Clinical trial results:
A randomized phase II study of MCS110 combined with carboplatin and gemcitabine in advanced Triple Negative Breast Cancer (TNBC)

Summary

EudraCT number	2015-000179-29
Trial protocol	CZ DE AT ES BE FR IT
Global end of trial date	23 March 2020

Results information

Result version number	v1 (current)
This version publication date	02 April 2021
First version publication date	02 April 2021

Trial information

Trial identification

Sponsor protocol code	CMCS110Z2201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02435680
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, novartis.email@novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, novartis.email@novartis.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	23 March 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	23 March 2020
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main objective for this trial was to assess the anti-tumor activity of MCS110 combined with carboplatin/gemcitabine, as compared to carboplatin/gemcitabine alone, by comparing progression-free survival (PFS) as per response evaluation criteria in solid tumors (RECIST) (v) 1.1

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 August 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 5
Country: Number of subjects enrolled	Austria: 4
Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	France: 8
Country: Number of subjects enrolled	Germany: 9
Country: Number of subjects enrolled	Hong Kong: 2
Country: Number of subjects enrolled	Italy: 4
Country: Number of subjects enrolled	Korea, Republic of: 4
Country: Number of subjects enrolled	Spain: 7
Country: Number of subjects enrolled	Taiwan: 1
Country: Number of subjects enrolled	Turkey: 1
Country: Number of subjects enrolled	United States: 4
Worldwide total number of subjects	50
EEA total number of subjects	33

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	37
From 65 to 84 years	13
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

In total, 50 subjects were enrolled into the study and 49 subjects received study treatment.
Number of subjects in Safety Set and PK set was higher than in Full Analysis Set for the MCS110 Arm with additional MCS110 dose on C1D8. Explanations in screening details field.

Pre-assignment

Screening details:

This was because some subjects received MCS110 dose on C1D8, while it was already instructed to the sites (after first safety review meeting) to omit this dose. These were reported as protocol deviations.
- MCS110+carbo+gem PK/safety set:19
- MCS110+C1D8+carbo+gem PK/safety:15
- Carbo/Gem PK/safety:15

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	MCS110+carboplatin+gemcitabine

Arm description:
experimental

Arm type	Experimental
Investigational medicinal product name	MCS110
Investigational medicinal product code	MCS110
Other name	lacnotuzumab
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:
MCS110 Intravenous (iv) infusion 10, 5 or 2.5 mg/kg Day 1

Arm title	MCS110 with C1D8 dose+carboplatin+gemcitabine

Arm description:
experimental

Arm type	Experimental
Investigational medicinal product name	MCS110
Investigational medicinal product code	MCS110
Other name	lacnotuzumab
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:
MCS110 Intravenous (iv) infusion 10, 5 or 2.5 mg/kg Day 1 with additional dose on C1D8

Arm title	carboplatin+gemcitabine

Arm description:
comparator

Arm type	Active comparator

Investigational medicinal product name	carboplatin, gemcitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

- Gemcitabine iv infusion 1000 mg/m2 Days 1 & 8
- Carboplatin iv infusion AUC 2 Days 1 & 8. Area under curve (AUC) 2 dose in milligrams = AUC x (Glomerular filtration rate + 25) according to Calvert's formula.

Number of subjects in period 1	MCS110+carboplatin+gemcitabine	MCS110 with C1D8 dose+carboplatin+gemcitabine	carboplatin+gemcitabine
Started	21	13	16
Completed	0	0	0
Not completed	21	13	16
Physician decision	3	-	-
not treated	-	-	1
Adverse event, non-fatal	8	3	2
progressive disease	10	7	11
subject / guardian decision	-	3	2

Baseline characteristics

Reporting groups	
Reporting group title	MCS110+carboplatin+gemcitabine
Reporting group description: experimental	
Reporting group title	MCS110 with C1D8 dose+carboplatin+gemcitabine
Reporting group description: experimental	
Reporting group title	carboplatin+gemcitabine
Reporting group description: comparator	

Reporting group values	MCS110+carboplatin+gemcitabine	MCS110 with C1D8 dose+carboplatin+gemcitabine	carboplatin+gemcitabine
Number of subjects	21	13	16
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)	15	10	12
From 65-84 years	6	3	4
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	55.5	56.2	55.1
standard deviation	± 13.20	± 12.97	± 13.20
Sex: Female, Male Units: participants			
Female	21	13	16
Male	0	0	0
Race/Ethnicity, Customized Units: Subjects			
Caucasian	15	10	11
Asian	2	2	3
Unknown	3	1	1
Other	1	0	1

Reporting group values	Total		
Number of subjects	50		
Age categorical Units: Subjects			
In utero	0		

Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	37		
From 65-84 years	13		
85 years and over	0		
Age Continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male			
Units: participants			
Female	50		
Male	0		
Race/Ethnicity, Customized			
Units: Subjects			
Caucasian	36		
Asian	7		
Unknown	5		
Other	2		

End points

End points reporting groups

Reporting group title	MCS110+carboplatin+gemcitabine
Reporting group description: experimental	
Reporting group title	MCS110 with C1D8 dose+carboplatin+gemcitabine
Reporting group description: experimental	
Reporting group title	carboplatin+gemcitabine
Reporting group description: comparator	
Subject analysis set title	All MCS110+Carbo+Gem participants
Subject analysis set type	Per protocol
Subject analysis set description: experimental	
Subject analysis set title	gemcitabine+carboplatin
Subject analysis set type	Per protocol
Subject analysis set description: comparator	
Subject analysis set title	MCS110+carbo/gem safety and PK set
Subject analysis set type	Safety analysis
Subject analysis set description: experimental	
Subject analysis set title	MCS110+C1D8+carbo/gem safety and PK set
Subject analysis set type	Safety analysis
Subject analysis set description: experimental	

Primary: Progression free survival (PFS) as per RECIST v1.1 (by local investigator assessment)

End point title	Progression free survival (PFS) as per RECIST v1.1 (by local investigator assessment)[1][2]
End point description:	
End point type	Primary
End point timeframe: 4 years	

Notes:

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

[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 was performed

End point values	MCS110 with C1D8 dose+carboplatin+gemcitabine	carboplatin+gemcitabine	All MCS110+Carbo+Gem participants	gemcitabine+carboplatin
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	13[3]	16[4]	34	16
Units: months				
median (confidence interval 90%)				
25th percentile	0 (0 to 0)	0 (0 to 0)	4.3 (1.8 to 4.7)	3.5 (1.0 to 4.5)
median	0 (0 to 0)	0 (0 to 0)	5.6 (4.5 to 8.7)	5.5 (3.5 to 7.5)
75th percentile	0 (0 to 0)	0 (0 to 0)	10.9 (6.0 to 44.0)	7.7 (6.4 to 14.5)

Notes:

[3] - All MCS participants (13 +21) were analyzed together. Refer to the subject analysis set

[4] - Refer to the subject analysis set

Statistical analyses

No statistical analyses for this end point

Secondary: Free MCS110 : derived Pharmacokinetics (PK) parameters: AUCtau

End point title	Free MCS110 : derived Pharmacokinetics (PK) parameters: AUCtau[5]

End point description:

AUC tau derived from day 0 to 21 (cycle 1) from day 0 to 21 (cycle 4) Cycle duration is 21 days. PK set.

End point type	Secondary

End point timeframe:

day 21 (end cycle 1); day 84 (end cycle 4)

Notes:

[5] - 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 was performed

End point values	MCS110+carboplatin+gemcitabine	MCS110 with C1D8 dose+carboplatin+gemcitabine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	9		
Units: day x microgram / mL				
geometric mean (geometric coefficient of variation)				
day 21	1430 (± 23.5)	2960 (± 22.7)		
day 84	1840 (± 34.9)	3240 (± 30.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Free MCS110 : derived Pharmacokinetics (PK) parameters: Cmax

End point title	Free MCS110 : derived Pharmacokinetics (PK) parameters: Cmax[6]

End point description:	
PK set.	
End point type	Secondary
End point timeframe:	
day 21 (end cycle 1); day 84 (end cycle 4)	

Notes:

[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 was performed

End point values	MCS110+carboplatin+gemcitabine	MCS110 with C1D8 dose+carboplatin+gemcitabine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	12		
Units: microgram / mL				
geometric mean (geometric coefficient of variation)				
day 21	186 (± 28.5)	281 (± 21.2)		
day 84	240 (± 14.8)	319 (± 27.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax derived from Plasma concentration of carboplatin, gemcitabine and 2',2'-difluoro-deoxyuridine (dFdU)

End point title	Cmax derived from Plasma concentration of carboplatin, gemcitabine and 2',2'-difluoro-deoxyuridine (dFdU)
End point description:	
day 21 (end cycle 1); day 84 (end cycle 4)	
End point type	Secondary
End point timeframe:	
day 21, day 84	

End point values	MCS110+carboplatin+gemcitabine	MCS110 with C1D8 dose+carboplatin+gemcitabine	carboplatin+gemcitabine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	16	13	14	
Units: nanogram /mL				
geometric mean (geometric coefficient of variation)				
Cmax Carboplatin Day 21	12400 (± 37.3)	12500 (± 33.2)	11200 (± 70.9)	
Cmax Carboplatin Day 84	9550 (± 33.0)	10000 (± 28.9)	11600 (± 55.0)	
Cmax Gemcitabine Day 21	2750 (± 194.5)	5480 (± 95.1)	2370 (± 484.9)	
Cmax Gemcitabine Day 84	2470 (± 227.3)	3400 (± 173.9)	8630 (± 101.2)	
Cmax dFdU Day 21	39100 (± 21.6)	33900 (± 19.5)	37700 (± 28.2)	

Cmax dFdU Day 84	36600 (± 88.6)	30300 (± 11.8)	32300 (± 12.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: AUClast derived from Plasma concentration of carboplatin, gemcitabine and 2',2'-difluoro-deoxyuridine (dFdU)

End point title	AUClast derived from Plasma concentration of carboplatin, gemcitabine and 2',2'-difluoro-deoxyuridine (dFdU)
End point description: day 21 (end cycle 1); day 84 (end cycle 4)	
End point type	Secondary
End point timeframe: day 21, day 84	

End point values	MCS110+carboplatin+gemcitabine	MCS110 with C1D8 dose+carboplatin+gemcitabine	carboplatin+gemcitabine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	16	13	14	
Units: hours * nanogram /mL				
geometric mean (geometric coefficient of variation)				
AUC Carboplatin Day 21	24500 (± 31.1)	21400 (± 27.3)	21800 (± 56.0)	
AUC Carboplatin Day 84	18300 (± 21.8)	17500 (± 25.0)	20500 (± 34.6)	
AUC Gemcitabine Day 21	2390 (± 157.3)	4270 (± 79.3)	2620 (± 225.5)	
AUC Gemcitabine Day 84	2410 (± 115.2)	2770 (± 118.8)	6320 (± 76.2)	
AUC dFdU Day 21	230000 (± 34.7)	181000 (± 37.7)	231000 (± 25.2)	
AUC dFdU Day 84	229000 (± 31.9)	147000 (± 28.7)	211000 (± 24.7)	

Statistical analyses

No statistical analyses for this end point

Secondary: Total Colony stimulation factor -1 (CSF-I) circulating levels

End point title	Total Colony stimulation factor -1 (CSF-I) circulating levels[7]
End point description: results expressed as a the ratio change from baseline expressed in percentage. Absolute values were expressed in pg/mL. Cycle duration is 21 days. Safety set.	
End point type	Secondary

End point timeframe:

baseline, day 1, 4, 15, 22, 43, 64, 85, 106, 127, 148

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 was performed

End point values	MCS110+carboplatin+gemcitabine	MCS110 with C1D8 dose+carboplatin+gemcitabine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	13		
Units: % change from baseline				
arithmetic mean (standard deviation)				
Day 1	110 (± 19.8)	115 (± 34.8)		
Day 4	4930 (± 2280)	4350 (± 1620)		
Day 15	21600 (± 8290)	19500 (± 6130)		
Day 22 (cycle 2 day 1)	32000 (± 9190)	34400 (± 14900)		
Day 43 (cycle 3 day 1)	57900 (± 14100)	70000 (± 27400)		
Day 64 (cycle 4 day 1)	73600 (± 16200)	78000 (± 41200)		
Day 85 (cycle 5 day 1)	79300 (± 27000)	107000 (± 51400)		
Day 106 (cycle 6 day 1)	97500 (± 15600)	103000 (± 50700)		
Day 127 (cycle 7 day 1)	110000 (± 33800)	109000 (± 40100)		
Day 148 (cycle 8 day 1)	108000 (± 30300)	111000 (± 58800)		

Statistical analyses

No statistical analyses for this end point

Secondary: Serum C-terminal telopeptide of type I collagen (CTX-I)

End point title	Serum C-terminal telopeptide of type I collagen (CTX-I)[8]

End point description:

results expressed as a the ratio change from baseline expressed in percentage. Absolute values were expressed in ng/mL. Cycle duration is 21 days. Safety set.

End point type	Secondary

End point timeframe:

baseline, day 2, 4, 15, 22, 43, 64, 85, 106, 127, 148

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 was performed

End point values	MCS110+carboplatin+gemcitabine	MCS110 with C1D8 dose+carboplatin+gemcitabine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	12		
Units: % change from baseline				
arithmetic mean (standard deviation)				
Day 2	79.4 (± 22.8)	85.0 (± 44.0)		
Day 4	72.5 (± 25.4)	80.2 (± 39.6)		
Day 15	65.6 (± 44.3)	69.4 (± 27.4)		
Day 22 (cycle 2 day 1)	67.9 (± 43.6)	52.9 (± 26.5)		
Day 43 (cycle 3 day 1)	64.3 (± 58.7)	39.3 (± 23.8)		
Day 64 (cycle 4 day 1)	69.7 (± 62.2)	29.5 (± 23.7)		
Day 85 (cycle 5 day 1)	102 (± 124)	40.6 (± 34.8)		
Day 106 (cycle 6 day 1)	41.2 (± 13.2)	50.2 (± 45.3)		
Day 127 (cycle 7 day 1)	38.7 (± 14.9)	68.7 (± 66.5)		
Day 148 (cycle 8 day 1)	40.5 (± 13.7)	75.3 (± 103)		

Statistical analyses

No statistical analyses for this end point

Secondary: Tumor response per RECIST v1.1 (by local investigator assessment)

End point title	Tumor response per RECIST v1.1 (by local investigator assessment)[9]

End point description:

CR: complete response. PR: partial response. SD: stable disease: CBR: clinical benefit rate =CR + PR + SD lasting at least for 6 months. ORR = CR + PR

End point type	Secondary

End point timeframe:

4 years

Notes:

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

End point values	MCS110 with C1D8 dose+carboplatin+gemcitabine	carboplatin+gemcitabine	All MCS110+Carbo+Gem participants	gemcitabine+carboplatin
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	13[10]	16[11]	34	16
Units: participants				
PR	0	0	8	6
Non-CR/ Non-progressive disease	0	0	1	0
SD	0	0	19	7
progressive disease	0	0	4	1
unknown	0	0	2	2
clinical benefit	0	0	10	7
ORR	0	0	8	6

Notes:

[10] - All MCS110 participants were analyzed together. Refer to the subject analysis set

[11] - Refer to the subject analysis set

Statistical analyses

No statistical analyses for this end point

Secondary: Tumor response per RECIST v1.1 (by local investigator assessment) Duration of response

End point title	Tumor response per RECIST v1.1 (by local investigator assessment) Duration of response[12]

