



Clinical trial results:

A Phase III, Multicenter, Randomized, Open-Label Study Comparing Atezolizumab (Anti PD-L1 Antibody) in Combination With Adjuvant Anthracycline/Taxane-Based Chemotherapy Versus Chemotherapy Alone in Patients With Operable Triple Negative Breast Cancer

Summary

EudraCT number	2016-003695-47
Trial protocol	IE DE GB PL CZ ES HU DK AT BE IT RO
Global end of trial date	14 August 2023

Results information

Result version number	v1 (current)
This version publication date	14 August 2024
First version publication date	14 August 2024

Trial information

Trial identification

Sponsor protocol code	WO39391
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03498716
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Hoffmann-La Roche
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4058
Public contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com
Scientific contact	Medical Communications, Hoffmann-La Roche, +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	18 August 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 August 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The objective of this trial was to evaluate the efficacy, safety, and pharmacokinetics of adjuvant atezolizumab in combination with paclitaxel, followed by atezolizumab, dose-dense doxorubicin or epirubicin (investigator's choice), and cyclophosphamide, compared with paclitaxel followed by dose-dense doxorubicin or epirubicin (investigator's choice) and cyclophosphamide alone in patients with Stage II-III triple negative breast cancer (TNBC).

Protection of trial subjects:

All study participants were required to read and sign an informed consent form (ICF).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 August 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	Argentina: 17
Country: Number of subjects enrolled	Australia: 27
Country: Number of subjects enrolled	Austria: 10
Country: Number of subjects enrolled	Belgium: 26
Country: Number of subjects enrolled	Brazil: 58
Country: Number of subjects enrolled	Switzerland: 8
Country: Number of subjects enrolled	China: 268
Country: Number of subjects enrolled	Czechia: 12
Country: Number of subjects enrolled	Germany: 52
Country: Number of subjects enrolled	Denmark: 22
Country: Number of subjects enrolled	Spain: 75
Country: Number of subjects enrolled	France: 143
Country: Number of subjects enrolled	United Kingdom: 11
Country: Number of subjects enrolled	Hong Kong: 14
Country: Number of subjects enrolled	Hungary: 7
Country: Number of subjects enrolled	Ireland: 17
Country: Number of subjects enrolled	Israel: 12
Country: Number of subjects enrolled	Italy: 73
Country: Number of subjects enrolled	Japan: 249

Country: Number of subjects enrolled	Korea, Republic of: 158
Country: Number of subjects enrolled	Mexico: 74
Country: Number of subjects enrolled	Peru: 10
Country: Number of subjects enrolled	Poland: 14
Country: Number of subjects enrolled	Romania: 21
Country: Number of subjects enrolled	Russian Federation: 367
Country: Number of subjects enrolled	Singapore: 3
Country: Number of subjects enrolled	Thailand: 56
Country: Number of subjects enrolled	Türkiye: 6
Country: Number of subjects enrolled	Taiwan: 70
Country: Number of subjects enrolled	Ukraine: 288
Country: Number of subjects enrolled	United States: 31
Worldwide total number of subjects	2199
EEA total number of subjects	472

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)	1821
From 65 to 84 years	376
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

Participants with newly diagnosed Stage II-III primary invasive Breast cancer (BC) that is of triple negative phenotype and who were to be treated with adjuvant systemic chemotherapy following definitive surgery, were enrolled in 342 centers in 31 countries.

Pre-assignment

Screening details:

A total of 2199 participants were enrolled in the study. Participants were randomized in a 1:1 ratio to receive Atezolizumab and Chemotherapy or Chemotherapy alone.

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	Chemotherapy

Arm description:

Participants were administered paclitaxel, 80 milligram per square meter (mg/m^2), intravenous (IV) infusion weekly (QW) for maximum of 36 weeks followed by dose-dense doxorubicin, 60 mg/m^2 or dose-dense epirubicin, 90 mg/m^2 IV (investigator's choice) plus cyclophosphamide, 600 mg/m^2 , IV repeated every 2 weeks (Q2W) for a maximum of 20 weeks supported with granulocyte colony-stimulating factor (G-CSF) or granulocyte-macrophage colony-stimulating factor (GM-CSF) treatment.

Arm type	Active comparator
Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Paclitaxel 80 mg/m^2 QW IV infusion.

Investigational medicinal product name	Cyclophosphamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Cyclophosphamide, 600 mg/m^2 Q2W IV infusion.

Investigational medicinal product name	Epirubicin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Epirubicin 90 mg/m^2 IV infusion.

Investigational medicinal product name	Doxorubicin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection

Routes of administration	Intravenous use
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Dosage and administration details:

Dxorubicin, 60 mg/m² IV infusion.

Arm title	Atezolizumab and Chemotherapy
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Arm description:

Participants were administered atezolizumab 840 mg, IV infusion, Q2W in combination with chemotherapy (paclitaxel 80 mg/m², IV infusion QW for maximum of 22 weeks followed by dose-dense doxorubicin, 60 mg/m² or dose-dense epirubicin, 90 mg/m², IV (investigator's choice) plus cyclophosphamide, 600 mg/m², IV repeated Q2W for maximum of 17 weeks supported with G-CSF or GM-CSF treatment followed by atezolizumab, 1200 mg IV infusion every 3 weeks (Q3W) as a maintenance therapy to complete 1 year of atezolizumab treatment from the first dose.

Arm type	Experimental
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Investigational medicinal product name	Doxorubicin
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Investigational medicinal product code	
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Other name	
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Pharmaceutical forms	Solution for injection
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Routes of administration	Intravenous use
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Dosage and administration details:

Dxorubicin, 60 mg/m² IV infusion.

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

Paclitaxel 80 mg/m² QW IV infusion.

Investigational medicinal product name	Cyclophosphamide
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Investigational medicinal product code	
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Other name	
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Pharmaceutical forms	Solution for injection
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Routes of administration	Intravenous use
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Dosage and administration details:

Cyclophosphamide, 600 mg/m² Q2W IV infusion.

Investigational medicinal product name	Atezolizumab
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Investigational medicinal product code	
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Other name	Tecentriq
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Pharmaceutical forms	Solution for injection
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Routes of administration	Intravenous use
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Dosage and administration details:

Atezolizumab 840 mg, Q2W and 1200 mg Q3W IV infusion.

Investigational medicinal product name	Epirubicin
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Investigational medicinal product code	
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Other name	
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Pharmaceutical forms	Solution for injection
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Routes of administration	Intravenous use
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Dosage and administration details:

Epirubicin 90 mg/m² IV infusion.

Number of subjects in period 1	Chemotherapy	Atezolizumab and Chemotherapy
Started	1098	1101
Safety Evaluable Population	1084	1093
Completed	0	0
Not completed	1098	1101
Adverse event, serious fatal	58	72
Consent withdrawn by subject	88	73
Physician decision	4	2
Disease Relapse	-	1
Study Terminated By Sponsor	933	927
Lost to follow-up	15	26

Baseline characteristics

Reporting groups

Reporting group title	Chemotherapy
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Reporting group description:

Participants were administered paclitaxel, 80 milligram per square meter (mg/m²), intravenous (IV) infusion weekly (QW) for maximum of 36 weeks followed by dose-dense doxorubicin, 60 mg/m² or dose-dense epirubicin, 90 mg/m² IV (investigator's choice) plus cyclophosphamide, 600 mg/m², IV repeated every 2 weeks (Q2W) for a maximum of 20 weeks supported with granulocyte colony-stimulating factor (G-CSF) or granulocyte-macrophage colony-stimulating factor (GM-CSF) treatment.

Reporting group title	Atezolizumab and Chemotherapy
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Reporting group description:

Participants were administered atezolizumab 840 mg, IV infusion, Q2W in combination with chemotherapy (paclitaxel 80 mg/m², IV infusion QW for maximum of 22 weeks followed by dose-dense doxorubicin, 60 mg/m² or dose-dense epirubicin, 90 mg/m², IV (investigator's choice) plus cyclophosphamide, 600 mg/m², IV repeated Q2W for maximum of 17 weeks supported with G-CSF or GM-CSF treatment followed by atezolizumab, 1200 mg IV infusion every 3 weeks (Q3W) as a maintenance therapy to complete 1 year of atezolizumab treatment from the first dose.

Reporting group values	Chemotherapy	Atezolizumab and Chemotherapy	Total
Number of subjects	1098	1101	2199
Age categorical Units: Subjects			

Age Continuous Units: years arithmetic mean standard deviation	52.8 ± 11.4	52.3 ± 11.9	-
Sex: Female, Male Units: participants			
Female	1094	1101	2195
Male	4	0	4
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	28	29	57
Asian	401	423	824
Native Hawaiian or Other Pacific Islander	1	0	1
Black or African American	2	8	10
White	567	554	1121
More than one race	0	1	1
Unknown or Not Reported	99	86	185
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	100	75	175
Not Hispanic or Latino	906	950	1856
Unknown or Not Reported	92	76	168

End points

End points reporting groups

Reporting group title	Chemotherapy
Reporting group description:	
Participants were administered paclitaxel, 80 milligram per square meter (mg/m ²), intravenous (IV) infusion weekly (QW) for maximum of 36 weeks followed by dose-dense doxorubicin, 60 mg/m ² or dose-dense epirubicin, 90 mg/m ² IV (investigator's choice) plus cyclophosphamide, 600 mg/m ² , IV repeated every 2 weeks (Q2W) for a maximum of 20 weeks supported with granulocyte colony-stimulating factor (G-CSF) or granulocyte-macrophage colony-stimulating factor (GM-CSF) treatment.	
Reporting group title	Atezolizumab and Chemotherapy
Reporting group description:	
Participants were administered atezolizumab 840 mg, IV infusion, Q2W in combination with chemotherapy (paclitaxel 80 mg/m ² , IV infusion QW for maximum of 22 weeks followed by dose-dense doxorubicin, 60 mg/m ² or dose-dense epirubicin, 90 mg/m ² , IV (investigator's choice) plus cyclophosphamide, 600 mg/m ² , IV repeated Q2W for maximum of 17 weeks supported with G-CSF or GM-CSF treatment followed by atezolizumab, 1200 mg IV infusion every 3 weeks (Q3W) as a maintenance therapy to complete 1 year of atezolizumab treatment from the first dose.	

Primary: Invasive Disease-Free Survival (iDFS)

End point title	Invasive Disease-Free Survival (iDFS)
End point description:	
iDFS=time from randomization until date of first occurrence of 1 of the events: Ipsilateral invasive breast tumor recurrence (an invasive breast cancer involving same breast parenchyma as the original primary lesion); Ipsilateral local-regional invasive breast cancer recurrence (an invasive breast cancer in axilla, regional lymph nodes, chest wall, &/or skin of ipsilateral breast); Ipsilateral second primary invasive breast cancer; Contralateral invasive breast cancer; Distant recurrence (evidence of breast cancer in any anatomic site) that is histologically confirmed &/or clinically/radiographically diagnosed as recurrent invasive breast cancer; & Death attributable to any cause, including breast cancer, non-breast cancer, or unknown cause. Analysis using Kaplan-Meier estimates where participants with no events at time of analysis/no post-baseline data were censored. ITT population. 9999=Median & 95% CI were not estimable due to too few events having occurred.	
End point type	Primary
End point timeframe:	
From randomization until the occurrence of an iDFS event or death from any cause, whichever occurred earlier (up to 5 years)	

End point values	Chemotherapy	Atezolizumab and Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1098	1101		
Units: months				
median (confidence interval 95%)	9999 (9999 to 9999)	9999 (9999 to 9999)		

Statistical analyses

Statistical analysis title	Chemotherapy Vs Atezolizumab and Chemotherapy
Comparison groups	Chemotherapy v Atezolizumab and Chemotherapy
Number of subjects included in analysis	2199
Analysis specification	Pre-specified
Analysis type	superiority ^[1]
P-value	= 0.3846
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.87
upper limit	1.42

Notes:

[1] - Stratified Analysis: The stratification factors used in the analysis are axillary nodal status, surgery (breast conserving vs. mastectomy), and tumor PD-L1 status.

Secondary: iDFS in the Subpopulation With Programmed Death-ligand 1 (PD-L1) Selected Tumor Status (IC1/2/3)

End point title	iDFS in the Subpopulation With Programmed Death-ligand 1 (PD-L1) Selected Tumor Status (IC1/2/3)
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End point description:

iDFS=time from randomization until date of first occurrence of 1 of the events: Ipsilateral invasive breast tumor recurrence (an invasive breast cancer involving same breast parenchyma as the original primary lesion); Ipsilateral local-regional invasive breast cancer recurrence (an invasive breast cancer in axilla, regional lymph nodes, chest wall, &/or skin of ipsilateral breast); Ipsilateral second primary invasive breast cancer; Contralateral invasive breast cancer; Distant recurrence (evidence of breast cancer in any anatomic site) that is histologically confirmed &/or clinically/radiographically diagnosed as recurrent invasive breast cancer; & Death attributable to any cause, including breast cancer, non-breast cancer, or unknown cause. Analysis = Kaplan-Meier estimates where participants with no events at time of analysis/no post-baseline data were censored. PD-L1-positive subpopulation. 9999=Median & 95% CI were not estimable due to too few events having occurred.

End point type	Secondary
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End point timeframe:

From randomization until the occurrence of an iDFS event or death from any cause, whichever occurred earlier (up to 5 years)

End point values	Chemotherapy	Atezolizumab and Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	782	785		
Units: months				
median (confidence interval 95%)	9999 (9999 to 9999)	9999 (9999 to 9999)		

Statistical analyses

No statistical analyses for this end point

Secondary: iDFS in the Node Positive Subpopulation

End point title	iDFS in the Node Positive Subpopulation
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End point description:

iDFS=time from randomization until date of first occurrence of 1 of the events: Ipsilateral invasive breast tumor recurrence (an invasive breast cancer involving same breast parenchyma as the original primary lesion); Ipsilateral local-regional invasive breast cancer recurrence (an invasive breast cancer in axilla, regional lymph nodes, chest wall, &/or skin of ipsilateral breast); Ipsilateral second primary invasive breast cancer; Contralateral invasive breast cancer; Distant recurrence (evidence of breast cancer in any anatomic site) that is histologically confirmed &/or clinically/radiographically diagnosed as recurrent invasive breast cancer; & Death attributable to any cause, including breast cancer, non-breast cancer, or unknown cause. Analysis = Kaplan-Meier estimates where participants with no events at time of analysis/no post-baseline data were censored. Node positive subpopulation. 9999=Median & 95% CI were not estimable due to too few events having occurred.

End point type	Secondary
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End point timeframe:

From randomization until the occurrence of an iDFS event or death from any cause, whichever occurred earlier (up to 5 years)

End point values	Chemotherapy	Atezolizumab and Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	533	534		
Units: months				
median (confidence interval 95%)	9999 (9999 to 9999)	9999 (9999 to 9999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

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

OS is defined as the time from randomization to the date of death due to any cause. Analysis used Kaplan-Meier estimates where participants with no events at the time of analysis or no post-baseline information were censored. ITT population included all randomized participants, whether or not the assigned study treatment was received. 9999 = Median and 95%CI for OS were not estimable due to too few events having occurred.

End point type	Secondary
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End point timeframe:

From randomization up to death from any cause, up to 5 years

End point values	Chemotherapy	Atezolizumab and Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1098	1101		
Units: months				
median (confidence interval 95%)	9999 (9999 to 9999)	9999 (9999 to 9999)		

Statistical analyses

No statistical analyses for this end point

Secondary: iDFS Including Second Primary Non-Breast Invasive Cancer

End point title	iDFS Including Second Primary Non-Breast Invasive Cancer
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End point description:

iDFS=time from randomization until date of first occurrence of 1 of the events: Ipsilateral invasive breast tumor recurrence (an invasive breast cancer involving same breast parenchyma as original primary lesion); Ipsilateral local-regional invasive breast cancer recurrence (invasive breast cancer in axilla, regional lymph nodes, chest wall, &/or skin of ipsilateral breast); Ipsilateral 2nd primary invasive breast cancer; 2nd primary non-breast invasive cancer; Contralateral invasive breast cancer; Distant recurrence (evidence of breast cancer in any anatomic site) histologically confirmed &/or clinically/radiographically diagnosed as recurrent invasive breast cancer; Death attributable to any cause, including breast cancer, non-breast cancer/unknown cause. Analysis=Kaplan-Meier estimates where participants with no events at time of analysis/no post-baseline data were censored. ITT population. 9999=Median & 95% CI were not estimable due to too few events having occurred.

End point type	Secondary
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End point timeframe:

From randomization up to death from any cause (up to 5 years)

End point values	Chemotherapy	Atezolizumab and Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1098	1101		
Units: months				
median (confidence interval 95%)	9999 (9999 to 9999)	9999 (9999 to 9999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Recurrence-Free Interval (RFI)

End point title	Recurrence-Free Interval (RFI)
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End point description:

RFI was defined as the time from randomization to the first occurrence of any recurrence (local, regional [including invasive ipsilateral tumor and invasive locoregional tumor], or distant), as determined by investigators. Analysis used Kaplan-Meier estimates where participants with no events at the time of

analysis, participants with no events who died, or participants with no post-baseline information were censored. ITT population included all randomized participants, whether or not the assigned study treatment was received. 9999=Median and 95%CI for RFI were not estimable due to too few events having occurred.

End point type	Secondary
End point timeframe:	
From randomization up to 5 years	

End point values	Chemotherapy	Atezolizumab and Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1098	1101		
Units: months				
median (confidence interval 95%)	9999 (9999 to 9999)	9999 (9999 to 9999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Distant Recurrence-Free Interval (DRFI)

End point title	Distant Recurrence-Free Interval (DRFI)
End point description:	
DRFI was defined as the time from randomization to the distant breast cancer recurrence. Analysis used Kaplan-Meier estimates where participants with no events at the time of analysis, participants with no events who died, or participants with no post-baseline information were censored. ITT population included all randomized participants, whether or not the assigned study treatment was received. 9999=Median and 95%CI for DRFI were not estimable due to too few events having occurred.	
End point type	Secondary
End point timeframe:	
From randomization up to 5 years	

End point values	Chemotherapy	Atezolizumab and Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1098	1101		
Units: months				
median (confidence interval 95%)	9999 (9999 to 9999)	9999 (9999 to 9999)		

Statistical analyses

Secondary: Change from Baseline (CFB) in European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire Core 30 (QLQ-C30) Patient reported Function (Role functioning [Q6, Q7])

End point title	Change from Baseline (CFB) in European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire Core 30 (QLQ-C30) Patient reported Function (Role functioning [Q6, Q7])
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End point description:

EORTC QLQ-C30=cancer specific health-related quality-of life (QoL) questionnaire. For role functioning scale, participant responses to 2 questions "Q6: Were you limited in doing either your work or daily activities" & "Q7: Were you limited in pursuing your hobbies or other leisure time activities" were scored on a 4-point scale (1=Not at All to 4=Very Much). Scores were linearly transformed on a scale of 0 to 100, with a low score indicating better functioning. Negative change from baseline indicated improvement. Patient-reported outcome (PRO)-evaluable populations = all randomized participants, whether or not assigned study treatment was received with baseline PRO assessment & at least one post-baseline PRO assessment in the EORTC QLQ-C30. Overall number analyzed = number of participants with data available for analyses. Number analyzed = number of participants with data available for analyses at the specified timepoint. 9999=standard deviation was not estimable for one participant.

End point type	Secondary
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End point timeframe:

Baseline (Cycle 1 Day 1), Day 1 of Cycles 4, 6, 8, 10, 12, 14 & 16; end of treatment/discontinuation (approximately at Day 351); Follow up: Months 3 to 48 (Total duration is up to 5 years) Cycles 1-5= 28 day cycles; Cycles 6-16: 21 day cycles

End point values	Chemotherapy	Atezolizumab and Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1083	1088		
Units: score on scale				
arithmetic mean (standard deviation)				
Baseline (n= 1083, 1088)	87.26 (± 18.92)	86.43 (± 19.66)		
CFB: Cycle 4 Day 1 (n= 1025, 1040)	-10.88 (± 25.00)	-10.26 (± 24.87)		
CFB: Cycle 6 Day 1 (n= 938, 924)	-17.31 (± 29.94)	-16.56 (± 29.18)		
CFB: Cycle 8 Day 1 (n= 902, 881)	-4.58 (± 23.58)	-4.58 (± 24.31)		
CFB: Cycle 10 Day 1 (n= 898, 851)	-3.77 (± 23.59)	-3.43 (± 22.77)		
CFB: Cycle 12 Day 1 (n= 869, 806)	-1.53 (± 22.39)	-1.59 (± 23.05)		
CFB: Cycle 14 Day 1 (n= 830, 736)	-1.02 (± 21.69)	-0.70 (± 20.61)		
CFB: Cycle 16 Day 1 (n= 628, 489)	-1.09 (± 23.16)	-0.10 (± 21.77)		
Drug Completion/Early Discontinuation(n=896,964)	-2.66 (± 23.48)	-4.37 (± 26.12)		
CFB: Follow-up Month 3 (n= 845, 872)	-0.26 (± 22.62)	-0.40 (± 23.34)		
CFB: Follow-up Month 6 (n= 815, 818)	0.20 (± 24.08)	0.02 (± 24.03)		
CFB: Follow-up Month 9 (n= 758, 741)	-0.18 (± 23.52)	0.47 (± 23.35)		

CFB: Follow-up Month 12 (n= 677, 697)	0.32 (± 22.42)	1.22 (± 21.95)		
CFB: Follow-up Month 18 (n= 528, 548)	-0.47 (± 24.41)	1.52 (± 21.82)		
CFB: Follow-up Month 24 (n= 374, 393)	0.67 (± 23.54)	1.74 (± 22.28)		
CFB: Follow-up Month 30 (n= 223, 249)	2.24 (± 23.36)	2.01 (± 24.19)		
CFB: Follow-up Month 36 (n= 119, 130)	3.08 (± 23.57)	4.74 (± 20.36)		
CFB: Follow-up Month 48 (n= 1, 5)	0.00 (± 9999)	13.33 (± 13.94)		

Statistical analyses

No statistical analyses for this end point

Secondary: Disease-Free Survival (DFS)

End point title	Disease-Free Survival (DFS)
End point description:	
DFS was defined as the time from randomization to the first occurrence of disease recurrence or death from any cause. DFS events include: Ipsilateral invasive breast tumor recurrence; Ipsilateral local-regional invasive breast cancer recurrence; Distant recurrence that has either been histologically confirmed or clinically diagnosed as recurrent invasive breast cancer; Contralateral invasive breast cancer; Ipsilateral or contralateral DCIS; Second primary non-breast invasive cancer; Death attributable to any cause. Analysis using Kaplan-Meier estimates where participants with no events at the time of analysis or no post-baseline information were censored. ITT population included all randomized participants, whether or not the assigned study treatment was received. 9999=Median and 95%CI for DFS were not estimable due to too few events having occurred.	
End point type	Secondary
End point timeframe:	
From randomization up to first disease recurrence or death from any cause (up to 5 years)	

End point values	Chemotherapy	Atezolizumab and Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1098	1101		
Units: months				
median (confidence interval 95%)	9999 (9999 to 9999)	9999 (9999 to 9999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in EORTC QLQ-C30 Patient-reported Function (Physical functioning [Q1-Q5])

End point title	Change from Baseline in EORTC QLQ-C30 Patient-reported Function (Physical functioning [Q1-Q5])
End point description:	
EORTC QLQ-C30 = cancer specific health-related quality-of life (QoL) questionnaire. For physical	

functioning scale, participant responses to 5 questions about daily activities (strenuous activities, long walks, short walks, bed/chair rest & needing help with eating, dressing, washing themselves, or using the toilet) were scored on a 4-point scale (1=Not at All to 4=Very Much). Scores were linearly transformed on a scale of 0 to 100, with a high score indicating worst functioning. Negative change from baseline = improvement in functioning. PRO-evaluable populations=all randomized participants, whether or not the assigned study treatment was received with baseline PRO assessment and at least one post-baseline PRO assessment in the EORTC QLQC30. Overall number analyzed = number of participants with data available for analyses. Number analyzed=number of participants with data available for analyses at the specified timepoint. 9999=standard deviation was not estimable for one participant.

End point type	Secondary
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End point timeframe:

Baseline (Cycle 1 Day 1), Day 1 of Cycles 4, 6, 8, 10, 12, 14 & 16; end of treatment/discontinuation (approximately at Day 351); Follow up: Months 3 to 48 (Total duration is up to 5 years) Cycles 1-5= 28 day cycles; Cycles 6-16: 21 day cycles

End point values	Chemotherapy	Atezolizumab and Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1083	1089		
Units: score on scale				
arithmetic mean (standard deviation)				
CFB: Cycle 4 Day 1 (n=1025,1042)	-8.93 (± 14.97)	-8.69 (± 14.91)		
CFB: Cycle 6 Day 1 (n=938, 925)	-13.30 (± 18.63)	-13.55 (± 18.47)		
CFB: Cycle 8 Day 1 (n=901, 882)	-5.33 (± 13.79)	-6.42 (± 14.41)		
CFB: Cycle 10 Day 1 (n=898, 852)	-3.71 (± 13.28)	-4.42 (± 13.15)		
CFB: Cycle 12 Day 1 (n=871, 807)	-2.41 (± 12.87)	-3.42 (± 12.95)		
CFB: Cycle 14 Day 1 (n=829, 736)	-1.41 (± 12.87)	-1.92 (± 12.11)		
CFB: Cycle 16 Day 1 (n=627, 489)	-1.65 (± 12.78)	-1.82 (± 12.12)		
Drug Completion/Early Discontinuation(n=895, 965)	-2.56 (± 13.72)	-4.68 (± 16.69)		
CFB: Follow-up Month 3 (n=844, 871)	-1.62 (± 12.71)	-2.29 (± 13.47)		
CFB: Follow-up Month 6 (n=815, 818)	-1.70 (± 13.46)	-1.96 (± 13.78)		
CFB: Follow-up Month 9 (n=757, 741)	-1.55 (± 13.75)	-1.33 (± 13.91)		
CFB: Follow-up Month 12 (n=676, 697)	-1.70 (± 13.85)	-1.37 (± 13.39)		
CFB: Follow-up Month 18 (n=527, 548)	-1.92 (± 13.60)	-0.91 (± 13.79)		
CFB: Follow-up Month 24 (n=374, 392)	-1.37 (± 13.89)	-0.72 (± 12.91)		
Follow-up Month 30 (n=223, 249)	-1.61 (± 15.61)	-0.74 (± 12.72)		
CFB: Follow-up Month 36 (n=119, 130)	-0.42 (± 14.40)	0.82 (± 13.18)		
CFB: Follow-up Month 48 (n=1, 5)	-13.33 (± 9999)	-2.67 (± 3.65)		
Baseline (n=1083, 1089)	89.86 (± 12.14)	89.92 (± 11.57)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in EORTC QLQ-C30 Global Health Status (GHS) [Q29] and Health-Related Quality of Life (HRQoL) [Q30] Combined Score

End point title	Change From Baseline in EORTC QLQ-C30 Global Health Status (GHS) [Q29] and Health-Related Quality of Life (HRQoL) [Q30] Combined Score
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End point description:

EORTC QLQ-C30=cancer specific health-related quality-of life (QoL) questionnaire. Participant responses to questions regarding GHS (Q29: "How would you rate your overall health during past week?") & QoL (Q30: "How would you rate your overall quality of life during the past week?") are scored on a 7-point scale (1= Very poor to 7=Excellent). Using linear transformation, raw scores are standardized, so that scores range from 0 to 100. Higher score = a better outcome. Negative change from Baseline values indicated deterioration in QoL or functioning and positive values indicated improvement. PRO-evaluable populations = participants in ITT population with baseline PRO assessment and at least one post-baseline PRO assessment in EORTC QLQC30. Overall number analyzed = number of participants with data available for analyses. Number analyzed = number of participants with data available for analysis at the specified time point. 9999=standard deviation was not estimable for 1 participant.

End point type	Secondary
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End point timeframe:

Baseline (Cycle 1 Day 1), Day 1 of Cycles 4, 6, 8, 10, 12, 14 & 16; end of treatment/discontinuation (approximately at Day 351); Follow up: Months 3 to 48 (Total duration is up to 5 years) Cycles 1-5= 28 day cycles; Cycles 6-16: 21 day cycles

End point values	Chemotherapy	Atezolizumab and Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1081	1087		
Units: score on scale				
arithmetic mean (standard deviation)				
Baseline (n=1081, 1087)	76.26 (± 18.15)	75.90 (± 18.52)		
CFB:Cycle 4 Day 1 (n=1022, 1040)	-10.49 (± 20.25)	-10.02 (± 19.48)		
CFB:Cycle 6 Day 1 (n= 933, 924)	-15.87 (± 23.83)	-15.68 (± 22.32)		
CFB:Cycle 8 Day 1 (n= 899, 881)	-3.54 (± 19.72)	-5.09 (± 18.88)		
CFB:Cycle 10 Day 1(n= 893, 851)	-1.84 (± 19.57)	-2.82 (± 18.38)		
CFB:Cycle 12 Day 1 (n= 869, 805)	-0.71 (± 19.41)	-2.31 (± 18.91)		
CFB:Cycle 14 Day 1 (n= 828, 736)	-0.37 (± 19.04)	-1.25 (± 18.35)		
CFB:Cycle 16 Day 1 (n= 627, 489)	0.08 (± 18.56)	-1.30 (± 18.34)		

Drug Completion/Early Discontinuation(n= 894, 962)	-1.56 (± 20.68)	-4.39 (± 22.01)		
CFB: Follow-up Month 3 (n= 843, 871)	1.01 (± 20.25)	-0.74 (± 20.50)		
CFB: Follow-up Month 6 (n= 813, 815)	1.10 (± 20.23)	-0.90 (± 20.72)		
CFB: Follow-up Month 9 (n= 756, 740)	0.62 (± 20.47)	0.07 (± 20.83)		
CFB: Follow-up Month 12 (n= 675, 697)	1.21 (± 20.42)	0.19 (± 19.84)		
CFB: Follow-up Month 18 (n= 526, 547)	1.09 (± 22.18)	0.47 (± 20.77)		
CFB: Follow-up Month 24 (n= 373, 390)	2.32 (± 22.30)	0.43 (± 21.33)		
CFB: Follow-up Month 30 (n= 222, 248)	1.54 (± 21.36)	-0.57 (± 22.43)		
CFB: Follow-up Month 36 (n= 117, 129)	2.64 (± 20.95)	0.58 (± 23.57)		
CFB: Follow-up Month 48 (n=1, 4)	0.00 (± 9999)	6.25 (± 31.46)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Adverse Events

End point title	Number of Participants With Adverse Events
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End point description:

An AE is any untoward medical occurrence in a participant administered a pharmaceutical product, regardless of causal attribution. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a pharmaceutical product, whether or not considered related to the pharmaceutical product. Preexisting conditions which worsen during a study are also considered as adverse events. AEs are reported based on the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE), Version 5.0. Safety Evaluable Population included all participants who received any amount of any study drug.

End point type	Secondary
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End point timeframe:

Up to 5 years

End point values	Chemotherapy	Atezolizumab and Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1084	1093		
Units: participants	1074	1090		

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Concentration of Atezolizumab

End point title	Serum Concentration of Atezolizumab ^[2]
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End point description:

Pharmacokinetic (PK)-evaluable population included all participants who received any dose of study medication and who have at least one evaluable postbaseline PK sample. Overall number analyzed is the number of participants with data available for analyses. Number analyzed is the number of participants with data available for analysis at the specified time point. Number analyzed=number of participants with data available for analyses at the specified timepoint.

End point type	Secondary
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End point timeframe:

Postdose Day 1 of Cycle 1; Predose Day 1 of Cycles 2, 3, and 4; Predose Cycles 6, 10, and 14; Predose Day 1 of Cycle 16;

Cycles 1-5= 28-day cycles; Cycles 6-16: 21-day cycles

Notes:

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

Justification: Only descriptive statistic were planned to be analyzed for this end point.

End point values	Atezolizumab and Chemotherapy			
Subject group type	Reporting group			
Number of subjects analysed	952			
Units: microgram per milliliter (µg/mL)				
geometric mean (geometric coefficient of variation)				
Postdose Cycle 1 Day 1 (n=853)	319 (± 43.3)			
Pre-dose: Cycle 2 Day 1 (n=854)	153 (± 85.2)			
Pre-dose: Cycle 3 Day 1 (n=833)	220 (± 62.0)			
Pre-dose: Cycle 4 Day 1 (n=819)	221 (± 120.4)			
Pre-dose: Cycle 6 (n=727)	239 (± 146.9)			
Pre-dose: Cycle 10 (n=650)	250 (± 92.2)			
Pre-dose: Cycle 14 (n=556)	258 (± 118.7)			
Pre-dose: Cycle 16 Day 2 (n=2)	355 (± 29.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Anti-Drug Antibodies (ADAs) to Atezolizumab

End point title	Percentage of Participants with Anti-Drug Antibodies (ADAs) to Atezolizumab ^[3]
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End point description:

Baseline evaluable participant= participant with an ADA assay result from a baseline sample(s). Post-baseline evaluable participant= participant with an ADA assay result from at least one postbaseline sample. Number analyzed at baseline and postbaseline are unique number of participants out of all the assessed participants who may have been ADA positive at that timepoint. Different participants may have contributed data for baseline and postbaseline. Safety Evaluable Population included all participants who received any amount of any study drug.

End point type	Secondary
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End point timeframe:

Up to 5 years

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only descriptive statistic were planned to be analyzed for this end point.

End point values	Atezolizumab and Chemotherapy			
Subject group type	Reporting group			
Number of subjects analysed	1093			
Units: percentage of participants				
number (not applicable)				
Baseline (n=899)	2.1			
Post-baseline (n=901)	11.5			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 5 years

Adverse event reporting additional description:

All-cause Mortality: ITT population population included all randomized participants, whether or not the assigned study treatment was received; Adverse Events: Safety Evaluable Population included all participants who received any amount of any study drug.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	26.1
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Reporting groups

Reporting group title	Chemotherapy
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Reporting group description:

Participants were administered paclitaxel, 80 mg/m², IV infusion QW for maximum of 36 weeks followed by dose-dense doxorubicin, 60 mg/m² or dose-dense epirubicin, 90 mg/m² IV (investigator's choice) plus cyclophosphamide, 600 mg/m², IV repeated Q2W for a maximum of 20 weeks supported with G-CSF or GM-CSF treatment.

Reporting group title	Atezolizumab and Chemotherapy
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Reporting group description:

Participants were administered atezolizumab 840 mg, IV infusion, Q2W in combination with chemotherapy (paclitaxel 80 mg/m², IV infusion QW for maximum of 22 weeks followed by dose-dense doxorubicin, 60 mg/m² or dose-dense epirubicin, 90 mg/m², IV (investigator's choice) plus cyclophosphamide, 600 mg/m², IV repeated Q2W for maximum of 17 weeks supported with G-CSF or GM-CSF treatment followed by atezolizumab, 1200 mg IV infusion Q3W as a maintenance therapy to complete 1 year of atezolizumab treatment from the first dose.

Serious adverse events	Chemotherapy	Atezolizumab and Chemotherapy	
Total subjects affected by serious adverse events			
subjects affected / exposed	173 / 1084 (15.96%)	280 / 1093 (25.62%)	
number of deaths (all causes)	58	72	
number of deaths resulting from adverse events	1	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Thyroid cancer			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1093 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign neoplasm of thyroid gland			
subjects affected / exposed	1 / 1084 (0.09%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Lobular breast carcinoma in situ subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm malignant subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Papillary thyroid cancer subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Venous thrombosis subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombophlebitis subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subclavian vein thrombosis subjects affected / exposed	1 / 1084 (0.09%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis limb subjects affected / exposed	1 / 1084 (0.09%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jugular vein thrombosis subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			

subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brachiocephalic vein thrombosis			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral ischaemia			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1093 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Postoperative care			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 1084 (0.09%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	2 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cyst			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	0 / 1084 (0.00%)	3 / 1093 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 3	
Device related thrombosis			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Fatigue			
subjects affected / exposed	1 / 1084 (0.09%)	2 / 1093 (0.18%)	
occurrences causally related to treatment / all	1 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	1 / 1084 (0.09%)	2 / 1093 (0.18%)	
occurrences causally related to treatment / all	1 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Implant site inflammation			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza like illness			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	4 / 1084 (0.37%)	0 / 1093 (0.00%)	
occurrences causally related to treatment / all	3 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mucosal inflammation			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	1 / 1084 (0.09%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	1 / 1084 (0.09%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 1	4 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			

subjects affected / exposed	10 / 1084 (0.92%)	13 / 1093 (1.19%)	
occurrences causally related to treatment / all	4 / 10	10 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	2 / 1084 (0.18%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Cytokine release syndrome			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersensitivity			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1093 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sarcoidosis			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Ovarian vein thrombosis			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			

subjects affected / exposed	4 / 1084 (0.37%)	3 / 1093 (0.27%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	1 / 1084 (0.09%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	4 / 1084 (0.37%)	18 / 1093 (1.65%)	
occurrences causally related to treatment / all	4 / 4	17 / 20	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			
subjects affected / exposed	3 / 1084 (0.28%)	6 / 1093 (0.55%)	
occurrences causally related to treatment / all	3 / 3	6 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperventilation			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1093 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthma			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis chronic			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			

subjects affected / exposed	1 / 1084 (0.09%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eosinophilic pneumonia			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1093 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Confusional state			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1093 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	0 / 1084 (0.00%)	2 / 1093 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression suicidal			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Neutrophil count decreased			
subjects affected / exposed	14 / 1084 (1.29%)	11 / 1093 (1.01%)	
occurrences causally related to treatment / all	14 / 14	16 / 16	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphocyte count decreased			
subjects affected / exposed	0 / 1084 (0.00%)	7 / 1093 (0.64%)	
occurrences causally related to treatment / all	0 / 0	6 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gamma-glutamyltransferase			

increased			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatinine increased			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 1084 (0.18%)	2 / 1093 (0.18%)	
occurrences causally related to treatment / all	1 / 2	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alanine aminotransferase increased			
subjects affected / exposed	2 / 1084 (0.18%)	3 / 1093 (0.27%)	
occurrences causally related to treatment / all	2 / 2	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oxygen saturation decreased			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1093 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SARS-CoV-2 test positive			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1093 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
White blood cell count decreased			
subjects affected / exposed	6 / 1084 (0.55%)	10 / 1093 (0.91%)	
occurrences causally related to treatment / all	6 / 6	13 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
Platelet count decreased			
subjects affected / exposed	0 / 1084 (0.00%)	2 / 1093 (0.18%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			

Foot fracture			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
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	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin laceration			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1093 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seroma			
subjects affected / exposed	1 / 1084 (0.09%)	3 / 1093 (0.27%)	
occurrences causally related to treatment / all	1 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post lumbar puncture syndrome			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic fracture			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1093 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ligament sprain			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infusion related reaction			

subjects affected / exposed	0 / 1084 (0.00%)	6 / 1093 (0.55%)	
occurrences causally related to treatment / all	0 / 0	7 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immunisation reaction			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fracture			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Synovial rupture			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound complication			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular access site inflammation			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1093 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac asthma			

subjects affected / exposed	1 / 1084 (0.09%)	0 / 1093 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	0 / 1084 (0.00%)	2 / 1093 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure acute			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1093 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Extrasystoles			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1093 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Left ventricular dysfunction			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve incompetence			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial ischaemia			
subjects affected / exposed	0 / 1084 (0.00%)	2 / 1093 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Myocarditis			

subjects affected / exposed	0 / 1084 (0.00%)	3 / 1093 (0.27%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus tachycardia			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular extrasystoles			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1093 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1093 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Dizziness			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1093 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalopathy			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			

subjects affected / exposed	0 / 1084 (0.00%)	2 / 1093 (0.18%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	1 / 1084 (0.09%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1093 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Posterior reversible encephalopathy syndrome			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
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 / 1084 (0.09%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tremor			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1093 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 1084 (0.28%)	6 / 1093 (0.55%)	
occurrences causally related to treatment / all	3 / 3	4 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia macrocytic			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
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	23 / 1084 (2.12%)	29 / 1093 (2.65%)	
occurrences causally related to treatment / all	25 / 25	35 / 35	
deaths causally related to treatment / all	0 / 0	0 / 0	
Autoimmune haemolytic anaemia			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Granulocytopenia			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1093 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukopenia			
subjects affected / exposed	5 / 1084 (0.46%)	18 / 1093 (1.65%)	
occurrences causally related to treatment / all	6 / 6	28 / 28	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenopathy mediastinal			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1093 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Methaemoglobinaemia			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelosuppression			
subjects affected / exposed	3 / 1084 (0.28%)	4 / 1093 (0.37%)	
occurrences causally related to treatment / all	4 / 4	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			

subjects affected / exposed	31 / 1084 (2.86%)	40 / 1093 (3.66%)	
occurrences causally related to treatment / all	41 / 41	76 / 76	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphopenia			
subjects affected / exposed	1 / 1084 (0.09%)	2 / 1093 (0.18%)	
occurrences causally related to treatment / all	1 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Deafness neurosensory			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1093 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertigo			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Cataract			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1093 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal detachment			
subjects affected / exposed	1 / 1084 (0.09%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	2 / 1084 (0.18%)	3 / 1093 (0.27%)	
occurrences causally related to treatment / all	2 / 2	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	

Colitis			
subjects affected / exposed	0 / 1084 (0.00%)	3 / 1093 (0.27%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 1084 (0.00%)	3 / 1093 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal inflammation			
subjects affected / exposed	0 / 1084 (0.00%)	2 / 1093 (0.18%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoidal haemorrhage			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1093 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune-mediated enterocolitis			
subjects affected / exposed	0 / 1084 (0.00%)	2 / 1093 (0.18%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mesenteric artery thrombosis			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1093 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Nausea			
subjects affected / exposed	2 / 1084 (0.18%)	2 / 1093 (0.18%)	
occurrences causally related to treatment / all	3 / 3	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			

subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Proctitis			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1093 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stomatitis			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1093 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatic failure			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1093 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Autoimmune hepatitis			
subjects affected / exposed	0 / 1084 (0.00%)	2 / 1093 (0.18%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis chronic			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1093 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	1 / 1084 (0.09%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug-induced liver injury			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic function abnormal			

subjects affected / exposed	1 / 1084 (0.09%)	2 / 1093 (0.18%)	
occurrences causally related to treatment / all	1 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune-mediated hepatitis			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 1084 (0.00%)	3 / 1093 (0.27%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Photosensitivity reaction			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis acneiform			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1093 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash maculo-papular			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
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	0 / 1084 (0.00%)	4 / 1093 (0.37%)	
occurrences causally related to treatment / all	0 / 0	2 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis noninfective			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tubulointerstitial nephritis			

subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Adrenocorticotrophic hormone deficiency			
subjects affected / exposed	0 / 1084 (0.00%)	2 / 1093 (0.18%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Addison's disease			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adrenal insufficiency			
subjects affected / exposed	0 / 1084 (0.00%)	6 / 1093 (0.55%)	
occurrences causally related to treatment / all	0 / 0	6 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperthyroidism			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypopituitarism			
subjects affected / exposed	0 / 1084 (0.00%)	4 / 1093 (0.37%)	
occurrences causally related to treatment / all	0 / 0	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypothyroidism			
subjects affected / exposed	0 / 1084 (0.00%)	2 / 1093 (0.18%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inappropriate antidiuretic hormone secretion			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypophysitis			

subjects affected / exposed	0 / 1084 (0.00%)	3 / 1093 (0.27%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscular weakness			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma muscle			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	1 / 1084 (0.09%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Soft tissue disorder			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Torticollis			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1093 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Device related infection			
subjects affected / exposed	1 / 1084 (0.09%)	2 / 1093 (0.18%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Anal abscess			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1093 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atypical pneumonia			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1093 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast abscess			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1093 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cellulitis			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	0 / 1084 (0.00%)	2 / 1093 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopulmonary aspergillosis			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1093 (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	7 / 1084 (0.65%)	9 / 1093 (0.82%)	
occurrences causally related to treatment / all	0 / 7	0 / 9	
deaths causally related to treatment / all	0 / 1	0 / 2	
COVID-19 pneumonia			

subjects affected / exposed	2 / 1084 (0.18%)	3 / 1093 (0.27%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 2	
Cellulitis			
subjects affected / exposed	2 / 1084 (0.18%)	2 / 1093 (0.18%)	
occurrences causally related to treatment / all	0 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile infection			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Complicated appendicitis			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronavirus infection			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis infectious			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			

subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	2 / 1084 (0.18%)	2 / 1093 (0.18%)	
occurrences causally related to treatment / all	1 / 2	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected seroma			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	0 / 1084 (0.00%)	2 / 1093 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1093 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Klebsiella infection			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1093 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenitis bacterial			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasopharyngitis			

subjects affected / exposed	1 / 1084 (0.09%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Necrotising fasciitis			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic sepsis			
subjects affected / exposed	0 / 1084 (0.00%)	2 / 1093 (0.18%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ophthalmic herpes zoster			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paronychia			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1093 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periorbital cellulitis			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1093 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 1084 (0.00%)	2 / 1093 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	17 / 1084 (1.57%)	18 / 1093 (1.65%)	
occurrences causally related to treatment / all	8 / 17	13 / 18	
deaths causally related to treatment / all	1 / 1	0 / 0	
Pneumonia bacterial			

subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous abscess			
subjects affected / exposed	2 / 1084 (0.18%)	0 / 1093 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Soft tissue infection			
subjects affected / exposed	0 / 1084 (0.00%)	2 / 1093 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin infection			
subjects affected / exposed	1 / 1084 (0.09%)	2 / 1093 (0.18%)	
occurrences causally related to treatment / all	1 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	1 / 1084 (0.09%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Sepsis			
subjects affected / exposed	1 / 1084 (0.09%)	2 / 1093 (0.18%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	1 / 1084 (0.09%)	3 / 1093 (0.27%)	
occurrences causally related to treatment / all	0 / 1	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1093 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia viral			

subjects affected / exposed	2 / 1084 (0.18%)	0 / 1093 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis			
subjects affected / exposed	1 / 1084 (0.09%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tubo-ovarian abscess			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1093 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 1084 (0.09%)	2 / 1093 (0.18%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 1084 (0.09%)	4 / 1093 (0.37%)	
occurrences causally related to treatment / all	0 / 1	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular device infection			
subjects affected / exposed	0 / 1084 (0.00%)	2 / 1093 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral rash			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection			

subjects affected / exposed	1 / 1084 (0.09%)	0 / 1093 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal sepsis			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1093 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 1084 (0.09%)	2 / 1093 (0.18%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	3 / 1084 (0.28%)	0 / 1093 (0.00%)	
occurrences causally related to treatment / all	4 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus			
subjects affected / exposed	0 / 1084 (0.00%)	2 / 1093 (0.18%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ketoacidosis			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercalcaemia			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Type 1 diabetes mellitus			

subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	2 / 1084 (0.18%)	0 / 1093 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypocalcaemia			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1093 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertriglyceridaemia			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1093 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Chemotherapy	Atezolizumab and Chemotherapy	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1068 / 1084 (98.52%)	1082 / 1093 (98.99%)	
Vascular disorders			
Hot flush			
subjects affected / exposed	50 / 1084 (4.61%)	63 / 1093 (5.76%)	
occurrences (all)	52	65	
General disorders and administration			

site conditions			
Asthenia			
subjects affected / exposed	230 / 1084 (21.22%)	234 / 1093 (21.41%)	
occurrences (all)	373	455	
Fatigue			
subjects affected / exposed	268 / 1084 (24.72%)	325 / 1093 (29.73%)	
occurrences (all)	348	490	
Malaise			
subjects affected / exposed	73 / 1084 (6.73%)	81 / 1093 (7.41%)	
occurrences (all)	83	92	
Oedema peripheral			
subjects affected / exposed	76 / 1084 (7.01%)	73 / 1093 (6.68%)	
occurrences (all)	84	83	
Pyrexia			
subjects affected / exposed	105 / 1084 (9.69%)	160 / 1093 (14.64%)	
occurrences (all)	126	211	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	79 / 1084 (7.29%)	132 / 1093 (12.08%)	
occurrences (all)	85	158	
Dyspnoea			
subjects affected / exposed	56 / 1084 (5.17%)	84 / 1093 (7.69%)	
occurrences (all)	64	105	
Epistaxis			
subjects affected / exposed	73 / 1084 (6.73%)	56 / 1093 (5.12%)	
occurrences (all)	92	63	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	116 / 1084 (10.70%)	140 / 1093 (12.81%)	
occurrences (all)	122	158	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	240 / 1084 (22.14%)	296 / 1093 (27.08%)	
occurrences (all)	319	457	
Aspartate aminotransferase increased			

subjects affected / exposed	159 / 1084 (14.67%)	246 / 1093 (22.51%)	
occurrences (all)	215	372	
Blood alkaline phosphatase increased			
subjects affected / exposed	38 / 1084 (3.51%)	61 / 1093 (5.58%)	
occurrences (all)	43	92	
Blood lactate dehydrogenase increased			
subjects affected / exposed	57 / 1084 (5.26%)	51 / 1093 (4.67%)	
occurrences (all)	106	67	
Lymphocyte count decreased			
subjects affected / exposed	86 / 1084 (7.93%)	113 / 1093 (10.34%)	
occurrences (all)	162	214	
Neutrophil count decreased			
subjects affected / exposed	254 / 1084 (23.43%)	273 / 1093 (24.98%)	
occurrences (all)	473	558	
White blood cell count decreased			
subjects affected / exposed	196 / 1084 (18.08%)	232 / 1093 (21.23%)	
occurrences (all)	392	526	
Weight decreased			
subjects affected / exposed	27 / 1084 (2.49%)	63 / 1093 (5.76%)	
occurrences (all)	30	67	
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	70 / 1084 (6.46%)	74 / 1093 (6.77%)	
occurrences (all)	95	90	
Radiation skin injury			
subjects affected / exposed	13 / 1084 (1.20%)	95 / 1093 (8.69%)	
occurrences (all)	13	98	
Nervous system disorders			
Dizziness			
subjects affected / exposed	58 / 1084 (5.35%)	71 / 1093 (6.50%)	
occurrences (all)	68	104	
Dysgeusia			
subjects affected / exposed	117 / 1084 (10.79%)	116 / 1093 (10.61%)	
occurrences (all)	127	129	

Headache			
subjects affected / exposed	135 / 1084 (12.45%)	176 / 1093 (16.10%)	
occurrences (all)	178	284	
Hypoaesthesia			
subjects affected / exposed	94 / 1084 (8.67%)	91 / 1093 (8.33%)	
occurrences (all)	106	111	
Neuropathy peripheral			
subjects affected / exposed	151 / 1084 (13.93%)	158 / 1093 (14.46%)	
occurrences (all)	179	181	
Paraesthesia			
subjects affected / exposed	75 / 1084 (6.92%)	72 / 1093 (6.59%)	
occurrences (all)	99	117	
Peripheral sensory neuropathy			
subjects affected / exposed	185 / 1084 (17.07%)	196 / 1093 (17.93%)	
occurrences (all)	193	207	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	422 / 1084 (38.93%)	420 / 1093 (38.43%)	
occurrences (all)	546	586	
Neutropenia			
subjects affected / exposed	240 / 1084 (22.14%)	236 / 1093 (21.59%)	
occurrences (all)	437	474	
Leukopenia			
subjects affected / exposed	139 / 1084 (12.82%)	137 / 1093 (12.53%)	
occurrences (all)	274	317	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	61 / 1084 (5.63%)	72 / 1093 (6.59%)	
occurrences (all)	73	79	
Vomiting			
subjects affected / exposed	146 / 1084 (13.47%)	177 / 1093 (16.19%)	
occurrences (all)	212	242	
Stomatitis			
subjects affected / exposed	120 / 1084 (11.07%)	143 / 1093 (13.08%)	
occurrences (all)	133	166	

Nausea subjects affected / exposed occurrences (all)	531 / 1084 (48.99%) 865	553 / 1093 (50.59%) 958	
Dyspepsia subjects affected / exposed occurrences (all)	58 / 1084 (5.35%) 73	65 / 1093 (5.95%) 71	
Diarrhoea subjects affected / exposed occurrences (all)	188 / 1084 (17.34%) 260	287 / 1093 (26.26%) 430	
Constipation subjects affected / exposed occurrences (all)	210 / 1084 (19.37%) 252	231 / 1093 (21.13%) 270	
Abdominal pain upper subjects affected / exposed occurrences (all)	52 / 1084 (4.80%) 53	79 / 1093 (7.23%) 92	
Skin and subcutaneous tissue disorders			
Rash maculo-papular subjects affected / exposed occurrences (all)	41 / 1084 (3.78%) 50	79 / 1093 (7.23%) 91	
Rash subjects affected / exposed occurrences (all)	89 / 1084 (8.21%) 110	167 / 1093 (15.28%) 200	
Pruritus subjects affected / exposed occurrences (all)	50 / 1084 (4.61%) 56	127 / 1093 (11.62%) 160	
Nail discolouration subjects affected / exposed occurrences (all)	99 / 1084 (9.13%) 108	106 / 1093 (9.70%) 113	
Dry skin subjects affected / exposed occurrences (all)	36 / 1084 (3.32%) 38	55 / 1093 (5.03%) 57	
Alopecia subjects affected / exposed occurrences (all)	715 / 1084 (65.96%) 733	735 / 1093 (67.25%) 752	
Endocrine disorders			

Hypothyroidism subjects affected / exposed occurrences (all)	6 / 1084 (0.55%) 6	161 / 1093 (14.73%) 173	
Hyperthyroidism subjects affected / exposed occurrences (all)	3 / 1084 (0.28%) 3	62 / 1093 (5.67%) 65	
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	73 / 1084 (6.73%) 92	116 / 1093 (10.61%) 145	
Arthralgia subjects affected / exposed occurrences (all)	150 / 1084 (13.84%) 246	218 / 1093 (19.95%) 333	
Bone pain subjects affected / exposed occurrences (all)	62 / 1084 (5.72%) 72	68 / 1093 (6.22%) 79	
Pain in extremity subjects affected / exposed occurrences (all)	50 / 1084 (4.61%) 58	66 / 1093 (6.04%) 82	
Myalgia subjects affected / exposed occurrences (all)	175 / 1084 (16.14%) 309	202 / 1093 (18.48%) 347	
Infections and infestations COVID-19 subjects affected / exposed occurrences (all)	34 / 1084 (3.14%) 34	71 / 1093 (6.50%) 72	
Metabolism and nutrition disorders Hyperglycaemia subjects affected / exposed occurrences (all)	51 / 1084 (4.70%) 64	73 / 1093 (6.68%) 89	
Decreased appetite subjects affected / exposed occurrences (all)	144 / 1084 (13.28%) 185	213 / 1093 (19.49%) 275	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 November 2017	Protocol Amendment 1: The guidelines for managing patients who experienced atezolizumab-associated adverse events were revised to include guidelines for hypophysitis and myocarditis. The interval for the periodic safety iDMC reviews was established to occur on a 6-month basis.
20 May 2018	Protocol Amendment 2: The study design was modified to align with recommendations by European Health authorities, including clarifying the secondary efficacy endpoint related to recurrence-free interval and some eligibility criteria.
15 November 2018	Protocol Amendment 3: The protocol was amended primarily to update safety information, including risks for atezolizumab and management guidelines, eligibility criteria, and changes to the adverse event severity grading scale.
12 November 2019	Protocol Amendment 4: Safety information was updated and recommendations implemented in response to Health Authority request.
14 February 2020	Protocol Amendment 5: The protocol converged country-specific criteria into the global amendment. In addition, requirements for membership in the iDMC were clarified. Additional safety-related updates were also added.
17 February 2021	Protocol Amendment 6: The protocol was amended to update the risks and management guidelines for atezolizumab to align with the latest Atezolizumab Investigator's Brochure (Version 17).
24 November 2021	Protocol Amendment 7: The interim analysis timeline was updated and the adverse event management guidelines were revised to align with the latest Atezolizumab Investigator's Brochure (Version 18).
01 March 2023	Protocol Amendment 8: A formal efficacy and futility analysis was added due to FDA request to determine the ability of the study to provide an acceptable benefit-risk assessment upon trial conclusion.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported