Clinical trial results:
A phase III randomized, double-blinded trial of platinum-based chemotherapy with or without atezolizumab followed by niraparib maintenance with or without atezolizumab in patients with recurrent ovarian, tubal or peritoneal cancer and platinum treatment-free interval (TFIp) >6 months.

Summary

EudraCT number	2018-000366-11
Trial protocol	ES FR DE BE IT
Global end of trial date	04 March 2025

Results information

Result version number	v1 (current)
This version publication date	14 June 2025
First version publication date	14 June 2025

Trial information

Trial identification

Sponsor protocol code	ENGOT-Ov41/GEICO69-O/ANITA

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03598270
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Grupo Español de Investigación en Cáncer Ginecologico (GEICO)
Sponsor organisation address	Santa Engracia, 151, 5th floor, 2nd door.;, Madrid, Spain, 28003
Public contact	Iratxe Puebla, Grupo Español de Investigación en Cáncer Ginecologico (GEICO), ipuebla@grupogeico.net
Scientific contact	Iratxe Puebla, Grupo Español de Investigación en Cáncer Ginecologico (GEICO), ipuebla@grupogeico.net

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	04 March 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 March 2025
Global end of trial reached?	Yes
Global end of trial date	04 March 2025
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Determine whether the addition of atezolizumab to carboplatin-based chemotherapy followed by maintenance niraparib improves progression-free survival (PFS) compared to placebo combined with carboplatin-based chemotherapy followed by maintenance niraparib, in patients with relapsed epithelial ovarian, fallopian tube, or peritoneal cancer after a platinum treatment free interval (TFIp) of at least 6 months (platinum-sensitive).

Protection of trial subjects:

The patient signed the informed consent before carrying out any procedure related to the study. Physical examination, vital signs, 12-lead ECG, hematology, biochemistry, urinalysis, pregnancy test if applicable and tumor evaluation were made before to start study treatment and during their participation in the study, according to the protocol.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 November 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Israel: 3
Country: Number of subjects enrolled	Spain: 222
Country: Number of subjects enrolled	Belgium: 33
Country: Number of subjects enrolled	France: 89
Country: Number of subjects enrolled	Germany: 36
Country: Number of subjects enrolled	Italy: 34
Worldwide total number of subjects	417
EEA total number of subjects	414

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	233
From 65 to 84 years	183
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

417 patients were recruited during the study

Pre-assignment

Screening details:

Of the 548 patients that signed the ICF, 131 were screening failures and 417 started treatment in the trial.
131 patients were screening failures, most of them because they did not meet the eligibility criteria of the trial.

Period 1

Period 1 title	Global (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor

Arms

Are arms mutually exclusive?	Yes
Arm title	ARM A (control arm)

Arm description:

Placebo of atezolizumab in combination with one of the platinum based regimens below (investigator's choice) followed by maintenance niraparib with placebo q3 wk:
•Carboplatin (AUC = 5, d1) combined with paclitaxel (175 mg/m², d1) and placebo (volume equivalent to 1200 mg of atezolizumab drug product, d1) IV q3 wk.
•Carboplatin (AUC = 4, d1) combined with gemcitabine (1000 mg/m2, d1 & d8) and placebo (volume equivalent to 1200 mg of atezolizumab drug product, d1) IV q3 wk.
•Carboplatin (AUC = 5, d1) combined with pegylated liposomal doxorubicin (PLD) (30 mg/m², d1) and placebo (volume equivalent to 840 mg of atezolizumab drug product, d1 & d15) IV q4 wk.

Arm type	Placebo
Investigational medicinal product name	Placebo of atezolizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1- Carboplatin (AUC = 5, d1) combined with paclitaxel (175 mg/m², d1) and placebo (volume equivalent to 1200 mg of atezolizumab drug product, d1) IV q3 wk.
2- Carboplatin (AUC = 4, d1) combined with gemcitabine (1000 mg/m2, d1 & d8) and placebo (volume equivalent to 1200 mg of atezolizumab drug product, d1) IV q3 wk.
3- Carboplatin (AUC = 5, d1) combined with pegylated liposomal doxorubicin (PLD) (30 mg/m², d1) and placebo (volume equivalent to 840 mg of atezolizumab drug product, d1 & d15) IV q4 wk.

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

Dosage and administration details:

1- Carboplatin (AUC = 5, d1) combined with paclitaxel (175 mg/m², d1) and placebo (volume equivalent to 1200 mg of atezolizumab drug product, d1) IV q3 wk.
2- Carboplatin (AUC = 4, d1) combined with gemcitabine (1000 mg/m2, d1 & d8) and placebo (volume equivalent to 1200 mg of atezolizumab drug product, d1) IV q3 wk.
3- Carboplatin (AUC = 5, d1) combined with pegylated liposomal doxorubicin (PLD) (30 mg/m², d1) and placebo (volume equivalent to 840 mg of atezolizumab drug product, d1 & d15) IV q4 wk.

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

Dosage and administration details:

Carboplatin (AUC = 5, d1) combined with paclitaxel (175 mg/m², d1) and placebo (volume equivalent to 1200 mg of atezolizumab drug product, d1) IV q3 wk.

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

Dosage and administration details:

Carboplatin (AUC = 4, d1) combined with gemcitabine (1000 mg/m2, d1 & d8) and placebo (volume equivalent to 1200 mg of atezolizumab drug product, d1) IV q3 wk.

Investigational medicinal product name	Pegylated liposomal doxorubicin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Carboplatin (AUC = 5, d1) combined with pegylated liposomal doxorubicin (PLD) (30 mg/m², d1) and placebo (volume equivalent to 840 mg of atezolizumab drug product, d1 & d15) IV q4 wk.

Arm title	ARM B (experimental arm)

Arm description:

Atezolizumab in combination with one of the platinum based regimens below (investigator's choice) followed by maintenance niraparib with atezolizumab q3 wk:
•Carboplatin (AUC = 5, d1) combined with paclitaxel (175 mg/m², d1) and atezolizumab (1200 mg, d1) IV q3 wk.
•Carboplatin (AUC = 4, d1) combined with gemcitabine (1000 mg/m2, d1 & d8) and atezolizumab (1200 mg, d1) IV q3 wk.
•Carboplatin (AUC = 5, d1) combined with pegylated liposomal doxorubicin (PLD) (30 mg/m², d1) and atezolizumab (840 mg, d1& d15) IV q4 wk.

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

Dosage and administration details:

1- Carboplatin (AUC = 5, d1) combined with paclitaxel (175 mg/m², d1) and atezolizumab (1200 mg, d1) IV q3 wk.
2- Carboplatin (AUC = 4, d1) combined with gemcitabine (1000 mg/m2, d1 & d8) and atezolizumab (1200 mg, d1) IV q3 wk.
3- Carboplatin (AUC = 5, d1) combined with pegylated liposomal doxorubicin (PLD) (30 mg/m², d1) and atezolizumab (840 mg, d1& d15) IV q4 wk.

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

Dosage and administration details:

1- Carboplatin (AUC = 5, d1) combined with paclitaxel (175 mg/m², d1) and atezolizumab (1200 mg,

d1) IV q3 wk.
2- Carboplatin (AUC = 4, d1) combined with gemcitabine (1000 mg/m2, d1 & d8) and atezolizumab (1200 mg, d1) IV q3 wk.
3- Carboplatin (AUC = 5, d1) combined with pegylated liposomal doxorubicin (PLD) (30 mg/m², d1) and atezolizumab (840 mg, d1& d15) IV q4 wk.

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

Dosage and administration details:

Carboplatin (AUC = 5, d1) combined with paclitaxel (175 mg/m², d1) and atezolizumab (1200 mg, d1) IV q3 wk.

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

Dosage and administration details:

Carboplatin (AUC = 4, d1) combined with gemcitabine (1000 mg/m2, d1 & d8) and atezolizumab (1200 mg, d1) IV q3 wk.

Investigational medicinal product name	Pegylated liposomal doxorubicin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Carboplatin (AUC = 5, d1) combined with pegylated liposomal doxorubicin (PLD) (30 mg/m², d1) and atezolizumab (840 mg, d1& d15) IV q4 wk.

Number of subjects in period 1	ARM A (control arm)	ARM B (experimental arm)
Started	209	208
Completed	209	208

Baseline characteristics

Reporting groups	
Reporting group title	ARM A (control arm)
Reporting group description:	
Placebo of atezolizumab in combination with one of the platinum based regimens below (investigator's choice) followed by maintenance niraparib with placebo q3 wk: •Carboplatin (AUC = 5, d1) combined with paclitaxel (175 mg/m², d1) and placebo (volume equivalent to 1200 mg of atezolizumab drug product, d1) IV q3 wk. •Carboplatin (AUC = 4, d1) combined with gemcitabine (1000 mg/m2, d1 & d8) and placebo (volume equivalent to 1200 mg of atezolizumab drug product, d1) IV q3 wk. •Carboplatin (AUC = 5, d1) combined with pegylated liposomal doxorubicin (PLD) (30 mg/m², d1) and placebo (volume equivalent to 840 mg of atezolizumab drug product, d1 & d15) IV q4 wk.	
Reporting group title	ARM B (experimental arm)
Reporting group description:	
Atezolizumab in combination with one of the platinum based regimens below (investigator's choice) followed by maintenance niraparib with atezolizumab q3 wk: •Carboplatin (AUC = 5, d1) combined with paclitaxel (175 mg/m², d1) and atezolizumab (1200 mg, d1) IV q3 wk. •Carboplatin (AUC = 4, d1) combined with gemcitabine (1000 mg/m2, d1 & d8) and atezolizumab (1200 mg, d1) IV q3 wk. •Carboplatin (AUC = 5, d1) combined with pegylated liposomal doxorubicin (PLD) (30 mg/m², d1) and atezolizumab (840 mg, d1& d15) IV q4 wk.	

Reporting group values	ARM A (control arm)	ARM B (experimental arm)	Total
Number of subjects	209	208	417
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	120	113	233
From 65-84 years	89	94	183
85 years and over	0	1	1
Age continuous Units: years			
median	62	63	
inter-quartile range (Q1-Q3)	56 to 69	55 to 70	-
Gender categorical Units: Subjects			
Female	209	208	417
Screening visit 1 ECOG/PS Units: Subjects			
ECOG 0	128	134	262
ECOG 1	81	74	155
Histologic diagnosis Units: Subjects			
High Grade Serous Ovarian Cancer	196	187	383

High Grade Endometroid Ovarian Cancer	5	11	16
Mixed histology	5	7	12
Undifferentiated	3	3	6
Origin Units: Subjects			
Ovarian	188	189	377
Tubal carcinoma	15	10	25
Primary peritoneal	6	9	15
BRCA status Units: Subjects			
Not-Mutated	178	181	359
Mutated	31	27	58
Number of previous anticancer treatment lines Units: Subjects			
1 Line	181	181	362
2 Lines	28	27	55
Previous treatment with Bevacizumab Units: Subjects			
No	98	89	187
Yes	111	119	230
Previous treatment with PARPi Units: Subjects			
No	182	188	370
Yes	27	20	47
Time from last dose of platinum to progression Units: Subjects			
6-12 months	70	73	143
>12 months	139	135	274
1st line: Primary debulking surgery? Units: Subjects			
No	93	90	183
Yes	116	118	234
1st line: Primary debulking surgery result Units: Subjects			
Optimal	73	82	155
Suboptimal	29	18	47
Unknown	14	18	32
Not applicable	93	90	183
1st line: Interval debulking surgery (IDS) done? Units: Subjects			
No	128	131	259
Yes	81	77	158
1st line: IDS result Units: Subjects			
Optimal	56	51	107
Suboptimal	19	18	37
Unknown	5	8	13
Not applicable	129	131	260

1st line: Treatment with antiangiogenic agent in a clinical trial Units: Subjects			
No	175	164	339
Yes	34	44	78
1st line: Treatment with PARPi inhibitor in a clinical trial Units: Subjects			
No	185	194	379
Yes	24	14	38
2nd line: Primary debulking surgery? Units: Subjects			
No	16	17	33
Yes	11	10	21
Not applicable	182	181	363
2nd line: Primary debulking surgery result Units: Subjects			
Optimal	8	8	16
Suboptimal	3	2	5
Not applicable	198	198	396
2nd line: Secondary debulking surgery after some cycles of chemotherapy Units: Subjects			
No	26	25	51
Yes	1	2	3
Not applicable	182	181	363
2nd line: Treatment with antiangiogenic agent in a clinical trial Units: Subjects			
No	25	22	47
Yes	3	5	8
Not applicable	181	181	362
2nd line: Treatment with PARPi inhibitor in a clinical trial Units: Subjects			
No	27	27	54
Yes	1	0	1
Not applicable	181	181	362
Number of affected locations per patient Units: Subjects			
1 lesion	35	39	74
2 lesions	73	65	138
3 lesions	51	47	98
4 lesions	34	28	62
5 lesions	11	22	33
6 lesions	2	6	8
7 lesions	2	1	3
8 lesions	1	0	1
Treatment Regimen Units: Subjects			
Regimen 1	25	29	54
Regimen 2	33	32	65

Regimen 3	151	147	298

End points

End points reporting groups

Reporting group title	ARM A (control arm)

Reporting group description:

Placebo of atezolizumab in combination with one of the platinum based regimens below (investigator's choice) followed by maintenance niraparib with placebo q3 wk:
•Carboplatin (AUC = 5, d1) combined with paclitaxel (175 mg/m², d1) and placebo (volume equivalent to 1200 mg of atezolizumab drug product, d1) IV q3 wk.
•Carboplatin (AUC = 4, d1) combined with gemcitabine (1000 mg/m2, d1 & d8) and placebo (volume equivalent to 1200 mg of atezolizumab drug product, d1) IV q3 wk.
•Carboplatin (AUC = 5, d1) combined with pegylated liposomal doxorubicin (PLD) (30 mg/m², d1) and placebo (volume equivalent to 840 mg of atezolizumab drug product, d1 & d15) IV q4 wk.

Reporting group title	ARM B (experimental arm)

Reporting group description:

Atezolizumab in combination with one of the platinum based regimens below (investigator's choice) followed by maintenance niraparib with atezolizumab q3 wk:
•Carboplatin (AUC = 5, d1) combined with paclitaxel (175 mg/m², d1) and atezolizumab (1200 mg, d1) IV q3 wk.
•Carboplatin (AUC = 4, d1) combined with gemcitabine (1000 mg/m2, d1 & d8) and atezolizumab (1200 mg, d1) IV q3 wk.
•Carboplatin (AUC = 5, d1) combined with pegylated liposomal doxorubicin (PLD) (30 mg/m², d1) and atezolizumab (840 mg, d1& d15) IV q4 wk.

Primary: Progression-free survival (PFS)

End point title	Progression-free survival (PFS)

End point description:

The primary endpoint of the study is progression-free survival (PFS) from randomization until progression based on investigator assessment determined by RECIST (version v1.1).

End point type	Primary

End point timeframe:

Every 9 weeks during the chemotherapy phase and every 12 weeks during the maintenance phase until progression up to a maximum of 64 months.

End point values	ARM A (control arm)	ARM B (experimental arm)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	209	208		
Units: months				
median (confidence interval 95%)	9.901 (9.243 to 11.09)	10.63 (9.901 to 11.78)		

Statistical analyses

Statistical analysis title	PFS
Comparison groups	ARM A (control arm) v ARM B (experimental arm)

Number of subjects included in analysis	417
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.929
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.757
upper limit	1.139

Secondary: Overall survival (OS)

End point title	Overall survival (OS)

End point description:

Overall survival (OS), defined as the observed length of life from entry into the study (day of randomization) to death from any cause, or the date of last contact

End point type	Secondary

End point timeframe:

Every study visit until a maximun of 66 months

End point values	ARM A (control arm)	ARM B (experimental arm)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	209	208		
Units: months				
median (confidence interval 95%)	27.11 (23.22 to 32.34)	32.17 (27.14 to 34.80)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time from randomization to first subsequent therapy or death (TFST)

End point title	Time from randomization to first subsequent therapy or death (TFST)

End point description:

Time from randomization to first subsequent therapy or death (TFST)

End point type	Secondary

End point timeframe:

Every 12 weeks until end of study, withdrawal of consent or the patient is lost to follow up. Maximun 66 months

End point values	ARM A (control arm)	ARM B (experimental arm)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	209	208		
Units: months				
median (confidence interval 95%)	13.45 (12.11 to 13.95)	12.89 (11.78 to 14.77)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time from randomization to second subsequent therapy or death (TSST)

End point title	Time from randomization to second subsequent therapy or death (TSST)

End point description:

Time from randomization to second subsequent therapy or death (TSST)

End point type	Secondary

End point timeframe:

Every 12 weeks until end of study, withdrawal of consent or the patient is lost to follow up. Maximun 66 months

End point values	ARM A (control arm)	ARM B (experimental arm)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	209	208		
Units: months				
median (confidence interval 95%)	19.51 (17.43 to 22.37)	20.03 (17.99 to 21.91)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time from randomization to second progression or death (PFS2)

End point title	Time from randomization to second progression or death (PFS2)

End point description:

Time from randomization to second progression or death (PFS2)

End point type	Secondary

End point timeframe:

Every 12 weeks until end of study, withdrawal of consent or the patient is lost to follow up. Maximun 66 months

End point values	ARM A (control arm)	ARM B (experimental arm)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	209	208		
Units: months				
median (confidence interval 95%)	18.39 (16.71 to 20.59)	19.70 (17.30 to 20.59)		

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate (ORR) during the chemotherapy phase

End point title	Objective Response Rate (ORR) during the chemotherapy phase

End point description:

Objective Response Rate (ORR) as assessed by RECIST v1.1 during the chemotherapy phase (complete and partial responses)

End point type	Secondary

End point timeframe:

Every 9 weeks during the chemotherapy phase and every 12 weeks during the maintenance phase until progression up to a maximum of 64 months.

End point values	ARM A (control arm)	ARM B (experimental arm)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	209	208		
Units: Percentage				
median (confidence interval 95%)	43.06 (36.35 to 49.78)	46.63 (39.85 to 53.41)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Response Rate (ORR) during maintenance

End point title	Overall Response Rate (ORR) during maintenance

End point description:

Objective Response Rate (ORR) as assessed by RECIST v1.1 during the maintenance phase (complete and partial responses).

End point type	Secondary

End point timeframe:

Every 9 weeks during the chemotherapy phase and every 12 weeks during the maintenance phase until progression up to a maximum of 64 months.

End point values	ARM A (control arm)	ARM B (experimental arm)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	158	156		
Units: percentage				
median (confidence interval 95%)	28.5 (21.4 to 35.5)	41.0 (33.3 to 48.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of response (DOR)

End point title	Duration of response (DOR)

End point description:

Duration of response (DOR) by RECIST v1.1

End point type	Secondary

End point timeframe:

Every 9 weeks during the chemotherapy phase and every 12 weeks during the maintenance phase until progression up to a maximum of 64 months.

End point values	ARM A (control arm)	ARM B (experimental arm)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	120		
Units: months				
median (confidence interval 95%)	9.243 (7.895 to 11.12)	10.66 (9.211 to 12.43)		

Statistical analyses

No statistical analyses for this end point

Secondary: PFS by treatment arm and BRCA

End point title	PFS by treatment arm and BRCA

End point description:

PFS by treatment arm and BRCA

End point type	Secondary

End point timeframe:

Every 9 weeks during the chemotherapy phase and every 12 weeks during the maintenance phase until progression up to a maximum of 64 months.

End point values	ARM A (control arm)	ARM B (experimental arm)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	209	208		
Units: months				
median (confidence interval 95%)				
Mutated	11.94 (9.803 to 26.97)	12.70 (8.322 to 16.84)		
Not-Mutated	9.704 (8.816 to 10.49)	10.59 (9.572 to 11.55)		

Statistical analyses

No statistical analyses for this end point

Secondary: PFS by treatment arm and PDL1 status

End point title	PFS by treatment arm and PDL1 status

End point description:

PFS by treatment arm and PDL1 status

End point type	Secondary

End point timeframe:

Every 9 weeks during the chemotherapy phase and every 12 weeks during the maintenance phase until progression up to a maximum of 64 months.

End point values	ARM A (control arm)	ARM B (experimental arm)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	206	207		
Units: months				
median (confidence interval 95%)				
PD-L1 Negative	9.24 (8.32 to 11.09)	10.36 (9.01 to 11.32)		
PD-L1 Positive	10.49 (9.34 to 12.17)	12.53 (10.20 to 14.80)		
PD-L1 Non-informative	9.44 (6.51 to 12.99)	9.77 (2.76 to 11.78)		

Statistical analyses

No statistical analyses for this end point

Secondary: Abdominal/GI symptom change from baseline to latest evaluation available (EORTC QLQ-OV28)

End point title	Abdominal/GI symptom change from baseline to latest evaluation available (EORTC QLQ-OV28)

End point description:

Clinically-meaningful improvement in patient-reported abdominal pain or bloating, defined as a 10-point decrease from the baseline score on either of the two items of the EORTC QLQ-OV28 abdominal/GI symptom scale (items 31 and 32)

End point type	Secondary

End point timeframe:

Every study visit during chemotherapy phase and then every 12 weeks until PFS2 or a maximum of 4 years

End point values	ARM A (control arm)	ARM B (experimental arm)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	183	168		
Units: percentage				
arithmetic mean (standard deviation)	1.4 (± 20.3)	2.8 (± 20.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: QLQ-OV28: Abdominal/GI symptom change from baseline to latest evaluation available (Clinical improvement/Deterioration)

End point title	QLQ-OV28: Abdominal/GI symptom change from baseline to latest evaluation available (Clinical improvement/Deterioration)

End point description:

Clinically-meaningful improvement in patient-reported abdominal pain or bloating, defined as a 10-point decrease from the baseline score on either of the two items of the EORTC QLQ-OV28 abdominal/GI symptom scale (items 31 and 32)

End point type	Secondary

End point timeframe:

Every study visit during chemotherapy phase and then every 12 weeks until PFS2 or a maximum of 4 years

End point values	ARM A (control arm)	ARM B (experimental arm)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	183	168		
Units: patients				
Clinical improvement	52	45		
Remaining stable	71	66		
Deterioration	60	57		

Statistical analyses

No statistical analyses for this end point

Secondary: QLQ-C30: Global health status changes from baseline to latest evaluation available

End point title	QLQ-C30: Global health status changes from baseline to latest evaluation available

End point description:

Clinical improvement, remaining stable, or deterioration in patient-reported function and HRQoL, defined as a 10-point increase, changes within 10 points, and a 10-point decrease, respectively, from the baseline score on each of the functional (physical, role, emotional, and social) and global health status/HRQoL scales of EORTC QLQ-C30

End point type	Secondary

End point timeframe:

Every study visit during chemotherapy phase and then every 12 weeks until PFS2 or a maximum of 4 years

End point values	ARM A (control arm)	ARM B (experimental arm)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	185	179		
Units: subjects				
Clinical improvement	45	26		
Remaining stable	86	79		
Deterioration	54	74		

Statistical analyses

No statistical analyses for this end point

Secondary: QLQ-C30: role functioning changes from baseline to latest evaluation

available

End point title	QLQ-C30: role functioning changes from baseline to latest evaluation available

End point description:

Clinical improvement, remaining stable, or deterioration in patient-reported function and HRQoL, defined as a 10-point increase, changes within 10 points, and a 10-point decrease, respectively, from the baseline score on each of the functional (physical, role, emotional, and social) and global health status/HRQoL scales of EORTC QLQ-C30

End point type	Secondary

End point timeframe:

Every study visit during chemotherapy phase and then every 12 weeks until PFS2 or a maximum of 4 years

End point values	ARM A (control arm)	ARM B (experimental arm)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	188	179		
Units: subjects				
Clinical improvement	21	17		
Remaining stable	128	113		
Deterioration	39	49		

Statistical analyses

No statistical analyses for this end point

Secondary: QLQ-C30: Emotional functioning changes from baseline to latest evaluation available

End point title	QLQ-C30: Emotional functioning changes from baseline to latest evaluation available

End point description:

Clinical improvement, remaining stable, or deterioration in patient-reported function and HRQoL, defined as a 10-point increase, changes within 10 points, and a 10-point decrease, respectively, from the baseline score on each of the functional (physical, role, emotional, and social) and global health status/HRQoL scales of EORTC QLQ-C30

End point type	Secondary

End point timeframe:

Every study visit during chemotherapy phase and then every 12 weeks until PFS2 or a maximum of 4 years

End point values	ARM A (control arm)	ARM B (experimental arm)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	182	175		
Units: subjects				
Clinical improvement	28	20		
Remaining stable	123	126		
Deterioration	31	29		

Statistical analyses

No statistical analyses for this end point

Secondary: QLQ-C30: Cognitive functioning changes from baseline to latest evaluation available

End point title	QLQ-C30: Cognitive functioning changes from baseline to latest evaluation available

End point description:

Clinical improvement, remaining stable, or deterioration in patient-reported function and HRQoL, defined as a 10-point increase, changes within 10 points, and a 10-point decrease, respectively, from the baseline score on each of the functional (physical, role, emotional, and social) and global health status/HRQoL scales of EORTC QLQ-C30

End point type	Secondary

End point timeframe:

Every study visit during chemotherapy phase and then every 12 weeks until PFS2 or a maximum of 4 years

End point values	ARM A (control arm)	ARM B (experimental arm)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	182	177		
Units: subjects				
Clinical improvement	15	4		
Remaining stable	141	148		
Deterioration	26	25		

Statistical analyses

No statistical analyses for this end point

Secondary: QLQ-C30: Social functioning changes from baseline to latest evaluation available

End point title	QLQ-C30: Social functioning changes from baseline to latest evaluation available

End point description:

Clinical improvement, remaining stable, or deterioration in patient-reported function and HRQoL, defined as a 10-point increase, changes within 10 points, and a 10-point decrease, respectively, from the baseline score on each of the functional (physical, role, emotional, and social) and global health status/HRQoL scales of EORTC QLQ-C30

End point type	Secondary

End point timeframe:

Every study visit during chemotherapy phase and then every 12 weeks until PFS2 or a maximum of 4 years

End point values	ARM A (control arm)	ARM B (experimental arm)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	182	170		
Units: subjects				
Clinical improvement	24	17		
Remaining stable	121	107		
Deterioration	37	46		

Statistical analyses

No statistical analyses for this end point

Secondary: QLQ-C30: Physical functioning changes from baseline to latest evaluation available

End point title	QLQ-C30: Physical functioning changes from baseline to latest evaluation available

End point description:

Clinical improvement, remaining stable, or deterioration in patient-reported function and HRQoL, defined as a 10-point increase, changes within 10 points, and a 10-point decrease, respectively, from the baseline score on each of the functional (physical, role, emotional, and social) and global health status/HRQoL scales of EORTC QLQ-C30

End point type	Secondary

End point timeframe:

Every study visit during chemotherapy phase and then every 12 weeks until PFS2 or a maximum of 4 years

End point values	ARM A (control arm)	ARM B (experimental arm)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	184	169		
Units: subjects				
Clinical improvement	17	15		
Remaining stable	134	123		
Deterioration	33	31		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The safety profile of patients will be monitored throughout the treatment and up to 30 days after the last treatment infusion. SAEs and AESIs until 90 days after the last dose of atezolizumab/placebo or until initiation of new systemic anti-cancer therapy

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.1

Reporting groups

Reporting group title	ARM A (control arm)

Reporting group description:

ARM A (control arm): Placebo of atezolizumab in combination with one of the platinum based regimens (investigator's choice) followed by maintenance niraparib with placebo:

Reporting group title	ARM B (experimental arm)

Reporting group description:

ARM B (experimental arm): Atezolizumab in combination with one of the platinum based regimens (investigator's choice) followed by maintenance niraparib with atezolizumab:

Serious adverse events	ARM A (control arm)	ARM B (experimental arm)	
Total subjects affected by serious adverse events			
subjects affected / exposed	63 / 209 (30.14%)	80 / 208 (38.46%)	
number of deaths (all causes)	133	125	
number of deaths resulting from adverse events	4	4	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	1 / 209 (0.48%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Breast cancer			
subjects affected / exposed	2 / 209 (0.96%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lentigo maligna			
subjects affected / exposed	1 / 209 (0.48%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelodysplastic syndrome			

subjects affected / exposed	0 / 209 (0.00%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraneoplastic encephalomyelitis			
subjects affected / exposed	1 / 209 (0.48%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Undifferentiated nasopharyngeal carcinoma			
subjects affected / exposed	1 / 209 (0.48%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Embolism			
subjects affected / exposed	1 / 209 (0.48%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
General physical health deterioration			
subjects affected / exposed	2 / 209 (0.96%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	0 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalised oedema			
subjects affected / exposed	0 / 209 (0.00%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple organ dysfunction syndrome			
subjects affected / exposed	1 / 209 (0.48%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 209 (0.48%)	3 / 208 (1.44%)	
occurrences causally related to treatment / all	1 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	

Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 209 (0.00%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaphylactic shock			
subjects affected / exposed	0 / 209 (0.00%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug hypersensitivity			
subjects affected / exposed	0 / 209 (0.00%)	2 / 208 (0.96%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infusion related hypersensitivity reaction			
subjects affected / exposed	1 / 209 (0.48%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Bronchopneumopathy			
subjects affected / exposed	0 / 209 (0.00%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cough			
subjects affected / exposed	0 / 209 (0.00%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	2 / 209 (0.96%)	2 / 208 (0.96%)	
occurrences causally related to treatment / all	0 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			

subjects affected / exposed	0 / 209 (0.00%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	1 / 209 (0.48%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	1 / 209 (0.48%)	2 / 208 (0.96%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	1 / 209 (0.48%)	3 / 208 (1.44%)	
occurrences causally related to treatment / all	0 / 1	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	0 / 209 (0.00%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	0 / 209 (0.00%)	2 / 208 (0.96%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood bilirubin increased			
subjects affected / exposed	0 / 209 (0.00%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	0 / 209 (0.00%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Ankle fracture			
subjects affected / exposed	1 / 209 (0.48%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clavicle fracture			
subjects affected / exposed	1 / 209 (0.48%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	0 / 209 (0.00%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	1 / 209 (0.48%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	1 / 209 (0.48%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pericarditis			
subjects affected / exposed	0 / 209 (0.00%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Supraventricular tachycardia			
subjects affected / exposed	0 / 209 (0.00%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia			
subjects affected / exposed	1 / 209 (0.48%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			

Cerebrovascular accident			
subjects affected / exposed	0 / 209 (0.00%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalitis autoimmune			
subjects affected / exposed	0 / 209 (0.00%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalopathy			
subjects affected / exposed	0 / 209 (0.00%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrocephalus			
subjects affected / exposed	0 / 209 (0.00%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune-mediated encephalitis			
subjects affected / exposed	0 / 209 (0.00%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	1 / 209 (0.48%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	0 / 209 (0.00%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vestibular neuronitis			
subjects affected / exposed	0 / 209 (0.00%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	1 / 209 (0.48%)	4 / 208 (1.92%)	
occurrences causally related to treatment / all	0 / 1	3 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile bone marrow aplasia			
subjects affected / exposed	0 / 209 (0.00%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	4 / 209 (1.91%)	13 / 208 (6.25%)	
occurrences causally related to treatment / all	5 / 5	10 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune thrombocytopenia			
subjects affected / exposed	1 / 209 (0.48%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	2 / 209 (0.96%)	7 / 208 (3.37%)	
occurrences causally related to treatment / all	2 / 2	10 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	2 / 209 (0.96%)	2 / 208 (0.96%)	
occurrences causally related to treatment / all	2 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	13 / 209 (6.22%)	6 / 208 (2.88%)	
occurrences causally related to treatment / all	15 / 16	4 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 209 (0.00%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertigo positional			

subjects affected / exposed	0 / 209 (0.00%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Diplopia			
subjects affected / exposed	1 / 209 (0.48%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	3 / 209 (1.44%)	4 / 208 (1.92%)	
occurrences causally related to treatment / all	1 / 4	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	1 / 209 (0.48%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	1 / 209 (0.48%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	2 / 209 (0.96%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	1 / 209 (0.48%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	1 / 209 (0.48%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric haemorrhage			

subjects affected / exposed	0 / 209 (0.00%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 209 (0.48%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gastrointestinal obstruction			
subjects affected / exposed	0 / 209 (0.00%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematochezia			
subjects affected / exposed	1 / 209 (0.48%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	7 / 209 (3.35%)	6 / 208 (2.88%)	
occurrences causally related to treatment / all	0 / 7	1 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestinal obstruction			
subjects affected / exposed	2 / 209 (0.96%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	0 / 209 (0.00%)	2 / 208 (0.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic colitis			
subjects affected / exposed	0 / 209 (0.00%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			

subjects affected / exposed	0 / 209 (0.00%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	1 / 209 (0.48%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	2 / 209 (0.96%)	4 / 208 (1.92%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal perforation			
subjects affected / exposed	0 / 209 (0.00%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subileus			
subjects affected / exposed	1 / 209 (0.48%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 209 (0.48%)	4 / 208 (1.92%)	
occurrences causally related to treatment / all	0 / 1	3 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 209 (0.48%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholestasis			
subjects affected / exposed	0 / 209 (0.00%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cytolysis			

subjects affected / exposed	0 / 209 (0.00%)	2 / 208 (0.96%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatotoxicity			
subjects affected / exposed	1 / 209 (0.48%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Skin toxicity			
subjects affected / exposed	0 / 209 (0.00%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stevens-Johnson syndrome			
subjects affected / exposed	0 / 209 (0.00%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Vitiligo			
subjects affected / exposed	0 / 209 (0.00%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 209 (0.48%)	2 / 208 (0.96%)	
occurrences causally related to treatment / all	1 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydronephrosis			
subjects affected / exposed	0 / 209 (0.00%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephritis			
subjects affected / exposed	0 / 209 (0.00%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			

subjects affected / exposed	1 / 209 (0.48%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	1 / 209 (0.48%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Adrenal disorder			
subjects affected / exposed	0 / 209 (0.00%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal infection			
subjects affected / exposed	1 / 209 (0.48%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	0 / 209 (0.00%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
subjects affected / exposed	0 / 209 (0.00%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial diarrhoea			
subjects affected / exposed	1 / 209 (0.48%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	2 / 209 (0.96%)	2 / 208 (0.96%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19 pneumonia			

subjects affected / exposed	0 / 209 (0.00%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	1 / 209 (0.48%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related sepsis			
subjects affected / exposed	2 / 209 (0.96%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis infectious			
subjects affected / exposed	0 / 209 (0.00%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile infection			
subjects affected / exposed	1 / 209 (0.48%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Groin abscess			
subjects affected / exposed	1 / 209 (0.48%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected lymphocele			
subjects affected / exposed	1 / 209 (0.48%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver abscess			
subjects affected / exposed	1 / 209 (0.48%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media			

subjects affected / exposed	1 / 209 (0.48%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	3 / 209 (1.44%)	2 / 208 (0.96%)	
occurrences causally related to treatment / all	1 / 3	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 209 (0.00%)	3 / 208 (1.44%)	
occurrences causally related to treatment / all	0 / 0	2 / 3	
deaths causally related to treatment / all	0 / 0	1 / 2	
Stoma site infection			
subjects affected / exposed	1 / 209 (0.48%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth infection			
subjects affected / exposed	1 / 209 (0.48%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	0 / 209 (0.00%)	2 / 208 (0.96%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Food intolerance			
subjects affected / exposed	0 / 209 (0.00%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	1 / 209 (0.48%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			

subjects affected / exposed	0 / 209 (0.00%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malnutrition			
subjects affected / exposed	1 / 209 (0.48%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	ARM A (control arm)	ARM B (experimental arm)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	206 / 209 (98.56%)	207 / 208 (99.52%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	22 / 209 (10.53%)	34 / 208 (16.35%)	
occurrences (all)	30	49	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	126 / 209 (60.29%)	131 / 208 (62.98%)	
occurrences (all)	367	425	
Fatigue			
subjects affected / exposed	38 / 209 (18.18%)	47 / 208 (22.60%)	
occurrences (all)	64	102	
Mucosal inflammation			
subjects affected / exposed	44 / 209 (21.05%)	49 / 208 (23.56%)	
occurrences (all)	78	92	
Oedema peripheral			
subjects affected / exposed	12 / 209 (5.74%)	16 / 208 (7.69%)	
occurrences (all)	14	28	
Pyrexia			
subjects affected / exposed	25 / 209 (11.96%)	48 / 208 (23.08%)	
occurrences (all)	32	72	
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	21 / 209 (10.05%)	24 / 208 (11.54%)	
occurrences (all)	30	31	
Dyspnoea			
subjects affected / exposed	31 / 209 (14.83%)	33 / 208 (15.87%)	
occurrences (all)	46	42	
Dyspnoea exertional			
subjects affected / exposed	11 / 209 (5.26%)	0 / 208 (0.00%)	
occurrences (all)	12	0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	16 / 209 (7.66%)	16 / 208 (7.69%)	
occurrences (all)	21	27	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	18 / 209 (8.61%)	20 / 208 (9.62%)	
occurrences (all)	42	51	
Aspartate aminotransferase increased			
subjects affected / exposed	21 / 209 (10.05%)	22 / 208 (10.58%)	
occurrences (all)	37	56	
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 209 (0.00%)	14 / 208 (6.73%)	
occurrences (all)	0	26	
Blood creatinine increased			
subjects affected / exposed	22 / 209 (10.53%)	28 / 208 (13.46%)	
occurrences (all)	39	45	
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 209 (0.00%)	14 / 208 (6.73%)	
occurrences (all)	0	23	
White blood cell count decreased			
subjects affected / exposed	23 / 209 (11.00%)	18 / 208 (8.65%)	
occurrences (all)	190	150	
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 209 (0.00%)	11 / 208 (5.29%)	
occurrences (all)	0	13	

Nervous system disorders			
Dizziness			
subjects affected / exposed	16 / 209 (7.66%)	11 / 208 (5.29%)	
occurrences (all)	16	11	
Dysgeusia			
subjects affected / exposed	23 / 209 (11.00%)	25 / 208 (12.02%)	
occurrences (all)	27	38	
Headache			
subjects affected / exposed	33 / 209 (15.79%)	42 / 208 (20.19%)	
occurrences (all)	52	61	
Insomnia			
subjects affected / exposed	28 / 209 (13.40%)	31 / 208 (14.90%)	
occurrences (all)	36	46	
Neuropathy peripheral			
subjects affected / exposed	19 / 209 (9.09%)	0 / 208 (0.00%)	
occurrences (all)	23	0	
Paraesthesia			
subjects affected / exposed	0 / 209 (0.00%)	17 / 208 (8.17%)	
occurrences (all)	0	25	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	142 / 209 (67.94%)	141 / 208 (67.79%)	
occurrences (all)	577	552	
Febrile neutropenia			
subjects affected / exposed	0 / 209 (0.00%)	19 / 208 (9.13%)	
occurrences (all)	0	21	
Leukopenia			
subjects affected / exposed	0 / 209 (0.00%)	17 / 208 (8.17%)	
occurrences (all)	0	31	
Lymphopenia			
subjects affected / exposed	0 / 209 (0.00%)	13 / 208 (6.25%)	
occurrences (all)	0	31	
Neutropenia			
subjects affected / exposed	141 / 209 (67.46%)	125 / 208 (60.10%)	
occurrences (all)	767	650	
Thrombocytopenia			

subjects affected / exposed	134 / 209 (64.11%)	129 / 208 (62.02%)	
occurrences (all)	579	488	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	11 / 209 (5.26%)	11 / 208 (5.29%)	
occurrences (all)	13	16	
Abdominal distension			
subjects affected / exposed	12 / 209 (5.74%)	16 / 208 (7.69%)	
occurrences (all)	14	17	
Abdominal pain			
subjects affected / exposed	55 / 209 (26.32%)	58 / 208 (27.88%)	
occurrences (all)	94	89	
Abdominal pain lower			
subjects affected / exposed	11 / 209 (5.26%)	0 / 208 (0.00%)	
occurrences (all)	11	0	
Abdominal pain upper			
subjects affected / exposed	48 / 209 (22.97%)	35 / 208 (16.83%)	
occurrences (all)	72	45	
Constipation			
subjects affected / exposed	99 / 209 (47.37%)	100 / 208 (48.08%)	
occurrences (all)	189	187	
Diarrhoea			
subjects affected / exposed	49 / 209 (23.44%)	61 / 208 (29.33%)	
occurrences (all)	81	98	
Dry mouth			
subjects affected / exposed	0 / 209 (0.00%)	11 / 208 (5.29%)	
occurrences (all)	0	15	
Dyspepsia			
subjects affected / exposed	17 / 209 (8.13%)	15 / 208 (7.21%)	
occurrences (all)	23	23	
Nausea			
subjects affected / exposed	138 / 209 (66.03%)	134 / 208 (64.42%)	
occurrences (all)	326	320	
Vomiting			
subjects affected / exposed	65 / 209 (31.10%)	63 / 208 (30.29%)	
occurrences (all)	119	105	

Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	24 / 209 (11.48%)	17 / 208 (8.17%)	
occurrences (all)	25	21	
Dry skin			
subjects affected / exposed	0 / 209 (0.00%)	17 / 208 (8.17%)	
occurrences (all)	0	18	
Erythema			
subjects affected / exposed	0 / 209 (0.00%)	17 / 208 (8.17%)	
occurrences (all)	0	22	
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	16 / 209 (7.66%)	27 / 208 (12.98%)	
occurrences (all)	25	53	
Pruritus			
subjects affected / exposed	16 / 209 (7.66%)	32 / 208 (15.38%)	
occurrences (all)	21	54	
Rash			
subjects affected / exposed	26 / 209 (12.44%)	41 / 208 (19.71%)	
occurrences (all)	44	89	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 209 (0.00%)	30 / 208 (14.42%)	
occurrences (all)	0	34	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	43 / 209 (20.57%)	44 / 208 (21.15%)	
occurrences (all)	66	73	
Back pain			
subjects affected / exposed	30 / 209 (14.35%)	33 / 208 (15.87%)	
occurrences (all)	34	48	
Myalgia			
subjects affected / exposed	14 / 209 (6.70%)	14 / 208 (6.73%)	
occurrences (all)	20	20	
Pain in extremity			
subjects affected / exposed	14 / 209 (6.70%)	20 / 208 (9.62%)	
occurrences (all)	18	25	

Infections and infestations			
COVID-19			
subjects affected / exposed	21 / 209 (10.05%)	27 / 208 (12.98%)	
occurrences (all)	23	27	
Urinary tract infection			
subjects affected / exposed	23 / 209 (11.00%)	31 / 208 (14.90%)	
occurrences (all)	40	49	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	53 / 209 (25.36%)	50 / 208 (24.04%)	
occurrences (all)	90	76	
Hyperglycaemia			
subjects affected / exposed	17 / 209 (8.13%)	16 / 208 (7.69%)	
occurrences (all)	25	29	
Hypokalaemia			
subjects affected / exposed	14 / 209 (6.70%)	19 / 208 (9.13%)	
occurrences (all)	28	29	
Hypomagnesaemia			
subjects affected / exposed	44 / 209 (21.05%)	40 / 208 (19.23%)	
occurrences (all)	91	91	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 April 2019	The rationale for the amended includes several relevant issues: Safety information has been updated due to the update of niraparib and atezolizumab investigator brochure: - Thromboembolic events has been added as a potential AESI of niraparib, exclusion criteria related to niraparib has been modified. - Atezolizumab immune-related nephritis and immune-related myositis management guidelines have been included. - A new exploratory objective and exploratory endpoint have been added. - Eligibility criteria have been modified. - Clarifications in both arms of the study have been added related to administration of medication. - Study calendar has been updated to add new clarifications and for consistency. - Indications for sample management have been referred to the lab manual. - Minor text accuracy edits/corrections have been performed.
06 June 2019	The rationale for the amended includes several relevant issues: PD-L1 has been considered as a new stratification factor, thus, rationale for stratification has been added and some sections of the protocol have been modified accordingly: - Study schema - Study flow chart - Table of assessments - Randomization process - Statistical considerations - Study objectives - Eligibility criteria: Mandatory de novo tumor biopsy sent to central laboratory for PD-L1 status determination has been added as an inclusion criterion. In addition, two additional tumour samples are needed for exploratory PD-L1 testing and biomarkers. - Tumor samples management directions Permitted time to hold the atezolizumab/placebo treatment in patients tapered off steroids used to treat adverse events has been updated from > 42 days to > 12 weeks. Left ventricular ejection fraction defined by MUGA/ECHO below the institutional lower limit of normal is no longer limited to patient treated with pegylated liposomal doxorubicin only. Administration of a live, attenuated vaccine (including against influenza) is not permitted within 5 months after the final dose of atezolizumab. Safety information has been updated: occurrence of auto-immune disease will be declared as an adverse event of special interest at any time during atezolizumab/placebo treatment and at any time after the treatment has been stopped (previously declared as serious adverse event (SAE)). Protocol Deviations term and definition has been updated to “Serious Breaches” as per current regulation. Minor text accuracy edits/corrections have been performed.

11 August 2020	Due to Atezolizumab IB update from version 14 to version 15 addendum 2, management of adverse events associated with atezolizumab and other safety issues has been updated: - Changes in atezolizumab AESIs. - Different wording of immunological AEs: immune-mediated instead of immune-related. - Changes in atezolizumab SAEs management wording and procedure and possibility to use another corticosteroid different than prednisone. - New section added in SAEs management: Hemophagocytic Lymphohistiocytosis and Macrophage Activation Syndrome. "Fresh tumor" specimens for PD-L1 status determination has been referenced as "de novo" tumor specimens to avoid misunderstandings. Eligibility criteria: Exclusion Criteria 24: the following exceptions to patients with history of autoimmune disease have been added: Patients with eczema, psoriasis, lichen simplex chronicus, or vitiligo with dermatologic manifestations only (e.g., patients with psoriasis arthritis would be excluded) provided that they meet all of the following conditions: - Rash must cover less than 10% of body surface area. - Disease is well controlled at baseline and requires only low potency topical steroids: • No acute exacerbations of underlying condition within the previous 12 months (i.e., does not require psoralen plus ultraviolet A radiation, methotrexate, retinoids, biologic agents, oral calcineurin inhibitors, high-potency or oral steroids) Exclusion Criteria 32: New requisition on the iPARP exposure duration has been added: The duration of exposure to PARPi following front line therapy need to be ≥18 months for BRCA mutated patients and ≥ 12 months for BRCA wild type patients. Tumor Samples: Requirements on the "de novo" biopsy have been added: In order to have a very low percentage on non-informative PD-L1, blocks must be provided with a maximal of tumoral cellularity. Sample fixation conditions have been modified.
26 May 2021	The following amendment has been performed mainly due to new safety information related with the study investigational medicinal products. Management guidelines of adverse events associated with atezolizumab has been updated. After discussion with the Independent Data Monitoring Committee and in the Steering Committee, it was agreed and proposed that FFPE from archival tissue may be acceptable for ANITA patient randomization if the mandatory de novo biopsy is technically not possible or failed to produce enough representative tumor tissue, and after sponsor approval. The current protocol states that mandatory de novo tumor biopsy (collected within 3 months prior to randomization) is needed for patient randomization. This change, which modifies inclusion criteria 9, is implemented at the request of principal investigators, who claim that the novo biopsy is sometimes technically not possible or failed to produce enough representative tumor tissue, causing patient screening failures, with a detrimental effect in the trial recruitment rate that should be finalised by August 2021. Due to the request by the principal investigators, as it was not previously defined, GEICO has considered to added apixaban as an allowed medication in patients who require therapeutic anticoagulation. In the original protocol, the analysis of PFS, which is the primary endpoint, was determined to be performed after 254 events had occurred, which correspond to approximately 60% of events. Based on the results of recent phase III trials with checkpoint inhibitors in ovarian cancer, both in the front line (IMAGYN050) and recurrent setting (JAVELIN 200), we have learned that the differences in PFS are better observed and detected with longer follow-up. Based on this observation, we plan to perform the primary analysis when 332 events have occurred, which is approximately 80% of events. With this change, we will improve the power of detecting a positive effect with the addition of atezolizumab.
24 August 2022	Due to Atezolizumab IB update from version 17 to version 18, protocol was updated with new safety information regarding changes in the management of Atezolizumab-specific adverse events. Also study personnel, study timelines, atezolizumab clinical experience section and other minor changes have been updated.

13 July 2023	Due to the update of the Atezolizumab IB from version 18 to version 19, the protocol was updated with new safety information. Based on previous data, patients will receive a maximum of 24 months of treatment. ATA and PK will not be analysed. An unblinded pre-final analysis will be performed once the expected number of events has been reached.
28 May 2024	Due to Atezolizumab IB update from version 19 to version 20, protocol was updated with new safety information, including changes in the management of atezolizumab-specific adverse events and new warnings and precautions. Atezolizumab indications have also been updated.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
21 June 2019	The sponsor processed a relevant modification related to the protocol of the reference trial to determine the PD-L1 status of the patients to be included in the trial, with the aim of exploring the correlation between PD-L1 expression status in archival tissue and in fresh tumour samples in line with what has been done in other clinical trials, and echoing the latest results obtained in similar clinical trials. Given that recruitment for the study was ahead of schedule and that it would take several weeks to process the relevant modification until authorisation, which would imply the inclusion of a large number of patients for whom PD-L1 determination would not be available, the sponsor decided to halt recruitment until authorisation of the relevant modification in order to have as many patients as possible with PD-L1 determination available for data analysis.	22 October 2019

Notes:

Limitations and caveats

None reported