End point description:

9.6 months [90% CI: 3.6, 42.5]) as compared Arm 2 (5.0 months [90% CI: 2.7, 13.3]

End point type	Secondary

End point timeframe:

4 years

Notes:

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

End point values	MCS110 with C1D8 dose+carboplatin+gemcitabine	carboplatin+gemcitabine	All MCS110+Carbo+Gem participants	gemcitabine+carboplatin
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	13[13]	16[14]	34	16
Units: months				
median (confidence interval 90%)	0 (0 to 0)	0 (0 to 0)	9.6 (3.6 to 42.5)	5 (2.7 to 13.3)

Notes:

[13] - All MCS110 participants (34) were analyzed together. Refer to the subject analysis set

[14] - Refer to the subject analysis set

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with at least one dose reduction, and number of patients with at least one dose interruption

End point title	Number of patients with at least one dose reduction, and number of patients with at least one dose interruption[15]

End point description:

Safety set

End point type	Secondary

End point timeframe:

4 years

Notes:

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

End point values	MCS110+carboplatin+gemcitabine	MCS110 with C1D8 dose+carboplatin+gemcitabine	MCS110+carbo/gem safety and PK set	MCS110+C1D8+carbo/gem safety and PK set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	21[16]	13[17]	19	15
Units: participants				
MCS110 dose reduction	0	0	3	5
MCS110 dose interruption	0	0	6	9

Notes:

[16] - please refer to the subject analysis set

[17] - please refer to the subject analysis set

Statistical analyses

No statistical analyses for this end point

Secondary: Dose intensity

End point title	Dose intensity[18]

End point description:

Relative dose intensity by categories. Safety set.

End point type	Secondary

End point timeframe:

4 years

Notes:

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

End point values	MCS110+carboplatin+gemcitabine	MCS110 with C1D8 dose+carboplatin+gemcitabine	MCS110+carbo/gem safety and PK set	MCS110+C1D8+carbo/gem safety and PK set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	21[19]	13[20]	19	15
Units: participants				
<50	0	0	1	4
50-<75	0	0	8	3
75-<90	0	0	7	5
90-<110	0	0	3	3

Notes:

[19] - please refer to the subject analysis set

[20] - please refer to the subject analysis set

Statistical analyses

No statistical analyses for this end point

Secondary: Tumor associated macrophage (TAM) and Tumor infiltrating lymphocyte (TIL) content in pre- and post-dose tumor biopsies.

End point title	Tumor associated macrophage (TAM) and Tumor infiltrating lymphocyte (TIL) content in pre- and post-dose tumor biopsies.[21]

End point description:

results expressed as a the ratio change from baseline expressed in percentage: Biopsies were taken at baseline and between Day 29 and Day 43. Safety set.

End point type	Secondary

End point timeframe:

Baseline, Day 29-43

Notes:

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

End point values	MCS110+carboplatin+gemcitabine	MCS110 with C1D8 dose+carboplatin+gemcitabine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	5		
Units: % change from baseline				
geometric mean (geometric coefficient of variation)				
CD163	42.1 (± 62.1)	43.5 (± 239.5)		
CD8	102 (± 747.3)	99.0 (± 92.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Circulating monocytes cells in blood

End point title	Circulating monocytes cells in blood[22]

End point description:

Cycle duration is 21 days results expressed in percentage of cells. Results available for 1 patient only. Safety set.

End point type	Secondary

End point timeframe:

day 15, 29, 43, 50

Notes:

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

End point values	MCS110 with C1D8 dose+carboplatin+gemcitabine			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: percentage				
number (not applicable)				
day 15 CD14+CD16-	43.5			
day 15 CD14+CD16+	54.8			
day 29 (cycle 2 day 8) CD14+CD16-	86.6			
day 29 (cycle 2 day 8) CD14+CD16+	12.2			
day 43 (cycle 3 day 1) CD14+CD16-	9.1			
day 43 (cycle 3 day 1) CD14+CD16+	89.7			
day 50 (cycle 3 day 8) CD14+CD16-	86			
day 50 (cycle 3 day 8) CD14+CD16+	10			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Adverse events and serious adverse events were collected from the first patient first visit until the last patient last visit.	
Adverse event reporting additional description: AE additional description	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	23.0
Reporting groups	
Reporting group title	MCS110 + Carbo/Gem
Reporting group description: MCS110 + Carbo/Gem	
Reporting group title	MCS110 with C1D8@dose + Carbo/Gem
Reporting group description: MCS110 with C1D8@dose + Carbo/Gem	
Reporting group title	All MCS110 + @Carbo/Gem Patients
Reporting group description: All MCS110 + @Carbo/Gem Patients	
Reporting group title	Carbo/Gem
Reporting group description: Carbo/Gem	
Reporting group title	All@Patients
Reporting group description: All@Patients	

Serious adverse events	MCS110 + Carbo/Gem	MCS110 with C1D8@dose + Carbo/Gem	All MCS110 + @Carbo/Gem Patients
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 19 (52.63%)	7 / 15 (46.67%)	17 / 34 (50.00%)
number of deaths (all causes)	1	1	2
number of deaths resulting from adverse events	1	1	2
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour associated fever			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour pain			

subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive crisis			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Generalised oedema			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 19 (5.26%)	2 / 15 (13.33%)	3 / 34 (8.82%)
occurrences causally related to treatment / all	0 / 1	1 / 3	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			

subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung disorder			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Ankle fracture			

subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Myocardial ischaemia			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atypical haemolytic uraemic syndrome			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 19 (0.00%)	3 / 15 (20.00%)	3 / 34 (8.82%)
occurrences causally related to treatment / all	0 / 0	4 / 4	4 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obstructive pancreatitis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 19 (0.00%)	2 / 15 (13.33%)	2 / 34 (5.88%)
occurrences causally related to treatment / all	0 / 0	1 / 2	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	1 / 19 (5.26%)	1 / 15 (6.67%)	2 / 34 (5.88%)
occurrences causally related to treatment / all	1 / 1	1 / 1	2 / 2
deaths causally related to treatment / all	1 / 1	1 / 1	2 / 2
Infections and infestations			
Device related infection			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Genital infection			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mastitis			

subjects affected / exposed	0 / 19 (0.00%)	0 / 15 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Carbo/Gem	All@Patients	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 15 (6.67%)	18 / 49 (36.73%)	
number of deaths (all causes)	1	3	
number of deaths resulting from adverse events	0	2	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour associated fever			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour pain			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive crisis			

subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
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			
Fatigue			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalised oedema			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
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			
Dyspnoea			
subjects affected / exposed	0 / 15 (0.00%)	3 / 49 (6.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epistaxis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung disorder			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pneumothorax			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Myocardial ischaemia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atypical haemolytic uraemic syndrome			

subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	0 / 15 (0.00%)	3 / 49 (6.12%)	
occurrences causally related to treatment / all	0 / 0	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive pancreatitis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 15 (0.00%)	2 / 49 (4.08%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	0 / 15 (0.00%)	2 / 49 (4.08%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	2 / 2	
Infections and infestations			
Device related infection			

subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Genital infection			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
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 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mastitis			
subjects affected / exposed	1 / 15 (6.67%)	1 / 49 (2.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
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: 0 %

Non-serious adverse events	MCS110 + Carbo/Gem	MCS110 with C1D8@dose + Carbo/Gem	All MCS110 + @Carbo/Gem Patients
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 19 (100.00%)	15 / 15 (100.00%)	34 / 34 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences (all)	0	1	1
Vascular disorders			
Flushing			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	2	0	2
Haematoma			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	2	0	2
Hot flush			
subjects affected / exposed	0 / 19 (0.00%)	0 / 15 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	3 / 19 (15.79%)	1 / 15 (6.67%)	4 / 34 (11.76%)
occurrences (all)	3	5	8
Hypotension			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Jugular vein thrombosis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Peripheral venous disease			
subjects affected / exposed	0 / 19 (0.00%)	0 / 15 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Phlebitis			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences (all)	0	1	1
Poor venous access			

subjects affected / exposed	0 / 19 (0.00%)	0 / 15 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Thrombophlebitis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 15 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Thrombosis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	5 / 19 (26.32%)	3 / 15 (20.00%)	8 / 34 (23.53%)
occurrences (all)	8	4	12
Chest discomfort			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences (all)	0	1	1
Chills			
subjects affected / exposed	2 / 19 (10.53%)	2 / 15 (13.33%)	4 / 34 (11.76%)
occurrences (all)	2	2	4
Device related thrombosis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 15 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Face oedema			
subjects affected / exposed	4 / 19 (21.05%)	3 / 15 (20.00%)	7 / 34 (20.59%)
occurrences (all)	5	3	8
Facial pain			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Fatigue			
subjects affected / exposed	6 / 19 (31.58%)	9 / 15 (60.00%)	15 / 34 (44.12%)
occurrences (all)	6	11	17
Gait disturbance			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences (all)	0	1	1
General physical health deterioration			

subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Influenza like illness			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences (all)	0	2	2
Infusion site extravasation			
subjects affected / exposed	0 / 19 (0.00%)	0 / 15 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Infusion site pain			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences (all)	0	1	1
Injection site reaction			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences (all)	0	1	1
Injection site swelling			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences (all)	0	1	1
Non-cardiac chest pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 15 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	3 / 19 (15.79%)	4 / 15 (26.67%)	7 / 34 (20.59%)
occurrences (all)	4	4	8
Peripheral swelling			
subjects affected / exposed	1 / 19 (5.26%)	1 / 15 (6.67%)	2 / 34 (5.88%)
occurrences (all)	1	2	3
Pyrexia			
subjects affected / exposed	4 / 19 (21.05%)	3 / 15 (20.00%)	7 / 34 (20.59%)
occurrences (all)	4	5	9
Swelling			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Swelling face			
subjects affected / exposed	2 / 19 (10.53%)	0 / 15 (0.00%)	2 / 34 (5.88%)
occurrences (all)	2	0	2
Xerosis			

subjects affected / exposed	0 / 19 (0.00%)	0 / 15 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences (all)	0	1	1
Hypersensitivity			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences (all)	0	1	1
Reproductive system and breast disorders			
Breast oedema			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences (all)	0	1	1
Breast pain			
subjects affected / exposed	1 / 19 (5.26%)	2 / 15 (13.33%)	3 / 34 (8.82%)
occurrences (all)	1	2	3
Menorrhagia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Pelvic pain			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Respiratory, thoracic and mediastinal disorders			
Aphonia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Apnoea			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Bronchospasm			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences (all)	0	1	1
Cough			
subjects affected / exposed	3 / 19 (15.79%)	4 / 15 (26.67%)	7 / 34 (20.59%)
occurrences (all)	4	4	8
Dysphonia			

subjects affected / exposed	2 / 19 (10.53%)	1 / 15 (6.67%)	3 / 34 (8.82%)
occurrences (all)	2	1	3
Dyspnoea			
subjects affected / exposed	6 / 19 (31.58%)	5 / 15 (33.33%)	11 / 34 (32.35%)
occurrences (all)	7	7	14
Epistaxis			
subjects affected / exposed	1 / 19 (5.26%)	3 / 15 (20.00%)	4 / 34 (11.76%)
occurrences (all)	1	8	9
Hypoxia			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences (all)	0	1	1
Nasal congestion			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Pharyngeal oedema			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences (all)	0	1	1
Pleural effusion			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Productive cough			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences (all)	0	1	1
Pulmonary oedema			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences (all)	0	1	1
Rhinorrhoea			
subjects affected / exposed	2 / 19 (10.53%)	0 / 15 (0.00%)	2 / 34 (5.88%)
occurrences (all)	2	0	2
Snoring			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	2	0	2
Upper-airway cough syndrome			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences (all)	0	1	1
Vocal cord polyp			

subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences (all)	0	1	1
Psychiatric disorders			
Anxiety			
subjects affected / exposed	2 / 19 (10.53%)	2 / 15 (13.33%)	4 / 34 (11.76%)
occurrences (all)	2	2	4
Depressed mood			
subjects affected / exposed	1 / 19 (5.26%)	1 / 15 (6.67%)	2 / 34 (5.88%)
occurrences (all)	1	1	2
Depression			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	2	0	2
Hallucination			
subjects affected / exposed	0 / 19 (0.00%)	0 / 15 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	2	0	2
Product issues			
Device dislocation			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences (all)	0	1	1
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	12 / 19 (63.16%)	12 / 15 (80.00%)	24 / 34 (70.59%)
occurrences (all)	17	16	33
Amylase increased			
subjects affected / exposed	1 / 19 (5.26%)	1 / 15 (6.67%)	2 / 34 (5.88%)
occurrences (all)	1	2	3
Aspartate aminotransferase increased			
subjects affected / exposed	16 / 19 (84.21%)	12 / 15 (80.00%)	28 / 34 (82.35%)
occurrences (all)	22	13	35
Blood alkaline phosphatase increased			
subjects affected / exposed	4 / 19 (21.05%)	1 / 15 (6.67%)	5 / 34 (14.71%)
occurrences (all)	4	1	5
Blood creatine phosphokinase MB increased			

subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Blood creatine phosphokinase increased			
subjects affected / exposed	9 / 19 (47.37%)	7 / 15 (46.67%)	16 / 34 (47.06%)
occurrences (all)	9	8	17
Blood creatinine increased			
subjects affected / exposed	1 / 19 (5.26%)	2 / 15 (13.33%)	3 / 34 (8.82%)
occurrences (all)	1	2	3
Blood iron decreased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 15 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	2 / 19 (10.53%)	1 / 15 (6.67%)	3 / 34 (8.82%)
occurrences (all)	2	1	3
C-reactive protein increased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 15 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	5 / 19 (26.32%)	1 / 15 (6.67%)	6 / 34 (17.65%)
occurrences (all)	5	1	6
Haemoglobin decreased			
subjects affected / exposed	1 / 19 (5.26%)	1 / 15 (6.67%)	2 / 34 (5.88%)
occurrences (all)	1	1	2
Hepatic enzyme increased			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	3	0	3
Lipase			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Lipase increased			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences (all)	0	1	1
Lymphocyte count decreased			

subjects affected / exposed	2 / 19 (10.53%)	1 / 15 (6.67%)	3 / 34 (8.82%)
occurrences (all)	3	1	4
Neutrophil count decreased			
subjects affected / exposed	6 / 19 (31.58%)	5 / 15 (33.33%)	11 / 34 (32.35%)
occurrences (all)	16	21	37
Platelet count decreased			
subjects affected / exposed	3 / 19 (15.79%)	3 / 15 (20.00%)	6 / 34 (17.65%)
occurrences (all)	9	28	37
Weight decreased			
subjects affected / exposed	1 / 19 (5.26%)	1 / 15 (6.67%)	2 / 34 (5.88%)
occurrences (all)	1	2	3
Weight increased			
subjects affected / exposed	0 / 19 (0.00%)	2 / 15 (13.33%)	2 / 34 (5.88%)
occurrences (all)	0	2	2
White blood cell count decreased			
subjects affected / exposed	3 / 19 (15.79%)	4 / 15 (26.67%)	7 / 34 (20.59%)
occurrences (all)	7	7	14
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Chemical cystitis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Contusion			
subjects affected / exposed	2 / 19 (10.53%)	1 / 15 (6.67%)	3 / 34 (8.82%)
occurrences (all)	2	1	3
Humerus fracture			
subjects affected / exposed	0 / 19 (0.00%)	0 / 15 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Oral contusion			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences (all)	0	1	1
Post procedural haematoma			

subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Seroma			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	3	0	3
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences (all)	0	1	1
Bradycardia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Palpitations			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Tachycardia			
subjects affected / exposed	1 / 19 (5.26%)	1 / 15 (6.67%)	2 / 34 (5.88%)
occurrences (all)	1	1	2
Nervous system disorders			
Ageusia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Balance disorder			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Dizziness			
subjects affected / exposed	0 / 19 (0.00%)	2 / 15 (13.33%)	2 / 34 (5.88%)
occurrences (all)	0	5	5
Dysaesthesia			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences (all)	0	1	1
Dysgeusia			
subjects affected / exposed	1 / 19 (5.26%)	1 / 15 (6.67%)	2 / 34 (5.88%)
occurrences (all)	1	1	2
Headache			

subjects affected / exposed	4 / 19 (21.05%)	3 / 15 (20.00%)	7 / 34 (20.59%)
occurrences (all)	11	3	14
Myelopathy			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences (all)	0	1	1
Neuralgia			
subjects affected / exposed	2 / 19 (10.53%)	0 / 15 (0.00%)	2 / 34 (5.88%)
occurrences (all)	3	0	3
Neuropathy peripheral			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences (all)	0	1	1
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 19 (0.00%)	3 / 15 (20.00%)	3 / 34 (8.82%)
occurrences (all)	0	3	3
Vocal cord paralysis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	13 / 19 (68.42%)	10 / 15 (66.67%)	23 / 34 (67.65%)
occurrences (all)	22	27	49
Leukocytosis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	2	0	2
Leukopenia			
subjects affected / exposed	1 / 19 (5.26%)	5 / 15 (33.33%)	6 / 34 (17.65%)
occurrences (all)	4	12	16
Neutropenia			
subjects affected / exposed	10 / 19 (52.63%)	8 / 15 (53.33%)	18 / 34 (52.94%)
occurrences (all)	24	20	44
Thrombocytopenia			
subjects affected / exposed	8 / 19 (42.11%)	8 / 15 (53.33%)	16 / 34 (47.06%)
occurrences (all)	16	18	34
Thrombotic thrombocytopenic purpura			

subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences (all)	0	1	1
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 19 (5.26%)	1 / 15 (6.67%)	2 / 34 (5.88%)
occurrences (all)	1	1	2
Eye disorders			
Conjunctival haemorrhage			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences (all)	0	3	3
Diplopia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 15 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Dry eye			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Eye oedema			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences (all)	0	1	1
Eye pain			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Eyelid oedema			
subjects affected / exposed	2 / 19 (10.53%)	0 / 15 (0.00%)	2 / 34 (5.88%)
occurrences (all)	3	0	3
Foreign body sensation in eyes			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Lacrimation increased			
subjects affected / exposed	2 / 19 (10.53%)	1 / 15 (6.67%)	3 / 34 (8.82%)
occurrences (all)	2	1	3
Orbital oedema			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences (all)	0	1	1
Periorbital oedema			

subjects affected / exposed	8 / 19 (42.11%)	6 / 15 (40.00%)	14 / 34 (41.18%)
occurrences (all)	8	8	16
Periorbital swelling			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Vision blurred			
subjects affected / exposed	1 / 19 (5.26%)	1 / 15 (6.67%)	2 / 34 (5.88%)
occurrences (all)	1	1	2
Xerophthalmia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 15 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 19 (0.00%)	0 / 15 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	4 / 19 (21.05%)	3 / 15 (20.00%)	7 / 34 (20.59%)
occurrences (all)	6	3	9
Abdominal pain upper			
subjects affected / exposed	2 / 19 (10.53%)	1 / 15 (6.67%)	3 / 34 (8.82%)
occurrences (all)	2	2	4
Chapped lips			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Constipation			
subjects affected / exposed	5 / 19 (26.32%)	3 / 15 (20.00%)	8 / 34 (23.53%)
occurrences (all)	15	5	20
Diarrhoea			
subjects affected / exposed	5 / 19 (26.32%)	2 / 15 (13.33%)	7 / 34 (20.59%)
occurrences (all)	6	4	10
Dry mouth			
subjects affected / exposed	2 / 19 (10.53%)	0 / 15 (0.00%)	2 / 34 (5.88%)
occurrences (all)	2	0	2
Dyspepsia			
subjects affected / exposed	2 / 19 (10.53%)	1 / 15 (6.67%)	3 / 34 (8.82%)
occurrences (all)	6	1	7

Flatulence			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Gastritis			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences (all)	0	2	2
Gingival bleeding			
subjects affected / exposed	1 / 19 (5.26%)	1 / 15 (6.67%)	2 / 34 (5.88%)
occurrences (all)	1	3	4
Gingival pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 15 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Gingival recession			
subjects affected / exposed	0 / 19 (0.00%)	0 / 15 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Haemorrhoidal haemorrhage			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Lip oedema			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Nausea			
subjects affected / exposed	10 / 19 (52.63%)	12 / 15 (80.00%)	22 / 34 (64.71%)
occurrences (all)	14	22	36
Odynophagia			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences (all)	0	1	1
Periodontal disease			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences (all)	0	1	1
Rectal haemorrhage			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Salivary hypersecretion			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1

Stomatitis			
subjects affected / exposed	2 / 19 (10.53%)	5 / 15 (33.33%)	7 / 34 (20.59%)
occurrences (all)	3	8	11
Vomiting			
subjects affected / exposed	5 / 19 (26.32%)	3 / 15 (20.00%)	8 / 34 (23.53%)
occurrences (all)	9	4	13
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	1 / 19 (5.26%)	2 / 15 (13.33%)	3 / 34 (8.82%)
occurrences (all)	1	2	3
Blood blister			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Dermatitis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Dermatitis acneiform			
subjects affected / exposed	0 / 19 (0.00%)	3 / 15 (20.00%)	3 / 34 (8.82%)
occurrences (all)	0	3	3
Dry skin			
subjects affected / exposed	2 / 19 (10.53%)	2 / 15 (13.33%)	4 / 34 (11.76%)
occurrences (all)	2	2	4
Erythema			
subjects affected / exposed	0 / 19 (0.00%)	3 / 15 (20.00%)	3 / 34 (8.82%)
occurrences (all)	0	3	3
Hyperhidrosis			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences (all)	0	1	1
Nail disorder			
subjects affected / exposed	0 / 19 (0.00%)	0 / 15 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	2 / 19 (10.53%)	3 / 15 (20.00%)	5 / 34 (14.71%)
occurrences (all)	3	3	6
Purpura			

subjects affected / exposed	0 / 19 (0.00%)	0 / 15 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	5 / 19 (26.32%)	5 / 15 (33.33%)	10 / 34 (29.41%)
occurrences (all)	7	8	15
Rash maculo-papular			
subjects affected / exposed	1 / 19 (5.26%)	1 / 15 (6.67%)	2 / 34 (5.88%)
occurrences (all)	1	1	2
Rash pruritic			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Skin fissures			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences (all)	0	1	1
Skin lesion			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences (all)	0	1	1
Stasis dermatitis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Toxic skin eruption			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences (all)	0	1	1
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Dysuria			
subjects affected / exposed	0 / 19 (0.00%)	0 / 15 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Nocturia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Endocrine disorders			
Hypothyroidism			

subjects affected / exposed	2 / 19 (10.53%)	0 / 15 (0.00%)	2 / 34 (5.88%)
occurrences (all)	2	0	2
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 19 (10.53%)	0 / 15 (0.00%)	2 / 34 (5.88%)
occurrences (all)	2	0	2
Back pain			
subjects affected / exposed	1 / 19 (5.26%)	1 / 15 (6.67%)	2 / 34 (5.88%)
occurrences (all)	1	2	3
Bone pain			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences (all)	0	1	1
Fracture pain			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences (all)	0	1	1
Joint swelling			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Muscle spasms			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Muscular weakness			
subjects affected / exposed	0 / 19 (0.00%)	0 / 15 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences (all)	0	1	1
Musculoskeletal pain			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Musculoskeletal stiffness			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Myalgia			

subjects affected / exposed	3 / 19 (15.79%)	1 / 15 (6.67%)	4 / 34 (11.76%)
occurrences (all)	4	1	5
Neck pain			
subjects affected / exposed	1 / 19 (5.26%)	1 / 15 (6.67%)	2 / 34 (5.88%)
occurrences (all)	1	1	2
Pain in extremity			
subjects affected / exposed	2 / 19 (10.53%)	1 / 15 (6.67%)	3 / 34 (8.82%)
occurrences (all)	2	1	3
Soft tissue necrosis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Tendonitis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Infections and infestations			
Bronchitis viral			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Candida infection			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Catheter site infection			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Cellulitis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 15 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Cystitis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Ear infection			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Folliculitis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1

Fungal oesophagitis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Gingivitis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Influenza			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Lower respiratory tract infection			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Lymphangitis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Mastitis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Nail infection			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Oral candidiasis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	4	0	4
Oral herpes			
subjects affected / exposed	1 / 19 (5.26%)	1 / 15 (6.67%)	2 / 34 (5.88%)
occurrences (all)	1	1	2
Oral infection			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Oropharyngeal candidiasis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Pneumonia			
subjects affected / exposed	0 / 19 (0.00%)	2 / 15 (13.33%)	2 / 34 (5.88%)
occurrences (all)	0	3	3

Sinusitis			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences (all)	0	3	3
Spinal cord infection			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Tinea pedis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 15 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Tonsillitis			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences (all)	0	4	4
Upper respiratory tract infection			
subjects affected / exposed	1 / 19 (5.26%)	2 / 15 (13.33%)	3 / 34 (8.82%)
occurrences (all)	2	3	5
Urinary tract infection			
subjects affected / exposed	1 / 19 (5.26%)	2 / 15 (13.33%)	3 / 34 (8.82%)
occurrences (all)	2	2	4
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	3 / 19 (15.79%)	4 / 15 (26.67%)	7 / 34 (20.59%)
occurrences (all)	3	5	8
Dehydration			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences (all)	0	1	1
Fluid retention			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Hypercalcaemia			
subjects affected / exposed	2 / 19 (10.53%)	0 / 15 (0.00%)	2 / 34 (5.88%)
occurrences (all)	2	0	2
Hyperglycaemia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Hypoalbuminaemia			

subjects affected / exposed	1 / 19 (5.26%)	1 / 15 (6.67%)	2 / 34 (5.88%)
occurrences (all)	1	1	2
Hypocalcaemia			
subjects affected / exposed	2 / 19 (10.53%)	0 / 15 (0.00%)	2 / 34 (5.88%)
occurrences (all)	2	0	2
Hypokalaemia			
subjects affected / exposed	2 / 19 (10.53%)	1 / 15 (6.67%)	3 / 34 (8.82%)
occurrences (all)	2	1	3
Hypomagnesaemia			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences (all)	0	1	1
Hyponatraemia			
subjects affected / exposed	2 / 19 (10.53%)	1 / 15 (6.67%)	3 / 34 (8.82%)
occurrences (all)	2	1	3

Non-serious adverse events	Carbo/Gem	All@Patients	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 15 (100.00%)	49 / 49 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Vascular disorders			
Flushing			
subjects affected / exposed	1 / 15 (6.67%)	2 / 49 (4.08%)	
occurrences (all)	1	3	
Haematoma			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	2	
Hot flush			
subjects affected / exposed	1 / 15 (6.67%)	1 / 49 (2.04%)	
occurrences (all)	1	1	
Hypertension			
subjects affected / exposed	0 / 15 (0.00%)	4 / 49 (8.16%)	
occurrences (all)	0	8	
Hypotension			

subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Jugular vein thrombosis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Peripheral venous disease			
subjects affected / exposed	1 / 15 (6.67%)	1 / 49 (2.04%)	
occurrences (all)	1	1	
Phlebitis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Poor venous access			
subjects affected / exposed	1 / 15 (6.67%)	1 / 49 (2.04%)	
occurrences (all)	1	1	
Thrombophlebitis			
subjects affected / exposed	2 / 15 (13.33%)	2 / 49 (4.08%)	
occurrences (all)	2	2	
Thrombosis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	4 / 15 (26.67%)	12 / 49 (24.49%)	
occurrences (all)	6	18	
Chest discomfort			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Chills			
subjects affected / exposed	0 / 15 (0.00%)	4 / 49 (8.16%)	
occurrences (all)	0	4	
Device related thrombosis			
subjects affected / exposed	1 / 15 (6.67%)	1 / 49 (2.04%)	
occurrences (all)	1	1	
Face oedema			

subjects affected / exposed	0 / 15 (0.00%)	7 / 49 (14.29%)	
occurrences (all)	0	8	
Facial pain			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Fatigue			
subjects affected / exposed	4 / 15 (26.67%)	19 / 49 (38.78%)	
occurrences (all)	7	24	
Gait disturbance			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
General physical health deterioration			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Influenza like illness			
subjects affected / exposed	1 / 15 (6.67%)	2 / 49 (4.08%)	
occurrences (all)	1	3	
Infusion site extravasation			
subjects affected / exposed	1 / 15 (6.67%)	1 / 49 (2.04%)	
occurrences (all)	1	1	
Infusion site pain			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Injection site reaction			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Injection site swelling			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Non-cardiac chest pain			
subjects affected / exposed	1 / 15 (6.67%)	1 / 49 (2.04%)	
occurrences (all)	1	1	
Oedema peripheral			
subjects affected / exposed	1 / 15 (6.67%)	8 / 49 (16.33%)	
occurrences (all)	1	9	
Peripheral swelling			

subjects affected / exposed	0 / 15 (0.00%)	2 / 49 (4.08%)	
occurrences (all)	0	3	
Pyrexia			
subjects affected / exposed	2 / 15 (13.33%)	9 / 49 (18.37%)	
occurrences (all)	3	12	
Swelling			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Swelling face			
subjects affected / exposed	0 / 15 (0.00%)	2 / 49 (4.08%)	
occurrences (all)	0	2	
Xerosis			
subjects affected / exposed	1 / 15 (6.67%)	1 / 49 (2.04%)	
occurrences (all)	1	1	
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Hypersensitivity			
subjects affected / exposed	2 / 15 (13.33%)	3 / 49 (6.12%)	
occurrences (all)	3	4	
Reproductive system and breast disorders			
Breast oedema			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Breast pain			
subjects affected / exposed	0 / 15 (0.00%)	3 / 49 (6.12%)	
occurrences (all)	0	3	
Menorrhagia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Pelvic pain			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			

Aphonia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Apnoea			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Bronchospasm			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Cough			
subjects affected / exposed	0 / 15 (0.00%)	7 / 49 (14.29%)	
occurrences (all)	0	8	
Dysphonia			
subjects affected / exposed	0 / 15 (0.00%)	3 / 49 (6.12%)	
occurrences (all)	0	3	
Dyspnoea			
subjects affected / exposed	2 / 15 (13.33%)	13 / 49 (26.53%)	
occurrences (all)	2	16	
Epistaxis			
subjects affected / exposed	0 / 15 (0.00%)	4 / 49 (8.16%)	
occurrences (all)	0	9	
Hypoxia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Nasal congestion			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Pharyngeal oedema			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Pleural effusion			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Productive cough			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	

Pulmonary oedema			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Rhinorrhoea			
subjects affected / exposed	0 / 15 (0.00%)	2 / 49 (4.08%)	
occurrences (all)	0	2	
Snoring			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	2	
Upper-airway cough syndrome			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Vocal cord polyp			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 15 (6.67%)	5 / 49 (10.20%)	
occurrences (all)	1	5	
Depressed mood			
subjects affected / exposed	0 / 15 (0.00%)	2 / 49 (4.08%)	
occurrences (all)	0	2	
Depression			
subjects affected / exposed	2 / 15 (13.33%)	3 / 49 (6.12%)	
occurrences (all)	2	4	
Hallucination			
subjects affected / exposed	1 / 15 (6.67%)	1 / 49 (2.04%)	
occurrences (all)	1	1	
Insomnia			
subjects affected / exposed	1 / 15 (6.67%)	2 / 49 (4.08%)	
occurrences (all)	1	3	
Product issues			
Device dislocation			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Investigations			

Alanine aminotransferase increased			
subjects affected / exposed	2 / 15 (13.33%)	26 / 49 (53.06%)	
occurrences (all)	4	37	
Amylase increased			
subjects affected / exposed	0 / 15 (0.00%)	2 / 49 (4.08%)	
occurrences (all)	0	3	
Aspartate aminotransferase increased			
subjects affected / exposed	4 / 15 (26.67%)	32 / 49 (65.31%)	
occurrences (all)	8	43	
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 15 (0.00%)	5 / 49 (10.20%)	
occurrences (all)	0	5	
Blood creatine phosphokinase MB increased			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 15 (0.00%)	16 / 49 (32.65%)	
occurrences (all)	0	17	
Blood creatinine increased			
subjects affected / exposed	0 / 15 (0.00%)	3 / 49 (6.12%)	
occurrences (all)	0	3	
Blood iron decreased			
subjects affected / exposed	1 / 15 (6.67%)	1 / 49 (2.04%)	
occurrences (all)	1	1	
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 15 (0.00%)	3 / 49 (6.12%)	
occurrences (all)	0	3	
C-reactive protein increased			
subjects affected / exposed	1 / 15 (6.67%)	1 / 49 (2.04%)	
occurrences (all)	1	1	
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 15 (0.00%)	6 / 49 (12.24%)	
occurrences (all)	0	6	
Haemoglobin decreased			

subjects affected / exposed	0 / 15 (0.00%)	2 / 49 (4.08%)	
occurrences (all)	0	2	
Hepatic enzyme increased			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	3	
Lipase			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Lipase increased			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Lymphocyte count decreased			
subjects affected / exposed	0 / 15 (0.00%)	3 / 49 (6.12%)	
occurrences (all)	0	4	
Neutrophil count decreased			
subjects affected / exposed	5 / 15 (33.33%)	16 / 49 (32.65%)	
occurrences (all)	13	50	
Platelet count decreased			
subjects affected / exposed	6 / 15 (40.00%)	12 / 49 (24.49%)	
occurrences (all)	12	49	
Weight decreased			
subjects affected / exposed	0 / 15 (0.00%)	2 / 49 (4.08%)	
occurrences (all)	0	3	
Weight increased			
subjects affected / exposed	0 / 15 (0.00%)	2 / 49 (4.08%)	
occurrences (all)	0	2	
White blood cell count decreased			
subjects affected / exposed	1 / 15 (6.67%)	8 / 49 (16.33%)	
occurrences (all)	2	16	
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Chemical cystitis			

subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Contusion			
subjects affected / exposed	1 / 15 (6.67%)	4 / 49 (8.16%)	
occurrences (all)	1	4	
Humerus fracture			
subjects affected / exposed	1 / 15 (6.67%)	1 / 49 (2.04%)	
occurrences (all)	1	1	
Oral contusion			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Post procedural haematoma			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Seroma			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	3	
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Bradycardia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Palpitations			
subjects affected / exposed	1 / 15 (6.67%)	2 / 49 (4.08%)	
occurrences (all)	1	2	
Tachycardia			
subjects affected / exposed	0 / 15 (0.00%)	2 / 49 (4.08%)	
occurrences (all)	0	2	
Nervous system disorders			
Ageusia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Balance disorder			

subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Dizziness			
subjects affected / exposed	0 / 15 (0.00%)	2 / 49 (4.08%)	
occurrences (all)	0	5	
Dysaesthesia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Dysgeusia			
subjects affected / exposed	0 / 15 (0.00%)	2 / 49 (4.08%)	
occurrences (all)	0	2	
Headache			
subjects affected / exposed	4 / 15 (26.67%)	11 / 49 (22.45%)	
occurrences (all)	7	21	
Myelopathy			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Neuralgia			
subjects affected / exposed	0 / 15 (0.00%)	2 / 49 (4.08%)	
occurrences (all)	0	3	
Neuropathy peripheral			
subjects affected / exposed	1 / 15 (6.67%)	2 / 49 (4.08%)	
occurrences (all)	1	2	
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 15 (6.67%)	4 / 49 (8.16%)	
occurrences (all)	1	4	
Vocal cord paralysis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	10 / 15 (66.67%)	33 / 49 (67.35%)	
occurrences (all)	16	65	
Leukocytosis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	2	

Leukopenia			
subjects affected / exposed	3 / 15 (20.00%)	9 / 49 (18.37%)	
occurrences (all)	5	21	
Neutropenia			
subjects affected / exposed	8 / 15 (53.33%)	26 / 49 (53.06%)	
occurrences (all)	21	65	
Thrombocytopenia			
subjects affected / exposed	8 / 15 (53.33%)	24 / 49 (48.98%)	
occurrences (all)	16	50	
Thrombotic thrombocytopenic purpura			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 15 (0.00%)	2 / 49 (4.08%)	
occurrences (all)	0	2	
Eye disorders			
Conjunctival haemorrhage			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	3	
Diplopia			
subjects affected / exposed	1 / 15 (6.67%)	1 / 49 (2.04%)	
occurrences (all)	1	1	
Dry eye			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Eye oedema			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Eye pain			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Eyelid oedema			
subjects affected / exposed	0 / 15 (0.00%)	2 / 49 (4.08%)	
occurrences (all)	0	3	
Foreign body sensation in eyes			

subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Lacrimation increased			
subjects affected / exposed	0 / 15 (0.00%)	3 / 49 (6.12%)	
occurrences (all)	0	3	
Orbital oedema			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Periorbital oedema			
subjects affected / exposed	0 / 15 (0.00%)	14 / 49 (28.57%)	
occurrences (all)	0	16	
Periorbital swelling			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Vision blurred			
subjects affected / exposed	0 / 15 (0.00%)	2 / 49 (4.08%)	
occurrences (all)	0	2	
Xerophthalmia			
subjects affected / exposed	1 / 15 (6.67%)	1 / 49 (2.04%)	
occurrences (all)	1	1	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 15 (6.67%)	1 / 49 (2.04%)	
occurrences (all)	1	1	
Abdominal pain			
subjects affected / exposed	1 / 15 (6.67%)	8 / 49 (16.33%)	
occurrences (all)	3	12	
Abdominal pain upper			
subjects affected / exposed	0 / 15 (0.00%)	3 / 49 (6.12%)	
occurrences (all)	0	4	
Chapped lips			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Constipation			
subjects affected / exposed	2 / 15 (13.33%)	10 / 49 (20.41%)	
occurrences (all)	2	22	

Diarrhoea			
subjects affected / exposed	3 / 15 (20.00%)	10 / 49 (20.41%)	
occurrences (all)	4	14	
Dry mouth			
subjects affected / exposed	0 / 15 (0.00%)	2 / 49 (4.08%)	
occurrences (all)	0	2	
Dyspepsia			
subjects affected / exposed	3 / 15 (20.00%)	6 / 49 (12.24%)	
occurrences (all)	3	10	
Flatulence			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Gastritis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	2	
Gingival bleeding			
subjects affected / exposed	0 / 15 (0.00%)	2 / 49 (4.08%)	
occurrences (all)	0	4	
Gingival pain			
subjects affected / exposed	1 / 15 (6.67%)	1 / 49 (2.04%)	
occurrences (all)	1	1	
Gingival recession			
subjects affected / exposed	1 / 15 (6.67%)	1 / 49 (2.04%)	
occurrences (all)	1	1	
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Lip oedema			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	8 / 15 (53.33%)	30 / 49 (61.22%)	
occurrences (all)	15	51	
Odynophagia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	

Periodontal disease			
subjects affected / exposed	1 / 15 (6.67%)	2 / 49 (4.08%)	
occurrences (all)	1	2	
Rectal haemorrhage			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Salivary hypersecretion			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Stomatitis			
subjects affected / exposed	1 / 15 (6.67%)	8 / 49 (16.33%)	
occurrences (all)	1	12	
Vomiting			
subjects affected / exposed	2 / 15 (13.33%)	10 / 49 (20.41%)	
occurrences (all)	3	16	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	3 / 15 (20.00%)	6 / 49 (12.24%)	
occurrences (all)	3	6	
Blood blister			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Dermatitis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Dermatitis acneiform			
subjects affected / exposed	0 / 15 (0.00%)	3 / 49 (6.12%)	
occurrences (all)	0	3	
Dry skin			
subjects affected / exposed	0 / 15 (0.00%)	4 / 49 (8.16%)	
occurrences (all)	0	4	
Erythema			
subjects affected / exposed	0 / 15 (0.00%)	3 / 49 (6.12%)	
occurrences (all)	0	3	
Hyperhidrosis			

subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Nail disorder			
subjects affected / exposed	1 / 15 (6.67%)	1 / 49 (2.04%)	
occurrences (all)	1	1	
Pruritus			
subjects affected / exposed	0 / 15 (0.00%)	5 / 49 (10.20%)	
occurrences (all)	0	6	
Purpura			
subjects affected / exposed	1 / 15 (6.67%)	1 / 49 (2.04%)	
occurrences (all)	1	1	
Rash			
subjects affected / exposed	4 / 15 (26.67%)	14 / 49 (28.57%)	
occurrences (all)	6	21	
Rash maculo-papular			
subjects affected / exposed	0 / 15 (0.00%)	2 / 49 (4.08%)	
occurrences (all)	0	2	
Rash pruritic			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Skin fissures			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Skin lesion			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Stasis dermatitis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Toxic skin eruption			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	

Dysuria			
subjects affected / exposed	1 / 15 (6.67%)	1 / 49 (2.04%)	
occurrences (all)	1	1	
Nocturia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 15 (0.00%)	2 / 49 (4.08%)	
occurrences (all)	0	2	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 15 (6.67%)	3 / 49 (6.12%)	
occurrences (all)	1	3	
Back pain			
subjects affected / exposed	2 / 15 (13.33%)	4 / 49 (8.16%)	
occurrences (all)	2	5	
Bone pain			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Fracture pain			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Joint swelling			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Muscle spasms			
subjects affected / exposed	1 / 15 (6.67%)	2 / 49 (4.08%)	
occurrences (all)	1	2	
Muscular weakness			
subjects affected / exposed	1 / 15 (6.67%)	1 / 49 (2.04%)	
occurrences (all)	1	1	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Musculoskeletal pain			

subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Musculoskeletal stiffness			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Myalgia			
subjects affected / exposed	1 / 15 (6.67%)	5 / 49 (10.20%)	
occurrences (all)	1	6	
Neck pain			
subjects affected / exposed	0 / 15 (0.00%)	2 / 49 (4.08%)	
occurrences (all)	0	2	
Pain in extremity			
subjects affected / exposed	0 / 15 (0.00%)	3 / 49 (6.12%)	
occurrences (all)	0	3	
Soft tissue necrosis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Tendonitis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Infections and infestations			
Bronchitis viral			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Candida infection			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Catheter site infection			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Cellulitis			
subjects affected / exposed	1 / 15 (6.67%)	1 / 49 (2.04%)	
occurrences (all)	1	1	
Cystitis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	

Ear infection			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Folliculitis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Fungal oesophagitis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Gingivitis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Influenza			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Lower respiratory tract infection			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Lymphangitis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Mastitis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Nail infection			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Oral candidiasis			
subjects affected / exposed	1 / 15 (6.67%)	2 / 49 (4.08%)	
occurrences (all)	1	5	
Oral herpes			
subjects affected / exposed	2 / 15 (13.33%)	4 / 49 (8.16%)	
occurrences (all)	2	4	
Oral infection			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	

Oropharyngeal candidiasis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Pneumonia			
subjects affected / exposed	0 / 15 (0.00%)	2 / 49 (4.08%)	
occurrences (all)	0	3	
Sinusitis			
subjects affected / exposed	1 / 15 (6.67%)	2 / 49 (4.08%)	
occurrences (all)	1	4	
Spinal cord infection			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Tinea pedis			
subjects affected / exposed	1 / 15 (6.67%)	1 / 49 (2.04%)	
occurrences (all)	1	1	
Tonsillitis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	4	
Upper respiratory tract infection			
subjects affected / exposed	2 / 15 (13.33%)	5 / 49 (10.20%)	
occurrences (all)	4	9	
Urinary tract infection			
subjects affected / exposed	0 / 15 (0.00%)	3 / 49 (6.12%)	
occurrences (all)	0	4	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 15 (13.33%)	9 / 49 (18.37%)	
occurrences (all)	2	10	
Dehydration			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Fluid retention			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Hypercalcaemia			

subjects affected / exposed	0 / 15 (0.00%)	2 / 49 (4.08%)	
occurrences (all)	0	2	
Hyperglycaemia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Hypoalbuminaemia			
subjects affected / exposed	0 / 15 (0.00%)	2 / 49 (4.08%)	
occurrences (all)	0	2	
Hypocalcaemia			
subjects affected / exposed	0 / 15 (0.00%)	2 / 49 (4.08%)	
occurrences (all)	0	2	
Hypokalaemia			
subjects affected / exposed	0 / 15 (0.00%)	3 / 49 (6.12%)	
occurrences (all)	0	3	
Hypomagnesaemia			
subjects affected / exposed	1 / 15 (6.67%)	2 / 49 (4.08%)	
occurrences (all)	1	2	
Hyponatraemia			
subjects affected / exposed	0 / 15 (0.00%)	3 / 49 (6.12%)	
occurrences (all)	0	3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 March 2015	The main reason for this amendment is to add more specific guidance for dose modifications for creatine kinase elevation suspected to be related to MCS110, following Health Authority feed-back. Furthermore, a clarification has been added regarding severe periorbital edema
08 April 2016	The main purpose of this amendment is to provide additional flexibility for MCS110 dosing by introducing the option to skip the additional MCS110 dose on C1D8 for subsequent patients, should any safety concerns be revealed upon review of data from the dosing regimen currently being evaluated.
20 September 2016	The main purpose of this amendment is to extend the post-treatment contraception period from 60 to 90 days for patients receiving MCS110. In addition, the safety follow-up has been extended from 60 to 90 days
04 May 2017	The purpose of this amendment is to address requested changes from a Health Authority regarding the post-treatment contraception period for carboplatin and gemcitabine. The minimum required post-treatment contraception period has been revised and updated to 30 days.
11 October 2017	Following the recruitment halt, the purpose of this amendment is to reduce the schedule of assessments while still ensuring adequate safety monitoring in order to reduce the burden to patients who remain on study treatment.
08 October 2018	The main purpose of this amendment is to allow safety monitoring of creatine kinase elevations per local guidelines, to modify the language on Tumor associated macrophages content for patient selection, and to implement requested changes from Health Authorities.

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.

Enrollment in the study was terminated early as a result of challenges in enrollment due to the rapid evolution of the therapeutic landscape, and was not as a consequence of any safety concern. Ongoing patients continued according to the protocol.

Notes: