that they were not calculated for the "Not Evaluable" and "Missing" categories. The 95% CIs for the difference in rates were constructed using the Wald method with continuity correction.

End point type	Primary

End point timeframe:
From randomization until disease progression or loss of clinical benefit (up to 4 years)

End point values	Regorafenib (Control)	Atezolizumab + Imprime PGG + Bevacizumab	Atezolizumab + Isatuximab	Atezolizumab + Selicrelumab + Bevacizumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19	15	15	6
Units: Percentage of Participants				
number (confidence interval 95%)				
Responders (CR + PR)	0 (0 to 17.65)	0 (0 to 21.80)	0 (0 to 21.80)	0 (0 to 45.93)
Complete Response (CR)	0 (0 to 17.65)	0 (0 to 21.80)	0 (0 to 21.80)	0 (0 to 45.93)
Partial Response (PR)	0 (0 to 17.65)	0 (0 to 21.80)	0 (0 to 21.80)	0 (0 to 45.93)
Stable Disease (SD)	63.2 (38.36 to 83.71)	33.3 (11.82 to 61.62)	20.0 (4.33 to 48.09)	50 (11.81 to 88.19)
Progressive Disease (PD)	26.3 (9.15 to 51.20)	66.7 (38.38 to 88.18)	66.7 (38.38 to 88.18)	33.3 (4.33 to 77.72)
Not Evaluable	0 (0 to 999999)	0 (0 to 999999)	13.3 (0 to 999999)	0 (0 to 999999)
Missing	10.5 (0 to 999999)	0 (0 to 999999)	0 (0 to 999999)	16.7 (0 to 999999)

End point values	Atezolizumab + Idasanutlin	Atezolizumab + Regorafenib	Atezolizumab + Regorafenib + AB928	Atezolizumab + LOAd703
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	15	15	2
Units: Percentage of Participants				
number (confidence interval 95%)				
Responders (CR + PR)	0 (0 to 60.24)	6.7 (0.17 to 31.95)	6.7 (0.17 to 31.95)	0 (0 to 84.19)
Complete Response (CR)	0 (0 to 60.24)	0 (0 to 21.80)	0 (0 to 21.80)	0 (0 to 84.19)
Partial Response (PR)	0 (0 to 60.24)	6.7 (0.17 to 31.95)	6.7 (0.17 to 31.95)	0 (0 to 84.19)
Stable Disease (SD)	0 (0 to 60.24)	33.3 (11.82 to 61.62)	53.3 (26.59 to 78.73)	0 (0 to 84.19)
Progressive Disease (PD)	100 (39.76 to 100)	46.7 (21.27 to 73.41)	26.7 (7.79 to 55.10)	100 (15.81 to 100)
Not Evaluable	0 (0 to 999999)	0 (0 to 999999)	13.3 (0 to 999999)	0 (0 to 999999)
Missing	0 (0 to 999999)	13.3 (0 to 999999)	0 (0 to 999999)	0 (0 to 999999)

Statistical analyses

Statistical analysis title	The difference in ORR between arms
Comparison groups	Regorafenib (Control) v Atezolizumab + Regorafenib

Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in Overall Response Rate
Point estimate	6.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.92
upper limit	25.25

Statistical analysis title	The difference in ORR between arms
Comparison groups	Regorafenib (Control) v Atezolizumab + Regorafenib + AB928
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in Overall Response Rate
Point estimate	6.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.92
upper limit	25.25

Secondary: Progression-Free Survival (PFS) as Determined by Investigator According to RECIST v1.1

End point title	Progression-Free Survival (PFS) as Determined by Investigator According to RECIST v1.1

End point description:

Progression-free survival (PFS) after randomization, defined as the time from randomization to the first occurrence of disease progression or death from any cause (whichever occurs first), was determined by the investigator according to RECIST v1.1. For participants who did not have documented disease progression or death, PFS was censored at the day of the last tumor assessment. The Kaplan-Meier method was used to estimate the median for PFS with 95% confidence intervals (CIs) constructed through use of the Brookmeyer and Crowley method. The values "999999" indicate that the 95% CI could not be calculated because too few events had occurred.

End point type	Secondary

End point timeframe:

From randomization up to the first occurrence of disease or death from any cause (up to 4 years)

End point values	Regorafenib (Control)	Atezolizumab + Imprime PGG + Bevacizumab	Atezolizumab + Isatuximab	Atezolizumab + Selicrelumab + Bevacizumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19	15	15	6
Units: Months				
median (confidence interval 95%)	2.83 (2.20 to 3.02)	1.51 (1.38 to 2.79)	1.41 (1.41 to 1.77)	4.21 (1.68 to 999999)

End point values	Atezolizumab + Idasanutlin	Atezolizumab + Regorafenib	Atezolizumab + Regorafenib + AB928	Atezolizumab + LOAd703
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	15	15	2
Units: Months				
median (confidence interval 95%)	1.26 (0.82 to 999999)	1.81 (1.38 to 2.96)	4.60 (2.60 to 5.78)	1.58 (1.51 to 999999)

Statistical analyses

Statistical analysis title	PFS Hazard Ratio
Comparison groups	Regorafenib (Control) v Atezolizumab + Imprime PGG + Bevacizumab
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Hazard ratio (HR)
Point estimate	1.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	2.73

Statistical analysis title	PFS Hazard Ratio
Comparison groups	Regorafenib (Control) v Atezolizumab + Isatuximab
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Hazard ratio (HR)
Point estimate	2.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.08
upper limit	4.88

Statistical analysis title	PFS Hazard Ratio
Comparison groups	Regorafenib (Control) v Atezolizumab + Selicrelumab + Bevacizumab
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Hazard ratio (HR)
Point estimate	0.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.29
upper limit	2.18

Statistical analysis title	PFS Hazard Ratio
Comparison groups	Regorafenib (Control) v Atezolizumab + LOAd703
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Hazard ratio (HR)
Point estimate	5.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.94
upper limit	33.82

Statistical analysis title	PFS Hazard Ratio
Comparison groups	Regorafenib (Control) v Atezolizumab + Regorafenib
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Hazard ratio (HR)
Point estimate	1.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.83
upper limit	3.63

Statistical analysis title	PFS Hazard Ratio
Comparison groups	Regorafenib (Control) v Atezolizumab + Regorafenib + AB928
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Hazard ratio (HR)
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.39
upper limit	1.63

Statistical analysis title	PFS Hazard Ratio
Comparison groups	Regorafenib (Control) v Atezolizumab + Idasanutlin
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Hazard ratio (HR)
Point estimate	2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.64
upper limit	6.24

Secondary: Overall Survival (OS)	
End point title	Overall Survival (OS)

End point description:

Overall survival (OS) is defined as the time from randomization to death from any cause. Participants who were still alive at the time of OS analysis were censored at the last date they were known to be alive. The Kaplan-Meier method was used to estimate the median for OS with 95% confidence intervals (CIs) constructed through use of the Brookmeyer and Crowley method. The values "999999" indicate that the median or the 95% CI could not be calculated because too few events had occurred.

End point type	Secondary

End point timeframe:

From randomization up to death from any cause (up to 4 years)

End point values	Regorafenib (Control)	Atezolizumab + Imprime PGG + Bevacizumab	Atezolizumab + Isatuximab	Atezolizumab + Selicrelumab + Bevacizumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19	15	15	6
Units: Months				
median (confidence interval 95%)	10.15 (4.40 to	5.72 (4.37 to	5.13 (3.12 to	14.36 (3.22 to

12.29)	10.51)	7.75)	999999)

End point values	Atezolizumab + Idasanutlin	Atezolizumab + Regorafenib	Atezolizumab + Regorafenib + AB928	Atezolizumab + LOAd703
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	15	15	2
Units: Months				
median (confidence interval 95%)	5.93 (1.61 to 999999)	11.01 (5.29 to 16.66)	8.67 (6.60 to 14.62)	4.07 (0.999999 to 999999)

Statistical analyses

Statistical analysis title	OS Hazard Ratio
Statistical analysis description: Atezolizumab + Imprime PGG + Bevacizumab vs. Regorafenib (Control) Hazard Ratio for OS	
Comparison groups	Regorafenib (Control) v Atezolizumab + Imprime PGG + Bevacizumab
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Hazard ratio (HR)
Point estimate	1.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	2.93

Statistical analysis title	OS Hazard Ratio
Statistical analysis description: Atezolizumab + Isatuximab vs. Regorafenib (Control) Hazard Ratio for OS	
Comparison groups	Regorafenib (Control) v Atezolizumab + Isatuximab
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Hazard ratio (HR)
Point estimate	1.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	2.81

Statistical analysis title	OS Hazard Ratio
Statistical analysis description: Atezolizumab + Selicrelumab + Bevacizumab vs. Regorafenib (Control) Hazard Ratio for OS	
Comparison groups	Regorafenib (Control) v Atezolizumab + Selicrelumab + Bevacizumab
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Hazard ratio (HR)
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	2.72

Statistical analysis title	OS Hazard Ratio
Statistical analysis description: Atezolizumab + Idasanutlin vs. Regorafenib (Control) Hazard Ratio for OS	
Comparison groups	Regorafenib (Control) v Atezolizumab + Idasanutlin
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Hazard ratio (HR)
Point estimate	1.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.42
upper limit	3.84

Statistical analysis title	OS Hazard Ratio
Statistical analysis description: Atezolizumab + Regorafenib vs. Regorafenib (Control) Hazard Ratio for OS	
Comparison groups	Regorafenib (Control) v Atezolizumab + Regorafenib
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Hazard ratio (HR)
Point estimate	0.86

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.39
upper limit	1.88

Statistical analysis title	OS Hazard Ratio
Statistical analysis description:	
Atezolizumab + Regorafenib + AB928 vs. Regorafenib (Control) Hazard Ratio for OS	
Comparison groups	Atezolizumab + Regorafenib + AB928 v Regorafenib (Control)
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Hazard ratio (HR)
Point estimate	0.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.43
upper limit	1.96

Statistical analysis title	OS Hazard Ratio
Statistical analysis description:	
Atezolizumab + LOAd703 vs. Regorafenib (Control) Hazard Ratio for OS	
Comparison groups	Regorafenib (Control) v Atezolizumab + LOAd703
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Hazard ratio (HR)
Point estimate	2.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.33
upper limit	24.85

Secondary: Percentage of Participants Who Were Alive at Landmark Timepoints for Overall Survival (OS)

End point title	Percentage of Participants Who Were Alive at Landmark Timepoints for Overall Survival (OS)

End point description:

Overall survival (OS) is defined as the time from randomization to death from any cause. Participants who were still alive at the time of OS analysis were censored at the last date they were known to be alive. OS is shown as the percentage of participants who were event-free at the landmark timepoints of 3, 6, 12, and 18 months. The values "999999" indicate that the 95% CI could not be calculated because

too few events had occurred.

End point type	Secondary

End point timeframe:

3, 6, 12, and 18 months

End point values	Regorafenib (Control)	Atezolizumab + Imprime PGG + Bevacizumab	Atezolizumab + Isatuximab	Atezolizumab + Selicrelumab + Bevacizumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19	15	15	6
Units: Percentage of Participants				
number (confidence interval 95%)				
3 Months	84.21 (67.81 to 100.00)	100 (100 to 100)	73.33 (50.95 to 95.71)	100 (100 to 100)
6 Months	63.16 (41.47 to 84.85)	46.67 (21.42 to 71.91)	40.00 (15.21 to 64.79)	80.00 (44.94 to 100)
12 Months	34.45 (12.42 to 56.48)	20.00 (0.00 to 40.24)	26.67 (4.29 to 49.05)	53.33 (4.68 to 100)
18 Months	17.22 (0.00 to 34.87)	6.67 (0.00 to 19.29)	20.00 (0.00 to 40.24)	26.67 (0.00 to 70.91)

End point values	Atezolizumab + Idasanutlin	Atezolizumab + Regorafenib	Atezolizumab + Regorafenib + AB928	Atezolizumab + LOAd703
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	15	15	2
Units: Percentage of Participants				
number (confidence interval 95%)				
3 Months	75.00 (32.57 to 100)	78.97 (57.78 to 100.00)	86.67 (69.46 to 100.00)	100 (100 to 100)
6 Months	50.00 (1.00 to 99.00)	71.79 (48.32 to 95.27)	73.33 (50.95 to 95.71)	0 (0 to 999999)
12 Months	25.00 (0.00 to 67.43)	39.89 (13.18 to 66.59)	33.33 (9.48 to 57.19)	0 (0 to 999999)
18 Months	25.00 (0.00 to 67.43)	23.93 (0.48 to 47.39)	26.67 (4.29 to 49.05)	0 (0 to 999999)

Statistical analyses

Statistical analysis title	Difference in OS Event-Free Rate

Statistical analysis description:

Difference in OS event-free rate at 6 months for the Atezolizumab + Imprime PGG + Bevacizumab vs. Regorafenib (Control) arms

Comparison groups	Regorafenib (Control) v Atezolizumab + Imprime PGG + Bevacizumab

Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in OS Event-Free Rate
Point estimate	-16.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	-49.78
upper limit	16.79

Statistical analysis title	Difference in OS Event-Free Rate
Statistical analysis description:	
Difference in OS event-free rate at 3 months for the Atezolizumab + Imprime PGG + Bevacizumab vs. Regorafenib (Control) arms	
Comparison groups	Regorafenib (Control) v Atezolizumab + Imprime PGG + Bevacizumab
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in OS Event-Free Rate
Point estimate	15.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.61
upper limit	32.19

Statistical analysis title	Difference in OS Event-Free Rate
Statistical analysis description:	
Difference in OS event-free rate at 3 months for the Atezolizumab + Isatuximab vs. Regorafenib (Control) arms	
Comparison groups	Regorafenib (Control) v Atezolizumab + Isatuximab
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in OS Event-Free Rate
Point estimate	-10.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	-38.62
upper limit	16.87

Statistical analysis title	Difference in OS Event-Free Rate

Statistical analysis description:	
Difference in OS event-free rate at 18 months for the Atezolizumab + Imprime PGG + Bevacizumab vs. Regorafenib (Control) arms	
Comparison groups	Regorafenib (Control) v Atezolizumab + Imprime PGG + Bevacizumab
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in OS Event-Free Rate
Point estimate	-10.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	-32.25
upper limit	11.14

Statistical analysis title	Difference in OS Event-Free Rate
Statistical analysis description:	
Difference in OS event-free rate at 12 months for the Atezolizumab + Imprime PGG + Bevacizumab vs. Regorafenib (Control) arms	
Comparison groups	Regorafenib (Control) v Atezolizumab + Imprime PGG + Bevacizumab
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in OS Event-Free Rate
Point estimate	-14.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	-44.37
upper limit	15.47

Statistical analysis title	Difference in OS Event-Free Rate
Statistical analysis description:	
Difference in OS event-free rate at 12 months for the Atezolizumab + Selicrelumab + Bevacizumab vs. Regorafenib (Control) arms	
Comparison groups	Regorafenib (Control) v Atezolizumab + Selicrelumab + Bevacizumab
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in OS Event-Free Rate
Point estimate	18.88

Confidence interval	
level	95 %
sides	2-sided
lower limit	-34.53
upper limit	72.3

Statistical analysis title	Difference in OS Event-Free Rate
Statistical analysis description:	
Difference in OS event-free rate at 18 months for the Atezolizumab + Selicrelumab + Bevacizumab vs. Regorafenib (Control) arms	
Comparison groups	Regorafenib (Control) v Atezolizumab + Selicrelumab + Bevacizumab
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in OS Event-Free Rate
Point estimate	9.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	-38.19
upper limit	57.08

Statistical analysis title	Difference in OS Event-Free Rate
Statistical analysis description:	
Difference in OS event-free rate at 6 months for the Atezolizumab + Selicrelumab + Bevacizumab vs. Regorafenib (Control) arms	
Comparison groups	Regorafenib (Control) v Atezolizumab + Selicrelumab + Bevacizumab
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in OS Event-Free Rate
Point estimate	16.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	-24.39
upper limit	58.07

Statistical analysis title	Difference in OS Event-Free Rate
Statistical analysis description:	
Difference in OS event-free rate at 3 months for the Atezolizumab + Selicrelumab + Bevacizumab vs. Regorafenib (Control) arms	
Comparison groups	Regorafenib (Control) v Atezolizumab + Selicrelumab + Bevacizumab

Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in OS Event-Free Rate
Point estimate	15.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.61
upper limit	32.19

Statistical analysis title	Difference in OS Event-Free Rate

Statistical analysis description:

Difference in OS event-free rate at 18 months for the Atezolizumab + Isatuximab vs. Regorafenib (Control) arms

Comparison groups	Regorafenib (Control) v Atezolizumab + Isatuximab
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in OS Event-Free Rate
Point estimate	2.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	-24.08
upper limit	29.63

Statistical analysis title	Difference in OS Event-Free Rate

Statistical analysis description:

Difference in OS event-free rate at 12 months for the Atezolizumab + Isatuximab vs. Regorafenib (Control) arms

Comparison groups	Regorafenib (Control) v Atezolizumab + Isatuximab
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in OS Event-Free Rate
Point estimate	-7.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	-39.19
upper limit	23.62

Statistical analysis title	Difference in OS Event-Free Rate

Statistical analysis description:

Difference in OS event-free rate at 6 months for the Atezolizumab + Isatuximab vs. Regorafenib (Control) arms

Comparison groups	Regorafenib (Control) v Atezolizumab + Isatuximab
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in OS Event-Free Rate
Point estimate	-23.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-56.1
upper limit	9.78

Statistical analysis title	Difference in OS Event-Free Rate

Statistical analysis description:

Difference in OS event-free rate at 3 months for the Atezolizumab + Idasanutlin vs. Regorafenib (Control) arms

Comparison groups	Regorafenib (Control) v Atezolizumab + Idasanutlin
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in OS Event-Free Rate
Point estimate	-9.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	-54.7
upper limit	36.28

Statistical analysis title	Difference in OS Event-Free Rate

Statistical analysis description:

Difference in OS event-free rate at 3 months for the Atezolizumab + Regorafenib vs. Regorafenib (Control) arms

Comparison groups	Regorafenib (Control) v Atezolizumab + Regorafenib
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in OS Event-Free Rate
Point estimate	-5.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-32.03
upper limit	21.56

Statistical analysis title	Difference in OS Event-Free Rate
Statistical analysis description:	
Difference in OS event-free rate at 18 months for the Atezolizumab + Idasanutlin vs. Regorafenib (Control) arms	
Comparison groups	Regorafenib (Control) v Atezolizumab + Idasanutlin
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in OS Event-Free Rate
Point estimate	7.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	-38.18
upper limit	53.73

Statistical analysis title	Difference in OS Event-Free Rate
Statistical analysis description:	
Difference in OS event-free rate at 12 months for the Atezolizumab + Idasanutlin vs. Regorafenib (Control) arms	
Comparison groups	Regorafenib (Control) v Atezolizumab + Idasanutlin
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in OS Event-Free Rate
Point estimate	-9.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	-57.26
upper limit	38.36

Statistical analysis title	Difference in OS Event-Free Rate
Statistical analysis description:	
Difference in OS event-free rate at 6 months for the Atezolizumab + Idasanutlin vs. Regorafenib (Control) arms	
Comparison groups	Regorafenib (Control) v Atezolizumab + Idasanutlin
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in OS Event-Free Rate
Point estimate	-13.16

Confidence interval	
level	95 %
sides	2-sided
lower limit	-66.74
upper limit	40.43

Statistical analysis title	Difference in OS Event-Free Rate
Statistical analysis description:	
Difference in OS event-free rate at 6 months for the Atezolizumab + Regorafenib vs. Regorafenib (Control) arms	
Comparison groups	Regorafenib (Control) v Atezolizumab + Regorafenib
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in OS Event-Free Rate
Point estimate	8.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	-23.33
upper limit	40.6

Statistical analysis title	Difference in OS Event-Free Rate
Statistical analysis description:	
Difference in OS event-free rate at 12 months for the Atezolizumab + Regorafenib vs. Regorafenib (Control) arms	
Comparison groups	Regorafenib (Control) v Atezolizumab + Regorafenib + AB928
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in OS Event-Free Rate
Point estimate	5.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	-29.19
upper limit	40.06

Statistical analysis title	Difference in OS Event-Free Rate
Statistical analysis description:	
Difference in OS event-free rate at 18 months for the Atezolizumab + Regorafenib vs. Regorafenib (Control) arms	
Comparison groups	Regorafenib (Control) v Atezolizumab + Regorafenib

Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in OS Event-Free Rate
Point estimate	6.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	-22.64
upper limit	36.06

Statistical analysis title	Difference in OS Event-Free Rate

Statistical analysis description:

Difference in OS event-free rate at 18 months for the Atezolizumab + Regorafenib + AB928 vs. Regorafenib (Control) arms

Comparison groups	Regorafenib (Control) v Atezolizumab + Regorafenib + AB928
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in OS Event-Free Rate
Point estimate	9.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.06
upper limit	37.94

Statistical analysis title	Difference in OS Event-Free Rate

Statistical analysis description:

Difference in OS event-free rate at 12 months for the Atezolizumab + Regorafenib + AB928 vs. Regorafenib (Control) arms

Comparison groups	Regorafenib (Control) v Atezolizumab + Regorafenib + AB928
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in OS Event-Free Rate
Point estimate	-1.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-33.59
upper limit	31.36

Statistical analysis title	Difference in OS Event-Free Rate

Statistical analysis description:

Difference in OS event-free rate at 6 months for the Atezolizumab + Regorafenib + AB928 vs. Regorafenib (Control) arms

Comparison groups	Regorafenib (Control) v Atezolizumab + Regorafenib + AB928
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in OS Event-Free Rate
Point estimate	10.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-20.99
upper limit	41.34

Statistical analysis title	Difference in OS Event-Free Rate

Statistical analysis description:

Difference in OS event-free rate at 3 months for the Atezolizumab + Regorafenib + AB928 vs. Regorafenib (Control) arms

Comparison groups	Regorafenib (Control) v Atezolizumab + Regorafenib + AB928
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in OS Event-Free Rate
Point estimate	2.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	-21.31
upper limit	26.22

Statistical analysis title	Difference in OS Event-Free Rate

Statistical analysis description:

Difference in OS event-free rate at 3 months for the Atezolizumab + LOAd703 vs. Regorafenib (Control) arms

Comparison groups	Regorafenib (Control) v Atezolizumab + LOAd703
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in OS Event-Free Rate
Point estimate	15.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.61
upper limit	32.19

Secondary: Duration of Response (DOR) as Determined by the Investigator According to RECIST v1.1

End point title	Duration of Response (DOR) as Determined by the Investigator According to RECIST v1.1

End point description:

Duration of response is defined as the time from the first occurrence of a documented objective response to disease progression or death from any cause, whichever occurs first. In both arms where DOR was measured only 1 participant had a confirmed response; 95% CI could not be calculated.

End point type	Secondary

End point timeframe:

From the date of first occurrence of a documented objective response to disease progression or death from any cause, whichever occurs first (up to 4 years)

End point values	Regorafenib (Control)	Atezolizumab + Imprime PGG + Bevacizumab	Atezolizumab + Isatuximab	Atezolizumab + Selicrelumab + Bevacizumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[1]	0[2]	0[3]	0[4]
Units: Months				
median (confidence interval 95%)	(to)	(to)	(to)	(to)

Notes:

[1] - None of the patients in this arm had a confirmed response.

[2] - None of the patients in this arm had a confirmed response.

[3] - None of the patients in this arm had a confirmed response.

[4] - None of the patients in this arm had a confirmed response.

End point values	Atezolizumab + Idasanutlin	Atezolizumab + Regorafenib	Atezolizumab + Regorafenib + AB928	Atezolizumab + LOAd703
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[5]	1[6]	1[7]	0[8]
Units: Months				
median (confidence interval 95%)	(to)	3.12 (0 to 999999)	5.75 (0 to 999999)	(to)

Notes:

[5] - None of the patients in this arm had a confirmed response.

[6] - 1 patient with a confirmed response; 95% CI could not be calculated.

[7] - 1 patient with a confirmed response; 95% CI could not be calculated.

[8] - None of the patients in this arm had a confirmed response.

Statistical analyses

No statistical analyses for this end point

Secondary: Disease Control Rate (DCR), as Determined by the Investigator per RECIST v1.1

End point title	Disease Control Rate (DCR), as Determined by the Investigator per RECIST v1.1

End point description:

Disease control rate is defined as the percentage of participants with stable disease for ≥12 weeks or a complete or partial response, as determined by the investigator according to RECIST v1.1.

End point type	Secondary

End point timeframe:

From randomization until disease progression or loss of clinical benefit (up to 4 years)

End point values	Regorafenib (Control)	Atezolizumab + Imprime PGG + Bevacizumab	Atezolizumab + Isatuximab	Atezolizumab + Selicrelumab + Bevacizumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19	15	15	6
Units: Percentage of Participants				
number (confidence interval 95%)	15.8 (3.38 to 39.58)	13.3 (1.66 to 40.46)	6.7 (0.17 to 31.95)	33.3 (4.33 to 77.72)

End point values	Atezolizumab + Idasanutlin	Atezolizumab + Regorafenib	Atezolizumab + Regorafenib + AB928	Atezolizumab + LOAd703
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	15	15	2
Units: Percentage of Participants				
number (confidence interval 95%)	0 (0.00 to 60.24)	13.3 (1.66 to 40.46)	40.0 (16.34 to 67.71)	0 (0.00 to 84.19)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with at Least One Adverse Event (AE)

End point title	Percentage of Participants with at Least One Adverse Event (AE)

End point description:

The incidence, nature, and severity of adverse events (AEs) are reported, with severity determined according to NCI CTCAE v4.0. AEs were reported for the safety-evaluable population, which included all patients who received any amount of dose of any component of study treatment. All AEs were reported until 30 days after the last study dose or until start of new systemic anti-cancer therapy. Serious AEs and AEs of special interest were reported until 135 days (or 180 days for the Atezolizumab + LOAd703 arm only) after the last dose of study treatment.

End point type	Secondary

End point timeframe:

Adverse event data were collected from baseline up to 6 months after the last dose of study treatment (up to 640 days); deaths (all-cause) were reported from baseline through survival follow-up (up to 4 years)

End point values	Regorafenib (Control)	Atezolizumab + Imprime PGG + Bevacizumab	Atezolizumab + Isatuximab	Atezolizumab + Selicrelumab + Bevacizumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19	15	15	6
Units: Percentage of Participants				
number (not applicable)				
Adverse Event (AE)	100	100	100	100
Death	89.5	100	100	66.7
Withdrawn from Stage due to an AE	15.8	6.7	0	0
AE with a Fatal Outcome	10.5	0	0	0
Serious AE (SAE)	26.3	6.7	33.3	50.0
SAE Leading to Withdrawal from any Treatment	21.1	6.7	0	0
SAE Leading to Dose Modification/Interruption	5.3	0	6.7	50.0
Related SAE	5.3	6.7	0	50.0
AE Leading to Withdrawal from any Treatment	26.3	6.7	0	0
AE Leading to Dose Modification/Interruption	63.2	40.0	13.3	50.0
Related AE	94.7	86.7	86.7	100
Related AE Leading to Withdrawal from Treatment	10.5	6.7	0	0
Related AE Leading to Dose Modified/Interruption	47.4	33.3	0	33.3
Grade 3-5 AE	68.4	20.0	46.7	50.0
Worst Grade AE: 5	10.5	0	0	0
Worst Grade AE: 4	5.3	0	6.7	0
Worst Grade AE: 3	52.6	20.0	40.0	50.0

End point values	Atezolizumab + Idasanutlin	Atezolizumab + Regorafenib	Atezolizumab + Regorafenib + AB928	Atezolizumab + LOAd703
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	15	15	2
Units: Percentage of Participants				
number (not applicable)				
Adverse Event (AE)	100	100	100	100
Death	100	73.3	80.0	50.0
Withdrawn from Stage due to an AE	0	6.7	6.7	0
AE with a Fatal Outcome	0	6.7	0	0
Serious AE (SAE)	25.0	46.7	46.7	50.0
SAE Leading to Withdrawal from any Treatment	0	6.7	0	0
SAE Leading to Dose Modification/Interruption	0	26.7	46.7	0
Related SAE	25.0	26.7	33.3	50.0
AE Leading to Withdrawal from any Treatment	0	20.0	6.7	0
AE Leading to Dose Modification/Interruption	75.0	86.7	93.3	0
Related AE	100	93.3	100	50.0

Related AE Leading to Withdrawal from Treatment	0	6.7	6.7	0
Related AE Leading to Dose Modified/Interruption	75.0	73.3	93.3	0
Grade 3-5 AE	75.0	66.7	60.0	0
Worst Grade AE: 5	0	6.7	0	0
Worst Grade AE: 4	25.0	6.7	13.3	0
Worst Grade AE: 3	50.0	53.3	46.7	0

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

Adverse event (AE) data were collected from baseline up to 6 months after the last dose of study treatment (up to 640 days); the total number of deaths (all-cause) reported include survival follow-up (up to 4 years)

Adverse event reporting additional description:

AEs were reported for the safety population, defined as all those who received ≥1 dose of study treatment. All AEs were reported until 30 days after the last study dose or until start of new systemic anti-cancer therapy. Serious AEs and AEs of special interest were reported until 135 days (180 days for Atezo + LOAd703) after the last study dose.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	Atezolizumab + Selicrelumab + Bevacizumab

Reporting group description:

Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator.

Reporting group title	Atezolizumab + Isatuximab

Reporting group description:

Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator.

Reporting group title	Regorafenib (Control)

Reporting group description:

Participants will receive treatment until unacceptable toxicity or disease progression per Response Evaluation Criteria in Solid Tumors (RECIST) Version 1.1.

Reporting group title	Atezolizumab + Imprime PGG + Bevacizumab

Reporting group description:

Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator.

Reporting group title	Atezolizumab + Idasanutlin

Reporting group description:

Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator.

Reporting group title	Atezolizumab + Regorafenib + AB928

Reporting group description:

Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator.

Reporting group title	Atezolizumab + Regorafenib

Reporting group description:

Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator.

Reporting group title	Atezolizumab + LOAd703

Reporting group description:

Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator.

Serious adverse events	Atezolizumab + Selicrelumab + Bevacizumab	Atezolizumab + Isatuximab	Regorafenib (Control)
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 6 (50.00%)	5 / 15 (33.33%)	5 / 19 (26.32%)
number of deaths (all causes)	4	15	17
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Perforation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Cytokine release syndrome			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypersensitivity			

subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	0 / 19 (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
Respiratory failure			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 19 (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
Haemoptysis			
subjects affected / exposed	1 / 6 (16.67%)	1 / 15 (6.67%)	0 / 19 (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
Hypoxia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood bilirubin increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Injury, poisoning and procedural complications			
Lumbar vertebral fracture			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial flutter			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	0 / 19 (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
Nervous system disorders			
Syncope			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukocytosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombotic microangiopathy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			

subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 19 (5.26%)
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 intestinal obstruction			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 19 (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
Diarrhoea			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	1 / 6 (16.67%)	1 / 15 (6.67%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Biliary obstruction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash maculo-papular			

subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Fistula			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bacteraemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Biliary tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	2 / 19 (10.53%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Pyelonephritis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterocolitis infectious			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 19 (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

Serious adverse events	Atezolizumab + Imprime PGG + Bevacizumab	Atezolizumab + Idasanutlin	Atezolizumab + Regorafenib + AB928
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 15 (6.67%)	1 / 4 (25.00%)	7 / 15 (46.67%)
number of deaths (all causes)	15	4	12
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour haemorrhage			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Perforation			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	2 / 15 (13.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Immune system disorders			
Cytokine release syndrome			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypersensitivity			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Investigations			
Blood bilirubin increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Lumbar vertebral fracture			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial flutter			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukocytosis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 4 (25.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombotic microangiopathy			

subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestinal obstruction			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Biliary obstruction			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			

Rash			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash maculo-papular			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Fistula			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bacteraemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Biliary tract infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Enterocolitis infectious			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Atezolizumab + Regorafenib	Atezolizumab + LOAd703	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 15 (46.67%)	1 / 2 (50.00%)	
number of deaths (all causes)	11	1	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour haemorrhage			
subjects affected / exposed	1 / 15 (6.67%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perforation			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			

subjects affected / exposed	3 / 15 (20.00%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	2 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Cytokine release syndrome			
subjects affected / exposed	0 / 15 (0.00%)	1 / 2 (50.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersensitivity			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epistaxis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Hypoxia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood bilirubin increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Lumbar vertebral fracture			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial flutter			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukocytosis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			

subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombotic microangiopathy			
subjects affected / exposed	1 / 15 (6.67%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestinal obstruction			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	1 / 15 (6.67%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			

Biliary obstruction			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash maculo-papular			
subjects affected / exposed	1 / 15 (6.67%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Fistula			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bacteraemia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary tract infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 15 (6.67%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			

subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis infectious			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Atezolizumab + Selicrelumab + Bevacizumab	Atezolizumab + Isatuximab	Regorafenib (Control)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	15 / 15 (100.00%)	19 / 19 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour fistulisation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Tumour pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Vascular disorders			
Vena cava thrombosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Hypertension			

subjects affected / exposed	1 / 6 (16.67%)	1 / 15 (6.67%)	6 / 19 (31.58%)
occurrences (all)	5	1	7
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 6 (33.33%)	1 / 15 (6.67%)	2 / 19 (10.53%)
occurrences (all)	3	2	2
Chest discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	0 / 6 (0.00%)	2 / 15 (13.33%)	3 / 19 (15.79%)
occurrences (all)	0	3	3
Chills			
subjects affected / exposed	0 / 6 (0.00%)	4 / 15 (26.67%)	0 / 19 (0.00%)
occurrences (all)	0	6	0
Inflammation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
General physical health deterioration			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	1 / 6 (16.67%)	1 / 15 (6.67%)	1 / 19 (5.26%)
occurrences (all)	1	1	1
Mucosal inflammation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	2
Medical device site erythema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Injection site reaction			
subjects affected / exposed	5 / 6 (83.33%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	9	0	0
Influenza like illness			

subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Device related thrombosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Face oedema			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Fatigue			
subjects affected / exposed	2 / 6 (33.33%)	9 / 15 (60.00%)	8 / 19 (42.11%)
occurrences (all)	2	11	8
Oedema			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	3 / 19 (15.79%)
occurrences (all)	1	0	4
Peripheral swelling			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Oedema peripheral			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Swelling face			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Hypersensitivity			

subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Cytokine release syndrome			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Intermenstrual bleeding			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Perineal fistula			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Vaginal haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea exertional			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Aspiration			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Cough			
subjects affected / exposed	1 / 6 (16.67%)	4 / 15 (26.67%)	2 / 19 (10.53%)
occurrences (all)	1	5	2
Dysphonia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	5 / 19 (26.32%)
occurrences (all)	1	0	7
Dyspnoea			
subjects affected / exposed	1 / 6 (16.67%)	2 / 15 (13.33%)	4 / 19 (21.05%)
occurrences (all)	1	2	4
Aphonia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Epistaxis			

subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Haemoptysis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Hypoxia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 6 (0.00%)	2 / 15 (13.33%)	0 / 19 (0.00%)
occurrences (all)	0	2	0
Nasal dryness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Sinus congestion			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Wheezing			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Oropharyngeal pain			
subjects affected / exposed	1 / 6 (16.67%)	1 / 15 (6.67%)	1 / 19 (5.26%)
occurrences (all)	1	1	1
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Anxiety			
subjects affected / exposed	1 / 6 (16.67%)	1 / 15 (6.67%)	0 / 19 (0.00%)
occurrences (all)	1	1	0
Depression			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 19 (0.00%)
occurrences (all)	0	1	0

Insomnia			
subjects affected / exposed	2 / 6 (33.33%)	2 / 15 (13.33%)	3 / 19 (15.79%)
occurrences (all)	2	2	3
Sleep disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Product issues			
Device occlusion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Investigations			
Blood bilirubin increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	4 / 19 (21.05%)
occurrences (all)	0	0	5
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	3
Blood creatinine increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
C-reactive protein increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	3 / 19 (15.79%)
occurrences (all)	0	0	4
Alanine aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	4 / 19 (21.05%)
occurrences (all)	0	1	5
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	2 / 19 (10.53%)
occurrences (all)	0	1	2

Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Lipase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Lymphocyte count decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Platelet count decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	2
Weight decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	2
White blood cell count decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Intentional overdose			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Injection related reaction			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
Infusion related reaction			

subjects affected / exposed	0 / 6 (0.00%)	11 / 15 (73.33%)	0 / 19 (0.00%)
occurrences (all)	0	13	0
Gastrointestinal anastomotic leak			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Facial bones fracture			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Corneal abrasion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Accidental overdose			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Stoma site rash			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Palpitations			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Sinus tachycardia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Dizziness			

subjects affected / exposed	1 / 6 (16.67%)	2 / 15 (13.33%)	0 / 19 (0.00%)
occurrences (all)	1	2	0
Cerebellar syndrome			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Disturbance in attention			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Dysgeusia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Hyperaesthesia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Myoclonus			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Peripheral motor neuropathy			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Sciatica			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Neuropathy peripheral			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			

Thrombocytopenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	2
Anaemia			
subjects affected / exposed	1 / 6 (16.67%)	3 / 15 (20.00%)	2 / 19 (10.53%)
occurrences (all)	1	3	2
Lymphopenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	2
Ear and labyrinth disorders			
Ear haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Ear discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Cerumen impaction			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Lacrimation increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Vision blurred			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Ascites			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	1 / 19 (5.26%)
occurrences (all)	0	1	3
Anal haemorrhage			

subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Abdominal pain lower			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	0 / 6 (0.00%)	4 / 15 (26.67%)	5 / 19 (26.32%)
occurrences (all)	0	4	5
Abdominal distension			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Colitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Dry mouth			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	2
Diarrhoea			
subjects affected / exposed	2 / 6 (33.33%)	2 / 15 (13.33%)	6 / 19 (31.58%)
occurrences (all)	2	3	9
Constipation			
subjects affected / exposed	2 / 6 (33.33%)	3 / 15 (20.00%)	4 / 19 (21.05%)
occurrences (all)	2	3	4
Dyspepsia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Odynophagia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	0 / 6 (0.00%)	6 / 15 (40.00%)	7 / 19 (36.84%)
occurrences (all)	0	8	7
Haemorrhoids			

subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Dysphagia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 6 (16.67%)	1 / 15 (6.67%)	1 / 19 (5.26%)
occurrences (all)	1	1	1
Frequent bowel movements			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Enterocolitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Gingival bleeding			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	1 / 6 (16.67%)	3 / 15 (20.00%)	1 / 19 (5.26%)
occurrences (all)	1	4	1
Stomatitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Salivary duct inflammation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Rectal haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Proctalgia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Post-tussive vomiting			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Oral pain			

subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	2 / 19 (10.53%)
occurrences (all)	1	0	2
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	2
Hepatic vein thrombosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Jaundice			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Dermatitis acneiform			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Alopecia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Dry skin			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Erythema			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Hair colour changes			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Hyperhidrosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Night sweats			

subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	12 / 19 (63.16%)
occurrences (all)	0	0	18
Pruritus			
subjects affected / exposed	1 / 6 (16.67%)	1 / 15 (6.67%)	0 / 19 (0.00%)
occurrences (all)	1	1	0
Psoriasis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Hyperkeratosis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Rash macular			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Rash maculo-papular			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Rash papular			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Seborrhoeic dermatitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Urticaria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Xeroderma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Skin exfoliation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0

Renal and urinary disorders			
Urinary incontinence			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Haematuria			
subjects affected / exposed	2 / 6 (33.33%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
Proteinuria			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Renal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Acute kidney injury			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Urinary retention			
subjects affected / exposed	1 / 6 (16.67%)	1 / 15 (6.67%)	0 / 19 (0.00%)
occurrences (all)	1	1	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	1 / 6 (16.67%)	1 / 15 (6.67%)	2 / 19 (10.53%)
occurrences (all)	1	1	2
Hyperthyroidism			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 6 (16.67%)	1 / 15 (6.67%)	1 / 19 (5.26%)
occurrences (all)	2	1	1
Arthritis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0

Groin pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Bone pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Flank pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Fracture pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Muscle discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Muscle spasms			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Musculoskeletal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	1 / 6 (16.67%)	2 / 15 (13.33%)	1 / 19 (5.26%)
occurrences (all)	1	2	1
Neck pain			
subjects affected / exposed	2 / 6 (33.33%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
Pain in extremity			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	5 / 19 (26.32%)
occurrences (all)	0	0	5
Infections and infestations			
Nasopharyngitis			

subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Influenza			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Gingivitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Otitis media			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	3	0	0
Sepsis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Rash pustular			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Pneumonia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Soft tissue infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Tooth infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	1 / 6 (16.67%)	2 / 15 (13.33%)	1 / 19 (5.26%)
occurrences (all)	2	2	1
Upper respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	3 / 15 (20.00%)	0 / 19 (0.00%)
occurrences (all)	0	3	0
Metabolism and nutrition disorders			

Decreased appetite			
subjects affected / exposed	2 / 6 (33.33%)	4 / 15 (26.67%)	6 / 19 (31.58%)
occurrences (all)	2	4	6
Dehydration			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Hyperkalaemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Hyperphosphataemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Hypoalbuminaemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Malnutrition			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	1 / 6 (16.67%)	2 / 15 (13.33%)	3 / 19 (15.79%)
occurrences (all)	1	2	3
Hypomagnesaemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Hyponatraemia			
subjects affected / exposed	1 / 6 (16.67%)	1 / 15 (6.67%)	2 / 19 (10.53%)
occurrences (all)	1	1	2
Hypophosphataemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	2 / 19 (10.53%)
occurrences (all)	1	0	2
Hypocalcaemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0

Vitamin D deficiency			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1

Non-serious adverse events	Atezolizumab + Imprime PGG + Bevacizumab	Atezolizumab + Idasanutlin	Atezolizumab + Regorafenib + AB928
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 15 (100.00%)	4 / 4 (100.00%)	15 / 15 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour fistulisation			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Tumour pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Vascular disorders			
Vena cava thrombosis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	3 / 15 (20.00%)	1 / 4 (25.00%)	3 / 15 (20.00%)
occurrences (all)	3	1	4
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	2 / 15 (13.33%)
occurrences (all)	0	0	2
Chest discomfort			
subjects affected / exposed	0 / 15 (0.00%)	1 / 4 (25.00%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Chest pain			
subjects affected / exposed	2 / 15 (13.33%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	2	0	0
Chills			
subjects affected / exposed	4 / 15 (26.67%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	4	0	1
Inflammation			

subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
General physical health deterioration			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Mucosal inflammation			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	2 / 15 (13.33%)
occurrences (all)	0	0	2
Medical device site erythema			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Injection site reaction			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Device related thrombosis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Face oedema			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	7 / 15 (46.67%)	1 / 4 (25.00%)	4 / 15 (26.67%)
occurrences (all)	11	2	6
Oedema			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 15 (0.00%)	1 / 4 (25.00%)	0 / 15 (0.00%)
occurrences (all)	0	1	0

Pyrexia			
subjects affected / exposed	4 / 15 (26.67%)	0 / 4 (0.00%)	7 / 15 (46.67%)
occurrences (all)	5	0	9
Peripheral swelling			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	2	0	0
Pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Oedema peripheral			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Swelling face			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Cytokine release syndrome			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Intermenstrual bleeding			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Perineal fistula			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Vaginal haemorrhage			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea exertional			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0

Aspiration			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	3 / 15 (20.00%)	1 / 4 (25.00%)	2 / 15 (13.33%)
occurrences (all)	4	1	2
Dysphonia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Dyspnoea			
subjects affected / exposed	2 / 15 (13.33%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	2	0	1
Aphonia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 4 (25.00%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Haemoptysis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Hypoxia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Nasal congestion			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Nasal dryness			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Sinus congestion			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0

Wheezing			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	2 / 15 (13.33%)
occurrences (all)	0	0	2
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Depression			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Insomnia			
subjects affected / exposed	2 / 15 (13.33%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	2	0	1
Sleep disorder			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Product issues			
Device occlusion			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Investigations			
Blood bilirubin increased			
subjects affected / exposed	1 / 15 (6.67%)	2 / 4 (50.00%)	3 / 15 (20.00%)
occurrences (all)	1	2	3
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	3 / 15 (20.00%)
occurrences (all)	0	0	3

Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
C-reactive protein increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 15 (13.33%)	2 / 4 (50.00%)	3 / 15 (20.00%)
occurrences (all)	2	2	3
Alanine aminotransferase increased			
subjects affected / exposed	3 / 15 (20.00%)	1 / 4 (25.00%)	2 / 15 (13.33%)
occurrences (all)	4	1	2
Blood alkaline phosphatase increased			
subjects affected / exposed	2 / 15 (13.33%)	1 / 4 (25.00%)	2 / 15 (13.33%)
occurrences (all)	2	1	2
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	2 / 15 (13.33%)
occurrences (all)	0	0	2
Lipase increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Lymphocyte count decreased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Lymphocyte count increased			
subjects affected / exposed	0 / 15 (0.00%)	1 / 4 (25.00%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Neutrophil count decreased			
subjects affected / exposed	1 / 15 (6.67%)	1 / 4 (25.00%)	0 / 15 (0.00%)
occurrences (all)	1	1	0
Platelet count decreased			

subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	2 / 15 (13.33%)
occurrences (all)	1	0	2
Weight decreased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
White blood cell count decreased			
subjects affected / exposed	0 / 15 (0.00%)	1 / 4 (25.00%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Intentional overdose			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Injection related reaction			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Infusion related reaction			
subjects affected / exposed	8 / 15 (53.33%)	0 / 4 (0.00%)	4 / 15 (26.67%)
occurrences (all)	16	0	7
Gastrointestinal anastomotic leak			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Facial bones fracture			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Corneal abrasion			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Accidental overdose			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Stoma site rash			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Procedural pain			

subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Palpitations			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Sinus tachycardia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Tachycardia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	3 / 15 (20.00%)
occurrences (all)	0	0	4
Cerebellar syndrome			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Disturbance in attention			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	1 / 15 (6.67%)	1 / 4 (25.00%)	2 / 15 (13.33%)
occurrences (all)	1	1	2
Hyperaesthesia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Myoclonus			

subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Peripheral motor neuropathy			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	2
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	2
Sciatica			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Syncope			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Neuropathy peripheral			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	2 / 15 (13.33%)
occurrences (all)	1	0	2
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	1 / 15 (6.67%)	1 / 4 (25.00%)	2 / 15 (13.33%)
occurrences (all)	1	1	2
Anaemia			
subjects affected / exposed	1 / 15 (6.67%)	1 / 4 (25.00%)	3 / 15 (20.00%)
occurrences (all)	1	1	4
Lymphopenia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	2 / 15 (13.33%)
occurrences (all)	0	0	2
Neutropenia			
subjects affected / exposed	1 / 15 (6.67%)	1 / 4 (25.00%)	0 / 15 (0.00%)
occurrences (all)	1	1	0
Ear and labyrinth disorders			
Ear haemorrhage			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Ear discomfort			

subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Cerumen impaction			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Lacrimation increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Ascites			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Anal haemorrhage			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Abdominal pain upper			
subjects affected / exposed	3 / 15 (20.00%)	1 / 4 (25.00%)	0 / 15 (0.00%)
occurrences (all)	5	1	0
Abdominal pain lower			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Abdominal pain			
subjects affected / exposed	3 / 15 (20.00%)	1 / 4 (25.00%)	4 / 15 (26.67%)
occurrences (all)	3	1	4
Abdominal distension			
subjects affected / exposed	0 / 15 (0.00%)	1 / 4 (25.00%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Colitis			

subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	0 / 15 (0.00%)	1 / 4 (25.00%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Diarrhoea			
subjects affected / exposed	6 / 15 (40.00%)	2 / 4 (50.00%)	4 / 15 (26.67%)
occurrences (all)	9	4	6
Constipation			
subjects affected / exposed	3 / 15 (20.00%)	0 / 4 (0.00%)	3 / 15 (20.00%)
occurrences (all)	3	0	3
Dyspepsia			
subjects affected / exposed	4 / 15 (26.67%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	4	0	1
Odynophagia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	3 / 15 (20.00%)	4 / 4 (100.00%)	2 / 15 (13.33%)
occurrences (all)	5	11	2
Haemorrhoids			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Dysphagia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Frequent bowel movements			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Enterocolitis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Gingival bleeding			

subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	4 / 15 (26.67%)	4 / 4 (100.00%)	2 / 15 (13.33%)
occurrences (all)	7	6	2
Stomatitis			
subjects affected / exposed	2 / 15 (13.33%)	0 / 4 (0.00%)	4 / 15 (26.67%)
occurrences (all)	2	0	6
Salivary duct inflammation			
subjects affected / exposed	0 / 15 (0.00%)	1 / 4 (25.00%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Rectal haemorrhage			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Proctalgia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Post-tussive vomiting			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Oral pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Hepatic vein thrombosis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Jaundice			
subjects affected / exposed	0 / 15 (0.00%)	1 / 4 (25.00%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Dermatitis acneiform			

subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	2 / 15 (13.33%)
occurrences (all)	0	0	2
Alopecia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	2 / 15 (13.33%)
occurrences (all)	0	0	2
Dry skin			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Erythema			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Hair colour changes			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Rash			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Night sweats			
subjects affected / exposed	0 / 15 (0.00%)	1 / 4 (25.00%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	4 / 15 (26.67%)
occurrences (all)	0	0	6
Pruritus			
subjects affected / exposed	2 / 15 (13.33%)	0 / 4 (0.00%)	3 / 15 (20.00%)
occurrences (all)	2	0	3
Psoriasis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Hyperkeratosis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0

Rash macular			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Rash maculo-papular			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	6 / 15 (40.00%)
occurrences (all)	1	0	8
Rash papular			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Seborrhoeic dermatitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Xeroderma			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Skin exfoliation			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	2	0	0
Renal and urinary disorders			
Urinary incontinence			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Dysuria			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Haematuria			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Proteinuria			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	2 / 15 (13.33%)
occurrences (all)	0	0	2
Renal pain			

subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Acute kidney injury			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Urinary retention			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 15 (0.00%)	1 / 4 (25.00%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Hyperthyroidism			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 15 (6.67%)	1 / 4 (25.00%)	2 / 15 (13.33%)
occurrences (all)	1	1	2
Arthritis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Groin pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Bone pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Fracture pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Back pain			

subjects affected / exposed	3 / 15 (20.00%)	1 / 4 (25.00%)	3 / 15 (20.00%)
occurrences (all)	3	1	3
Muscle discomfort			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Myalgia			
subjects affected / exposed	2 / 15 (13.33%)	1 / 4 (25.00%)	0 / 15 (0.00%)
occurrences (all)	3	1	0
Neck pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Pain in extremity			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Gingivitis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Otitis media			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Sinusitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0

Sepsis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Rash pustular			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Soft tissue infection			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Tooth infection			
subjects affected / exposed	0 / 15 (0.00%)	1 / 4 (25.00%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Urinary tract infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	5 / 15 (33.33%)	1 / 4 (25.00%)	5 / 15 (33.33%)
occurrences (all)	6	1	7
Dehydration			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Hyperkalaemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Hyperphosphataemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia			

subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	2
Malnutrition			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Hypokalaemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Hypomagnesaemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Hyponatraemia			
subjects affected / exposed	3 / 15 (20.00%)	0 / 4 (0.00%)	3 / 15 (20.00%)
occurrences (all)	3	0	3
Hypophosphataemia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 4 (25.00%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Hypocalcaemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Vitamin D deficiency			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Atezolizumab + Regorafenib	Atezolizumab + LOAd703	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 15 (100.00%)	2 / 2 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour fistulisation			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Tumour pain			

subjects affected / exposed	1 / 15 (6.67%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			
Vena cava thrombosis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Hypertension			
subjects affected / exposed	2 / 15 (13.33%)	0 / 2 (0.00%)	
occurrences (all)	2	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	5 / 15 (33.33%)	0 / 2 (0.00%)	
occurrences (all)	5	0	
Chest discomfort			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Chest pain			
subjects affected / exposed	2 / 15 (13.33%)	0 / 2 (0.00%)	
occurrences (all)	2	0	
Chills			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Inflammation			
subjects affected / exposed	1 / 15 (6.67%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
General physical health deterioration			
subjects affected / exposed	1 / 15 (6.67%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Non-cardiac chest pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Mucosal inflammation			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Medical device site erythema			

subjects affected / exposed	1 / 15 (6.67%)	0 / 2 (0.00%)		
occurrences (all)	1	0		
Injection site reaction				
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)		
occurrences (all)	0	0		
Influenza like illness				
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)		
occurrences (all)	0	0		
Device related thrombosis				
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)		
occurrences (all)	0	0		
Face oedema				
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)		
occurrences (all)	0	0		
Fatigue				
subjects affected / exposed	7 / 15 (46.67%)	2 / 2 (100.00%)		
occurrences (all)	8	2		
Oedema				
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)		
occurrences (all)	0	0		
Systemic inflammatory response syndrome				
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)		
occurrences (all)	0	0		
Pyrexia				
subjects affected / exposed	2 / 15 (13.33%)	0 / 2 (0.00%)		
occurrences (all)	3	0		
Peripheral swelling				
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)		
occurrences (all)	0	0		
Pain				
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)		
occurrences (all)	0	0		
Oedema peripheral				
subjects affected / exposed	2 / 15 (13.33%)	0 / 2 (0.00%)		
occurrences (all)	2	0		

Swelling face			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Cytokine release syndrome			
subjects affected / exposed	0 / 15 (0.00%)	1 / 2 (50.00%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
Intermenstrual bleeding			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Perineal fistula			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Vaginal haemorrhage			
subjects affected / exposed	1 / 15 (6.67%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea exertional			
subjects affected / exposed	1 / 15 (6.67%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Aspiration			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Cough			
subjects affected / exposed	2 / 15 (13.33%)	0 / 2 (0.00%)	
occurrences (all)	2	0	
Dysphonia			
subjects affected / exposed	3 / 15 (20.00%)	0 / 2 (0.00%)	
occurrences (all)	3	0	
Dyspnoea			
subjects affected / exposed	3 / 15 (20.00%)	1 / 2 (50.00%)	
occurrences (all)	3	2	

Aphonia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Epistaxis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Haemoptysis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Hypoxia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Nasal congestion			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Nasal dryness			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Rhinorrhoea			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Sinus congestion			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Wheezing			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Oropharyngeal pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Anxiety			

subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Depression			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Insomnia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Sleep disorder			
subjects affected / exposed	1 / 15 (6.67%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Product issues			
Device occlusion			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Investigations			
Blood bilirubin increased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 2 (0.00%)	
occurrences (all)	2	0	
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Blood creatinine increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
C-reactive protein increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Aspartate aminotransferase increased			
subjects affected / exposed	3 / 15 (20.00%)	0 / 2 (0.00%)	
occurrences (all)	3	0	
Alanine aminotransferase increased			

subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Blood alkaline phosphatase increased			
subjects affected / exposed	2 / 15 (13.33%)	0 / 2 (0.00%)	
occurrences (all)	2	0	
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Lipase increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Lymphocyte count decreased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Lymphocyte count increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Neutrophil count decreased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Platelet count decreased			
subjects affected / exposed	3 / 15 (20.00%)	0 / 2 (0.00%)	
occurrences (all)	4	0	
Weight decreased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
White blood cell count decreased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Injury, poisoning and procedural complications			

Intentional overdose			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Injection related reaction			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Infusion related reaction			
subjects affected / exposed	2 / 15 (13.33%)	0 / 2 (0.00%)	
occurrences (all)	2	0	
Gastrointestinal anastomotic leak			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Facial bones fracture			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Corneal abrasion			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Accidental overdose			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Stoma site rash			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Procedural pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Palpitations			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Sinus tachycardia			

subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Tachycardia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Cerebellar syndrome			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Disturbance in attention			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Dysgeusia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Headache			
subjects affected / exposed	1 / 15 (6.67%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Hyperaesthesia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Myoclonus			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Peripheral motor neuropathy			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Sciatica			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	

Syncope			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Neuropathy peripheral			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	2 / 15 (13.33%)	0 / 2 (0.00%)	
occurrences (all)	2	0	
Anaemia			
subjects affected / exposed	3 / 15 (20.00%)	0 / 2 (0.00%)	
occurrences (all)	3	0	
Lymphopenia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Neutropenia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Ear and labyrinth disorders			
Ear haemorrhage			
subjects affected / exposed	1 / 15 (6.67%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Ear discomfort			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Cerumen impaction			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Eye disorders			
Lacrimation increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Vision blurred			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			

Abdominal discomfort			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Ascites			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Anal haemorrhage			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Abdominal pain upper			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Abdominal pain lower			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Abdominal pain			
subjects affected / exposed	1 / 15 (6.67%)	1 / 2 (50.00%)	
occurrences (all)	2	1	
Abdominal distension			
subjects affected / exposed	1 / 15 (6.67%)	1 / 2 (50.00%)	
occurrences (all)	1	1	
Colitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Dry mouth			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Diarrhoea			
subjects affected / exposed	7 / 15 (46.67%)	0 / 2 (0.00%)	
occurrences (all)	8	0	
Constipation			
subjects affected / exposed	1 / 15 (6.67%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Dyspepsia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 2 (0.00%)	
occurrences (all)	1	0	

Odynophagia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Nausea			
subjects affected / exposed	3 / 15 (20.00%)	1 / 2 (50.00%)	
occurrences (all)	3	1	
Haemorrhoids			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Dysphagia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Frequent bowel movements			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Enterocolitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Gingival bleeding			
subjects affected / exposed	1 / 15 (6.67%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Vomiting			
subjects affected / exposed	3 / 15 (20.00%)	0 / 2 (0.00%)	
occurrences (all)	4	0	
Stomatitis			
subjects affected / exposed	3 / 15 (20.00%)	0 / 2 (0.00%)	
occurrences (all)	3	0	
Salivary duct inflammation			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Rectal haemorrhage			
subjects affected / exposed	1 / 15 (6.67%)	0 / 2 (0.00%)	
occurrences (all)	1	0	

Proctalgia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Post-tussive vomiting			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Oral pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Hepatic vein thrombosis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Jaundice			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			
Dermatitis acneiform			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Alopecia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Dry skin			
subjects affected / exposed	1 / 15 (6.67%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Erythema			
subjects affected / exposed	1 / 15 (6.67%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Hair colour changes			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Hyperhidrosis			

subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)		
occurrences (all)	0	0		
Rash				
subjects affected / exposed	2 / 15 (13.33%)	0 / 2 (0.00%)		
occurrences (all)	2	0		
Night sweats				
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)		
occurrences (all)	0	0		
Palmar-plantar erythrodysaesthesia syndrome				
subjects affected / exposed	5 / 15 (33.33%)	0 / 2 (0.00%)		
occurrences (all)	7	0		
Pruritus				
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)		
occurrences (all)	0	0		
Psoriasis				
subjects affected / exposed	1 / 15 (6.67%)	0 / 2 (0.00%)		
occurrences (all)	1	0		
Hyperkeratosis				
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)		
occurrences (all)	0	0		
Rash macular				
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)		
occurrences (all)	0	0		
Rash maculo-papular				
subjects affected / exposed	3 / 15 (20.00%)	1 / 2 (50.00%)		
occurrences (all)	4	1		
Rash papular				
subjects affected / exposed	1 / 15 (6.67%)	0 / 2 (0.00%)		
occurrences (all)	1	0		
Seborrhoeic dermatitis				
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)		
occurrences (all)	0	0		
Urticaria				
subjects affected / exposed	1 / 15 (6.67%)	0 / 2 (0.00%)		
occurrences (all)	1	0		

Xeroderma			
subjects affected / exposed	1 / 15 (6.67%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Skin exfoliation			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Renal and urinary disorders			
Urinary incontinence			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Dysuria			
subjects affected / exposed	1 / 15 (6.67%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Haematuria			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Proteinuria			
subjects affected / exposed	1 / 15 (6.67%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Renal pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Acute kidney injury			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Urinary retention			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	1 / 15 (6.67%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Hyperthyroidism			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	2 / 15 (13.33%)	0 / 2 (0.00%)	
occurrences (all)	3	0	
Arthritis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Groin pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Bone pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Flank pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Fracture pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Back pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Muscle discomfort			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Muscle spasms			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Myalgia			
subjects affected / exposed	4 / 15 (26.67%)	0 / 2 (0.00%)	
occurrences (all)	4	0	
Neck pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 2 (0.00%)	
occurrences (all)	1	0	

Pain in extremity			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Influenza			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Gingivitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Otitis media			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Sinusitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Sepsis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Rash pustular			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Pneumonia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Soft tissue infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Tooth infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Urinary tract infection			

subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	6 / 15 (40.00%)	1 / 2 (50.00%)	
occurrences (all)	6	1	
Dehydration			
subjects affected / exposed	1 / 15 (6.67%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Hyperkalaemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Hyperphosphataemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Hypoalbuminaemia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Malnutrition			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Hypokalaemia			
subjects affected / exposed	2 / 15 (13.33%)	0 / 2 (0.00%)	
occurrences (all)	2	0	
Hypomagnesaemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Hyponatraemia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Hypophosphataemia			
subjects affected / exposed	2 / 15 (13.33%)	0 / 2 (0.00%)	
occurrences (all)	2	0	

Hypocalcaemia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Type 2 diabetes mellitus			
subjects affected / exposed	1 / 15 (6.67%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Vitamin D deficiency			
subjects affected / exposed	0 / 15 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 October 2018	Amended to allow enrollment into one new experimental arm for the existing cohort of patients who progressed during or following two separate lines of treatment for metastatic colorectal cancer (mCRC). The new arm is Atezolizumab + Selicrelumab + Bevacizumab.
10 July 2019	Amended primarily to reflect the addition of an experimental arm Atezolizumab + Idasanutlin in Stage 1, to clarify discrepancies and errors identified in Version 2 of the protocol, and to align the adverse event management guidelines with the recent updates to the Atezolizumab Investigator Brochure (Version 13).
29 October 2019	Protocol CO39612 has been amended primarily to reflect the changes requested by French National Agency for the Safety of Medicines and Health Products (ANSM) in relation to the substantial amendment for protocol version 3 dated 10th July 2019.
12 November 2019	Amended primarily to reflect the addition of two new experimental arms Atezolizumab + Regorafenib, and Atezolizumab + Regorafenib + AB928 in Stage 1, to clarify discrepancies and errors identified in Version 3 of the protocol, and to align the adverse event management guidelines with recent updates to the Atezolizumab Investigator's Brochure (Version 14).
10 January 2020	Amended primarily to reflect the changes requested by French National Agency for the Safety of Medicines and Health Products (ANSM) in relation to the substantial amendment for protocol Version 3 (10 July 2019) that was implemented in Version 4 (France) and to align the adverse event management guidelines with recent updates to the Atezolizumab Investigator's Brochure (Version 15).
22 March 2020	Version 7, is a merging of the global protocol (previously Version 5) and the country-specific Version 6 (France, Switzerland, and United Kingdom). This amendment includes cumulative changes to the protocol from Version 5 along with global changes specific to this amendment.
16 January 2021	Amended primarily to reflect the addition of a new experimental arm in Stage 1: Atezolizumab + Lokon oncolytic adenovirus (LOAd703).
16 February 2021	Amended primarily to update the eligibility criteria in Stage 1 of the Atezolizumab + Lokon oncolytic adenovirus (LOAd703) arm.
30 August 2021	Amended to update contraception duration following a request by the U.K. Medicines and Healthcare products Regulatory Agency (MHRA).
22 March 2022	Amended primarily to reflect the removal of Imprime PGG arm, alignment with Morpheus Platform Template (including removal of iRECIST language), and alignment with Atezolizumab IB v18, and Atezolizumab model document.

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.

This study is not designed to make explicit power and Type I error considerations for a hypothesis test. Instead, this study is designed to obtain preliminary data. Due to the limited sample size, the results need to be interpreted with caution.

Notes: