



Clinical trial results:

Randomized, Placebo Controlled Phase 3 Study of ABT-414 with Concurrent Chemoradiation and Adjuvant Temozolomide in Subjects with Newly Diagnosed Glioblastoma (GBM) with Epidermal Growth Factor Receptor (EGFR) Amplification (Intelligence1)

Summary

EudraCT number	2015-001166-26
Trial protocol	CZ NL IE DE BE AT GB PT ES FR
Global end of trial date	04 April 2022

Results information

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

Trial information

Trial identification

Sponsor protocol code	M13-813
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02573324
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AbbVie Deutschland GmbH & Co. KG
Sponsor organisation address	AbbVie House, Vanwall Business Park, Vanwall Road, Maidenhead, Berkshire, United Kingdom, SL6 4UB
Public contact	Global Medical Services, AbbVie, 001 8006339110, abbvieclinicaltrials@abbvie.com
Scientific contact	Global Medical Services, AbbVie, 001 8006339110, abbvieclinicaltrials@abbvie.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	04 April 2022
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	04 April 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to determine whether the addition of ABT-414 to concomitant radiotherapy and temozolomide (TMZ) plus adjuvant TMZ prolongs Overall Survival (OS) among subjects with newly diagnosed GBM harboring EGFR amplification.

Protection of trial subjects:

The study was conducted in accordance with the protocol, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) guidelines, applicable regulations and guidelines governing clinical study conduct and ethical principles that have their origin in the Declaration of Helsinki. Prior to the initiation of any screening or study-specific procedures, the investigator or his or her representative explained the nature of the study to the subject or his or her representative and answered all questions regarding this study. The informed consent statement was reviewed and signed and dated by the subject and/or the subject's parent or legal guardian and the person who administered the informed consent.

Background therapy: -

Evidence for comparator:

During the Chemoradiation Phase, all subjects underwent focal radiotherapy (RT), with one treatment given daily 5 days per week over approximately 6 weeks (and no more than 7 weeks). TMZ was administered 75 mg/m² orally once daily continuously from Day 1 of RT to the last day of radiation for a maximum of 49 days.

During the Adjuvant Phase, all subjects received oral TMZ 150 – 200 mg/m² once daily on Days 1 – 5 of each 28-day cycle for 6 cycles.

Actual start date of recruitment	04 January 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 35
Country: Number of subjects enrolled	Austria: 14
Country: Number of subjects enrolled	Belgium: 31
Country: Number of subjects enrolled	Brazil: 15
Country: Number of subjects enrolled	Canada: 40
Country: Number of subjects enrolled	China: 48
Country: Number of subjects enrolled	Colombia: 16
Country: Number of subjects enrolled	Czechia: 14
Country: Number of subjects enrolled	France: 36
Country: Number of subjects enrolled	Germany: 34

Country: Number of subjects enrolled	Hong Kong: 3
Country: Number of subjects enrolled	Ireland: 7
Country: Number of subjects enrolled	Israel: 22
Country: Number of subjects enrolled	Italy: 21
Country: Number of subjects enrolled	Korea, Republic of: 18
Country: Number of subjects enrolled	Netherlands: 33
Country: Number of subjects enrolled	New Zealand: 2
Country: Number of subjects enrolled	Portugal: 23
Country: Number of subjects enrolled	Russian Federation: 22
Country: Number of subjects enrolled	Singapore: 4
Country: Number of subjects enrolled	South Africa: 4
Country: Number of subjects enrolled	Spain: 20
Country: Number of subjects enrolled	Switzerland: 16
Country: Number of subjects enrolled	Taiwan: 16
Country: Number of subjects enrolled	United Kingdom: 27
Country: Number of subjects enrolled	United States: 170
Worldwide total number of subjects	691
EEA total number of subjects	233

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)	504
From 65 to 84 years	187
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study includes a Screening Period of up to 7 weeks from surgery/biopsy.

Period 1

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

Blinding implementation details:

AbbVie, the Radiation Therapy Oncology Group (RTOG), the investigator, the study site personnel and subject will remain blinded to each subject's treatment with ABT-414 or placebo throughout the course of the study

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo, Radiation and Temozolomide (TMZ)

Arm description:

Placebo is given on Day 1 of Week 1, 3 and 5 along with the standard therapy of TMZ and radiation during the chemoradiation phase. Placebo is given on Day 1 and 15 of each cycle along with TMZ (Days 1-5 of each cycle) per standard of care during the adjuvant phase.

Arm type	Placebo
Investigational medicinal product name	Placebo for depatuxizumab mafodotin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

During the Chemoradiation Phase, subjects receive blinded placebo intravenous (IV) infusion over 30 – 40 minutes once every 2 weeks (Day 1 of Weeks 1, 3, and 5 of the 6-week regimen). The dosing interval must be at least 12 days after the previous dose of placebo, and the doses must be administered no later than the last day of radiation treatment.

Arm title	Depatuxizumab Mafodotin, Radiation and TMZ
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Arm description:

Depatuxizumab mafodotin is given on Day 1 of Week 1, 3 and 5 along with the standard therapy of TMZ and radiation during the chemoradiation phase. Depatuxizumab mafodotin is given on Day 1 & 15 of each cycle along with TMZ (Days 1-5 of each cycle) per standard of care during the adjuvant phase.

Arm type	Experimental
Investigational medicinal product name	Depatuxizumab mafodotin
Investigational medicinal product code	
Other name	ABT-414
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

During the Chemoradiation Phase, subjects will receive blinded ABT-414 at 2.0 mg/kg IV infusion over 30 – 40 minutes once every 2 weeks (Day 1 of Weeks 1, 3, and 5 of the 6-week regimen). The dosing interval must be at least 12 days after the previous dose of ABT-414, and the doses must be administered no later than the last day of radiation treatment.

Arm title	Open-Label Substudy Depatuxizumab Mafodotin, Radiation and
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Arm description:

Subjects with hepatic impairment will be assigned to depatuxizumab mafodotin is given on Day 1 of Week 1, 3 and 5 along with the standard therapy of TMZ and radiation during the chemoradiation phase. Depatuxizumab mafodotin is given on Day 1 & 15 of each cycle along with TMZ (Days 1-5 of each cycle) per standard of care during the adjuvant phase.

Arm type	Experimental
Investigational medicinal product name	Depatuxizumab mafodotin
Investigational medicinal product code	
Other name	ABT-414
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

During the Chemoradiation Phase, subjects will receive ABT-414 at 2.0 mg/kg IV infusion over 30 – 40 minutes once every 2 weeks (Day 1 of Weeks 1, 3, and 5 of the 6-week regimen). The dosing interval must be at least 12 days after the previous dose of ABT-414, and the doses must be administered no later than the last day of radiation treatment.

Number of subjects in period 1	Placebo, Radiation and Temozolomide (TMZ)	Depatuxizumab Mafodotin, Radiation and TMZ	Open-Label Substudy Depatuxizumab Mafodotin, Radiation and TMZ
Started	341	344	6
Received Randomized Study Drug	337	344	6
Entered Adjuvant Phase	285	273	6
Entered Follow-Up Phase	328	326	5
Completed	0	0	0
Not completed	341	344	6
Consent withdrawn by subject	26	23	3
Death	182	200	1
Other, not specified	20	27	-
Study terminated by sponsor	107	89	2
Unknown reason	2	-	-
Lost to follow-up	4	5	-

Baseline characteristics

Reporting groups

Reporting group title	Placebo, Radiation and Temozolomide (TMZ)
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Reporting group description:

Placebo is given on Day 1 of Week 1, 3 and 5 along with the standard therapy of TMZ and radiation during the chemoradiation phase. Placebo is given on Day 1 and 15 of each cycle along with TMZ (Days 1-5 of each cycle) per standard of care during the adjuvant phase.

Reporting group title	Depatuxizumab Mafodotin, Radiation and TMZ
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Reporting group description:

Depatuxizumab mafodotin is given on Day 1 of Week 1, 3 and 5 along with the standard therapy of TMZ and radiation during the chemoradiation phase. Depatuxizumab mafodotin is given on Day 1 & 15 of each cycle along with TMZ (Days 1-5 of each cycle) per standard of care during the adjuvant phase.

Reporting group title	Open-Label Substudy Depatuxizumab Mafodotin, Radiation and TMZ
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Reporting group description:

Subjects with hepatic impairment will be assigned to depatuxizumab mafodotin is given on Day 1 of Week 1, 3 and 5 along with the standard therapy of TMZ and radiation during the chemoradiation phase. Depatuxizumab mafodotin is given on Day 1 & 15 of each cycle along with TMZ (Days 1-5 of each cycle) per standard of care during the adjuvant phase.

Reporting group values	Placebo, Radiation and Temozolomide (TMZ)	Depatuxizumab Mafodotin, Radiation and TMZ	Open-Label Substudy Depatuxizumab Mafodotin, Radiation and TMZ
Number of subjects	341	344	6
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	58.1 ± 10.42	58.2 ± 10.14	55.3 ± 10.58
Gender categorical Units: Subjects			
Female	137	129	0
Male	204	215	6
Race Units: Subjects			
American Indian or Alaska Native	6	7	0
Asian	47	40	5
Native Hawaiian or Other Pacific Islander	1	1	0
Black or African American	4	5	0
White	282	289	1
More than one race	1	1	0
Unknown or Not Reported	0	1	0
Ethnicity Units: Subjects			
Hispanic or Latino	35	35	1
Han Chinese (First Generation)	28	23	2
Other, Not Specified	278	285	3

Missing	0	1	0
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Reporting group values	Total		
Number of subjects	691		
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	-		
Gender categorical Units: Subjects			
Female	266		
Male	425		
Race Units: Subjects			
American Indian or Alaska Native	13		
Asian	92		
Native Hawaiian or Other Pacific Islander	2		
Black or African American	9		
White	572		
More than one race	2		
Unknown or Not Reported	1		
Ethnicity Units: Subjects			
Hispanic or Latino	71		
Han Chinese (First Generation)	53		
Other, Not Specified	566		
Missing	1		

End points

End points reporting groups

Reporting group title	Placebo, Radiation and Temozolomide (TMZ)
Reporting group description: Placebo is given on Day 1 of Week 1, 3 and 5 along with the standard therapy of TMZ and radiation during the chemoradiation phase. Placebo is given on Day 1 and 15 of each cycle along with TMZ (Days 1-5 of each cycle) per standard of care during the adjuvant phase.	
Reporting group title	Depatuxizumab Mafodotin, Radiation and TMZ
Reporting group description: Depatuxizumab mafodotin is given on Day 1 of Week 1, 3 and 5 along with the standard therapy of TMZ and radiation during the chemoradiation phase. Depatuxizumab mafodotin is given on Day 1 & 15 of each cycle along with TMZ (Days 1-5 of each cycle) per standard of care during the adjuvant phase.	
Reporting group title	Open-Label Substudy Depatuxizumab Mafodotin, Radiation and TMZ
Reporting group description: Subjects with hepatic impairment will be assigned to depatuxizumab mafodotin is given on Day 1 of Week 1, 3 and 5 along with the standard therapy of TMZ and radiation during the chemoradiation phase. Depatuxizumab mafodotin is given on Day 1 & 15 of each cycle along with TMZ (Days 1-5 of each cycle) per standard of care during the adjuvant phase.	
Subject analysis set title	Full Analysis Set: Placebo, Radiation and TMZ
Subject analysis set type	Full analysis
Subject analysis set description: All participants randomized to placebo (regardless of whether they received study treatment) satisfying the following criteria: • Enrollment date was on or prior to 31-Mar-2018 • Enrolled in the main study (not in the open-label hepatic sub-study)	
Subject analysis set title	Full Analysis Set: Depatuxizumab Mafodotin, Radiation and TMZ
Subject analysis set type	Full analysis
Subject analysis set description: All participants randomized to depatuxizumab mafodotin (regardless of whether they received study treatment) satisfying the following criteria: • Enrollment date was on or prior to 31-Mar-2018 • Enrolled in the main study (not in the open-label hepatic sub-study)	
Primary: Overall Survival (OS)	
End point title	Overall Survival (OS)
End point description: Time to OS is defined as the number of days from the date of randomization to the date of death due to any cause.	
End point type	Primary
End point timeframe: Overall median duration of follow-up was 15.5 months (range: 0.1, 35.6).	

End point values	Full Analysis Set: Placebo, Radiation and TMZ	Full Analysis Set: Depatuxizumab Mafodotin, Radiation and TMZ		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	316	323		
Units: months				

median (confidence interval 95%)	18.7 (17.0 to 20.3)	18.9 (17.4 to 20.8)		
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Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Cox proportional hazard is based on multivariate Cox proportional hazards model including treatment, O6-methylguaninemethytransferase (MGMT) methylation status, Recursive Partitioning Analysis (RPA) class, region of the world, and EGFRde2-7 (EGFRvIII) mutation status as covariates.	
Comparison groups	Full Analysis Set: Placebo, Radiation and TMZ v Full Analysis Set: Depatuxizumab Mafodotin, Radiation and TMZ
Number of subjects included in analysis	639
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.633 ^[1]
Method	Logrank
Parameter estimate	Cox proportional hazard
Point estimate	1.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.82
upper limit	1.26

Notes:

[1] - Weighted log-rank P-value: Stratified Fleming-Harrington ($\rho = 0$, $\gamma = 0.2$) test was used. Stratified by randomization stratification factors namely: MGMT methylation status, RPA class, region of the world and EGFRvIII mutation status.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Full Analysis Set: Placebo, Radiation and TMZ v Full Analysis Set: Depatuxizumab Mafodotin, Radiation and TMZ
Number of subjects included in analysis	639
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.704 ^[2]
Method	Logrank

Notes:

[2] - Log-rank P-value (1-sided): Stratified by randomization stratification factors namely: MGMT methylation status, RPA class, region of the world and EGFRvIII mutation status.

Secondary: OS for the O6-methylguaninemethytransferase (MGMT) Unmethylated Group

End point title	OS for the O6-methylguaninemethytransferase (MGMT) Unmethylated Group
End point description:	
Time to OS is defined as the number of days from the date of randomization to the date of death due to any cause.	
Unmethylated MGMT promoter is associated with a worse prognosis in GBM.	
End point type	Secondary
End point timeframe:	
Overall median duration of follow-up was 15.5 months (range: 0.1, 35.6).	

End point values	Full Analysis Set: Placebo, Radiation and TMZ	Full Analysis Set: Depatuxizumab Mafodotin, Radiation and TMZ		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	199 ^[3]	205 ^[4]		
Units: months				
median (confidence interval 95%)	16.2 (14.7 to 17.7)	16.1 (14.6 to 18.5)		

Notes:

[3] - Participants with unmethylated MGMT promoter status.

[4] - Participants with unmethylated MGMT promoter status.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Cox proportional hazard estimate is based on multivariate Cox proportional hazards model including treatment, MGMT methylation status, RPA class, region of the world, and EGFRvIII mutation status as covariates.	
Comparison groups	Full Analysis Set: Placebo, Radiation and TMZ v Full Analysis Set: Depatuxizumab Mafodotin, Radiation and TMZ
Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.504 ^[5]
Method	Logrank
Parameter estimate	Cox proportional hazard
Point estimate	0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	1.24

Notes:

[5] - Weighted log-rank P-value: Stratified Fleming-Harrington ($\rho = 0$, $\gamma = 0.2$) test was used. Stratified by randomization stratification factors namely: MGMT methylation status, RPA class, region of the world and EGFRvIII mutation status.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Full Analysis Set: Placebo, Radiation and TMZ v Full Analysis Set: Depatuxizumab Mafodotin, Radiation and TMZ
Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.599 ^[6]
Method	Logrank

Notes:

[6] - Log-rank P-value (1-sided): Stratified by randomization stratification factors namely: MGMT methylation status, RPA class, region of the world and EGFRvIII mutation status.

Secondary: OS for the MGMT Methylated Group

End point title	OS for the MGMT Methylated Group
End point description: Time to OS is defined as the number of days from the date of randomization to the date of death due to any cause.	
End point type	Secondary
End point timeframe: Overall median duration of follow-up was 15.5 months (range: 0.1, 35.6).	

End point values	Full Analysis Set: Placebo, Radiation and TMZ	Full Analysis Set: Depatuxizumab Mafodotin, Radiation and TMZ		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	117 ^[7]	118 ^[8]		
Units: months				
median (confidence interval 95%)	99999 (21.2 to 99999)	25.4 (21.6 to 27.3)		

Notes:

[7] - Participants with methylated MGMT promoter status. 99999=not estimable due to small number of events

[8] - Participants with methylated MGMT promoter status.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: Cox Proportional Hazard is based on multivariate Cox proportional hazards model including treatment, MGMT methylation status, RPA class, region of the world, and EGFRvIII mutation status as covariates.	
Comparison groups	Full Analysis Set: Placebo, Radiation and TMZ v Full Analysis Set: Depatuxizumab Mafodotin, Radiation and TMZ
Number of subjects included in analysis	235
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.773 ^[9]
Method	Logrank
Parameter estimate	Cox proportional hazard
Point estimate	1.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	1.8

Notes:

[9] - Weighted log-rank P-value: Stratified Fleming-Harrington ($\rho = 0$, $\gamma = 0.2$) test was used. Stratified by randomization stratification factors namely: MGMT methylation status, RPA class, region of the world and EGFRvIII mutation status.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Full Analysis Set: Placebo, Radiation and TMZ v Full Analysis Set: Depatuxizumab Mafodotin, Radiation and TMZ

Number of subjects included in analysis	235
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.74 ^[10]
Method	Logrank

Notes:

[10] - Log-rank P-value (1-sided): Stratified by randomization stratification factors namely: MGMT methylation status, RPA class, region of the world and EGFRvIII mutation status.

Secondary: OS for the Epidermal Growth Factor Receptor (EGFR)vIII-Mutated Tumor Subgroup

End point title	OS for the Epidermal Growth Factor Receptor (EGFR)vIII-Mutated Tumor Subgroup
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End point description:

Time to OS is defined as the number of days from the date of randomization to the date of death due to any cause.

End point type	Secondary
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End point timeframe:

Overall median duration of follow-up was 15.5 months (range: 0.1, 35.6).

End point values	Full Analysis Set: Placebo, Radiation and TMZ	Full Analysis Set: Depatuxizumab Mafodotin, Radiation and TMZ		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	168 ^[11]	164 ^[12]		
Units: months				
median (confidence interval 95%)	18.2 (15.7 to 19.5)	19.8 (17.8 to 23.1)		

Notes:

[11] - Participants with EGFR-VIII mutation status=mutated.

[12] - Participants with EGFR-VIII mutation status=mutated.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
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Statistical analysis description:

Cox Proportional Hazard is based on multivariate Cox proportional hazards model including treatment, MGMT methylation status, RPA class, region of the world and EGFRvIII mutation status as covariates.

Comparison groups	Full Analysis Set: Placebo, Radiation and TMZ v Full Analysis Set: Depatuxizumab Mafodotin, Radiation and TMZ
Number of subjects included in analysis	332
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.381 ^[13]
Method	Logrank
Parameter estimate	Cox proportional hazard
Point estimate	0.95

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	1.27

Notes:

[13] - Weighted log-rank P-value: Stratified Fleming-Harrington ($\rho = 0$, $\gamma = 0.2$) test was used. Stratified by randomization stratification factors namely: MGMT methylation status, RPA class, region of the world and EGFRvIII mutation status.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Full Analysis Set: Placebo, Radiation and TMZ v Full Analysis Set: Depatuxizumab Mafodotin, Radiation and TMZ
Number of subjects included in analysis	332
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.409 ^[14]
Method	Logrank

Notes:

[14] - Log-rank P-value (1-sided): Stratified by randomization stratification factors namely: MGMT methylation status, RPA class, region of the world and EGFRvIII mutation status.

Secondary: Progression-Free Survival (PFS)

End point title	Progression-Free Survival (PFS)
End point description:	
PFS will be defined as the number of days from the date of randomization to the date of earliest disease progression based on Response Assessment in Neuro-Oncology (RANO) criteria (see Wen et al. J Clin Oncol. 2010 Apr 10;28(11):1963-72) or to the date of death, if disease progression does not occur.	
End point type	Secondary
End point timeframe:	
Overall median duration of follow-up was 15.5 months (range: 0.1, 35.6).	

End point values	Full Analysis Set: Placebo, Radiation and TMZ	Full Analysis Set: Depatuxizumab Mafodotin, Radiation and TMZ		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	316	323		
Units: months				
median (confidence interval 95%)	6.3 (5.9 to 7.9)	8.0 (6.2 to 9.6)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Cox Proportional Hazard is based on multivariate Cox proportional hazards model including treatment, MGMT methylation status, RPA class, region of the world and EGFRvIII mutation status as covariates.	
Comparison groups	Full Analysis Set: Placebo, Radiation and TMZ v Full Analysis Set: Depatuxizumab Mafodotin, Radiation and TMZ

Number of subjects included in analysis	639
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.029 ^[15]
Method	Logrank
Parameter estimate	Cox proportional hazard
Point estimate	0.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	1.01

Notes:

[15] - Stratified log-rank test was used. Stratified by randomization stratification factors namely: MGMT methylation status, RPA class, region of the world and EGFRvIII mutation status.

Secondary: PFS for EGFRvIII-Mutated Tumor Subgroup

End point title	PFS for EGFRvIII-Mutated Tumor Subgroup
End point description:	
PFS will be defined as the number of days from the date of randomization to the date of earliest disease progression based on Response Assessment in Neuro-Oncology (RANO) criteria or to the date of death, if disease progression does not occur.	
End point type	Secondary
End point timeframe:	
Overall median duration of follow-up was 15.5 months (range: 0.1, 35.6).	

End point values	Full Analysis Set: Placebo, Radiation and TMZ	Full Analysis Set: Depatuxizumab Mafodotin, Radiation and TMZ		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	168 ^[16]	164 ^[17]		
Units: months				
median (confidence interval 95%)	5.9 (4.8 to 7.7)	8.3 (6.1 to 10.7)		

Notes:

[16] - Participants with EGFR-VIII mutation status=mutated.

[17] - Participants with EGFR-VIII mutation status=mutated.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Cox Proportional Hazard is based on multivariate Cox proportional hazards model including treatment, MGMT methylation status, RPA class, region of the world and EGFRvIII mutation status as covariates.	
Comparison groups	Full Analysis Set: Placebo, Radiation and TMZ v Full Analysis Set: Depatuxizumab Mafodotin, Radiation and TMZ

Number of subjects included in analysis	332
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002 ^[18]
Method	Logrank
Parameter estimate	Cox proportional hazard
Point estimate	0.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.56
upper limit	0.93

Notes:

[18] - Stratified log-rank test was used. Stratified by randomization stratification factors namely: MGMT methylation status, RPA class, region of the world and EGFRvIII mutation status.

Secondary: Deterioration Free Survival in M.D. Anderson Symptom Inventory Brain Tumor Module (MDASI-BT) Symptom Severity Score

End point title	Deterioration Free Survival in M.D. Anderson Symptom Inventory Brain Tumor Module (MDASI-BT) Symptom Severity Score
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End point description:

The MDASI-BT assesses the severity of multiple brain tumor-related symptoms and the impact of these symptoms on daily functioning in the last 24 hours. It consists of 22 symptom items and 6 interference items, each rated from 0 to 10. MDASI-BT symptom severity score is defined as average over 13 core symptom items and 9 brain tumor symptom items, with a total score of 0 to 10, with higher score indicating worse symptoms/interference. Changes in symptom severity score were classified into 3 categories: improved (≤ -1), stable (> -1 and < 1), and deteriorated (≥ 1). Deterioration is defined as satisfying the deterioration criteria (i.e., increase in symptom severity score by ≥ 1 unit) without further improvement (i.e., failing to satisfy deterioration criteria) within 8 weeks or occurrence of death.

End point type	Secondary
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End point timeframe:

Overall median duration of follow-up was 15.5 months (range: 0.1, 35.6).

End point values	Full Analysis Set: Placebo, Radiation and TMZ	Full Analysis Set: Depatuxizumab, Mafodotin, Radiation and TMZ		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	316	323		
Units: months				
median (confidence interval 95%)	11.0 (8.05 to 12.71)	6.1 (4.57 to 8.02)		

Statistical analyses

No statistical analyses for this end point

Secondary: Deterioration Free Survival in MDASI-BT Symptom Interference Score

End point title	Deterioration Free Survival in MDASI-BT Symptom Interference Score
End point description:	
The MDASI-BT assesses the severity of multiple brain tumor-related symptoms and the impact of these symptoms on daily functioning in the last 24 hours. It consists of 22 symptom items and 6 interference items, each rated from 0 to 10. MDASI-BT symptom interference score is defined as an average of 6 interference items, with a total score of 0 to 10, where higher scores indicate worse interference. Changes in symptom interference score were classified into 3 categories: improved (≤ -1), stable (> -1 and < 1), and deteriorated (≥ 1). Deterioration is defined as satisfying the deterioration criteria (i.e., increase in symptom interference score by ≥ 1 unit) without further improvement (i.e., failing to satisfy deterioration criteria) within 8 weeks or occurrence of death.	
End point type	Secondary
End point timeframe:	
Overall median duration of follow-up was 15.5 months (range: 0.1, 35.6).	

End point values	Full Analysis Set: Placebo, Radiation and TMZ	Full Analysis Set: Depatuxizumab Mafodotin, Radiation and TMZ		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	316	323		
Units: months				
median (confidence interval 95%)	9.7 (7.79 to 12.19)	6.1 (4.57 to 8.84)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Cox Proportional Hazard is based on multivariate Cox proportional hazards model including treatment, MGMT methylation status, RPA class, region of the world and EGFRvIII mutation status as covariates.	
Comparison groups	Full Analysis Set: Placebo, Radiation and TMZ v Full Analysis Set: Depatuxizumab Mafodotin, Radiation and TMZ
Number of subjects included in analysis	639
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.938 ^[19]
Method	Logrank
Parameter estimate	Cox proportional hazard
Point estimate	1.185
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.972
upper limit	1.446

Notes:

[19] - Stratified log-rank test was used. Stratified by randomization stratification factors namely: MGMT methylation status, RPA class, region of the world and EGFRvIII mutation status.

Secondary: Deterioration Free Survival in Neurocognitive Functioning on the Hopkins Verbal Learning Test Revised (HVLTR) Total Recall Score

End point title	Deterioration Free Survival in Neurocognitive Functioning on the Hopkins Verbal Learning Test Revised (HVLTR) Total Recall Score
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End point description:

The HVLTR consists of 3 parts. Free call has a range of 0 to 36, delayed recall has a range from 0 to 12, and delayed recognition has a range of -12 to 12. Higher scores indicating better function in all 3 parts. When scoring the HVLTR, the 3 learning trials are combined to calculate a total recall score (range -12 to 60). Deterioration is defined as satisfying the deterioration criteria (i.e., decrease in HVLTR total recall score by 5 units) without further improvement within 8 weeks or occurrence of death.

End point type	Secondary
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End point timeframe:

Overall median duration of follow-up was 15.5 months (range: 0.1, 35.6).

End point values	Full Analysis Set: Placebo, Radiation and TMZ	Full Analysis Set: Depatuxizumab Mafodotin, Radiation and TMZ		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	316	323		
Units: months				
median (confidence interval 95%)	13.2 (11.53 to 14.59)	10.7 (8.18 to 13.14)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
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Statistical analysis description:

Cox Proportional Hazard is based on multivariate Cox proportional hazards model including treatment, MGMT methylation status, RPA class, region of the world and EGFRvIII mutation status as covariates.

Comparison groups	Full Analysis Set: Placebo, Radiation and TMZ v Full Analysis Set: Depatuxizumab Mafodotin, Radiation and TMZ
Number of subjects included in analysis	639
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.814 ^[20]
Method	Logrank
Parameter estimate	Cox proportional hazard
Point estimate	1.136
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.921
upper limit	1.402

Notes:

[20] - Stratified log-rank test was used. Stratified by randomization stratification factors namely: MGMT methylation status, RPA class, region of the world and EGFRvIII mutation status.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the first dose of any study drug during each study phase and no later than 49 days after the last dose of depatuxizumab mafodotin or placebo during each study phase, or the start of a new phase.

Adverse event reporting additional description:

Overall, the median duration of study drug treatment was 6.0 and 7.9 months in the depatuxizumab mafodotin and placebo treatment arms, respectively. Safety Analysis Set: all randomized participants who received at least one dose of study treatment (either RT, TMZ, placebo or depatuxizumab mafodotin), classified according to treatment received.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups

Reporting group title	Depatuxizumab Mafodotin, Radiation + TMZ: Chemoradiation Phase
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Reporting group description:

Depatuxizumab mafodotin given on Day 1 of Week 1, 3 and 5 along with the standard therapy of TMZ and radiation during the chemoradiation phase.

Reporting group title	Depatuxizumab Mafodotin, Radiation and TMZ: Adjuvant Phase
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Reporting group description:

Depatuxizumab mafodotin given on Day 1 of Week 1, 3 and 5 along with the standard therapy of TMZ and radiation during the chemoradiation phase. Depatuxizumab mafodotin given on Day 1 and 15 of each cycle, along with TMZ (Days 1-5 of each cycle) per standard of care during the adjuvant phase.

Reporting group title	Depatuxizumab Mafodotin, Radiation and TMZ: Follow Up Phase
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Reporting group description:

Participants who complete depatuxizumab mafodotin + TMZ adjuvant treatment or discontinue study drug prior to disease progression continue to undergo magnetic resonance imaging and assessment of neurocognitive functioning and patient reported outcomes approximately every 8 weeks up to and including at the time of disease progression, starting 8 weeks after the last scheduled assessments in the adjuvant phase. After disease progression, overall survival continues to be assessed quarterly.

Reporting group title	Placebo, Radiation and TMZ: Chemoradiation Phase
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Reporting group description:

Placebo given on Day 1 of Week 1, 3 and 5 along with the standard therapy of TMZ and radiation during the chemoradiation phase.

Reporting group title	Placebo, Radiation and TMZ: Adjuvant Phase
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Reporting group description:

Placebo given on Day 1 of Week 1, 3 and 5 along with the standard therapy of TMZ and radiation during the chemoradiation phase. Placebo given on Day 1 and 15 of each cycle, along with TMZ (Days 1-5 of each cycle) per standard of care during the adjuvant phase.

Reporting group title	OL Depatuxizumab Mafodotin, Radiation + TMZ: Chemoradiation Ph
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Reporting group description:

Open-label (OL) depatuxizumab mafodotin given to participants with hepatic impairment on Day 1 of Week 1, 3 and 5 along with the standard therapy of TMZ and radiation during the chemoradiation phase.

Reporting group title	Placebo, Radiation and TMZ: Follow Up Phase
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Reporting group description:

Participants who complete placebo + TMZ adjuvant treatment or discontinue study drug prior to disease progression continue to undergo magnetic resonance imaging and assessment of neurocognitive functioning and patient reported outcomes approximately every 8 weeks up to and including at the time of disease progression, starting 8 weeks after the last scheduled assessments in the adjuvant phase. After disease progression, overall survival continues to be assessed quarterly.

Reporting group title	OL Depatuxizumab Mafodotin, Radiation and TMZ: Adjuvant Phase
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Reporting group description:

Open-label (OL) depatuxizumab mafodotin given to participants with hepatic impairment on Day 1 of Week 1, 3 and 5 along with the standard therapy of TMZ and radiation during the chemoradiation phase. Depatuxizumab mafodotin given on Day 1 and 15 of each cycle, along with TMZ (Days 1-5 of each cycle) per standard of care during the adjuvant phase.

Reporting group title	OL Depatuxizumab Mafodotin, Radiation + TMZ: Follow-up Phase
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Reporting group description:

Participants who complete open-label depatuxizumab mafodotin + TMZ adjuvant treatment or discontinue study drug prior to disease progression continue to undergo magnetic resonance imaging and assessment of neurocognitive functioning and patient reported outcomes approximately every 8 weeks up to and including at the time of disease progression, starting 8 weeks after the last scheduled assessments in the adjuvant phase. After disease progression, overall survival continues to be assessed quarterly.

Serious adverse events	Depatuxizumab Mafodotin, Radiation + TMZ: Chemoradiation Phase	Depatuxizumab Mafodotin, Radiation and TMZ: Adjuvant Phase	Depatuxizumab Mafodotin, Radiation and TMZ: Follow Up Phase
Total subjects affected by serious adverse events			
subjects affected / exposed	68 / 342 (19.88%)	107 / 273 (39.19%)	2 / 326 (0.61%)
number of deaths (all causes)	4	22	188
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
BRAIN NEOPLASM			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BREAST CANCER			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GLIOBLASTOMA			
subjects affected / exposed	0 / 342 (0.00%)	2 / 273 (0.73%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GLIOBLASTOMA MULTIFORME			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LUNG NEOPLASM			

subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MALIGNANT NEOPLASM PROGRESSION			
subjects affected / exposed	1 / 342 (0.29%)	9 / 273 (3.30%)	2 / 326 (0.61%)
occurrences causally related to treatment / all	0 / 1	0 / 10	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 5	0 / 2
NEOPLASM PROGRESSION			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
NEOPLASM SWELLING			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
PAPILLARY THYROID CANCER			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
PLASMA CELL MYELOMA			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
PROSTATE CANCER			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
AORTIC STENOSIS			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
DEEP VEIN THROMBOSIS			

subjects affected / exposed	2 / 342 (0.58%)	0 / 273 (0.00%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HAEMATOMA			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERTENSION			
subjects affected / exposed	0 / 342 (0.00%)	2 / 273 (0.73%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPOTENSION			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUPERFICIAL VEIN THROMBOSIS			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
THROMBOSIS			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
Surgical and medical procedures			
EUTHANASIA			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	2 / 342 (0.58%)	3 / 273 (1.10%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

CHEST PAIN			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
CONDITION AGGRAVATED			
subjects affected / exposed	1 / 342 (0.29%)	0 / 273 (0.00%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FATIGUE			
subjects affected / exposed	0 / 342 (0.00%)	3 / 273 (1.10%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GENERAL PHYSICAL HEALTH DETERIORATION			
subjects affected / exposed	0 / 342 (0.00%)	3 / 273 (1.10%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
HYPOTHERMIA			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
IMPAIRED HEALING			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MALAISE			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MULTIPLE ORGAN DYSFUNCTION SYNDROME			

subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
OEDEMA PERIPHERAL			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PYREXIA			
subjects affected / exposed	1 / 342 (0.29%)	5 / 273 (1.83%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 1	3 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SYSTEMIC INFLAMMATORY RESPONSE SYNDROME			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
ANAPHYLACTIC REACTION			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
DRUG HYPERSENSITIVITY			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERSENSITIVITY			
subjects affected / exposed	3 / 342 (0.88%)	0 / 273 (0.00%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	4 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
UTERINE HAEMORRHAGE			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Respiratory, thoracic and mediastinal disorders			
ACUTE RESPIRATORY FAILURE			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
ATELECTASIS			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHRONIC OBSTRUCTIVE PULMONARY DISEASE			
subjects affected / exposed	1 / 342 (0.29%)	0 / 273 (0.00%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DYSPNOEA			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPOXIA			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
PULMONARY EMBOLISM			
subjects affected / exposed	2 / 342 (0.58%)	2 / 273 (0.73%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 2	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RESPIRATORY FAILURE			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
AGGRESSION			

subjects affected / exposed	1 / 342 (0.29%)	0 / 273 (0.00%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANXIETY			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CONFUSIONAL STATE			
subjects affected / exposed	2 / 342 (0.58%)	4 / 273 (1.47%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DELIRIUM			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
DEPRESSION			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MENTAL STATUS CHANGES			
subjects affected / exposed	1 / 342 (0.29%)	0 / 273 (0.00%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ORGANIC BRAIN SYNDROME			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
SUICIDAL IDEATION			
subjects affected / exposed	1 / 342 (0.29%)	0 / 273 (0.00%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			

subjects affected / exposed	3 / 342 (0.88%)	0 / 273 (0.00%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	4 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	1 / 342 (0.29%)	0 / 273 (0.00%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BLOOD ALKALINE PHOSPHATASE INCREASED			
subjects affected / exposed	1 / 342 (0.29%)	0 / 273 (0.00%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FIBRIN D DIMER INCREASED			
subjects affected / exposed	1 / 342 (0.29%)	0 / 273 (0.00%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GAMMA-GLUTAMYLTRANSFERASE INCREASED			
subjects affected / exposed	1 / 342 (0.29%)	0 / 273 (0.00%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GLOMERULAR FILTRATION RATE DECREASED			
subjects affected / exposed	1 / 342 (0.29%)	0 / 273 (0.00%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEUTROPHIL COUNT DECREASED			
subjects affected / exposed	1 / 342 (0.29%)	0 / 273 (0.00%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PLATELET COUNT DECREASED			
subjects affected / exposed	2 / 342 (0.58%)	4 / 273 (1.47%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	2 / 2	4 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

WHITE BLOOD CELL COUNT DECREASED			
subjects affected / exposed	1 / 342 (0.29%)	0 / 273 (0.00%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
BRAIN CONTUSION			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
EPIDURAL HAEMORRHAGE			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
EXPOSURE TO CONTAMINATED DEVICE			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
EXTRADURAL HAEMATOMA			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
FALL			
subjects affected / exposed	1 / 342 (0.29%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FEMUR FRACTURE			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
HAND FRACTURE			

subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
POST PROCEDURAL HAEMORRHAGE			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
RADIATION NECROSIS			
subjects affected / exposed	1 / 342 (0.29%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RIB FRACTURE			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ROAD TRAFFIC ACCIDENT			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
SPINAL COMPRESSION FRACTURE			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUBDURAL HAEMATOMA			
subjects affected / exposed	0 / 342 (0.00%)	2 / 273 (0.73%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SURGICAL PROCEDURE REPEATED			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
TRAUMATIC INTRACRANIAL HAEMORRHAGE			

subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
CORNEAL DYSTROPHY			
subjects affected / exposed	1 / 342 (0.29%)	0 / 273 (0.00%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
CARDIAC ARREST			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
VENTRICULAR ARRHYTHMIA			
subjects affected / exposed	1 / 342 (0.29%)	0 / 273 (0.00%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Nervous system disorders			
APHASIA			
subjects affected / exposed	1 / 342 (0.29%)	2 / 273 (0.73%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ATAXIA			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRAIN OEDEMA			
subjects affected / exposed	4 / 342 (1.17%)	7 / 273 (2.56%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	1 / 4	3 / 7	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
CENTRAL NERVOUS SYSTEM LESION			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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

CENTRAL NERVOUS SYSTEM NECROSIS			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CEREBRAL CYST			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CEREBRAL HAEMORRHAGE			
subjects affected / exposed	0 / 342 (0.00%)	2 / 273 (0.73%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
CEREBRAL VENTRICLE DILATATION			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
CEREBROVASCULAR ACCIDENT			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COGNITIVE DISORDER			
subjects affected / exposed	0 / 342 (0.00%)	2 / 273 (0.73%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CRANIAL NERVE DISORDER			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
DEPRESSED LEVEL OF CONSCIOUSNESS			
subjects affected / exposed	1 / 342 (0.29%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DYSKINESIA			

subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
ENCEPHALOPATHY			
subjects affected / exposed	0 / 342 (0.00%)	2 / 273 (0.73%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EPILEPSIA PARTIALIS CONTINUA			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
EPILEPSY			
subjects affected / exposed	5 / 342 (1.46%)	3 / 273 (1.10%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	1 / 5	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
FACIAL PARALYSIS			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
FACIAL PARESIS			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
FOCAL DYSCOGNITIVE SEIZURES			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GENERALISED TONIC-CLONIC SEIZURE			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HAEMORRHAGE INTRACRANIAL			

subjects affected / exposed	1 / 342 (0.29%)	3 / 273 (1.10%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEADACHE			
subjects affected / exposed	1 / 342 (0.29%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEMIPARESIS			
subjects affected / exposed	3 / 342 (0.88%)	3 / 273 (1.10%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	3 / 3	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYDROCEPHALUS			
subjects affected / exposed	1 / 342 (0.29%)	4 / 273 (1.47%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTRACRANIAL PRESSURE INCREASED			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ISCHAEMIC STROKE			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
LOSS OF CONSCIOUSNESS			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
MOTOR DYSFUNCTION			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NERVOUS SYSTEM DISORDER			

subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEUROLOGICAL DECOMPENSATION			
subjects affected / exposed	1 / 342 (0.29%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEUROPATHY PERIPHERAL			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
PARAESTHESIA			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
PARTIAL SEIZURES			
subjects affected / exposed	1 / 342 (0.29%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERIPHERAL MOTOR NEUROPATHY			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SEIZURE			
subjects affected / exposed	11 / 342 (3.22%)	25 / 273 (9.16%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	4 / 12	3 / 31	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SOMNOLENCE			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
STATUS EPILEPTICUS			

subjects affected / exposed	0 / 342 (0.00%)	2 / 273 (0.73%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SYNCOPE			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TRANSIENT ISCHAEMIC ATTACK			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VASOGENIC CEREBRAL OEDEMA			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	1 / 342 (0.29%)	0 / 273 (0.00%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
APLASTIC ANAEMIA			
subjects affected / exposed	1 / 342 (0.29%)	0 / 273 (0.00%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BONE MARROW FAILURE			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DISSEMINATED INTRAVASCULAR COAGULATION			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
FEBRILE NEUTROPENIA			

subjects affected / exposed	1 / 342 (0.29%)	0 / 273 (0.00%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
IMMUNE THROMBOCYTOPENIA			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
LEUKOPENIA			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
MYELOSUPPRESSION			
subjects affected / exposed	1 / 342 (0.29%)	0 / 273 (0.00%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEUTROPENIA			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
THROMBOCYTOPENIA			
subjects affected / exposed	10 / 342 (2.92%)	7 / 273 (2.56%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	14 / 14	8 / 8	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
THROMBOCYTOPENIC PURPURA			
subjects affected / exposed	1 / 342 (0.29%)	0 / 273 (0.00%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
VERTIGO			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
Eye disorders			

CATARACT			
subjects affected / exposed	0 / 342 (0.00%)	2 / 273 (0.73%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CATARACT NUCLEAR			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CORNEAL LESION			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EYELID FUNCTION DISORDER			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
KERATOPATHY			
subjects affected / exposed	2 / 342 (0.58%)	0 / 273 (0.00%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OPHTHALMOPLÉGIA			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
OPTIC ISCHAEMIC NEUROPATHY			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OPTIC NEUROPATHY			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
RETINAL DETACHMENT			

subjects affected / exposed	1 / 342 (0.29%)	0 / 273 (0.00%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ULCERATIVE KERATITIS			
subjects affected / exposed	1 / 342 (0.29%)	2 / 273 (0.73%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	1 / 1	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VISION BLURRED			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	0 / 342 (0.00%)	2 / 273 (0.73%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANAL INCONTINENCE			
subjects affected / exposed	1 / 342 (0.29%)	0 / 273 (0.00%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COLITIS			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CONSTIPATION			
subjects affected / exposed	0 / 342 (0.00%)	3 / 273 (1.10%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIARRHOEA			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
GASTRIC HAEMORRHAGE			

subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	1 / 342 (0.29%)	0 / 273 (0.00%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NAUSEA			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PANCREATITIS ACUTE			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VOMITING			
subjects affected / exposed	0 / 342 (0.00%)	2 / 273 (0.73%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
CHOLECYSTITIS			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEPATITIS			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
LIVER INJURY			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
NODULAR REGENERATIVE HYPERPLASIA			

subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
ANGIOEDEMA			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
DRUG REACTION WITH EOSINOPHILIA AND SYSTEMIC SYMPTOMS			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RASH MACULO-PAPULAR			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
URTICARIA			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
Renal and urinary disorders			
ACUTE KIDNEY INJURY			
subjects affected / exposed	0 / 342 (0.00%)	2 / 273 (0.73%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEPHROLITHIASIS			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
RENAL COLIC			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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

RENAL FAILURE			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY RETENTION			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
DIABETES INSIPIDUS			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
HAEMARTHROSIS			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTERVERTEBRAL DISC PROTRUSION			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LUMBAR SPINAL STENOSIS			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MUSCULAR WEAKNESS			
subjects affected / exposed	1 / 342 (0.29%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PAIN IN EXTREMITY			

subjects affected / exposed	0 / 342 (0.00%)	2 / 273 (0.73%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
ABDOMINAL SEPSIS			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ACUTE HEPATITIS B			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
APPENDICITIS			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
APPENDICITIS PERFORATED			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
BACTERAEMIA			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BACTERIAL INFECTION			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRONCHITIS			
subjects affected / exposed	1 / 342 (0.29%)	0 / 273 (0.00%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CLOSTRIDIUM DIFFICILE COLITIS			

subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIVERTICULITIS			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
ENCEPHALITIS			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENCEPHALITIS VIRAL			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
ESCHERICHIA BACTERAEMIA			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
EXTRADURAL ABSCESS			
subjects affected / exposed	1 / 342 (0.29%)	0 / 273 (0.00%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EYE INFECTION STAPHYLOCOCCAL			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HERPES SIMPLEX			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
HERPES SIMPLEX ENCEPHALITIS			

subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
HERPES SIMPLEX OESOPHAGITIS			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
HERPES ZOSTER			
subjects affected / exposed	0 / 342 (0.00%)	2 / 273 (0.73%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INFLUENZA			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OTITIS MEDIA			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMOCYSTIS JIROVECI PNEUMONIA			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA			
subjects affected / exposed	3 / 342 (0.88%)	8 / 273 (2.93%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	1 / 3	2 / 9	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 3	0 / 0
PNEUMONIA ASPIRATION			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
PNEUMONIA STREPTOCOCCAL			

subjects affected / exposed	1 / 342 (0.29%)	0 / 273 (0.00%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
POSTOPERATIVE WOUND INFECTION			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
PULMONARY SEPSIS			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SEPSIS			
subjects affected / exposed	1 / 342 (0.29%)	2 / 273 (0.73%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SEPTIC SHOCK			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
STAPHYLOCOCCAL INFECTION			
subjects affected / exposed	1 / 342 (0.29%)	0 / 273 (0.00%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUBDURAL ABSCESS			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY TRACT INFECTION			

subjects affected / exposed	1 / 342 (0.29%)	5 / 273 (1.83%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UROSEPSIS			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VIRAL INFECTION			
subjects affected / exposed	1 / 342 (0.29%)	0 / 273 (0.00%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	1 / 342 (0.29%)	0 / 273 (0.00%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DEHYDRATION			
subjects affected / exposed	1 / 342 (0.29%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERGLYCAEMIA			
subjects affected / exposed	2 / 342 (0.58%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPOCALCAEMIA			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (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
HYPOKALAEMIA			
subjects affected / exposed	1 / 342 (0.29%)	0 / 273 (0.00%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPONATRAEMIA			

subjects affected / exposed	1 / 342 (0.29%)	0 / 273 (0.00%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPOPHAGIA			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo, Radiation and TMZ: Chemoradiation Phase	Placebo, Radiation and TMZ: Adjuvant Phase	OL Depatuxizumab Mafodotin, Radiation + TMZ: Chemoradiation Ph
Total subjects affected by serious adverse events			
subjects affected / exposed	56 / 335 (16.72%)	85 / 285 (29.82%)	1 / 6 (16.67%)
number of deaths (all causes)	3	13	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
BRAIN NEOPLASM			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
BREAST CANCER			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GLIOBLASTOMA			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
GLIOBLASTOMA MULTIFORME			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
LUNG NEOPLASM			

subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
MALIGNANT NEOPLASM PROGRESSION			
subjects affected / exposed	2 / 335 (0.60%)	10 / 285 (3.51%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 10	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 3	0 / 0
NEOPLASM PROGRESSION			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
NEOPLASM SWELLING			
subjects affected / exposed	1 / 335 (0.30%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
PAPILLARY THYROID CANCER			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PLASMA CELL MYELOMA			
subjects affected / exposed	1 / 335 (0.30%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PROSTATE CANCER			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
AORTIC STENOSIS			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DEEP VEIN THROMBOSIS			

subjects affected / exposed	1 / 335 (0.30%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HAEMATOMA			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
HYPERTENSION			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
HYPOTENSION			
subjects affected / exposed	1 / 335 (0.30%)	2 / 285 (0.70%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUPERFICIAL VEIN THROMBOSIS			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
THROMBOSIS			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
EUTHANASIA			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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

CHEST PAIN			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CONDITION AGGRAVATED			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
FATIGUE			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GENERAL PHYSICAL HEALTH DETERIORATION			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
HYPOTHERMIA			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
IMPAIRED HEALING			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
MALAISE			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
MULTIPLE ORGAN DYSFUNCTION SYNDROME			

subjects affected / exposed	1 / 335 (0.30%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
OEDEMA PERIPHERAL			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PYREXIA			
subjects affected / exposed	1 / 335 (0.30%)	3 / 285 (1.05%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SYSTEMIC INFLAMMATORY RESPONSE SYNDROME			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
ANAPHYLACTIC REACTION			
subjects affected / exposed	1 / 335 (0.30%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DRUG HYPERSENSITIVITY			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERSENSITIVITY			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
Reproductive system and breast disorders			
UTERINE HAEMORRHAGE			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Respiratory, thoracic and mediastinal disorders			
ACUTE RESPIRATORY FAILURE			
subjects affected / exposed	1 / 335 (0.30%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ATELECTASIS			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
CHRONIC OBSTRUCTIVE PULMONARY DISEASE			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
DYSPNOEA			
subjects affected / exposed	1 / 335 (0.30%)	2 / 285 (0.70%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPOXIA			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PULMONARY EMBOLISM			
subjects affected / exposed	4 / 335 (1.19%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RESPIRATORY FAILURE			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
AGGRESSION			

subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
ANXIETY			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
CONFUSIONAL STATE			
subjects affected / exposed	1 / 335 (0.30%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DELIRIUM			
subjects affected / exposed	1 / 335 (0.30%)	2 / 285 (0.70%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DEPRESSION			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MENTAL STATUS CHANGES			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ORGANIC BRAIN SYNDROME			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUICIDAL IDEATION			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			

subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BLOOD ALKALINE PHOSPHATASE INCREASED			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
FIBRIN D DIMER INCREASED			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
GAMMA-GLUTAMYLTRANSFERASE INCREASED			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
GLOMERULAR FILTRATION RATE DECREASED			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
NEUTROPHIL COUNT DECREASED			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
PLATELET COUNT DECREASED			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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

WHITE BLOOD CELL COUNT DECREASED			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
BRAIN CONTUSION			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
EPIDURAL HAEMORRHAGE			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EXPOSURE TO CONTAMINATED DEVICE			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EXTRADURAL HAEMATOMA			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FALL			
subjects affected / exposed	1 / 335 (0.30%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FEMUR FRACTURE			
subjects affected / exposed	1 / 335 (0.30%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HAND FRACTURE			

subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
POST PROCEDURAL HAEMORRHAGE			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RADIATION NECROSIS			
subjects affected / exposed	0 / 335 (0.00%)	2 / 285 (0.70%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RIB FRACTURE			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
ROAD TRAFFIC ACCIDENT			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SPINAL COMPRESSION FRACTURE			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
SUBDURAL HAEMATOMA			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
SURGICAL PROCEDURE REPEATED			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TRAUMATIC INTRACRANIAL HAEMORRHAGE			

subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
Congenital, familial and genetic disorders			
CORNEAL DYSTROPHY			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
CARDIAC ARREST			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
VENTRICULAR ARRHYTHMIA			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
APHASIA			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
ATAXIA			
subjects affected / exposed	1 / 335 (0.30%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRAIN OEDEMA			
subjects affected / exposed	5 / 335 (1.49%)	5 / 285 (1.75%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	4 / 7	2 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CENTRAL NERVOUS SYSTEM LESION			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

CENTRAL NERVOUS SYSTEM NECROSIS			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CEREBRAL CYST			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
CEREBRAL HAEMORRHAGE			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
CEREBRAL VENTRICLE DILATATION			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
CEREBROVASCULAR ACCIDENT			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
COGNITIVE DISORDER			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
CRANIAL NERVE DISORDER			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DEPRESSED LEVEL OF CONSCIOUSNESS			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DYSKINESIA			

subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENCEPHALOPATHY			
subjects affected / exposed	1 / 335 (0.30%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EPILEPSIA PARTIALIS CONTINUA			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EPILEPSY			
subjects affected / exposed	2 / 335 (0.60%)	2 / 285 (0.70%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FACIAL PARALYSIS			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FACIAL PARESIS			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FOCAL DYSCOGNITIVE SEIZURES			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
GENERALISED TONIC-CLONIC SEIZURE			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HAEMORRHAGE INTRACRANIAL			

subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
HEADACHE			
subjects affected / exposed	0 / 335 (0.00%)	4 / 285 (1.40%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEMIPARESIS			
subjects affected / exposed	1 / 335 (0.30%)	3 / 285 (1.05%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	2 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYDROCEPHALUS			
subjects affected / exposed	1 / 335 (0.30%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTRACRANIAL PRESSURE INCREASED			
subjects affected / exposed	1 / 335 (0.30%)	3 / 285 (1.05%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ISCHAEMIC STROKE			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LOSS OF CONSCIOUSNESS			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MOTOR DYSFUNCTION			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NERVOUS SYSTEM DISORDER			

subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEUROLOGICAL DECOMPENSATION			
subjects affected / exposed	1 / 335 (0.30%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEUROPATHY PERIPHERAL			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PARAESTHESIA			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PARTIAL SEIZURES			
subjects affected / exposed	2 / 335 (0.60%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERIPHERAL MOTOR NEUROPATHY			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
SEIZURE			
subjects affected / exposed	12 / 335 (3.58%)	19 / 285 (6.67%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	5 / 13	7 / 22	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SOMNOLENCE			
subjects affected / exposed	1 / 335 (0.30%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
STATUS EPILEPTICUS			

subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
SYNCOPE			
subjects affected / exposed	1 / 335 (0.30%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TRANSIENT ISCHAEMIC ATTACK			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
VASOGENIC CEREBRAL OEDEMA			
subjects affected / exposed	2 / 335 (0.60%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
APLASTIC ANAEMIA			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
BONE MARROW FAILURE			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
DISSEMINATED INTRAVASCULAR COAGULATION			
subjects affected / exposed	1 / 335 (0.30%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FEBRILE NEUTROPENIA			

subjects affected / exposed	2 / 335 (0.60%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
IMMUNE THROMBOCYTOPENIA			
subjects affected / exposed	1 / 335 (0.30%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LEUKOPENIA			
subjects affected / exposed	1 / 335 (0.30%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MYELOSUPPRESSION			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
NEUTROPENIA			
subjects affected / exposed	2 / 335 (0.60%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
THROMBOCYTOPENIA			
subjects affected / exposed	5 / 335 (1.49%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	5 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
THROMBOCYTOPENIC PURPURA			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
Ear and labyrinth disorders			
VERTIGO			
subjects affected / exposed	1 / 335 (0.30%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			

CATARACT			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
CATARACT NUCLEAR			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
CORNEAL LESION			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
EYELID FUNCTION DISORDER			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
KERATOPATHY			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
OPHTHALMOPLÉGIA			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OPTIC ISCHAEMIC NEUROPATHY			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
OPTIC NEUROPATHY			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RETINAL DETACHMENT			

subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
ULCERATIVE KERATITIS			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
VISION BLURRED			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
ANAL INCONTINENCE			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
COLITIS			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
CONSTIPATION			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIARRHOEA			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTRIC HAEMORRHAGE			

subjects affected / exposed	1 / 335 (0.30%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NAUSEA			
subjects affected / exposed	1 / 335 (0.30%)	3 / 285 (1.05%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	2 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PANCREATITIS ACUTE			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VOMITING			
subjects affected / exposed	0 / 335 (0.00%)	3 / 285 (1.05%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
CHOLECYSTITIS			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
HEPATITIS			
subjects affected / exposed	1 / 335 (0.30%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LIVER INJURY			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
NODULAR REGENERATIVE HYPERPLASIA			

subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
ANGIOEDEMA			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DRUG REACTION WITH EOSINOPHILIA AND SYSTEMIC SYMPTOMS			
subjects affected / exposed	1 / 335 (0.30%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RASH MACULO-PAPULAR			
subjects affected / exposed	1 / 335 (0.30%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URTICARIA			
subjects affected / exposed	1 / 335 (0.30%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
ACUTE KIDNEY INJURY			
subjects affected / exposed	1 / 335 (0.30%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEPHROLITHIASIS			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RENAL COLIC			
subjects affected / exposed	1 / 335 (0.30%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

RENAL FAILURE			
subjects affected / exposed	1 / 335 (0.30%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY RETENTION			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
DIABETES INSIPIDUS			
subjects affected / exposed	1 / 335 (0.30%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
HAEMARTHROSIS			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
INTERVERTEBRAL DISC PROTRUSION			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
LUMBAR SPINAL STENOSIS			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
MUSCULAR WEAKNESS			
subjects affected / exposed	2 / 335 (0.60%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PAIN IN EXTREMITY			

subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
ABDOMINAL SEPSIS			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
ACUTE HEPATITIS B			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
APPENDICITIS			
subjects affected / exposed	0 / 335 (0.00%)	2 / 285 (0.70%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
APPENDICITIS PERFORATED			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BACTERAEMIA			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
BACTERIAL INFECTION			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
BRONCHITIS			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
CLOSTRIDIUM DIFFICILE COLITIS			

subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
DIVERTICULITIS			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENCEPHALITIS			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
ENCEPHALITIS VIRAL			
subjects affected / exposed	1 / 335 (0.30%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ESCHERICHIA BACTERAEMIA			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EXTRADURAL ABSCESS			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
EYE INFECTION STAPHYLOCOCCAL			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
HERPES SIMPLEX			
subjects affected / exposed	1 / 335 (0.30%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HERPES SIMPLEX ENCEPHALITIS			

subjects affected / exposed	1 / 335 (0.30%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HERPES SIMPLEX OESOPHAGITIS			
subjects affected / exposed	1 / 335 (0.30%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HERPES ZOSTER			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
INFLUENZA			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
OTITIS MEDIA			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
PNEUMOCYSTIS JIROVECI PNEUMONIA			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA			
subjects affected / exposed	4 / 335 (1.19%)	4 / 285 (1.40%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	5 / 5	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
PNEUMONIA ASPIRATION			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA STREPTOCOCCAL			

subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
POSTOPERATIVE WOUND INFECTION			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PULMONARY SEPSIS			
subjects affected / exposed	1 / 335 (0.30%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SEPSIS			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SEPTIC SHOCK			
subjects affected / exposed	1 / 335 (0.30%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
STAPHYLOCOCCAL INFECTION			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
SUBDURAL ABSCESS			
subjects affected / exposed	1 / 335 (0.30%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY TRACT INFECTION			

subjects affected / exposed	1 / 335 (0.30%)	2 / 285 (0.70%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UROSEPSIS			
subjects affected / exposed	1 / 335 (0.30%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VIRAL INFECTION			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	1 / 335 (0.30%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DEHYDRATION			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERGLYCAEMIA			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPOCALCAEMIA			
subjects affected / exposed	1 / 335 (0.30%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPOKALAEMIA			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPONATRAEMIA			

subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (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
HYPOPHAGIA			
subjects affected / exposed	1 / 335 (0.30%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo, Radiation and TMZ: Follow Up Phase	OL Depatuxizumab Mafodotin, Radiation and TMZ: Adjuvant Phase	OL Depatuxizumab Mafodotin, Radiation + TMZ: Follow-up Phase
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 326 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
number of deaths (all causes)	179	0	1
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
BRAIN NEOPLASM			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
BREAST CANCER			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
GLIOBLASTOMA			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
GLIOBLASTOMA MULTIFORME			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
LUNG NEOPLASM			

subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
MALIGNANT NEOPLASM PROGRESSION			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
NEOPLASM PROGRESSION			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
NEOPLASM SWELLING			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
PAPILLARY THYROID CANCER			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
PLASMA CELL MYELOMA			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
PROSTATE CANCER			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
AORTIC STENOSIS			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
DEEP VEIN THROMBOSIS			

subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
HAEMATOMA			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
HYPERTENSION			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
HYPOTENSION			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
SUPERFICIAL VEIN THROMBOSIS			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
THROMBOSIS			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
Surgical and medical procedures			
EUTHANASIA			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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

CHEST PAIN			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
CONDITION AGGRAVATED			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
FATIGUE			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GENERAL PHYSICAL HEALTH DETERIORATION			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
HYPOTHERMIA			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
IMPAIRED HEALING			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
MALAISE			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
MULTIPLE ORGAN DYSFUNCTION SYNDROME			

subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
OEDEMA PERIPHERAL			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PYREXIA			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SYSTEMIC INFLAMMATORY RESPONSE SYNDROME			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
ANAPHYLACTIC REACTION			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
DRUG HYPERSENSITIVITY			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERSENSITIVITY			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
Reproductive system and breast disorders			
UTERINE HAEMORRHAGE			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Respiratory, thoracic and mediastinal disorders			
ACUTE RESPIRATORY FAILURE			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
ATELECTASIS			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
CHRONIC OBSTRUCTIVE PULMONARY DISEASE			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
DYSPNOEA			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPOXIA			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
PULMONARY EMBOLISM			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RESPIRATORY FAILURE			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
AGGRESSION			

subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
ANXIETY			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
CONFUSIONAL STATE			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
DELIRIUM			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
DEPRESSION			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MENTAL STATUS CHANGES			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
ORGANIC BRAIN SYNDROME			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
SUICIDAL IDEATION			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			

subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BLOOD ALKALINE PHOSPHATASE INCREASED			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
FIBRIN D DIMER INCREASED			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
GAMMA-GLUTAMYLTRANSFERASE INCREASED			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
GLOMERULAR FILTRATION RATE DECREASED			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
NEUTROPHIL COUNT DECREASED			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
PLATELET COUNT DECREASED			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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

WHITE BLOOD CELL COUNT DECREASED			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
BRAIN CONTUSION			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
EPIDURAL HAEMORRHAGE			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
EXPOSURE TO CONTAMINATED DEVICE			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
EXTRADURAL HAEMATOMA			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
FALL			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
FEMUR FRACTURE			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
HAND FRACTURE			

subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
POST PROCEDURAL HAEMORRHAGE			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
RADIATION NECROSIS			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
RIB FRACTURE			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
ROAD TRAFFIC ACCIDENT			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
SPINAL COMPRESSION FRACTURE			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
SUBDURAL HAEMATOMA			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
SURGICAL PROCEDURE REPEATED			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
TRAUMATIC INTRACRANIAL HAEMORRHAGE			

subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
Congenital, familial and genetic disorders			
CORNEAL DYSTROPHY			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
CARDIAC ARREST			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
VENTRICULAR ARRHYTHMIA			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
APHASIA			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
ATAXIA			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
BRAIN OEDEMA			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
CENTRAL NERVOUS SYSTEM LESION			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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

CENTRAL NERVOUS SYSTEM NECROSIS				
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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	
CEREBRAL CYST				
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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	
CEREBRAL HAEMORRHAGE				
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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	
CEREBRAL VENTRICLE DILATATION				
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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	
CEREBROVASCULAR ACCIDENT				
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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	
COGNITIVE DISORDER				
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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	
CRANIAL NERVE DISORDER				
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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	
DEPRESSED LEVEL OF CONSCIOUSNESS				
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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	
DYSKINESIA				

subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
ENCEPHALOPATHY			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
EPILEPSIA PARTIALIS CONTINUA			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
EPILEPSY			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
FACIAL PARALYSIS			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
FACIAL PARESIS			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
FOCAL DYSCOGNITIVE SEIZURES			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
GENERALISED TONIC-CLONIC SEIZURE			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
HAEMORRHAGE INTRACRANIAL			

subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
HEADACHE			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
HEMIPARESIS			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
HYDROCEPHALUS			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
INTRACRANIAL PRESSURE INCREASED			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
ISCHAEMIC STROKE			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
LOSS OF CONSCIOUSNESS			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
MOTOR DYSFUNCTION			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NERVOUS SYSTEM DISORDER			

subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
NEUROLOGICAL DECOMPENSATION			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
NEUROPATHY PERIPHERAL			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
PARAESTHESIA			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
PARTIAL SEIZURES			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
PERIPHERAL MOTOR NEUROPATHY			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
SEIZURE			
subjects affected / exposed	0 / 326 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SOMNOLENCE			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
STATUS EPILEPTICUS			

subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
SYNCOPE			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
TRANSIENT ISCHAEMIC ATTACK			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
VASOGENIC CEREBRAL OEDEMA			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
APLASTIC ANAEMIA			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
BONE MARROW FAILURE			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
DISSEMINATED INTRAVASCULAR COAGULATION			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
FEBRILE NEUTROPENIA			

subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
IMMUNE THROMBOCYTOPENIA			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
LEUKOPENIA			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
MYELOSUPPRESSION			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
NEUTROPENIA			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
THROMBOCYTOPENIA			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
THROMBOCYTOPENIC PURPURA			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
Ear and labyrinth disorders			
VERTIGO			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
Eye disorders			

CATARACT			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
CATARACT NUCLEAR			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
CORNEAL LESION			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
EYELID FUNCTION DISORDER			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
KERATOPATHY			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
OPHTHALMOPLEGIA			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
OPTIC ISCHAEMIC NEUROPATHY			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
OPTIC NEUROPATHY			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
RETINAL DETACHMENT			

subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
ULCERATIVE KERATITIS			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
VISION BLURRED			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
ANAL INCONTINENCE			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
COLITIS			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
CONSTIPATION			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIARRHOEA			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
GASTRIC HAEMORRHAGE			

subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NAUSEA			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
PANCREATITIS ACUTE			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VOMITING			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
CHOLECYSTITIS			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
HEPATITIS			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
LIVER INJURY			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
NODULAR REGENERATIVE HYPERPLASIA			

subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
ANGIOEDEMA			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
DRUG REACTION WITH EOSINOPHILIA AND SYSTEMIC SYMPTOMS			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RASH MACULO-PAPULAR			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
URTICARIA			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
Renal and urinary disorders			
ACUTE KIDNEY INJURY			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
NEPHROLITHIASIS			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
RENAL COLIC			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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

RENAL FAILURE			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY RETENTION			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
Endocrine disorders			
DIABETES INSIPIDUS			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
HAEMARTHROSIS			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
INTERVERTEBRAL DISC PROTRUSION			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
LUMBAR SPINAL STENOSIS			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
MUSCULAR WEAKNESS			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
PAIN IN EXTREMITY			

subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
ABDOMINAL SEPSIS			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
ACUTE HEPATITIS B			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
APPENDICITIS			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
APPENDICITIS PERFORATED			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
BACTERAEemia			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
BACTERIAL INFECTION			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
BRONCHITIS			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
CLOSTRIDIUM DIFFICILE COLITIS			

subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
DIVERTICULITIS			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
ENCEPHALITIS			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
ENCEPHALITIS VIRAL			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
ESCHERICHIA BACTERAEMIA			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
EXTRADURAL ABSCESS			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
EYE INFECTION STAPHYLOCOCCAL			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
HERPES SIMPLEX			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
HERPES SIMPLEX ENCEPHALITIS			

subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
HERPES SIMPLEX OESOPHAGITIS			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
HERPES ZOSTER			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
INFLUENZA			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
OTITIS MEDIA			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
PNEUMOCYSTIS JIROVECI PNEUMONIA			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA ASPIRATION			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA STREPTOCOCCAL			

subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
POSTOPERATIVE WOUND INFECTION			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
PULMONARY SEPSIS			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SEPSIS			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
SEPTIC SHOCK			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
STAPHYLOCOCCAL INFECTION			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
SUBDURAL ABSCESS			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY TRACT INFECTION			

subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
UROSEPSIS			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
VIRAL INFECTION			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
DEHYDRATION			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
HYPERGLYCAEMIA			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
HYPOCALCAEMIA			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
HYPOKALAEMIA			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
HYPONATRAEMIA			

subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
HYPOPHAGIA			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (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

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

Non-serious adverse events	Depatuxizumab Mafodotin, Radiation + TMZ: Chemoradiation Phase	Depatuxizumab Mafodotin, Radiation and TMZ: Adjuvant Phase	Depatuxizumab Mafodotin, Radiation and TMZ: Follow Up Phase
Total subjects affected by non-serious adverse events			
subjects affected / exposed	337 / 342 (98.54%)	252 / 273 (92.31%)	2 / 326 (0.61%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps) MALIGNANT NEOPLASM PROGRESSION			
subjects affected / exposed	0 / 342 (0.00%)	2 / 273 (0.73%)	0 / 326 (0.00%)
occurrences (all)	0	2	0
Vascular disorders			
HYPERAEMIA			
subjects affected / exposed	2 / 342 (0.58%)	2 / 273 (0.73%)	0 / 326 (0.00%)
occurrences (all)	2	3	0
HYPERTENSION			
subjects affected / exposed	14 / 342 (4.09%)	18 / 273 (6.59%)	0 / 326 (0.00%)
occurrences (all)	15	29	0
HYPOTENSION			
subjects affected / exposed	1 / 342 (0.29%)	3 / 273 (1.10%)	0 / 326 (0.00%)
occurrences (all)	1	5	0
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	13 / 342 (3.80%)	17 / 273 (6.23%)	0 / 326 (0.00%)
occurrences (all)	15	21	0
CHILLS			

subjects affected / exposed	8 / 342 (2.34%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences (all)	8	1	0
FATIGUE			
subjects affected / exposed	132 / 342 (38.60%)	88 / 273 (32.23%)	0 / 326 (0.00%)
occurrences (all)	155	153	0
MALAISE			
subjects affected / exposed	1 / 342 (0.29%)	2 / 273 (0.73%)	0 / 326 (0.00%)
occurrences (all)	1	2	0
OEDEMA			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences (all)	0	1	0
PYREXIA			
subjects affected / exposed	10 / 342 (2.92%)	17 / 273 (6.23%)	0 / 326 (0.00%)
occurrences (all)	14	19	0
SWELLING			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	13 / 342 (3.80%)	26 / 273 (9.52%)	0 / 326 (0.00%)
occurrences (all)	13	27	0
HICCUPS			
subjects affected / exposed	2 / 342 (0.58%)	3 / 273 (1.10%)	0 / 326 (0.00%)
occurrences (all)	2	3	0
PULMONARY OEDEMA			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (0.00%)
occurrences (all)	0	0	0
STRIDOR			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
CONFUSIONAL STATE			
subjects affected / exposed	5 / 342 (1.46%)	18 / 273 (6.59%)	0 / 326 (0.00%)
occurrences (all)	5	21	0
DEPRESSION			

subjects affected / exposed	11 / 342 (3.22%)	20 / 273 (7.33%)	0 / 326 (0.00%)
occurrences (all)	11	21	0
INSOMNIA			
subjects affected / exposed	20 / 342 (5.85%)	15 / 273 (5.49%)	0 / 326 (0.00%)
occurrences (all)	20	15	0
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	57 / 342 (16.67%)	28 / 273 (10.26%)	1 / 326 (0.31%)
occurrences (all)	82	44	1
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	54 / 342 (15.79%)	29 / 273 (10.62%)	1 / 326 (0.31%)
occurrences (all)	76	52	1
BLOOD ALKALINE PHOSPHATASE INCREASED			
subjects affected / exposed	6 / 342 (1.75%)	18 / 273 (6.59%)	1 / 326 (0.31%)
occurrences (all)	8	27	1
GAMMA-GLUTAMYLTRANSFERASE INCREASED			
subjects affected / exposed	22 / 342 (6.43%)	45 / 273 (16.48%)	0 / 326 (0.00%)
occurrences (all)	39	87	0
LYMPHOCYTE COUNT DECREASED			
subjects affected / exposed	12 / 342 (3.51%)	10 / 273 (3.66%)	0 / 326 (0.00%)
occurrences (all)	18	25	0
NEUTROPHIL COUNT DECREASED			
subjects affected / exposed	6 / 342 (1.75%)	10 / 273 (3.66%)	0 / 326 (0.00%)
occurrences (all)	7	24	0
PLATELET COUNT DECREASED			
subjects affected / exposed	29 / 342 (8.48%)	21 / 273 (7.69%)	0 / 326 (0.00%)
occurrences (all)	59	47	0
WEIGHT DECREASED			
subjects affected / exposed	7 / 342 (2.05%)	27 / 273 (9.89%)	0 / 326 (0.00%)
occurrences (all)	7	33	0
WEIGHT INCREASED			
subjects affected / exposed	1 / 342 (0.29%)	3 / 273 (1.10%)	0 / 326 (0.00%)
occurrences (all)	1	6	0
WHITE BLOOD CELL COUNT DECREASED			

subjects affected / exposed occurrences (all)	6 / 342 (1.75%) 6	12 / 273 (4.40%) 21	0 / 326 (0.00%) 0
Injury, poisoning and procedural complications			
FALL			
subjects affected / exposed	8 / 342 (2.34%)	19 / 273 (6.96%)	0 / 326 (0.00%)
occurrences (all)	9	22	0
RADIATION SKIN INJURY			
subjects affected / exposed	18 / 342 (5.26%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences (all)	19	1	0
Nervous system disorders			
APHASIA			
subjects affected / exposed	7 / 342 (2.05%)	14 / 273 (5.13%)	0 / 326 (0.00%)
occurrences (all)	7	17	0
DIZZINESS			
subjects affected / exposed	11 / 342 (3.22%)	22 / 273 (8.06%)	0 / 326 (0.00%)
occurrences (all)	13	26	0
DYSGEUSIA			
subjects affected / exposed	15 / 342 (4.39%)	5 / 273 (1.83%)	0 / 326 (0.00%)
occurrences (all)	15	5	0
HEADACHE			
subjects affected / exposed	69 / 342 (20.18%)	66 / 273 (24.18%)	0 / 326 (0.00%)
occurrences (all)	80	92	0
HEMIPARESIS			
subjects affected / exposed	5 / 342 (1.46%)	17 / 273 (6.23%)	0 / 326 (0.00%)
occurrences (all)	6	25	0
MEMORY IMPAIRMENT			
subjects affected / exposed	8 / 342 (2.34%)	9 / 273 (3.30%)	0 / 326 (0.00%)
occurrences (all)	8	9	0
PARAESTHESIA			
subjects affected / exposed	5 / 342 (1.46%)	7 / 273 (2.56%)	0 / 326 (0.00%)
occurrences (all)	5	8	0
PAROSMIA			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences (all)	0	1	0
PERIPHERAL SENSORY NEUROPATHY			

subjects affected / exposed occurrences (all)	3 / 342 (0.88%) 3	5 / 273 (1.83%) 6	0 / 326 (0.00%) 0
SEIZURE			
subjects affected / exposed occurrences (all)	13 / 342 (3.80%) 14	22 / 273 (8.06%) 42	0 / 326 (0.00%) 0
SOMNOLENCE			
subjects affected / exposed occurrences (all)	3 / 342 (0.88%) 4	14 / 273 (5.13%) 17	0 / 326 (0.00%) 0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed occurrences (all)	15 / 342 (4.39%) 23	14 / 273 (5.13%) 27	0 / 326 (0.00%) 0
LEUKOPENIA			
subjects affected / exposed occurrences (all)	22 / 342 (6.43%) 35	22 / 273 (8.06%) 52	0 / 326 (0.00%) 0
LYMPHOPENIA			
subjects affected / exposed occurrences (all)	36 / 342 (10.53%) 66	26 / 273 (9.52%) 108	0 / 326 (0.00%) 0
NEUTROPENIA			
subjects affected / exposed occurrences (all)	15 / 342 (4.39%) 27	21 / 273 (7.69%) 54	0 / 326 (0.00%) 0
THROMBOCYTOPENIA			
subjects affected / exposed occurrences (all)	104 / 342 (30.41%) 190	119 / 273 (43.59%) 343	0 / 326 (0.00%) 0
Ear and labyrinth disorders			
TINNITUS			
subjects affected / exposed occurrences (all)	2 / 342 (0.58%) 2	0 / 273 (0.00%) 0	0 / 326 (0.00%) 0
Eye disorders			
CATARACT			
subjects affected / exposed occurrences (all)	2 / 342 (0.58%) 2	13 / 273 (4.76%) 18	0 / 326 (0.00%) 0
CORNEAL EPITHELIAL MICROCYSTS			
subjects affected / exposed occurrences (all)	22 / 342 (6.43%) 31	11 / 273 (4.03%) 25	0 / 326 (0.00%) 0
DRY EYE			

subjects affected / exposed	54 / 342 (15.79%)	15 / 273 (5.49%)	0 / 326 (0.00%)
occurrences (all)	61	17	0
EYE PAIN			
subjects affected / exposed	48 / 342 (14.04%)	20 / 273 (7.33%)	0 / 326 (0.00%)
occurrences (all)	57	29	0
KERATITIS			
subjects affected / exposed	39 / 342 (11.40%)	30 / 273 (10.99%)	0 / 326 (0.00%)
occurrences (all)	60	88	0
KERATOPATHY			
subjects affected / exposed	212 / 342 (61.99%)	89 / 273 (32.60%)	0 / 326 (0.00%)
occurrences (all)	333	274	0
LACRIMATION INCREASED			
subjects affected / exposed	20 / 342 (5.85%)	3 / 273 (1.10%)	0 / 326 (0.00%)
occurrences (all)	22	3	0
OCULAR HYPERAEMIA			
subjects affected / exposed	9 / 342 (2.63%)	8 / 273 (2.93%)	0 / 326 (0.00%)
occurrences (all)	10	11	0
PHOTOPHOBIA			
subjects affected / exposed	64 / 342 (18.71%)	33 / 273 (12.09%)	0 / 326 (0.00%)
occurrences (all)	88	57	0
PUNCTATE KERATITIS			
subjects affected / exposed	27 / 342 (7.89%)	18 / 273 (6.59%)	0 / 326 (0.00%)
occurrences (all)	38	47	0
VISION BLURRED			
subjects affected / exposed	84 / 342 (24.56%)	38 / 273 (13.92%)	0 / 326 (0.00%)
occurrences (all)	97	63	0
VISUAL FIELD DEFECT			
subjects affected / exposed	1 / 342 (0.29%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences (all)	1	1	0
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	6 / 342 (1.75%)	2 / 273 (0.73%)	0 / 326 (0.00%)
occurrences (all)	7	2	0
CONSTIPATION			
subjects affected / exposed	95 / 342 (27.78%)	56 / 273 (20.51%)	1 / 326 (0.31%)
occurrences (all)	100	65	1

DIARRHOEA			
subjects affected / exposed	16 / 342 (4.68%)	21 / 273 (7.69%)	0 / 326 (0.00%)
occurrences (all)	18	24	0
DRY MOUTH			
subjects affected / exposed	5 / 342 (1.46%)	4 / 273 (1.47%)	0 / 326 (0.00%)
occurrences (all)	5	6	0
DYSPEPSIA			
subjects affected / exposed	7 / 342 (2.05%)	7 / 273 (2.56%)	0 / 326 (0.00%)
occurrences (all)	8	7	0
FLATULENCE			
subjects affected / exposed	1 / 342 (0.29%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences (all)	1	1	0
GINGIVAL PAIN			
subjects affected / exposed	0 / 342 (0.00%)	0 / 273 (0.00%)	0 / 326 (0.00%)
occurrences (all)	0	0	0
HAEMORRHOIDAL HAEMORRHAGE			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences (all)	0	1	0
HYPERAESTHESIA TEETH			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences (all)	0	1	0
NAUSEA			
subjects affected / exposed	106 / 342 (30.99%)	64 / 273 (23.44%)	0 / 326 (0.00%)
occurrences (all)	130	90	0
VOMITING			
subjects affected / exposed	39 / 342 (11.40%)	47 / 273 (17.22%)	0 / 326 (0.00%)
occurrences (all)	44	58	0
Skin and subcutaneous tissue disorders			
ALOPECIA			
subjects affected / exposed	85 / 342 (24.85%)	10 / 273 (3.66%)	0 / 326 (0.00%)
occurrences (all)	93	11	0
DERMATITIS			
subjects affected / exposed	9 / 342 (2.63%)	2 / 273 (0.73%)	0 / 326 (0.00%)
occurrences (all)	9	2	0
ERYTHEMA			

subjects affected / exposed	20 / 342 (5.85%)	5 / 273 (1.83%)	0 / 326 (0.00%)
occurrences (all)	20	5	0
PHOTOSENSITIVITY REACTION			
subjects affected / exposed	3 / 342 (0.88%)	2 / 273 (0.73%)	0 / 326 (0.00%)
occurrences (all)	4	3	0
PRURITUS			
subjects affected / exposed	14 / 342 (4.09%)	21 / 273 (7.69%)	0 / 326 (0.00%)
occurrences (all)	15	25	0
RASH			
subjects affected / exposed	16 / 342 (4.68%)	17 / 273 (6.23%)	0 / 326 (0.00%)
occurrences (all)	17	22	0
RASH MACULO-PAPULAR			
subjects affected / exposed	4 / 342 (1.17%)	0 / 273 (0.00%)	0 / 326 (0.00%)
occurrences (all)	4	0	0
Renal and urinary disorders			
NOCTURIA			
subjects affected / exposed	0 / 342 (0.00%)	1 / 273 (0.37%)	0 / 326 (0.00%)
occurrences (all)	0	2	0
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	8 / 342 (2.34%)	32 / 273 (11.72%)	0 / 326 (0.00%)
occurrences (all)	8	45	0
BACK PAIN			
subjects affected / exposed	6 / 342 (1.75%)	22 / 273 (8.06%)	0 / 326 (0.00%)
occurrences (all)	6	23	0
MUSCLE SPASMS			
subjects affected / exposed	4 / 342 (1.17%)	7 / 273 (2.56%)	0 / 326 (0.00%)
occurrences (all)	4	9	0
MUSCULAR WEAKNESS			
subjects affected / exposed	8 / 342 (2.34%)	15 / 273 (5.49%)	0 / 326 (0.00%)
occurrences (all)	9	15	0
MYALGIA			
subjects affected / exposed	1 / 342 (0.29%)	9 / 273 (3.30%)	0 / 326 (0.00%)
occurrences (all)	1	9	0
PAIN IN EXTREMITY			

subjects affected / exposed occurrences (all)	4 / 342 (1.17%) 4	19 / 273 (6.96%) 23	0 / 326 (0.00%) 0
Infections and infestations BACTERIAL INFECTION subjects affected / exposed occurrences (all)	1 / 342 (0.29%) 1	0 / 273 (0.00%) 0	0 / 326 (0.00%) 0
NASOPHARYNGITIS subjects affected / exposed occurrences (all)	5 / 342 (1.46%) 6	18 / 273 (6.59%) 21	0 / 326 (0.00%) 0
ORAL HERPES subjects affected / exposed occurrences (all)	2 / 342 (0.58%) 2	3 / 273 (1.10%) 3	0 / 326 (0.00%) 0
Metabolism and nutrition disorders DECREASED APPETITE subjects affected / exposed occurrences (all)	40 / 342 (11.70%) 44	42 / 273 (15.38%) 53	0 / 326 (0.00%) 0
GOUT subjects affected / exposed occurrences (all)	1 / 342 (0.29%) 1	1 / 273 (0.37%) 1	0 / 326 (0.00%) 0
HYPOKALAEMIA subjects affected / exposed occurrences (all)	9 / 342 (2.63%) 11	10 / 273 (3.66%) 20	0 / 326 (0.00%) 0
HYPONATRAEMIA subjects affected / exposed occurrences (all)	2 / 342 (0.58%) 2	1 / 273 (0.37%) 1	0 / 326 (0.00%) 0

Non-serious adverse events	Placebo, Radiation and TMZ: Chemoradiation Phase	Placebo, Radiation and TMZ: Adjuvant Phase	OL Depatuxizumab Mafodotin, Radiation + TMZ: Chemoradiation Ph
Total subjects affected by non-serious adverse events subjects affected / exposed	290 / 335 (86.57%)	255 / 285 (89.47%)	6 / 6 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps) MALIGNANT NEOPLASM PROGRESSION subjects affected / exposed occurrences (all)	1 / 335 (0.30%) 1	2 / 285 (0.70%) 3	0 / 6 (0.00%) 0
Vascular disorders			

HYPERAEMIA			
subjects affected / exposed	1 / 335 (0.30%)	0 / 285 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
HYPERTENSION			
subjects affected / exposed	8 / 335 (2.39%)	15 / 285 (5.26%)	0 / 6 (0.00%)
occurrences (all)	10	23	0
HYPOTENSION			
subjects affected / exposed	9 / 335 (2.69%)	4 / 285 (1.40%)	0 / 6 (0.00%)
occurrences (all)	9	5	0
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	17 / 335 (5.07%)	17 / 285 (5.96%)	0 / 6 (0.00%)
occurrences (all)	22	21	0
CHILLS			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
FATIGUE			
subjects affected / exposed	110 / 335 (32.84%)	77 / 285 (27.02%)	0 / 6 (0.00%)
occurrences (all)	130	140	0
MALAISE			
subjects affected / exposed	3 / 335 (0.90%)	1 / 285 (0.35%)	1 / 6 (16.67%)
occurrences (all)	3	3	1
OEDEMA			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
PYREXIA			
subjects affected / exposed	12 / 335 (3.58%)	12 / 285 (4.21%)	0 / 6 (0.00%)
occurrences (all)	12	14	0
SWELLING			
subjects affected / exposed	2 / 335 (0.60%)	1 / 285 (0.35%)	1 / 6 (16.67%)
occurrences (all)	2	1	1
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	19 / 335 (5.67%)	25 / 285 (8.77%)	0 / 6 (0.00%)
occurrences (all)	20	26	0
HICCUPS			

subjects affected / exposed occurrences (all)	1 / 335 (0.30%) 1	2 / 285 (0.70%) 2	1 / 6 (16.67%) 1
PULMONARY OEDEMA subjects affected / exposed occurrences (all)	0 / 335 (0.00%) 0	0 / 285 (0.00%) 0	0 / 6 (0.00%) 0
STRIDOR subjects affected / exposed occurrences (all)	0 / 335 (0.00%) 0	0 / 285 (0.00%) 0	0 / 6 (0.00%) 0
Psychiatric disorders CONFUSIONAL STATE subjects affected / exposed occurrences (all)	2 / 335 (0.60%) 2	9 / 285 (3.16%) 11	0 / 6 (0.00%) 0
DEPRESSION subjects affected / exposed occurrences (all)	11 / 335 (3.28%) 12	11 / 285 (3.86%) 11	0 / 6 (0.00%) 0
INSOMNIA subjects affected / exposed occurrences (all)	18 / 335 (5.37%) 20	22 / 285 (7.72%) 25	0 / 6 (0.00%) 0
Investigations ALANINE AMINOTRANSFERASE INCREASED subjects affected / exposed occurrences (all)	26 / 335 (7.76%) 30	13 / 285 (4.56%) 16	2 / 6 (33.33%) 2
ASPARTATE AMINOTRANSFERASE INCREASED subjects affected / exposed occurrences (all)	23 / 335 (6.87%) 26	7 / 285 (2.46%) 7	2 / 6 (33.33%) 2
BLOOD ALKALINE PHOSPHATASE INCREASED subjects affected / exposed occurrences (all)	4 / 335 (1.19%) 4	0 / 285 (0.00%) 0	1 / 6 (16.67%) 1
GAMMA-GLUTAMYLTRANSFERASE INCREASED subjects affected / exposed occurrences (all)	7 / 335 (2.09%) 9	7 / 285 (2.46%) 11	2 / 6 (33.33%) 2
LYMPHOCYTE COUNT DECREASED subjects affected / exposed occurrences (all)	15 / 335 (4.48%) 22	16 / 285 (5.61%) 23	0 / 6 (0.00%) 0

NEUTROPHIL COUNT DECREASED subjects affected / exposed occurrences (all)	8 / 335 (2.39%) 10	10 / 285 (3.51%) 17	0 / 6 (0.00%) 0
PLATELET COUNT DECREASED subjects affected / exposed occurrences (all)	10 / 335 (2.99%) 12	14 / 285 (4.91%) 22	0 / 6 (0.00%) 0
WEIGHT DECREASED subjects affected / exposed occurrences (all)	7 / 335 (2.09%) 7	30 / 285 (10.53%) 31	0 / 6 (0.00%) 0
WEIGHT INCREASED subjects affected / exposed occurrences (all)	2 / 335 (0.60%) 3	8 / 285 (2.81%) 11	0 / 6 (0.00%) 0
WHITE BLOOD CELL COUNT DECREASED subjects affected / exposed occurrences (all)	10 / 335 (2.99%) 20	17 / 285 (5.96%) 45	0 / 6 (0.00%) 0
Injury, poisoning and procedural complications FALL subjects affected / exposed occurrences (all)	7 / 335 (2.09%) 9	21 / 285 (7.37%) 30	0 / 6 (0.00%) 0
RADIATION SKIN INJURY subjects affected / exposed occurrences (all)	21 / 335 (6.27%) 22	1 / 285 (0.35%) 1	1 / 6 (16.67%) 1
Nervous system disorders APHASIA subjects affected / exposed occurrences (all)	10 / 335 (2.99%) 10	15 / 285 (5.26%) 20	0 / 6 (0.00%) 0
DIZZINESS subjects affected / exposed occurrences (all)	19 / 335 (5.67%) 19	31 / 285 (10.88%) 38	1 / 6 (16.67%) 1
DYSGEUSIA subjects affected / exposed occurrences (all)	18 / 335 (5.37%) 20	5 / 285 (1.75%) 5	1 / 6 (16.67%) 1
HEADACHE subjects affected / exposed occurrences (all)	64 / 335 (19.10%) 73	52 / 285 (18.25%) 80	1 / 6 (16.67%) 1
HEMIPARESIS			

subjects affected / exposed	11 / 335 (3.28%)	21 / 285 (7.37%)	0 / 6 (0.00%)
occurrences (all)	13	28	0
MEMORY IMPAIRMENT			
subjects affected / exposed	7 / 335 (2.09%)	21 / 285 (7.37%)	0 / 6 (0.00%)
occurrences (all)	7	22	0
PARAESTHESIA			
subjects affected / exposed	6 / 335 (1.79%)	17 / 285 (5.96%)	0 / 6 (0.00%)
occurrences (all)	7	19	0
PAROSMIA			
subjects affected / exposed	2 / 335 (0.60%)	1 / 285 (0.35%)	1 / 6 (16.67%)
occurrences (all)	2	1	1
PERIPHERAL SENSORY NEUROPATHY			
subjects affected / exposed	5 / 335 (1.49%)	5 / 285 (1.75%)	0 / 6 (0.00%)
occurrences (all)	5	7	0
SEIZURE			
subjects affected / exposed	15 / 335 (4.48%)	19 / 285 (6.67%)	0 / 6 (0.00%)
occurrences (all)	16	31	0
SOMNOLENCE			
subjects affected / exposed	5 / 335 (1.49%)	10 / 285 (3.51%)	0 / 6 (0.00%)
occurrences (all)	5	12	0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	21 / 335 (6.27%)	14 / 285 (4.91%)	0 / 6 (0.00%)
occurrences (all)	29	21	0
LEUKOPENIA			
subjects affected / exposed	21 / 335 (6.27%)	26 / 285 (9.12%)	0 / 6 (0.00%)
occurrences (all)	37	86	0
LYMPHOPENIA			
subjects affected / exposed	50 / 335 (14.93%)	38 / 285 (13.33%)	1 / 6 (16.67%)
occurrences (all)	95	162	1
NEUTROPENIA			
subjects affected / exposed	27 / 335 (8.06%)	25 / 285 (8.77%)	0 / 6 (0.00%)
occurrences (all)	46	49	0
THROMBOCYTOPENIA			
subjects affected / exposed	47 / 335 (14.03%)	75 / 285 (26.32%)	3 / 6 (50.00%)
occurrences (all)	80	193	4

Ear and labyrinth disorders			
TINNITUS			
subjects affected / exposed	3 / 335 (0.90%)	6 / 285 (2.11%)	1 / 6 (16.67%)
occurrences (all)	3	6	1
Eye disorders			
CATARACT			
subjects affected / exposed	3 / 335 (0.90%)	10 / 285 (3.51%)	1 / 6 (16.67%)
occurrences (all)	4	11	2
CORNEAL EPITHELIAL MICROCYSTS			
subjects affected / exposed	0 / 335 (0.00%)	1 / 285 (0.35%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
DRY EYE			
subjects affected / exposed	20 / 335 (5.97%)	12 / 285 (4.21%)	0 / 6 (0.00%)
occurrences (all)	20	12	0
EYE PAIN			
subjects affected / exposed	8 / 335 (2.39%)	8 / 285 (2.81%)	1 / 6 (16.67%)
occurrences (all)	9	9	2
KERATITIS			
subjects affected / exposed	2 / 335 (0.60%)	3 / 285 (1.05%)	1 / 6 (16.67%)
occurrences (all)	2	4	1
KERATOPATHY			
subjects affected / exposed	16 / 335 (4.78%)	12 / 285 (4.21%)	6 / 6 (100.00%)
occurrences (all)	16	17	6
LACRIMATION INCREASED			
subjects affected / exposed	8 / 335 (2.39%)	2 / 285 (0.70%)	0 / 6 (0.00%)
occurrences (all)	8	2	0
OCULAR HYPERAEMIA			
subjects affected / exposed	3 / 335 (0.90%)	2 / 285 (0.70%)	0 / 6 (0.00%)
occurrences (all)	3	2	0
PHOTOPHOBIA			
subjects affected / exposed	16 / 335 (4.78%)	12 / 285 (4.21%)	4 / 6 (66.67%)
occurrences (all)	16	13	4
PUNCTATE KERATITIS			
subjects affected / exposed	3 / 335 (0.90%)	7 / 285 (2.46%)	0 / 6 (0.00%)
occurrences (all)	3	8	0
VISION BLURRED			

subjects affected / exposed	21 / 335 (6.27%)	15 / 285 (5.26%)	1 / 6 (16.67%)
occurrences (all)	22	17	1
VISUAL FIELD DEFECT			
subjects affected / exposed	0 / 335 (0.00%)	2 / 285 (0.70%)	1 / 6 (16.67%)
occurrences (all)	0	2	1
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	6 / 335 (1.79%)	20 / 285 (7.02%)	0 / 6 (0.00%)
occurrences (all)	6	21	0
CONSTIPATION			
subjects affected / exposed	79 / 335 (23.58%)	51 / 285 (17.89%)	2 / 6 (33.33%)
occurrences (all)	89	63	2
DIARRHOEA			
subjects affected / exposed	16 / 335 (4.78%)	24 / 285 (8.42%)	0 / 6 (0.00%)
occurrences (all)	19	29	0
DRY MOUTH			
subjects affected / exposed	3 / 335 (0.90%)	5 / 285 (1.75%)	1 / 6 (16.67%)
occurrences (all)	5	8	1
DYSPEPSIA			
subjects affected / exposed	5 / 335 (1.49%)	6 / 285 (2.11%)	1 / 6 (16.67%)
occurrences (all)	6	7	1
FLATULENCE			
subjects affected / exposed	0 / 335 (0.00%)	2 / 285 (0.70%)	1 / 6 (16.67%)
occurrences (all)	0	2	1
GINGIVAL PAIN			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
HAEMORRHOIDAL HAEMORRHAGE			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
HYPERAESTHESIA TEETH			
subjects affected / exposed	0 / 335 (0.00%)	0 / 285 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
NAUSEA			
subjects affected / exposed	79 / 335 (23.58%)	87 / 285 (30.53%)	2 / 6 (33.33%)
occurrences (all)	87	133	2

VOMITING subjects affected / exposed occurrences (all)	23 / 335 (6.87%) 24	50 / 285 (17.54%) 63	2 / 6 (33.33%) 2
Skin and subcutaneous tissue disorders			
ALOPECIA subjects affected / exposed occurrences (all)	97 / 335 (28.96%) 103	10 / 285 (3.51%) 10	4 / 6 (66.67%) 4
DERMATITIS subjects affected / exposed occurrences (all)	7 / 335 (2.09%) 7	0 / 285 (0.00%) 0	2 / 6 (33.33%) 2
ERYTHEMA subjects affected / exposed occurrences (all)	17 / 335 (5.07%) 17	9 / 285 (3.16%) 9	0 / 6 (0.00%) 0
PHOTOSENSITIVITY REACTION subjects affected / exposed occurrences (all)	0 / 335 (0.00%) 0	0 / 285 (0.00%) 0	0 / 6 (0.00%) 0
PRURITUS subjects affected / exposed occurrences (all)	14 / 335 (4.18%) 16	18 / 285 (6.32%) 23	1 / 6 (16.67%) 1
RASH subjects affected / exposed occurrences (all)	9 / 335 (2.69%) 9	14 / 285 (4.91%) 20	0 / 6 (0.00%) 0
RASH MACULO-PAPULAR subjects affected / exposed occurrences (all)	1 / 335 (0.30%) 1	5 / 285 (1.75%) 8	1 / 6 (16.67%) 1
Renal and urinary disorders			
NOCTURIA subjects affected / exposed occurrences (all)	0 / 335 (0.00%) 0	1 / 285 (0.35%) 1	1 / 6 (16.67%) 1
Musculoskeletal and connective tissue disorders			
ARTHRALGIA subjects affected / exposed occurrences (all)	6 / 335 (1.79%) 6	25 / 285 (8.77%) 32	0 / 6 (0.00%) 0
BACK PAIN subjects affected / exposed occurrences (all)	5 / 335 (1.49%) 5	18 / 285 (6.32%) 18	0 / 6 (0.00%) 0

MUSCLE SPASMS subjects affected / exposed occurrences (all)	6 / 335 (1.79%) 7	9 / 285 (3.16%) 10	0 / 6 (0.00%) 0
MUSCULAR WEAKNESS subjects affected / exposed occurrences (all)	8 / 335 (2.39%) 8	12 / 285 (4.21%) 18	0 / 6 (0.00%) 0
MYALGIA subjects affected / exposed occurrences (all)	4 / 335 (1.19%) 4	11 / 285 (3.86%) 12	0 / 6 (0.00%) 0
PAIN IN EXTREMITY subjects affected / exposed occurrences (all)	5 / 335 (1.49%) 5	18 / 285 (6.32%) 25	0 / 6 (0.00%) 0
Infections and infestations BACTERIAL INFECTION subjects affected / exposed occurrences (all)	0 / 335 (0.00%) 0	0 / 285 (0.00%) 0	0 / 6 (0.00%) 0
NASOPHARYNGITIS subjects affected / exposed occurrences (all)	9 / 335 (2.69%) 9	17 / 285 (5.96%) 20	0 / 6 (0.00%) 0
ORAL HERPES subjects affected / exposed occurrences (all)	4 / 335 (1.19%) 4	4 / 285 (1.40%) 5	0 / 6 (0.00%) 0
Metabolism and nutrition disorders DECREASED APPETITE subjects affected / exposed occurrences (all)	36 / 335 (10.75%) 36	44 / 285 (15.44%) 55	0 / 6 (0.00%) 0
GOUT subjects affected / exposed occurrences (all)	0 / 335 (0.00%) 0	1 / 285 (0.35%) 2	0 / 6 (0.00%) 0
HYPOKALAEMIA subjects affected / exposed occurrences (all)	12 / 335 (3.58%) 15	11 / 285 (3.86%) 14	0 / 6 (0.00%) 0
HYPONATRAEMIA subjects affected / exposed occurrences (all)	6 / 335 (1.79%) 6	4 / 285 (1.40%) 4	2 / 6 (33.33%) 2

Non-serious adverse events	Placebo, Radiation	OL Depatuxizumab	OL Depatuxizumab
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	and TMZ: Follow Up Phase	Mafodotin, Radiation and TMZ: Adjuvant Phase	Mafodotin, Radiation + TMZ: Follow-up Phase
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 326 (0.31%)	6 / 6 (100.00%)	0 / 5 (0.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
MALIGNANT NEOPLASM PROGRESSION			
subjects affected / exposed	0 / 326 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			
HYPERAEMIA			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
HYPERTENSION			
subjects affected / exposed	0 / 326 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
HYPOTENSION			
subjects affected / exposed	0 / 326 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
CHILLS			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
FATIGUE			
subjects affected / exposed	0 / 326 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
MALAISE			
subjects affected / exposed	0 / 326 (0.00%)	2 / 6 (33.33%)	0 / 5 (0.00%)
occurrences (all)	0	3	0
OEDEMA			
subjects affected / exposed	0 / 326 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
PYREXIA			

subjects affected / exposed	0 / 326 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
SWELLING			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
HICCUPS			
subjects affected / exposed	0 / 326 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
PULMONARY OEDEMA			
subjects affected / exposed	0 / 326 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
STRIDOR			
subjects affected / exposed	0 / 326 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
CONFUSIONAL STATE			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
DEPRESSION			
subjects affected / exposed	0 / 326 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
INSOMNIA			
subjects affected / exposed	0 / 326 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 326 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 326 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0

BLOOD ALKALINE PHOSPHATASE INCREASED			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
GAMMA-GLUTAMYLTRANSFERASE INCREASED			
subjects affected / exposed	0 / 326 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
LYMPHOCYTE COUNT DECREASED			
subjects affected / exposed	1 / 326 (0.31%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
NEUTROPHIL COUNT DECREASED			
subjects affected / exposed	0 / 326 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
PLATELET COUNT DECREASED			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
WEIGHT DECREASED			
subjects affected / exposed	0 / 326 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
WEIGHT INCREASED			
subjects affected / exposed	0 / 326 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
WHITE BLOOD CELL COUNT DECREASED			
subjects affected / exposed	0 / 326 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	4	0
Injury, poisoning and procedural complications			
FALL			
subjects affected / exposed	0 / 326 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
RADIATION SKIN INJURY			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
APHASIA			

subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
DIZZINESS			
subjects affected / exposed	0 / 326 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
DYSGEUSIA			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
HEADACHE			
subjects affected / exposed	0 / 326 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
HEMIPARESIS			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
MEMORY IMPAIRMENT			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
PARAESTHESIA			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
PAROSMIA			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
PERIPHERAL SENSORY NEUROPATHY			
subjects affected / exposed	0 / 326 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
SEIZURE			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
SOMNOLENCE			
subjects affected / exposed	0 / 326 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	0 / 326 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0

LEUKOPENIA			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
LYMPHOPENIA			
subjects affected / exposed	0 / 326 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	3	0
NEUTROPENIA			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
THROMBOCYTOPENIA			
subjects affected / exposed	0 / 326 (0.00%)	5 / 6 (83.33%)	0 / 5 (0.00%)
occurrences (all)	0	15	0
Ear and labyrinth disorders			
TINNITUS			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
CATARACT			
subjects affected / exposed	0 / 326 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
CORNEAL EPITHELIAL MICROCYSTS			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
DRY EYE			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
EYE PAIN			
subjects affected / exposed	0 / 326 (0.00%)	2 / 6 (33.33%)	0 / 5 (0.00%)
occurrences (all)	0	3	0
KERATITIS			
subjects affected / exposed	0 / 326 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
KERATOPATHY			
subjects affected / exposed	0 / 326 (0.00%)	3 / 6 (50.00%)	0 / 5 (0.00%)
occurrences (all)	0	12	0
LACRIMATION INCREASED			

subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
OCULAR HYPERAEMIA			
subjects affected / exposed	0 / 326 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
PHOTOPHOBIA			
subjects affected / exposed	0 / 326 (0.00%)	3 / 6 (50.00%)	0 / 5 (0.00%)
occurrences (all)	0	8	0
PUNCTATE KERATITIS			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
VISION BLURRED			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
VISUAL FIELD DEFECT			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
CONSTIPATION			
subjects affected / exposed	0 / 326 (0.00%)	2 / 6 (33.33%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
DIARRHOEA			
subjects affected / exposed	0 / 326 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
DRY MOUTH			
subjects affected / exposed	0 / 326 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
DYSPEPSIA			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
FLATULENCE			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

GINGIVAL PAIN	subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
	occurrences (all)	0	0	0
HAEMORRHOIDAL HAEMORRHAGE	subjects affected / exposed	0 / 326 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
	occurrences (all)	0	1	0
HYPERAESTHESIA TEETH	subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
	occurrences (all)	0	0	0
NAUSEA	subjects affected / exposed	0 / 326 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
	occurrences (all)	0	3	0
VOMITING	subjects affected / exposed	0 / 326 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
	occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders				
ALOPECIA	subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
	occurrences (all)	0	0	0
DERMATITIS	subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
	occurrences (all)	0	0	0
ERYTHEMA	subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
	occurrences (all)	0	0	0
PHOTOSENSITIVITY REACTION	subjects affected / exposed	0 / 326 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
	occurrences (all)	0	1	0
PRURITUS	subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
	occurrences (all)	0	0	0
RASH	subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
	occurrences (all)	0	0	0
RASH MACULO-PAPULAR				

subjects affected / exposed occurrences (all)	0 / 326 (0.00%) 0	1 / 6 (16.67%) 1	0 / 5 (0.00%) 0
Renal and urinary disorders NOCTURIA subjects affected / exposed occurrences (all)	0 / 326 (0.00%) 0	1 / 6 (16.67%) 1	0 / 5 (0.00%) 0
Musculoskeletal and connective tissue disorders ARTHRALGIA subjects affected / exposed occurrences (all)	0 / 326 (0.00%) 0	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0
BACK PAIN subjects affected / exposed occurrences (all)	0 / 326 (0.00%) 0	1 / 6 (16.67%) 1	0 / 5 (0.00%) 0
MUSCLE SPASMS subjects affected / exposed occurrences (all)	0 / 326 (0.00%) 0	1 / 6 (16.67%) 1	0 / 5 (0.00%) 0
MUSCULAR WEAKNESS subjects affected / exposed occurrences (all)	0 / 326 (0.00%) 0	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0
MYALGIA subjects affected / exposed occurrences (all)	0 / 326 (0.00%) 0	1 / 6 (16.67%) 1	0 / 5 (0.00%) 0
PAIN IN EXTREMITY subjects affected / exposed occurrences (all)	0 / 326 (0.00%) 0	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0
Infections and infestations BACTERIAL INFECTION subjects affected / exposed occurrences (all)	0 / 326 (0.00%) 0	1 / 6 (16.67%) 1	0 / 5 (0.00%) 0
NASOPHARYNGITIS subjects affected / exposed occurrences (all)	0 / 326 (0.00%) 0	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0
ORAL HERPES subjects affected / exposed occurrences (all)	0 / 326 (0.00%) 0	1 / 6 (16.67%) 1	0 / 5 (0.00%) 0
Metabolism and nutrition disorders			

DECREASED APPETITE			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
GOUT			
subjects affected / exposed	0 / 326 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
HYPOKALAEMIA			
subjects affected / exposed	0 / 326 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
HYPONATRAEMIA			
subjects affected / exposed	0 / 326 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 March 2016	Added a sub-study for subjects with mild or moderate hepatic impairment (Child-Pugh scores 5 to 9); revised exclusion criterion 16 to only exclude subjects with severe hepatic impairment (Child-Pugh C score ≥ 10) and to refer subjects with mild or moderate impairment to be evaluated for inclusion in substudy; clarified timing of screening MRI and that it should be performed with and without contrast.
07 December 2016	Revised inclusion criterion 4 to remove requirement for 72 hour post-surgical MRI.
13 January 2017	The screening interval between resection and start of Chemoradiation was increased from 6 to 7 weeks; removed inclusion criterion 3 (supratentorial tumor); updated inclusion criterion 8 regarding adequate hepatic function definition: aspartate aminotransferase (AST) and alanine aminotransferase (ALT) values (from 1.5 to ≤ 3 upper limit of normal).
06 December 2017	The original study design was a seamless Phase 2b/3 that allowed early termination of the study and reduced unnecessary subject exposures to an ineffective treatment if the Phase 2b results demonstrated futility. However, as further described in Amendment 6, based on rapid enrollment and other available information, the study design was modified to eliminate the progression-free survival (PFS)-based Phase 2b interim futility analysis and to complete the study as a Phase 3 study based on the most clinically relevant efficacy endpoint of OS, which became the primary endpoint. The amendment also adjusted the study overall sample size from 720 to 640, while maintaining the target number of 441 OS events for the overall study primary analysis. Reducing the enrollment from 720 to 640, while keeping the number of OS events planned for analysis at 441, was projected to increase the overall study duration by approximately 3 months, providing longer observation for the enrolled subjects and incorporating more information on longer term survival in the primary analysis while maintaining statistical power. With this amendment, an interim superiority and futility analysis was added to the study, which was to be performed when 75% (332) of the 441 required number of deaths are observed.
29 May 2018	Added depatuxizumab mafodotin/placebo dose modification guidelines and general toxicity management guidelines for hepatic laboratory abnormalities.
29 November 2018	Updated secondary objectives to clarify PFS is centrally assessed, add OS for MGMT unmethylated subgroup and to move MGMT subgroups higher in the order of secondary endpoints, and move OS and PFS for EGFRvIII lower in the order of secondary endpoints. Clarified and revised exploratory endpoints, which included but was not limited to adding PFS in MGMT methylation status subgroups. The window for reporting adverse events (AEs) was extended from 35 to 49 days following final dose of depatuxizumab mafodotin/placebo, and a 49-day Follow-up visit (which could be conducted via phone call) was added to reflect this change. Unblinding procedures were clarified.

26 May 2019	Added a brief summary of results for the protocol-specified interim efficacy analysis in the introduction. Provided modified study procedures and instructions for study drug dosing for those subjects currently receiving depatuxizumab mafodotin who chose to continue on the drug. No additional efficacy data would be collected, and procedures were minimized to include those necessary for study drug dosing, safety monitoring and collection of safety data related to AEs and serious adverse events (SAEs). Although the interim efficacy analysis results overall indicated no survival benefit for adding depatuxizumab mafodotin to standard RT/TMZ therapy in newly diagnosed GBM patients, given that no new clinically significant safety risks were identified it was decided to allow subjects currently receiving study drug to continue treatment if the investigator and subject believed it is in the subject's best interest.
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Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported