Clinical trial results:
An Open-Label, Dose-Finding and Expansion Phase IB Study to Evaluate the Safety, Pharmacokinetics and Clinical Activity of RO6870810 and Atezolizumab (PD-L1 Antibody) in Patients with Advanced Ovarian Cancer or Triple Negative Breast Cancer

Summary

EudraCT number	2017-001147-13
Trial protocol	
Global end of trial date	26 February 2019

Results information

Result version number	v1 (current)
This version publication date	
First version publication date	

Trial information

Trial identification

Sponsor protocol code	NP39487

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03292172
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
Public contact	Roche Trial Information Hotline, F. Hoffmann-La Roche AG, +41 61 6878333, global.trial_information@roche.com
Scientific contact	Roche Trial Information Hotline, F. Hoffmann-La Roche AG, +41 61 6878333, global.trial_information@roche.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	26 February 2019

Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	26 February 2019
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Study NP39487 was a Phase Ib, open-label, non-randomized study in patients with advanced OC and TNBC (with no alternative treatment options, or refusal to undergo an alternative treatment), to investigate the safety, PK, and anti-tumor activity of RO6870810 in combination with a fixed dose of atezolizumab.

Protection of trial subjects:

All study subjects were required to read and sign and Informed Consent Form. The study was conducted in accordance with the principles of the "Declaration of Helsinki" and Good Clinical Practice.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 November 2017
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	1 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 3
Country: Number of subjects enrolled	Canada: 10
Country: Number of subjects enrolled	Denmark: 8
Country: Number of subjects enrolled	United States: 15
Worldwide total number of subjects	36
EEA total number of subjects	8

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)	30
From 65 to 84 years	6
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment period: 08 November 2017 to 18 December 2018

Pre-assignment

Screening details:

Screening was performed from Day -14 to Day -1.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1 Cohort 1 - Escalation Dose

Arm description:

Subjects were administered escalating doses of RO6870810 (0.3 milligram per kilogram [mg/kg]) subcutaneously (SC) once daily (QD) along with fixed dose of atezolizumab 1200 mg intravenously (IV) on Day 1 of each cycle (21 day cycles), every 3 weeks. RO6870810 was given during the first 14 days.

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

Dosage and administration details:

Atezolizumab was given intravenously (IV) at a fixed dose of 1200 mg on Day 1 of each cycle, every 3 weeks.

Investigational medicinal product name	RO6870810
Investigational medicinal product code	
Other name	BETi
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

RO6870810 was injected SC, at initial planned doses of 0.30, 0.45, or 0.65 mg/kg, QD for the first 14 days of a 21-day cycle.

Arm title	Group 1 Cohort 2 - Escalation Dose

Arm description:

Subjects were administered escalating doses of RO6870810 (0.45 milligram per kilogram [mg/kg]) subcutaneously (SC) once daily (QD) along with fixed dose of atezolizumab 1200 mg intravenously (IV) on Day 1 of each cycle (21 day cycles), every 3 weeks. RO6870810 was given during the first 14 days.

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

Dosage and administration details:

Atezolizumab was given intravenously (IV) at a fixed dose of 1200 mg on Day 1 of each cycle, every 3

weeks.

Investigational medicinal product name	RO6870810
Investigational medicinal product code	
Other name	BETi
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

RO6870810 was injected SC, at initial planned doses of 0.30, 0.45, or 0.65 mg/kg, QD for the first 14 days of a 21-day cycle.

Arm title	Group 1 Cohort 3 - Escalation Dose

Arm description:

Subjects were administered escalating doses of RO6870810 (0.65 milligram per kilogram [mg/kg]) subcutaneously (SC) once daily (QD) along with fixed dose of atezolizumab 1200 mg intravenously (IV) on Day 1 of each cycle (21 day cycles), every 3 weeks. RO6870810 was given during the first 14 days.

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

Dosage and administration details:

Atezolizumab was given intravenously (IV) at a fixed dose of 1200 mg on Day 1 of each cycle, every 3 weeks.

Investigational medicinal product name	RO6870810
Investigational medicinal product code	
Other name	BETi
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

RO6870810 was injected SC, at initial planned doses of 0.30, 0.45, or 0.65 mg/kg, QD for the first 14 days of a 21-day cycle.

Arm title	Group 2 Cohort 1 - Sequential Dose

Arm description:

Subjects were administered RO6870810 monotherapy (starting dose 0.30 mg/kg) during the first 14 days of 21-day Run-in period. Following the Run-in period, Subjects continued to receive RO6870810 at the same dose in combination with fixed dose of atezolizumab 1200 mg IV every 3 weeks in 21-day cycles.

Arm type	Experimental
Investigational medicinal product name	RO6870810
Investigational medicinal product code	
Other name	BETi
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

RO6870810 was injected SC, at initial planned doses of 0.30, 0.45, or 0.65 mg/kg, QD for the first 14 days of a 21-day cycle.

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

Dosage and administration details:

Atezolizumab was given intravenously (IV) at a fixed dose of 1200 mg on Day 1 of each cycle, every 3 weeks.

Arm title	Group 2 Cohort 2 - Sequential Dose

Arm description:

Subjects were administered RO6870810 monotherapy (starting dose 0.45 mg/kg) during the first 14 days of 21-day Run-in period. Following the Run-in period, Subjects continued to receive RO6870810 at the same dose in combination with fixed dose of atezolizumab 1200 mg IV every 3 weeks in 21-day cycles.

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

Dosage and administration details:

Atezolizumab was given intravenously (IV) at a fixed dose of 1200 mg on Day 1 of each cycle, every 3 weeks.

Investigational medicinal product name	RO6870810
Investigational medicinal product code	
Other name	BETi
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

RO6870810 was injected SC, at initial planned doses of 0.30, 0.45, or 0.65 mg/kg, QD for the first 14 days of a 21-day cycle.

Arm title	Group 3 - Expansion in TNBC Group

Arm description:

Subjects were administered dose of RO6870810 established in Group 1 (either 0.3 mg/kg, 0.45 mg/kg, or 0.65 mg/kg) SC QD along with fixed dose of atezolizumab 1200 mg IV on Day 1 of each cycle (21 day cycles), every 3 weeks. RO6870810 was given during the first 14 days.

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

Dosage and administration details:

Atezolizumab was given intravenously (IV) at a fixed dose of 1200 mg on Day 1 of each cycle, every 3 weeks.

Investigational medicinal product name	RO6870810
Investigational medicinal product code	
Other name	BETi
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

RO6870810 was injected SC, at initial planned doses of 0.45 mg/kg, QD for the first 14 days of a 21-day cycle.

Arm title	Group 4 - Expansion in OC Group

Arm description:

Subjects were administered dose of RO6870810 established in Group 1 (either 0.3 mg/kg, 0.45 mg/kg, or 0.65 mg/kg) SC QD along with fixed dose of atezolizumab 1200 mg IV on Day 1 of each cycle (21 day cycles), every 3 weeks. RO6870810 was given during the first 14 days.

Arm type	Experimental

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

Dosage and administration details:

Atezolizumab was given intravenously (IV) at a fixed dose of 1200 mg on Day 1 of each cycle, every 3 weeks.

Investigational medicinal product name	RO6870810
Investigational medicinal product code	
Other name	BETi
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

RO6870810 was injected SC, at initial planned doses of 0.45 mg/kg, QD for the first 14 days of a 21-day cycle.

Number of subjects in period 1	Group 1 Cohort 1 - Escalation Dose	Group 1 Cohort 2 - Escalation Dose	Group 1 Cohort 3 - Escalation Dose
Started	4	7	6
Completed	1	1	3
Not completed	3	6	3
Death	3	1	3
Unknown Reason	-	2	-
Progressive Disease	-	1	-
Study Terminated By Sponsor	-	-	-
Consent withdrawn by subject	-	2	-

Number of subjects in period 1	Group 2 Cohort 1 - Sequential Dose	Group 2 Cohort 2 - Sequential Dose	Group 3 - Expansion in TNBC Group
Started	4	6	3
Completed	0	0	0
Not completed	4	6	3
Death	3	1	-
Unknown Reason	-	2	1
Progressive Disease	1	-	-
Study Terminated By Sponsor	-	1	1
Consent withdrawn by subject	-	2	1

Number of subjects in period 1	Group 4 - Expansion in OC Group
Started	6
Completed	2
Not completed	4
Death	1
Unknown Reason	2

Progressive Disease	-
Study Terminated By Sponsor	-
Consent withdrawn by subject	1

Baseline characteristics

Reporting groups	
Reporting group title	Group 1 Cohort 1 - Escalation Dose
Reporting group description:	
Subjects were administered escalating doses of RO6870810 (0.3 milligram per kilogram [mg/kg]) subcutaneously (SC) once daily (QD) along with fixed dose of atezolizumab 1200 mg intravenously (IV) on Day 1 of each cycle (21 day cycles), every 3 weeks. RO6870810 was given during the first 14 days.	
Reporting group title	Group 1 Cohort 2 - Escalation Dose
Reporting group description:	
Subjects were administered escalating doses of RO6870810 (0.45 milligram per kilogram [mg/kg]) subcutaneously (SC) once daily (QD) along with fixed dose of atezolizumab 1200 mg intravenously (IV) on Day 1 of each cycle (21 day cycles), every 3 weeks. RO6870810 was given during the first 14 days.	
Reporting group title	Group 1 Cohort 3 - Escalation Dose
Reporting group description:	
Subjects were administered escalating doses of RO6870810 (0.65 milligram per kilogram [mg/kg]) subcutaneously (SC) once daily (QD) along with fixed dose of atezolizumab 1200 mg intravenously (IV) on Day 1 of each cycle (21 day cycles), every 3 weeks. RO6870810 was given during the first 14 days.	
Reporting group title	Group 2 Cohort 1 - Sequential Dose
Reporting group description:	
Subjects were administered RO6870810 monotherapy (starting dose 0.30 mg/kg) during the first 14 days of 21-day Run-in period. Following the Run-in period, Subjects continued to receive RO6870810 at the same dose in combination with fixed dose of atezolizumab 1200 mg IV every 3 weeks in 21-day cycles.	
Reporting group title	Group 2 Cohort 2 - Sequential Dose
Reporting group description:	
Subjects were administered RO6870810 monotherapy (starting dose 0.45 mg/kg) during the first 14 days of 21-day Run-in period. Following the Run-in period, Subjects continued to receive RO6870810 at the same dose in combination with fixed dose of atezolizumab 1200 mg IV every 3 weeks in 21-day cycles.	
Reporting group title	Group 3 - Expansion in TNBC Group
Reporting group description:	
Subjects were administered dose of RO6870810 established in Group 1 (either 0.3 mg/kg, 0.45 mg/kg, or 0.65 mg/kg) SC QD along with fixed dose of atezolizumab 1200 mg IV on Day 1 of each cycle (21 day cycles), every 3 weeks. RO6870810 was given during the first 14 days.	
Reporting group title	Group 4 - Expansion in OC Group
Reporting group description:	
Subjects were administered dose of RO6870810 established in Group 1 (either 0.3 mg/kg, 0.45 mg/kg, or 0.65 mg/kg) SC QD along with fixed dose of atezolizumab 1200 mg IV on Day 1 of each cycle (21 day cycles), every 3 weeks. RO6870810 was given during the first 14 days.	

Reporting group values	Group 1 Cohort 1 - Escalation Dose	Group 1 Cohort 2 - Escalation Dose	Group 1 Cohort 3 - Escalation Dose
Number of subjects	4	7	6
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	3	6	6

From 65-84 years	1	1	0
85 years and over	0	0	0

Age continuous			
Units: years			
arithmetic mean	53.25	54.00	50.00
standard deviation	± 12.82	± 9.97	± 7.18
Gender categorical			
Units: Subjects			
Female	4	7	6
Male	0	0	0
Ethnicity			
Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	4	7	6
Not Stated	0	0	0
Race			
Units: Subjects			
Asian	0	0	0
White	4	7	6

Reporting group values	Group 2 Cohort 1 - Sequential Dose	Group 2 Cohort 2 - Sequential Dose	Group 3 - Expansion in TNBC Group
Number of subjects	4	6	3
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	3	5	3
From 65-84 years	1	1	0
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	51.50	51.17	51.33
standard deviation	± 12.23	± 11.20	± 2.52
Gender categorical			
Units: Subjects			
Female	4	6	3
Male	0	0	0
Ethnicity			
Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	4	5	3
Not Stated	0	1	0
Race			
Units: Subjects			

Asian	0	1	1
White	4	5	2

Reporting group values	Group 4 - Expansion in OC Group	Total	
Number of subjects	6	36	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	4	30	
From 65-84 years	2	6	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	60.50		
standard deviation	± 8.36	-	
Gender categorical Units: Subjects			
Female	6	36	
Male	0	0	
Ethnicity Units: Subjects			
Hispanic or Latino	1	1	
Not Hispanic or Latino	5	34	
Not Stated	0	1	
Race Units: Subjects			
Asian	0	2	
White	6	34	

End points

End points reporting groups

Reporting group title	Group 1 Cohort 1 - Escalation Dose

Reporting group description:

Subjects were administered escalating doses of RO6870810 (0.3 milligram per kilogram [mg/kg]) subcutaneously (SC) once daily (QD) along with fixed dose of atezolizumab 1200 mg intravenously (IV) on Day 1 of each cycle (21 day cycles), every 3 weeks. RO6870810 was given during the first 14 days.

Reporting group title	Group 1 Cohort 2 - Escalation Dose

Reporting group description:

Subjects were administered escalating doses of RO6870810 (0.45 milligram per kilogram [mg/kg]) subcutaneously (SC) once daily (QD) along with fixed dose of atezolizumab 1200 mg intravenously (IV) on Day 1 of each cycle (21 day cycles), every 3 weeks. RO6870810 was given during the first 14 days.

Reporting group title	Group 1 Cohort 3 - Escalation Dose

Reporting group description:

Subjects were administered escalating doses of RO6870810 (0.65 milligram per kilogram [mg/kg]) subcutaneously (SC) once daily (QD) along with fixed dose of atezolizumab 1200 mg intravenously (IV) on Day 1 of each cycle (21 day cycles), every 3 weeks. RO6870810 was given during the first 14 days.

Reporting group title	Group 2 Cohort 1 - Sequential Dose

Reporting group description:

Subjects were administered RO6870810 monotherapy (starting dose 0.30 mg/kg) during the first 14 days of 21-day Run-in period. Following the Run-in period, Subjects continued to receive RO6870810 at the same dose in combination with fixed dose of atezolizumab 1200 mg IV every 3 weeks in 21-day cycles.

Reporting group title	Group 2 Cohort 2 - Sequential Dose

Reporting group description:

Subjects were administered RO6870810 monotherapy (starting dose 0.45 mg/kg) during the first 14 days of 21-day Run-in period. Following the Run-in period, Subjects continued to receive RO6870810 at the same dose in combination with fixed dose of atezolizumab 1200 mg IV every 3 weeks in 21-day cycles.

Reporting group title	Group 3 - Expansion in TNBC Group

Reporting group description:

Subjects were administered dose of RO6870810 established in Group 1 (either 0.3 mg/kg, 0.45 mg/kg, or 0.65 mg/kg) SC QD along with fixed dose of atezolizumab 1200 mg IV on Day 1 of each cycle (21 day cycles), every 3 weeks. RO6870810 was given during the first 14 days.

Reporting group title	Group 4 - Expansion in OC Group

Reporting group description:

Subjects were administered dose of RO6870810 established in Group 1 (either 0.3 mg/kg, 0.45 mg/kg, or 0.65 mg/kg) SC QD along with fixed dose of atezolizumab 1200 mg IV on Day 1 of each cycle (21 day cycles), every 3 weeks. RO6870810 was given during the first 14 days.

Primary: Number of Subjects With Dose Limiting Toxicities (DLT)

End point title	Number of Subjects With Dose Limiting Toxicities (DLT)[1][2]

End point description:

A DLT is defined as a clinically significant adverse event (classified according to the NCI CTCAE v4.03, as applicable) or laboratory abnormality considered to be at least possibly related to study treatment (RO6870810 and/or atezolizumab) by the Investigator and is not attributed to disease progression or another clearly identifiable cause.

End point type	Primary

End point timeframe:

Cycle 1 (Day 1 to Day 21)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analysis provided.

[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: No statistical analysis provided.

End point values	Group 1 Cohort 1 - Escalation Dose	Group 1 Cohort 2 - Escalation Dose	Group 1 Cohort 3 - Escalation Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	7	6	
Units: Subjects				
Number of Subjects with DLT	0	0	1	

Statistical analyses

No statistical analyses for this end point

Primary: Best Overall Response as per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1

End point title	Best Overall Response as per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1[3][4]

End point description:

From first occurrence of objective response until disease progression or death from any cause (Up to 22 months).

End point type	Primary

End point timeframe:

Best response is defined as the best response across all time points as per to Response Evaluation Criteria in Solid Tumors (RECIST) v1.1

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis provided.

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis provided.

End point values	Group 3 - Expansion in TNBC Group	Group 4 - Expansion in OC Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	6		
Units: Subjects				
Overall Best Response: PR	0	0		
Overall Best Response: SD	2	0		
Overall Best Response: PD	0	4		
Overall Best Response: Missing	1	2		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects with Objective Response as per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1

End point title	Number of Subjects with Objective Response as per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1[5][6]

End point description:

Responder is defined as any subject who exhibits a complete response or partial response. Missing response is assumed as a non−responder

End point type	Primary

End point timeframe:

From first occurrence of objective response until disease progression or death from any cause (Up to 22 months)

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis provided.

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis provided.

End point values	Group 3 - Expansion in TNBC Group	Group 4 - Expansion in OC Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	6		
Units: Subjects				
Responder	0	0		
Non−Responder	3	6		

Statistical analyses

No statistical analyses for this end point

Secondary: Best Overall Response as per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1; Group 1 and 2

End point title	Best Overall Response as per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1; Group 1 and 2[7]

End point description:

Best response is defined as the best response across all time points as per to Response Evaluation Criteria in Solid Tumors (RECIST) v1.1

End point type	Secondary

End point timeframe:

From first occurrence of objective response until disease progression or death from any cause (Up to 22 months)

Notes:

[7] - 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: No statistical analysis provided.

End point values	Group 1 Cohort 1 - Escalation Dose	Group 1 Cohort 2 - Escalation Dose	Group 1 Cohort 3 - Escalation Dose	Group 2 Cohort 1 - Sequential Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	7	6	4
Units: Subjects				
Overall Best Response: PR	1	1	0	0
Overall Best Response: SD	1	2	4	1
Overall Best Response: PD	2	3	1	3
Overall Best Response: Missing	0	1	1	0

End point values	Group 2 Cohort 2 - Sequential Dose			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: Subjects				
Overall Best Response: PR	0			
Overall Best Response: SD	5			
Overall Best Response: PD	1			
Overall Best Response: Missing	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Objective Response as per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1; Group 1 and 2

End point title	Number of Subjects with Objective Response as per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1; Group 1 and 2[8]

End point description:

Responder is defined as any subject who exhibits a complete response or partial response. Missing response is assumed as a non−responder

End point type	Secondary

End point timeframe:

From first occurrence of objective response until disease progression or death from any cause (Up to 22 months)

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis provided.

End point values	Group 1 Cohort 1 - Escalation Dose	Group 1 Cohort 2 - Escalation Dose	Group 1 Cohort 3 - Escalation Dose	Group 2 Cohort 1 - Sequential Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	7	6	4
Units: Subjects				
Responder	1	1	0	0
Non−Responder	3	6	6	4

End point values	Group 2 Cohort 2 - Sequential Dose			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: Subjects				
Responder	0			
Non−Responder	6			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were recorded from the date of Screening until final database lock on 19 July 2019 (up to 22 months)

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups

Reporting group title	Group 1 Cohort 1 - Escalation Dose

Reporting group description:

Participants were administered escalating doses of RO6870810 (0.3 milligram per kilogram [mg/kg]) subcutaneously (SC) once daily (QD) along with fixed dose of atezolizumab 1200 mg intravenously (IV) on Day 1 of each cycle (21 day cycles), every 3 weeks. RO6870810 will be given during the first 14 days.

Reporting group title	Group 1 Cohort 3 - Escalation Dose

Reporting group description:

Participants were administered escalating doses of RO6870810 (0.65 milligram per kilogram [mg/kg]) subcutaneously (SC) once daily (QD) along with fixed dose of atezolizumab 1200 mg intravenously (IV) on Day 1 of each cycle (21 day cycles), every 3 weeks. RO6870810 will be given during the first 14 days.

Reporting group title	Group 1 Cohort 2 - Escalation Dose

Reporting group description:

Participants were administered escalating doses of RO6870810 (0.45 milligram per kilogram [mg/kg]) subcutaneously (SC) once daily (QD) along with fixed dose of atezolizumab 1200 mg intravenously (IV) on Day 1 of each cycle (21 day cycles), every 3 weeks. RO6870810 will be given during the first 14 days.

Reporting group title	Group 2 Cohort 1 - Sequential Dose

Reporting group description:

Participants were administered RO6870810 monotherapy (starting dose 0.30 mg/kg) during the first 14 days of 21-day Run-in period. Following the Run-in period, participants will continue to receive RO6870810 at the same dose in combination with fixed dose of atezolizumab 1200 mg IV every 3 weeks in 21-day cycles.

Reporting group title	Group 2 Cohort 2 - Sequential Dose

Reporting group description:

Participants were administered RO6870810 monotherapy (starting dose 0.45 mg/kg) during the first 14 days of 21-day Run-in period. Following the Run-in period, participants will continue to receive RO6870810 at the same dose in combination with fixed dose of atezolizumab 1200 mg IV every 3 weeks in 21-day cycles.

Reporting group title	Group 3 - Expansion in TNBC Group

Reporting group description:

Participants were administered dose of RO6870810 established in Group 1 (either 0.3 mg/kg, 0.45 mg/kg, or 0.65 mg/kg) SC QD along with fixed dose of atezolizumab 1200 mg IV on Day 1 of each cycle (21 day cycles), every 3 weeks. RO6870810 will be given during the first 14 days.

Reporting group title	Group 4 - Expansion in OC Group

Reporting group description:

Participants were administered dose of RO6870810 established in Group 1 (either 0.3 mg/kg, 0.45 mg/kg, or 0.65 mg/kg) SC QD along with fixed dose of atezolizumab 1200 mg IV on Day 1 of each cycle (21 day cycles), every 3 weeks. RO6870810 will be given during the first 14 days.

Serious adverse events	Group 1 Cohort 1 - Escalation Dose	Group 1 Cohort 3 - Escalation Dose	Group 1 Cohort 2 - Escalation Dose
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 4 (75.00%)	5 / 6 (83.33%)	4 / 7 (57.14%)
number of deaths (all causes)	3	3	2
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Post procedural haemorrhage			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Myocarditis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			

subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Autoimmune disorder			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Systemic immune activation			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0

deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mental status changes			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Infected bite			

subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Group 2 Cohort 1 - Sequential Dose	Group 2 Cohort 2 - Sequential Dose	Group 3 - Expansion in TNBC Group
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 4 (25.00%)	4 / 6 (66.67%)	2 / 3 (66.67%)
number of deaths (all causes)	4	1	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Post procedural haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0

deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Myocarditis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Autoimmune disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Systemic immune activation			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	2 / 3 (66.67%)
occurrences causally related to treatment / all	0 / 0	1 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			

Chest pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Confusional state			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mental status changes			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Small intestinal obstruction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Infected bite			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Group 4 - Expansion in OC Group		
Total subjects affected by serious adverse events			

subjects affected / exposed	2 / 6 (33.33%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Post procedural haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Myocarditis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypoxia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonitis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		

deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Autoimmune disorder			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Systemic immune activation			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fatigue			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Mental status changes			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intestinal obstruction			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Small intestinal obstruction			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Infected bite			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		

deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Upper respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Group 1 Cohort 1 - Escalation Dose	Group 1 Cohort 3 - Escalation Dose	Group 1 Cohort 2 - Escalation Dose
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)	6 / 6 (100.00%)	7 / 7 (100.00%)
Vascular disorders			
Embolism			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Flushing			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Haematoma			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hot flush			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
Hypertension			
subjects affected / exposed	0 / 4 (0.00%)	2 / 6 (33.33%)	0 / 7 (0.00%)
occurrences (all)	0	2	0

Hypotension			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	2 / 7 (28.57%)
occurrences (all)	0	0	2
Lymphoedema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Orthostatic hypotension			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Catheter site haematoma			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Catheter site pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Chills			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Early satiety			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Fatigue			
subjects affected / exposed	2 / 4 (50.00%)	4 / 6 (66.67%)	4 / 7 (57.14%)
occurrences (all)	2	5	4
Influenza like illness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Injection site reaction			
subjects affected / exposed	3 / 4 (75.00%)	4 / 6 (66.67%)	4 / 7 (57.14%)
occurrences (all)	10	8	13
Oedema peripheral			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Pyrexia			

subjects affected / exposed	3 / 4 (75.00%)	2 / 6 (33.33%)	4 / 7 (57.14%)
occurrences (all)	4	2	4
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Insomnia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Female genital tract fistula			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Vaginal haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Vulval oedema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0

Blood creatinine increased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Electrocardiogram T wave abnormal			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
International normalised ratio increased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Weight decreased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 4 (25.00%)	1 / 6 (16.67%)	3 / 7 (42.86%)
occurrences (all)	1	2	3
Dysphonia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Dyspnoea			
subjects affected / exposed	2 / 4 (50.00%)	2 / 6 (33.33%)	4 / 7 (57.14%)
occurrences (all)	3	3	4
Nasal dryness			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
Oropharyngeal pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Pleural effusion			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0

Rhinitis allergic			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Throat irritation			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 4 (25.00%)	1 / 6 (16.67%)	2 / 7 (28.57%)
occurrences (all)	1	1	4
Lymphadenopathy			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Neutropenia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Thrombocytopenia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
Nervous system disorders			
Balance disorder			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Dizziness			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Dysgeusia			
subjects affected / exposed	1 / 4 (25.00%)	2 / 6 (33.33%)	1 / 7 (14.29%)
occurrences (all)	1	2	1
Headache			
subjects affected / exposed	1 / 4 (25.00%)	2 / 6 (33.33%)	1 / 7 (14.29%)
occurrences (all)	2	2	1
Hypoaesthesia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Migraine			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)

occurrences (all)	0	0	1
Neuralgia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Neuropathy peripheral			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Optic neuritis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Paraesthesia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Presyncope			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Restless legs syndrome			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Taste disorder			
subjects affected / exposed	1 / 4 (25.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	1	2	0
Eye disorders			
Dry eye			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
Eye pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Eyelid function disorder			

subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Eyelid rash			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Keratitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Vision blurred			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Vitreous floaters			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Abdominal pain			
subjects affected / exposed	1 / 4 (25.00%)	1 / 6 (16.67%)	2 / 7 (28.57%)
occurrences (all)	1	1	2
Abdominal pain upper			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Anal incontinence			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Autoimmune colitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Constipation			
subjects affected / exposed	1 / 4 (25.00%)	1 / 6 (16.67%)	3 / 7 (42.86%)
occurrences (all)	1	1	3
Dental caries			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0

Diarrhoea			
subjects affected / exposed	2 / 4 (50.00%)	4 / 6 (66.67%)	4 / 7 (57.14%)
occurrences (all)	3	4	5
Dry mouth			
subjects affected / exposed	1 / 4 (25.00%)	4 / 6 (66.67%)	3 / 7 (42.86%)
occurrences (all)	2	4	3
Dyspepsia			
subjects affected / exposed	1 / 4 (25.00%)	1 / 6 (16.67%)	1 / 7 (14.29%)
occurrences (all)	1	1	1
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	3 / 4 (75.00%)	3 / 6 (50.00%)	2 / 7 (28.57%)
occurrences (all)	3	4	2
Stomatitis			
subjects affected / exposed	0 / 4 (0.00%)	2 / 6 (33.33%)	2 / 7 (28.57%)
occurrences (all)	0	2	2
Vomiting			
subjects affected / exposed	2 / 4 (50.00%)	1 / 6 (16.67%)	3 / 7 (42.86%)
occurrences (all)	2	1	4
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Dermatitis acneiform			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Dry skin			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Eczema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Hyperhidrosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)

occurrences (all)	0	0	1
Pain of skin			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Pruritus			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Rash			
subjects affected / exposed	1 / 4 (25.00%)	1 / 6 (16.67%)	2 / 7 (28.57%)
occurrences (all)	1	1	2
Rash maculo-papular			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	1 / 7 (14.29%)
occurrences (all)	0	2	1
Skin induration			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Skin lesion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Back pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Flank pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Groin pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Muscle fatigue			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0

Muscle spasms			
subjects affected / exposed	1 / 4 (25.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Muscular weakness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Musculoskeletal pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	1 / 4 (25.00%)	1 / 6 (16.67%)	2 / 7 (28.57%)
occurrences (all)	1	2	3
Pain in extremity			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 4 (50.00%)	4 / 6 (66.67%)	3 / 7 (42.86%)
occurrences (all)	3	5	3
Dehydration			
subjects affected / exposed	2 / 4 (50.00%)	1 / 6 (16.67%)	3 / 7 (42.86%)
occurrences (all)	2	1	5
Hyperglycaemia			
subjects affected / exposed	0 / 4 (0.00%)	2 / 6 (33.33%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Hyperkalaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	0 / 4 (0.00%)	2 / 6 (33.33%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Hypomagnesaemia			
subjects affected / exposed	1 / 4 (25.00%)	1 / 6 (16.67%)	2 / 7 (28.57%)

occurrences (all)	1	1	2
Hyponatraemia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	2 / 7 (28.57%)
occurrences (all)	1	0	2
Hypophosphataemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Abdominal infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Anal infection			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Conjunctivitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Cystitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Gastroenteritis viral			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Genital herpes			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Herpes simplex			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	1 / 4 (25.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Injection site infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Oral herpes			

subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
Upper respiratory tract infection			
subjects affected / exposed	1 / 4 (25.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Urinary tract infection			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Varicella zoster virus infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Group 2 Cohort 1 - Sequential Dose	Group 2 Cohort 2 - Sequential Dose	Group 3 - Expansion in TNBC Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)	6 / 6 (100.00%)	3 / 3 (100.00%)
Vascular disorders			
Embolism			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Flushing			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Haematoma			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hot flush			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypotension			
subjects affected / exposed	2 / 4 (50.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Lymphoedema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)

occurrences (all)	0	0	1
Orthostatic hypotension			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
General disorders and administration site conditions			
Catheter site haematoma			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Catheter site pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 4 (0.00%)	2 / 6 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Early satiety			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	3 / 4 (75.00%)	5 / 6 (83.33%)	1 / 3 (33.33%)
occurrences (all)	4	7	1
Influenza like illness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Injection site reaction			
subjects affected / exposed	3 / 4 (75.00%)	4 / 6 (66.67%)	2 / 3 (66.67%)
occurrences (all)	6	13	8
Oedema peripheral			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 4 (0.00%)	2 / 6 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Insomnia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Female genital tract fistula			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vaginal haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Vulval oedema			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Alanine aminotransferase increased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Blood bilirubin increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram T wave abnormal			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)

occurrences (all)	0	0	0
International normalised ratio increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 4 (0.00%)	3 / 6 (50.00%)	1 / 3 (33.33%)
occurrences (all)	0	3	1
Dysphonia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Dyspnoea			
subjects affected / exposed	0 / 4 (0.00%)	2 / 6 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Nasal dryness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rhinitis allergic			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Throat irritation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)

occurrences (all)	0	0	0

Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Lymphadenopathy			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Balance disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	1 / 4 (25.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Dysgeusia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	1 / 4 (25.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Hypoaesthesia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Migraine			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Neuralgia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)

occurrences (all)	1	0	0
Neuropathy peripheral			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Optic neuritis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Presyncope			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Restless legs syndrome			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Syncope			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Taste disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Dry eye			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Eye pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Eyelid function disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eyelid rash			

subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Keratitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vitreous floaters			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	0 / 4 (0.00%)	3 / 6 (50.00%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Abdominal pain upper			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Anal incontinence			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Autoimmune colitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Dental caries			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	1 / 4 (25.00%)	3 / 6 (50.00%)	1 / 3 (33.33%)
occurrences (all)	2	3	1

Dry mouth			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Dyspepsia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Nausea			
subjects affected / exposed	1 / 4 (25.00%)	3 / 6 (50.00%)	0 / 3 (0.00%)
occurrences (all)	2	3	0
Stomatitis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	2 / 4 (50.00%)	2 / 6 (33.33%)	0 / 3 (0.00%)
occurrences (all)	2	2	0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Dermatitis acneiform			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eczema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pain of skin			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)

occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	2 / 4 (50.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	2	0	1
Rash			
subjects affected / exposed	1 / 4 (25.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Rash maculo-papular			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Skin induration			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Skin lesion			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Back pain			
subjects affected / exposed	1 / 4 (25.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Flank pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Groin pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Muscle fatigue			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Muscle spasms			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1

Muscular weakness			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Musculoskeletal chest pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Myalgia			
subjects affected / exposed	2 / 4 (50.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	2	1	0
Pain in extremity			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 4 (50.00%)	1 / 6 (16.67%)	1 / 3 (33.33%)
occurrences (all)	2	1	1
Dehydration			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hyperglycaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperkalaemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hypokalaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypomagnesaemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hyponatraemia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	2 / 3 (66.67%)

occurrences (all)	1	0	2
Hypophosphataemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Abdominal infection			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Anal infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Cystitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis viral			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Genital herpes			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Herpes simplex			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Herpes zoster			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Injection site infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			

subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Varicella zoster virus infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Group 4 - Expansion in OC Group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)		
Vascular disorders			
Embolism			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Flushing			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Haematoma			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hot flush			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hypertension			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hypotension			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Lymphoedema			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Orthostatic hypotension			
subjects affected / exposed	0 / 6 (0.00%)		

occurrences (all)	0		

General disorders and administration site conditions			
Catheter site haematoma			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Catheter site pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Chills			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Early satiety			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Fatigue			
subjects affected / exposed	4 / 6 (66.67%)		
occurrences (all)	4		
Influenza like illness			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Injection site reaction			
subjects affected / exposed	4 / 6 (66.67%)		
occurrences (all)	7		
Oedema peripheral			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Insomnia			
subjects affected / exposed	0 / 6 (0.00%)		

occurrences (all)	0		

Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Female genital tract fistula			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Vaginal haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Vulval oedema			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Alanine aminotransferase increased			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Blood bilirubin increased			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Blood creatinine increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Electrocardiogram T wave abnormal			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		

International normalised ratio increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Weight decreased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Dysphonia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Dyspnoea			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Nasal dryness			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Oropharyngeal pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Pleural effusion			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Rhinitis allergic			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Throat irritation			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Lymphadenopathy			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Neutropenia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Thrombocytopenia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Nervous system disorders			
Balance disorder			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Dizziness			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Dysgeusia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Headache			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hypoaesthesia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Migraine			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Neuralgia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Neuropathy peripheral			
subjects affected / exposed	0 / 6 (0.00%)		

occurrences (all)	0		
Optic neuritis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Paraesthesia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Presyncope			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Restless legs syndrome			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Syncope			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Taste disorder			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Eye disorders			
Dry eye			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Eye pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Eyelid function disorder			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Eyelid rash			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Keratitis			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Vision blurred			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Vitreous floaters			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Abdominal pain			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Abdominal pain upper			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Anal incontinence			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Autoimmune colitis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Constipation			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Dental caries			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	3 / 6 (50.00%)		
occurrences (all)	3		
Dry mouth			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		

Dyspepsia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Gastrooesophageal reflux disease subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Nausea subjects affected / exposed occurrences (all)	4 / 6 (66.67%) 5		
Stomatitis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Vomiting subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1		
Renal and urinary disorders Acute kidney injury subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Skin and subcutaneous tissue disorders Dermatitis acneiform subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Dry skin subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Eczema subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Hyperhidrosis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Pain of skin subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Pruritus subjects affected / exposed	1 / 6 (16.67%)		

occurrences (all)	1		
Rash			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Rash maculo-papular			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Skin induration			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Skin lesion			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Back pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Flank pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Groin pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Muscle fatigue			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Muscle spasms			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Muscular weakness			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		

Musculoskeletal chest pain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Musculoskeletal pain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Myalgia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Pain in extremity subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	2 / 6 (33.33%) 2		
Dehydration subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Hyperglycaemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Hyperkalaemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Hypokalaemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Hypomagnesaemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Hyponatraemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Hypophosphataemia subjects affected / exposed	0 / 6 (0.00%)		

occurrences (all)	0		

Infections and infestations			
Abdominal infection			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Anal infection			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Conjunctivitis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Cystitis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Gastroenteritis viral			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Genital herpes			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Herpes simplex			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Herpes zoster			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Injection site infection			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Oral herpes			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		

Urinary tract infection subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Varicella zoster virus infection subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 July 2017	The IND number has been updated from 119114 to 136123 (title page and Protocol Acceptance Form).
24 April 2018	Expansion Groups 3 and 4 have been added; Inclusion criteria have been updated

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Due to the early termination of study NP39487, the planned PK/PD, biomarker and immunogenicity analyses were not performed for this sCSR. Only OR is presented. No other efficacy parameters (PFS, OS, OR, DoR) were analyzed.

Notes: