Clinical trial results:
A Phase Ib dose escalation/randomized Phase II, multicenter, open-label study of BYL719 in combination with cetuximab in patients with recurrent or metastatic head and neck squamous cell carcinoma

Summary

EudraCT number	2011-006017-34
Trial protocol	NL FR
Global end of trial date	09 May 2016

Results information

Result version number	v1 (current)
This version publication date	24 May 2017
First version publication date	24 May 2017

Trial information

Trial identification

Sponsor protocol code	CBYL719X2104

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, +41 613241111,
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, +41 613241111,

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	09 May 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 May 2016
Global end of trial reached?	Yes
Global end of trial date	09 May 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Phase Ib
•Arm A and B: To estimate the maximum tolerated dose (MTD(s)) and/or recommended Phase II dose (RP2D) of BYL719 in combination with cetuximab in patients with recurrent or metastatic head and neck squamous cell carcinoma (RM HNSCC) in the following two arms:
•Arm A: BYL719 administered orally as a film-coated whole tablet in patients able to swallow the tablets.
•Arm B: BYL719 administered orally as a drinkable suspension prepared from film-coated crushed tablets in patients with swallowing dysfunction.
•Arm C: To compare single-dose exposure of BYL719 dispersible tablet via G-tube in combination with cetuximab in RM HNSCC to that of Arm A (film-coated tablets).
Phase II
•Scheme 1: To assess the anti-tumor activity of BYL719 in combination with cetuximab vs. cetuximab as single-agent in RM HNSCC patients naïve to cetuximab.
•Scheme 2: To assess the anti-tumor activity of BYL719 in combination with cetuximab in RM HNSCC cetuximab resistant patients.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 November 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 9
Country: Number of subjects enrolled	Canada: 18
Country: Number of subjects enrolled	France: 25
Country: Number of subjects enrolled	Hong Kong: 1
Country: Number of subjects enrolled	Korea, Republic of: 21
Country: Number of subjects enrolled	Netherlands: 7
Country: Number of subjects enrolled	Singapore: 7
Country: Number of subjects enrolled	Taiwan: 31
Country: Number of subjects enrolled	United States: 61

Worldwide total number of subjects	180
EEA total number of subjects	32

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)	135
From 65 to 84 years	45
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

All patients have completed the trial.

Pre-assignment

Screening details:

45 patients enrolled in Phase Ib, 106 cetuximab naïve patients in Phase II were randomized to either BYL719+cet (N=71) or cet monotherapy (N=35). Of the 35 patients, 16 crossed over to BYL719+cet combo treatment. 29 patients enrolled in the non-randomized combo treatment arm (cet resistant patients).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A - 300mg BYL719+Cetuximab

Arm description:

300 mg BYL719 as film-coated (FC) whole tablets with cetuximab in Phase Ib

Arm type	Experimental
Investigational medicinal product name	BYL719
Investigational medicinal product code	BYL719
Other name	Alpelisib
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

BYL719 at 300mg once daily (film-coated tablets without swallowing dysfunction) with cetuximab at 400 mg/m2 on cycle 1 Day 1 and 250 mg/m2 weekly.

Arm title	Arm A - 400mg BYL719+Cetuximab

Arm description:

400 mg BYL719 as FC whole tablets with cetuximab in Phase Ib

Arm type	Experimental
Investigational medicinal product name	BYL719
Investigational medicinal product code	BYL719
Other name	Alpelisib
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

BYL719 at 400mg once daily (film-coated tablets without swallowing dysfunction) with cetuximab at 400 mg/m2 on cycle 1 Day 1 and 250 mg/m2 weekly.

Arm title	Arm B - BYL719 + Cetuximab, Oral suspension

Arm description:

300mg BYL719 as crushed FC tablets with cetuxumab in patients with swallowing dysfunction in Phase Ib.

Arm type	Experimental

Investigational medicinal product name	BYL719
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

BYL719 at 300mg once daily with cetuximab at 400 mg/m2 on cycle 1 Day 1 and 250 mg/m2 weekly. Patients with swallowing dysfunction without G tube, BYL719 film-coated tablets were administered as drinkable suspension by crushing the tablets and suspending them in water.

Arm title	Arm C - BYL719+Cetuximab, Dispersible tablets

Arm description:

300mg BYL719 dispersible tablets with cetuxumab in patients with swallowing dysfunction administered via G-tube in Phase Ib.

Arm type	Experimental
Investigational medicinal product name	BYL719
Investigational medicinal product code	BYL719
Other name	
Pharmaceutical forms	Dispersible tablet
Routes of administration	Gastroenteral use

Dosage and administration details:

BYL719 dispersible tablets were suspended in water and administered via the gastronomy tube (G-tube). BYL719 at 300mg once daily with cetuximab at 400 mg/m2 on cycle 1 Day 1 and 250 mg/m2 weekly.

Arm title	Arm 1 - BYL719+Cetuximab (randomized)

Arm description:

300mg BYL719 with cetuxumab (Phase II) in patients resistant to or intolerant/ineligible for platinum-based chemotherapy.

Arm type	Experimental
Investigational medicinal product name	BYL719
Investigational medicinal product code	
Other name	Alpelisib
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

300 mg BYL719 was administered as whole tablet. Patients were instructed to take BYL719 daily in the morning approximately 1 hour after the start of a light breakfast at approximately the same time each day. Patients were to fast for 1 hour after the administration of BYL719.
Cetuximab was administered intravenously weekly on Day 1, Day 8, Day 15, and Day 22 of every cycle at the study site with a ± 3 day time window.

Arm title	Arm 2 - Monotherapy Cetuximab (randomized)

Arm description:

Cetuximab in Phase II in patients resistant to or intolerant/ineligible for platinum-based chemotherapy.

Arm type	Active comparator
Investigational medicinal product name	Cetuximab
Investigational medicinal product code	
Other name	erbitux
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Cetuximab was administered intravenously weekly on Day 1, Day 8, Day 15, and Day 22 of every cycle at the study site with a ± 3 day time window. Cetuximab at 400 mg/m2 on cycle 1 Day 1 and 250 mg/m2 weekly

Arm title	Arm 3 - BYL719+Cetuximab (non-randomized)

Arm description:

300mg BYL719 with cetuximab in Phase II in patients resistant to platinum-based therapy and cetuximab

Arm type	Experimental
Investigational medicinal product name	BYL719
Investigational medicinal product code	
Other name	Alpelisib
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

300 mg BYL719 was administered as whole tablet. Patients were instructed to take BYL719 daily in the morning approximately 1 hour after the start of a light breakfast at approximately the same time each day. Patients were to fast for 1 hour after the administration of BYL719.
Cetuximab was administered intravenously weekly on Day 1, Day 8, Day 15, and Day 22 of every cycle at the study site with a ± 3 day time window.

Number of subjects in period 1	Arm A - 300mg BYL719+Cetuximab	Arm A - 400mg BYL719+Cetuximab	Arm B - BYL719 + Cetuximab, Oral suspension
Started	16	5	18
Completed	0	0	0
Not completed	16	5	18
Adverse event, serious fatal	1	1	1
Physician decision	2	-	-
Consent withdrawn by subject	2	-	2
Disease progression	6	3	10
Adverse event, non-fatal	5	1	5
Cross-over patients to combo treatment	-	-	-
Subject/guardian decision	-	-	-
Protocol deviation	-	-	-

Number of subjects in period 1	Arm C - BYL719+Cetuximab, Dispersible tablets	Arm 1 - BYL719+Cetuximab (randomized)	Arm 2 - Monotherapy Cetuximab (randomized)
Started	6	71	35
Completed	0	0	0
Not completed	6	71	35
Adverse event, serious fatal	1	7	2
Physician decision	-	2	1
Consent withdrawn by subject	-	6	-
Disease progression	1	41	12
Adverse event, non-fatal	4	15	3
Cross-over patients to combo treatment	-	-	16
Subject/guardian decision	-	-	-
Protocol deviation	-	-	1

Number of subjects in period 1	Arm 3 - BYL719+Cetuximab (non-randomized)
Started	29
Completed	0
Not completed	29
Adverse event, serious fatal	2
Physician decision	1
Consent withdrawn by subject	1
Disease progression	15
Adverse event, non-fatal	9
Cross-over patients to combo treatment	-
Subject/guardian decision	1
Protocol deviation	-

Baseline characteristics

Reporting groups	
Reporting group title	Arm A - 300mg BYL719+Cetuximab
Reporting group description:	
300 mg BYL719 as film-coated (FC) whole tablets with cetuximab in Phase Ib	
Reporting group title	Arm A - 400mg BYL719+Cetuximab
Reporting group description:	
400 mg BYL719 as FC whole tablets with cetuximab in Phase Ib	
Reporting group title	Arm B - BYL719 + Cetuximab, Oral suspension
Reporting group description:	
300mg BYL719 as crushed FC tablets with cetuxumab in patients with swallowing dysfunction in Phase Ib.	
Reporting group title	Arm C - BYL719+Cetuximab, Dispersible tablets
Reporting group description:	
300mg BYL719 dispersible tablets with cetuxumab in patients with swallowing dysfunction administered via G-tube in Phase Ib.	
Reporting group title	Arm 1 - BYL719+Cetuximab (randomized)
Reporting group description:	
300mg BYL719 with cetuxumab (Phase II) in patients resistant to or intolerant/ineligible for platinum-based chemotherapy.	
Reporting group title	Arm 2 - Monotherapy Cetuximab (randomized)
Reporting group description:	
Cetuximab in Phase II in patients resistant to or intolerant/ineligible for platinum-based chemotherapy.	
Reporting group title	Arm 3 - BYL719+Cetuximab (non-randomized)
Reporting group description:	
300mg BYL719 with cetuximab in Phase II in patients resistant to platinum-based therapy and cetuximab	

Reporting group values	Arm A - 300mg BYL719+Cetuximab	Arm A - 400mg BYL719+Cetuximab	Arm B - BYL719 + Cetuximab, Oral suspension
Number of subjects	16	5	18
Age categorical Units: Subjects			
Adults (18-64 years)	13	2	14
From 65-84 years	3	3	4
Age Continuous Units: years			
arithmetic mean	52.8	62.6	56.7
standard deviation	± 13.4	± 7.99	± 10.2
Gender, Male/Female Units: Subjects			
Female	7	1	4
Male	9	4	14

Reporting group values	Arm C - BYL719+Cetuximab, Dispersible tablets	Arm 1 - BYL719+Cetuximab (randomized)	Arm 2 - Monotherapy Cetuximab (randomized)
Number of subjects	6	71	35

Age categorical Units: Subjects			
Adults (18-64 years)	3	55	25
From 65-84 years	3	16	10
Age Continuous Units: years			
arithmetic mean	60.5	57.2	57.1
standard deviation	± 14.1	± 9.66	± 10.37
Gender, Male/Female Units: Subjects			
Female	2	16	4
Male	4	55	31

Reporting group values	Arm 3 - BYL719+Cetuximab (non-randomized)	Total	
Number of subjects	29	180	
Age categorical Units: Subjects			
Adults (18-64 years)	23	135	
From 65-84 years	6	45	
Age Continuous Units: years			
arithmetic mean	56.9		
standard deviation	± 8.25	-	
Gender, Male/Female Units: Subjects			
Female	10	44	
Male	19	136	

End points

End points reporting groups

Reporting group title	Arm A - 300mg BYL719+Cetuximab
Reporting group description:	
300 mg BYL719 as film-coated (FC) whole tablets with cetuximab in Phase Ib	
Reporting group title	Arm A - 400mg BYL719+Cetuximab
Reporting group description:	
400 mg BYL719 as FC whole tablets with cetuximab in Phase Ib	
Reporting group title	Arm B - BYL719 + Cetuximab, Oral suspension
Reporting group description:	
300mg BYL719 as crushed FC tablets with cetuxumab in patients with swallowing dysfunction in Phase Ib.	
Reporting group title	Arm C - BYL719+Cetuximab, Dispersible tablets
Reporting group description:	
300mg BYL719 dispersible tablets with cetuxumab in patients with swallowing dysfunction administered via G-tube in Phase Ib.	
Reporting group title	Arm 1 - BYL719+Cetuximab (randomized)
Reporting group description:	
300mg BYL719 with cetuxumab (Phase II) in patients resistant to or intolerant/ineligible for platinum-based chemotherapy.	
Reporting group title	Arm 2 - Monotherapy Cetuximab (randomized)
Reporting group description:	
Cetuximab in Phase II in patients resistant to or intolerant/ineligible for platinum-based chemotherapy.	
Reporting group title	Arm 3 - BYL719+Cetuximab (non-randomized)
Reporting group description:	
300mg BYL719 with cetuximab in Phase II in patients resistant to platinum-based therapy and cetuximab	
Subject analysis set title	0-0.16
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Posterior probabilities (%) that Pr(DLT) is in interval	
Subject analysis set title	0.16-0.35
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Posterior probabilities (%) that Pr(DLT) is in interval	
Subject analysis set title	0.35-1
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Posterior probabilities (%) that Pr(DLT) is in interval	
Subject analysis set title	All Patients
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
All patients in Phase Ib	
Subject analysis set title	BYL719+ Cetuximab (randomized)
Subject analysis set type	Full analysis
Subject analysis set description:	
300mg BYL719 with cetuximab (Phase II) in patients resistant to or intolerant/ineligible for platinum-based chemotherapy.	
Subject analysis set title	Monotherapy Cetuximab (randomized)
Subject analysis set type	Full analysis

Subject analysis set description:

Cetuximab in Phase II in patients resistant to or intolerant/ineligible for platinum-based chemotherapy.

Subject analysis set title	BYL719+ Cetuximab (non-randomized)
Subject analysis set type	Full analysis

Subject analysis set description:

300mg BYL719 with cetuximab in patients resistant to platinum-based therapy and cetuximab in Phase II

Subject analysis set title	Arm C: BYL719+Cetixumab, Dispersible tablets
Subject analysis set type	Full analysis

Subject analysis set description:

300mg BYL719 dispersible tablets with cetuxumab in patients with swallowing dysfunction administered via G-tube

Subject analysis set title	Arm A: 400mg BYL719 + Cetuximab
Subject analysis set type	Full analysis

Subject analysis set description:

400 mg BYL719 as FC whole tablets with cetuximab

Subject analysis set title	Arm 2B - BYL719+Cetuximab
Subject analysis set type	Full analysis

Subject analysis set description:

300mg BYL719 with cetuximab in Phase II in patients resistant to platinum-based therapy and cetuximab

Subject analysis set title	All Patients
Subject analysis set type	Full analysis

Subject analysis set description:

All patients

Subject analysis set title	Arm 3 - BYL719+Cetuximab
Subject analysis set type	Full analysis

Subject analysis set description:

300mg BYL719 with cetuximab in Phase II in patients resistant to platinum-based therapy and cetuximab

Subject analysis set title	All Patients (Phase II)
Subject analysis set type	Full analysis

Subject analysis set description:

All Patients in Phase II

Subject analysis set title	All Patients
Subject analysis set type	Full analysis

Subject analysis set description:

BYL719 + Cetuximab in Phase II (non-randomized) in patients resistant to or intolerant/ineligible for platinum-based

Subject analysis set title	Arm B: BYL719 + Cetuximab, Oral suspension
Subject analysis set type	Full analysis

Subject analysis set description:

300mg BYL719 as crushed FC tablets with cetuxumab in patients with swallowing dysfunction

Subject analysis set title	Arm 2B - BYL719+Cetuximab
Subject analysis set type	Full analysis

Subject analysis set description:

300mg BYL719 with cetuximab in Phase II in patients resistant to platinum-based therapy and cetuximab

Primary: Phase Ib Arms A: Posterior Distribution of Dose Limiting Toxicities (DLTs) at Recommended Phase 2 Dose in Cycle 1 (Cycle 1=28 days)

End point title	Phase Ib Arms A: Posterior Distribution of Dose Limiting Toxicities (DLTs) at Recommended Phase 2 Dose in Cycle 1 (Cycle 1=28 days)[1]

End point description:

Maximum Tolerated Doses (MTDs) and/or recommended Phase II doses (RP2Ds) of BYL719 in combination with cetuximab in patients with recurrent or metastatic head and neck squamous cell carcinoma (RM HNSCC) in arm A (BYL719 administered as a whole tablet in patients able to swallow the tablets). 6 months is an approximate timeframe.

End point type	Primary

End point timeframe:

until disease progression or intolerable toxicity (approximately 6 months)

Notes:

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

End point values	0-0.16	0.16-0.35	0.35-1	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	15	15	15	
Units: Percentages				
number (not applicable)				
200 mg	0.964	0.035	0.001	
300 mg	0.764	0.222	0.15	
350 mg	0.304	0.543	0.153	
400 mg	0.086	0.376	0.538	

Statistical analyses

No statistical analyses for this end point

Primary: Phase Ib Arms B: Posterior Distribution of Dose Limiting Toxicities (DLTs) at Recommended Phase 2 Dose in Cycle 1 (Cycle 1=28 days)

End point title	Phase Ib Arms B: Posterior Distribution of Dose Limiting Toxicities (DLTs) at Recommended Phase 2 Dose in Cycle 1 (Cycle 1=28 days)[2]

End point description:

Maximum Tolerated Doses (MTDs) and/or recommended Phase II doses (RP2Ds) of BYL719 in combination with cetuximab in patients with recurrent or metastatic head and neck squamous cell carcinoma (RM HNSCC) in arm B (crushed film-coated tablets as an oral suspension with swallowing dysfunction). 6 months is an approximate timeframe.

End point type	Primary

End point timeframe:

until disease progression or intolerable toxicity (approximately 6 months)

Notes:

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

End point values	0-0.16	0.16-0.35	0.35-1	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	15	15	15	
Units: Percentages				
number (not applicable)				
200 mg	0.836	0.16	0.004	
300 mg	0.267	0.664	0.069	
350 mg	0.054	0.585	0.361	
400 mg	0.017	0.346	0.638	

Statistical analyses

No statistical analyses for this end point

Primary: For Phase Ib: Incidence of Dose Limiting Toxicities (DLTs) in Cycle 1 (28 days)

End point title	For Phase Ib: Incidence of Dose Limiting Toxicities (DLTs) in Cycle 1 (28 days)[3][4]

End point description:

Estimation of Maximum Tolerated Doses (MTDs) and/or recommended Phase II doses (RP2Ds) of BYL719 in combination with cetuximab in patients with recurrent or metastatic head and neck squamous cell carcinoma (RM HNSCC) in arm A (BYL719 administered as a whole tablet in patients able to swallow the tablets) and arm B (BYL719 administered as a drinkable suspension in patients with swallowing dysfunction). 6 months is an approximate timeframe.

End point type	Primary

End point timeframe:

until disease progression or intolerable toxicity (approximately 6 months)

Notes:

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

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

End point values	Arm A - 300mg BYL719+Cetuximab	Arm A - 400mg BYL719+Cetuximab	Arm B - BYL719 + Cetuximab, Oral suspension	Arm C - BYL719+Cetuximab, Dispersible tablets
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	3	13	3
Units: Participants	1	2	4	2

End point values	All Patients			
Subject group type	Subject analysis set			
Number of subjects analysed	30			
Units: Participants	30			

Statistical analyses

No statistical analyses for this end point

Primary: Phase II Arms 1 and 2: Progression Free Survival (PFS) as per RECIST v1.1 by central radiology review

End point title	Phase II Arms 1 and 2: Progression Free Survival (PFS) as per RECIST v1.1 by central radiology review

End point description:

Assessment of the anti-tumor activity of BYL719 in combination with cetuximab vs. cetuximab as single-agent in RM HNSCC patients naive to cetuximab. 6 months is an approximate timeframe.

End point type	Primary

End point timeframe:

approximately 6 months

End point values	BYL719+ Cetuximab (randomized)	Monotherapy Cetuximab (randomized)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	71	35		
Units: participants				
Number of PFS events	46	27		
Progression	33	25		
Number of censored	25	8		
Death	13	2		

Statistical analyses

Statistical analysis title	PFS by central radiology review

Statistical analysis description:

The hazard ratio was estimated using the Bayesian Cox proportional hazard (PH) model.

Comparison groups	BYL719+ Cetuximab (randomized) v Monotherapy Cetuximab (randomized)
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	median HR
Point estimate	0.99

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.643
upper limit	1.529

Statistical analysis title	PFS by central radiology review
Comparison groups	BYL719+ Cetuximab (randomized) v Monotherapy Cetuximab (randomized)
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.643
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	1.82

Statistical analysis title	PFS by central radiology review
Statistical analysis description:	
Adjusted on Covariates: treatment, sum of longest diameters from central data [SLD (C)], Hemaglobin (Hgb) and White Blood Cells (WBC).	
Comparison groups	BYL719+ Cetuximab (randomized) v Monotherapy Cetuximab (randomized)
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.039
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	0.97

Primary: Phase II Arm 3: Progression Free Survival (PFS) as per RECIST V1.1	
End point title	Phase II Arm 3: Progression Free Survival (PFS) as per RECIST V1.1[5]

End point description:

Assessment of the anti-tumor activity of BYL719 in combination with cetuximab in patients resistant to platinum-based therapy and cetuximab.

End point type	Primary

End point timeframe:

approximately 6 months

Notes:

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

End point values	BYL719+ Cetuximab (non-randomized)			
Subject group type	Subject analysis set			
Number of subjects analysed	29			
Units: months				
median (confidence interval 95%)	3.896 (2.868 to 5.241)			

Statistical analyses

No statistical analyses for this end point

Primary: Phase Ib: Area under curve (AUC) 0-24 for BYL719 by Treatment

End point title	Phase Ib: Area under curve (AUC) 0-24 for BYL719 by Treatment[6][7]

End point description:

Comparison of single-dose exposure of BYL719 dispersible tablet via G-tube in combination with cetuximab in RM HNSCC to that of Arm A (film-coated tables)

End point type	Primary

End point timeframe:

6 months

Notes:

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

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

End point values	Arm A - 300mg BYL719+Cetuximab	Arm C: BYL719+Cetuximab, Dispersible tablets	Arm A: 400mg BYL719 + Cetuximab	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	15	6	5	
Units: hr*ng/mL				
median (full range (min-max))				
AUCinf	22600 (16600 to 48500)	24100 (9290 to 33200)	27800 (17200 to 60100)	

AUC0_24	18800 (5590 to 43400)	19400 (7580 to 32100)	26300 (16000 to 56100)	
AUClast	19200 (5830 to 42700)	22100 (4390 to 31800)	26200 (15800 to 55600)	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase II: Progression Free Survival (PFS) as per RECIST v 1.1

End point title	Phase II: Progression Free Survival (PFS) as per RECIST v 1.1

End point description:

Phase II, Scheme 1 (Arm 2B): To further assess the anti-tumor activity of BYL719 + cetuximab in the setting of resistance to single agent cetuximab

End point type	Secondary

End point timeframe:

approximately 6 months

End point values	Arm 2B - BYL719+Cetuximab			
Subject group type	Subject analysis set			
Number of subjects analysed	16			
Units: Participants				
Number of PFS	12			
Progression	9			
Death	3			
Number of Censored	4			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase Ib: Progression Free Survival (PFS) as per RECIST v1.1

End point title	Phase Ib: Progression Free Survival (PFS) as per RECIST

End point description:

Assessment of the preliminary anti-tumor activity of BYL719 in combination with cetuximab in arm A, B and C This endpoint was not analyzed because the trial terminated early.

End point type	Secondary

End point timeframe:

approximately 6 months

Notes:

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

End point values	Arm A - 300mg BYL719+Cetuximab	Arm A - 400mg BYL719+Cetuximab	Arm B - BYL719 + Cetuximab, Oral suspension	Arm C - BYL719+Cetuximab, Dispersible tablets
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[9]	0[10]	0[11]	0[12]
Units: Participants				

Notes:

[9] - This endpoint was not analyzed because the trial terminated early.

[10] - This endpoint was not analyzed because the trial terminated early.

[11] - This endpoint was not analyzed because the trial terminated early.

[12] - This endpoint was not analyzed because the trial terminated early.

Statistical analyses

No statistical analyses for this end point

Secondary: Phase II: Randomized Best overall response as per RECIST v1.1

End point title	Phase II: Randomized Best overall response as per RECIST v1.1[13]

End point description:

Scheme 1 (Arms 1 and 2): Further assessment of the anti-tumor activity of BYL719 in combination with cetuximab vs. cetuximab as single-agent in RM HNSCC patients naive to cetuximab

End point type	Secondary

End point timeframe:

approximately 6 months

Notes:

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

End point values	Arm 1 - BYL719+Cetuximab (randomized)	Arm 2 - Monotherapy Cetuximab (randomized)	All Patients	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	71	35	106	
Units: Participants				
Complete Response	1	0	1	
Partial Response	6	2	8	
Stable Disease	24	8	32	
Progressive Disease	17	12	29	
Non-CR/Non-PD (NCRNPD)	6	10	16	
Unknown	17	3	20	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase II: Non-Randomized Best overall response as per RECIST v1.1

End point title	Phase II: Non-Randomized Best overall response as per

	RECIST v1.1

End point description:

Scheme 1 (Arm 3): Further assessment of the anti-tumor activity of BYL719 in combination with cetuximab vs. cetuximab as single-agent in RM HNSCC patients naive to cetuximab

End point type	Secondary

End point timeframe:

approximately 6 months

End point values	Arm 3 - BYL719+Cetuximab			
Subject group type	Subject analysis set			
Number of subjects analysed	29			
Units: Participants				
Complete Response (CR)	1			
Partial Response (PR)	2			
Stable Disease (SD)	8			
Progressive Disease (PD)	5			
Non-CR/Non-PD (NCRNPD)	6			
Unknown	7			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase II: Randomized Overall Response Rate (ORR) and Disease Control Rate (DCR) as per RECIST v1.1

End point title	Phase II: Randomized Overall Response Rate (ORR) and Disease Control Rate (DCR) as per RECIST v1.1[14]

End point description:

Assessment of the preliminary anti-tumor activity of BYL719 in combination with cetuximab in arms 1 and 2.

End point type	Secondary

End point timeframe:

approximately 6 months

Notes:

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

End point values	Arm 1 - BYL719+Cetuximab (randomized)	Arm 2 - Monotherapy Cetuximab (randomized)	All Patients (Phase II)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	71	35	106	
Units: Percentages				
number (confidence interval 95%)				

Overall response rate (ORR) (CR or PR)	9.9 (4.1 to 19.3)	5.7 (0.7 to 19.2)	8.5 (4 to 15.5)	
Disease control rate 1 (DCR 1) (CR or PR or SD)	43.7 (31.9 to 56)	28.6 (14.6 to 46.3)	38.7 (29.4 to 48.6)	
DCR 2 (CR or PR or SD or Non-CR/Non-PD)	52.1 (39.9 to 64.1)	57.1 (39.4 to 73.7)	53.8 (43.8 to 63.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase II: Non-Randomized Overall Response Rate (ORR) and Disease Control Rate (DCR) as per RECIST v1.1

End point title	Phase II: Non-Randomized Overall Response Rate (ORR) and Disease Control Rate (DCR) as per RECIST v1.1

End point description:

Scheme 1 (arm 3): Assessment of the preliminary anti-tumor activity of BYL719 in combination with cetuximab in arm 3 (non-randomized arm)

End point type	Secondary

End point timeframe:

approximately 6 months

End point values	Arm 3 - BYL719+Cetuximab			
Subject group type	Subject analysis set			
Number of subjects analysed	29			
Units: Percentages				
number (confidence interval 95%)				
Overall response rate (ORR) (CR or PR)	10.3 (2.2 to 27.4)			
Disease control rate 1 (DCR 1) (CR or PR or SD)	37.9 (20.7 to 57.7)			
DCR 2 (CR or PR or SD or Non-CR/Non-PD)	58.6 (38.9 to 76.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase II: Randomized Overall Survival (OS) by treatment

End point title	Phase II: Randomized Overall Survival (OS) by treatment[15]

End point description:

Scheme 1 (Arms 1 and 2): Further assessment of the anti-tumor activity of BYL719 in combination with cetuximab vs. cetuximab as single-agent in RM HNSCC patients naive to cetuximab

End point type	Secondary

End point timeframe:

approximately 1 year

Notes:

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

Justification: Descriptive analyses.

End point values	Arm 1 - BYL719+Cetuximab (randomized)	Arm 2 - Monotherapy Cetuximab (randomized)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	35		
Units: Patients				
Number of deaths	51	26		
Number of censored	20	9		

Statistical analyses

Statistical analysis title	Radnomized OS by Treatment
Comparison groups	Arm 1 - BYL719+Cetuximab (randomized) v Arm 2 - Monotherapy Cetuximab (randomized)
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.313
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.79
upper limit	2.05

Secondary: Phase II: Non-Randomized Overall Survival (OS) by treatment

End point title	Phase II: Non-Randomized Overall Survival (OS) by treatment

End point description:

Scheme 1 (Arm 3): Further assessment of the anti-tumor activity of BYL719 in combination with cetuximab vs. cetuximab as single-agent in RM HNSCC patients naive to cetuximab

End point type	Secondary

End point timeframe:

approximately 1 year

End point values	Arm 3 - BYL719+Cetuximab			
Subject group type	Subject analysis set			
Number of subjects analysed	29			
Units: Patients				
Number of deaths	13			
Number of censored	10			

Statistical analyses

No statistical analyses for this end point

Secondary: For Phase Ib: Overall Response Rate (ORR) and Disease Control Rate (DCR) as per RECIST v1.1

End point title	For Phase Ib: Overall Response Rate (ORR) and Disease Control Rate (DCR) as per RECIST v1.1[16]

End point description:

Assessment of the preliminary anti-tumor activity of BYL719 in combination with cetuximab in arm A, B and C CR=complete response PR=partial response

End point type	Secondary

End point timeframe:

approximately 6 months

Notes:

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

End point values	Arm A - 300mg BYL719+Cetuximab	Arm A - 400mg BYL719+Cetuximab	Arm B - BYL719 + Cetuximab, Oral suspension	Arm C - BYL719+Cetuximab, Dispersible tablets
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	5	18	6
Units: Percentages				
number (confidence interval 95%)				
ORR (CR) or PR)	25.5 (7.3 to 52.4)	0 (0 to 52.2)	0 (0 to 18.5)	0 (0 to 45.9)
DCR (CR or PR or Stable Disease or non-CR/Non-PD)	75 (47.6 to 92.7)	20 (0.5 to 71.6)	50 (26 to 74)	16.7 (0.4 to 64.1)

End point values	All Patients			
Subject group type	Subject analysis set			
Number of subjects analysed	45			
Units: Percentages				
number (confidence interval 95%)				
ORR (CR) or PR)	8.9 (2.5 to 21.2)			

DCR (CR or PR or Stable Disease or non-CR/Non-PD)	51.1 (35.8 to 66.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase II, Scheme 1 (arm 2B): Overall Response Rate (ORR) and Disease Control Rate (DCR) as per RECIST v1.1

End point title	Phase II, Scheme 1 (arm 2B): Overall Response Rate (ORR) and Disease Control Rate (DCR) as per RECIST v1.1

End point description:

Phase II: Scheme 1 (Arm 2B): To further assess the anti-tumor activity of BYL719 + cetuximab in the setting of resistance to single agent cetuximab. This endpoint was not analyzed because the trial terminated early due to slow enrolment.

End point type	Secondary

End point timeframe:

Approximately 6 months

End point values	Arm 2B - BYL719+Cetuximab			
Subject group type	Subject analysis set			
Number of subjects analysed	0[17]			
Units: percentages				
number (confidence interval 95%)	(to)			

Notes:

[17] - This endpoint was not analyzed because the trial terminated early due to slow enrolment.

Statistical analyses

No statistical analyses for this end point

Secondary: Phase II, Scheme 2 (Arm 2B): OS from the time of crossing over

End point title	Phase II, Scheme 2 (Arm 2B): OS from the time of crossing over

End point description:

Phase II, Scheme 1 (Arm 2B): To further assess the anti-tumor activity of BYL719 + cetuximab in the setting of resistance to single agent cetuximab. This endpoint was not analyzed because the trial terminated early due to slow enrolment.

End point type	Secondary

End point timeframe:

approximately 1 year

End point values	Arm 2B - BYL719+Cetuximab			
Subject group type	Subject analysis set			
Number of subjects analysed	0[18]			
Units: Patients				

Notes:

[18] - This endpoint was not analyzed because the trial terminated early due to slow enrolment.

Statistical analyses

No statistical analyses for this end point

Secondary: Phase Ib: Primary Plasma Pharmacokinetic Parameters for BYL719 by Treatment

End point title	Phase Ib: Primary Plasma Pharmacokinetic Parameters for BYL719 by Treatment[19]

End point description:

Non compartmental PK parameters derived after single dose at Cycle 1 Day 1

End point type	Secondary

End point timeframe:

Day 1 Cycle 1

Notes:

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

End point values	Arm A - 300mg BYL719+Cetuximab	Arm C: BYL719+Cetuximab, Dispersible tablets	Arm A: 400mg BYL719 + Cetuximab	Arm B: BYL719 + Cetuximab, Oral suspension
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	15	6	5	17
Units: hr*ng/mL				
median (full range (min-max))				
AUCinf	22600 (16600 to 48500)	24100 (9290 to 33200)	27800 (17200 to 60100)	27300 (15700 to 47400)
AUC0_24	18800 (5590 to 43400)	19400 (7580 to 32100)	26300 (16000 to 56100)	25600 (14600 to 42100)
AUClast	19200 (5830 to 42700)	22100 (4390 to 31800)	26200 (15800 to 55600)	2370 (1330 to 3710)

Statistical analyses

No statistical analyses for this end point

Secondary: Phase Ib: Cmax for BYL719 by Treatment

End point title	Phase Ib: Cmax for BYL719 by Treatment[20]

End point description:

Non compartmental Cmax derived after single dose at Cycle 1 Day 1

End point type	Secondary

End point timeframe:

Day 1 Cycle 1

Notes:

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

End point values	Arm A - 300mg BYL719+Cetuximab	Arm C: BYL719+Cetuximab, Dispersible tablets	Arm A: 400mg BYL719 + Cetuximab	Arm B: BYL719 + Cetuximab, Oral suspension
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	15	6	5	17
Units: ng/mL				
median (full range (min-max))	2130 (303 to 4280)	2010 (682 to 2980)	2520 (1800 to 6240)	2340 (1330 to 3710)

Statistical analyses

No statistical analyses for this end point

Secondary: Phase Ib: Tmax for BYL719 by Treatment

End point title	Phase Ib: Tmax for BYL719 by Treatment[21]

End point description:

Non compartmental Cmax derived after single dose at Cycle 1 Day 1

End point type	Secondary

End point timeframe:

Day 1 Cycle 1

Notes:

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

End point values	Arm A - 300mg BYL719+Cetuximab	Arm C: BYL719+Cetuximab, Dispersible tablets	Arm A: 400mg BYL719 + Cetuximab	Arm B: BYL719 + Cetuximab, Oral suspension
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	15	6	5	17
Units: hr				
median (full range (min-max))	2.02 (1 to 24.8)	3 (0.767 to 6)	2.23 (1.58 to 3.02)	2.97 (1 to 5.87)

Statistical analyses

No statistical analyses for this end point

Secondary: Phase Ib: Plasma Pharmacokinetic Parameters for BYL719 after continuous dose administration (steady state)

End point title	Phase Ib: Plasma Pharmacokinetic Parameters for BYL719 after continuous dose administration (steady state)[22]

End point description:

Non compartmental PK parameters derived after single dose at Cycle 1 Day 1

End point type	Secondary

End point timeframe:

Day 1 Cycle 1

Notes:

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

End point values	Arm A - 300mg BYL719+Cetuximab	Arm C: BYL719+Cetuximab, Dispersible tablets	Arm B: BYL719 + Cetuximab, Oral suspension	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	15	6	17	
Units: hr*ng/mL				
median (full range (min-max))				
AUC (0-24)	24600 (17900 to 44400)	30500 (30500 to 30500)	28500 (12700 to 53900)	
AUClast	24500 (18000 to 76100)	22100 (4390 to 31800)	2370 (1330 to 3710)	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase Ib: Cmax for BYL719 after continuous dose administration (steady state)

End point title	Phase Ib: Cmax for BYL719 after continuous dose administration (steady state)[23]

End point description:

Non compartmental PK parameters derived after single dose at Cycle 1 Day 1

End point type	Secondary

End point timeframe:

Day 1 Cycle 1

Notes:

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

End point values	Arm A - 300mg BYL719+Cetuximab	Arm C: BYL719+Cetuximab, Dispersible tablets	Arm B: BYL719 + Cetuximab, Oral suspension	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	15	6	17	
Units: ng/mL				
median (full range (min-max))	2200 (1710 to 6520)	2750 (2750 to 2750)	2820 (373 to 4710)	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase Ib: Tmax for BYL719 after continuous dose administration (steady state)

End point title	Phase Ib: Tmax for BYL719 after continuous dose administration (steady state)[24]

End point description:

Non compartmental PK parameters derived after single dose at Cycle 1 Day 1

End point type	Secondary

End point timeframe:

Day 1 Cycle 1

Notes:

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

End point values	Arm A - 300mg BYL719+Cetuximab	Arm C: BYL719+Cetuximab, Dispersible tablets	Arm B: BYL719 + Cetuximab, Oral suspension	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	15	6	17	
Units: hr				
median (full range (min-max))	3.15 (1.5 to 7.13)	1 (1 to 1)	3.15 (1.03 to 8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase Ib: Notable Abnormal Vital Signs by Treatment

End point title	Phase Ib: Notable Abnormal Vital Signs by Treatment[25]

End point description:

Characterization of the safety and tolerability of BYL719 in combination with cetuximab in arm A, B and C.

End point type	Secondary

End point timeframe:

approximately 6 months

Notes:

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

End point values	Arm A - 300mg BYL719+Cetuximab	Arm A - 400mg BYL719+Cetuximab	Arm B - BYL719 + Cetuximab, Oral suspension	Arm C - BYL719+Cetuximab, Dispersible tablets
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	5	18	6
Units: Participants				
Sitting Pulse rate (bpm): High only	0	0	4	4
Sitting Pulse rate (bpm): Low only	0	0	0	0
Sitting Pulse rate (bpm): High and low	0	0	0	0
Sitting systolic B.P. (mmHg): High only	1	0	1	0
Sitting systolic B.P. (mmHg): Low only	1	0	0	1
Sitting systolic B.P. (mmHg): High and low	0	0	1	0
Sitting diastolic B.P. (mmHg): High only	0	0	1	0
Sitting diastolic B.P. (mmHg): Low only	1	0	2	0
Sitting diastolic B.P. (mmHg): High and low	0	0	0	0
Body Temperature (Celsius): High only	0	0	0	1
Body Temperature (Celsius): Low only	0	0	0	0
Body Temperature (Celsius): High and low	0	0	0	0
Weight (kg): High only	0	0	0	0
Weight (kg): Low only	7	1	3	3
Weight (kg): High and low	0	0	0	0
Respiratory Rate (bpm): High only	0	0	2	1
Respiratory Rate (bpm): Low only	0	0	0	0
Respiratory Rate (bpm): High and low	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Phase Ib: Number of patients with notable Electrocardiogram (ECG) abnormalities

End point title	Phase Ib: Number of patients with notable Electrocardiogram (ECG) abnormalities[26]

End point description:

Characterization of the safety and tolerability of BYL719 in combination with cetuximab in arm A, B and C.

End point type	Secondary

End point timeframe:

baseline, post baseline

Notes:

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

End point values	Arm A - 300mg BYL719+Cetuximab	Arm A - 400mg BYL719+Cetuximab	Arm B - BYL719 + Cetuximab, Oral suspension	Arm C - BYL719+Cetuximab, Dispersible tablets
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	5	18	6
Units: Participants				
QTcF (msec): Increase from baseline > 30	149	54	1810	61
QTcF (msec): Increase from baseline > 60	142	50	181	60
QTcB (msec): Increase from baseline > 30	1411	54	1812	61
QTcB (msec): Increase from baseline > 60	141	50	181	61
QT (msec): Increase from baseline > 30	1	54	1810	61
QT (msec): Increase from baseline > 60	144	50	183	60
VR (bpm): RR decrease > 25% & to a VR > 100	140	51	181	61
VR (bpm): RR decrease > 25% & to a VR < 50	140	50	180	60
PR (msec): increase > 25% & to a VR > 200	140	50	180	60
QRS (msec): increase > 25% & to a VR > 110	140	50	180	60

Statistical analyses

No statistical analyses for this end point

Secondary: For Phase II: Notable Abnormal Vital Signs by Treatment

End point title	For Phase II: Notable Abnormal Vital Signs by Treatment[27]

End point description:

Characterization of the safety and tolerability of BYL719 in combination with cetuximab in arm 1, 2 and 2B.

End point type	Secondary

End point timeframe:

approximately 6 months

Notes:

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

End point values	Arm 1 - BYL719+Cetuximab (randomized)	Arm 2 - Monotherapy Cetuximab (randomized)	Arm 2B - BYL719+Cetuximab	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	69	35	29	
Units: Participants				
Sitting Pulse rate (bpm): High only	4	3	5	
Sitting Pulse rate (bpm): Low only	1	0	1	
Sitting Pulse rate (bpm): High and low	0	0	0	
Sitting systolic B.P. (mmHg): High only	0	1	0	
Sitting systolic B.P. (mmHg): Low only	11	3	1	
Sitting systolic B.P. (mmHg): High and low	1	0	0	
Sitting diastolic B.P. (mmHg): High only	1	2	0	
Sitting diastolic B.P. (mmHg): Low only	4	3	2	
Sitting diastolic B.P. (mmHg): High and low	1	0	0	
Body Temperature (Celsius): High only	1	0	0	
Body Temperature (Celsius): Low only	3	1	2	
Body Temperature (Celsius): High and low	0	0	0	
Weight (kg): High only	1	4	0	
Weight (kg): Low only	31	3	9	
Weight (kg): High and low	0	0	0	
Respiratory Rate (bpm): High only	2	0	1	
Respiratory Rate (bpm): Low only	2	1	4	
Respiratory Rate (bpm): High and low	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: For Phase II: Number of patients with notable Electrocardiogram (ECG) abnormalities

End point title	For Phase II: Number of patients with notable Electrocardiogram (ECG) abnormalities[28]

End point description:

Characterization of the safety and tolerability of BYL719 in combination with cetuximab in arm 1, 2 and 2B.

End point type	Secondary

End point timeframe:

baseline, post baseline

Notes:

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

End point values	Arm 1 - BYL719+Cetuximab (randomized)	Arm 2 - Monotherapy Cetuximab (randomized)	Arm 2B - BYL719+Cetuximab	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	69	35	29	
Units: Participants				
QTcF (msec): Increase from baseline > 30	6335	324	2815	
QTcF (msec): Increase from baseline > 60	686	321	282	
QTcB (msec): Increase from baseline > 30	6840	3212	2815	
QTcB (msec): Increase from baseline > 60	687	320	282	
QT (msec): Increase from baseline > 30	6843	3213	2823	
QT (msec): Increase from baseline > 60	6817	322	285	
VR (bpm): RR decrease > 25% & to a VR > 100	689	324	283	
VR (bpm): RR decrease > 25% & to a VR < 50	681	320	280	
PR (msec): increase > 25% & to a VR > 200	680	310	270	
QRS (msec): increase > 25% & to a VR > 110	680	320	281	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase II: Progression Free Survival (PFS) based on Investigator's Assessment with treatment

End point title	Phase II: Progression Free Survival (PFS) based on Investigator's Assessment with treatment

End point description:

Assessment of the anti-tumor activity of BYL719 in combination with cetuximab vs. cetuximab as single-agent in RM HNSCC patients naive to cetuximab

End point type	Secondary

End point timeframe:

approximately 6 months

End point values	BYL719+ Cetuximab (randomized)	Monotherapy Cetuximab (randomized)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	71	35		
Units: Participants	71	35		

Statistical analyses

Statistical analysis title	PFS based on Investigator Assessment
Comparison groups	BYL719+ Cetuximab (randomized) v Monotherapy Cetuximab (randomized)
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.235
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.49
upper limit	1.19

Statistical analysis title	PFS based on Investigator Assessment
Statistical analysis description:	
Adjusted on Covariates: treatment, sum of longest diameters from local data [SLD (L)], Hemaglobin (Hgb) and White Blood Cells (WBC).	
Comparison groups	BYL719+ Cetuximab (randomized) v Monotherapy Cetuximab (randomized)
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.062
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	1.02

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Timeframe for AE	
Adverse event reporting additional description:	
AE additional description	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups	
Reporting group title	Phase Ib@Oral tablets@BYL719 300mg@+ CETU
Reporting group description:	
Phase Ib@Oral tablets@BYL719 300mg@+ CETU	
Reporting group title	Phase Ib@Oral tablets@BYL719 400mg@+ CETU
Reporting group description:	
Phase Ib@Oral tablets@BYL719 400mg@+ CETU	
Reporting group title	Phase Ib@Oral suspension@BYL719 300mg@+ CETU
Reporting group description:	
Phase Ib@Oral suspension@BYL719 300mg@+ CETU	
Reporting group title	Phase Ib@Disp. tablets@BYL719 300mg@+ CETU
Reporting group description:	
Phase Ib@Disp. tablets@BYL719 300mg@+ CETU	
Reporting group title	Phase II@randomized@BYL719 300mg + CETU
Reporting group description:	
Phase II@randomized@BYL719 300mg + CETU	
Reporting group title	Phase II@randomized@CETU
Reporting group description:	
Phase II@randomized@CETU	
Reporting group title	Phase II@open label@BYL719 300mg + CETU
Reporting group description:	
Phase II@open label@BYL719 300mg + CETU	
Reporting group title	All@patients
Reporting group description:	
All@patients	

Serious adverse events	Phase Ib@Oral tablets@BYL719 300mg@+ CETU	Phase Ib@Oral tablets@BYL719 400mg@+ CETU	Phase Ib@Oral suspension@BYL719 300mg@+ CETU
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 15 (60.00%)	4 / 5 (80.00%)	12 / 18 (66.67%)
number of deaths (all causes)	1	2	3
number of deaths resulting from adverse events	0	2	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Tumour haemorrhage			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour necrosis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
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			
Deep vein thrombosis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolism			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
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 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Hypotension			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (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
Surgical and medical procedures			
Gastrostomy			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
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 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chills			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
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 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
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 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
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			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
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 / 15 (6.67%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (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
Drug hypersensitivity			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
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			
Aspiration			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (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 / 15 (0.00%)	1 / 5 (20.00%)	0 / 18 (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
Interstitial lung disease			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngeal oedema			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
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 infiltration			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oropharyngeal pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	2 / 15 (13.33%)	0 / 5 (0.00%)	0 / 18 (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

Pneumonitis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (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
Pneumothorax			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Productive cough			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
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 air leakage			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
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 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
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 haemorrhage			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
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 distress			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (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
Respiratory failure			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stridor			

subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device dislocation			
subjects affected / exposed	0 / 15 (0.00%)	1 / 5 (20.00%)	0 / 18 (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
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
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			
Feeding tube complication			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumocephalus			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
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 fracture			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tracheal obstruction			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Wound secretion			

subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
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			
Atrial fibrillation			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial ischaemia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 5 (20.00%)	0 / 18 (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
Pulseless electrical activity			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
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			
Carotid artery perforation			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
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	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (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
Embolic cerebral infarction			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Somnolence			

subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
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 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
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 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
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			
Constipation			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
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 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterocolitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine perforation			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mouth haemorrhage			

subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
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 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal fistula			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal haemorrhage			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal ulcer			
subjects affected / exposed	0 / 15 (0.00%)	1 / 5 (20.00%)	0 / 18 (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
Oesophagitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
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 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
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			
Erythema nodosum			

subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (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
Swelling face			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ketonuria			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
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 injury			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
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			
Back pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
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 pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (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
Fistula			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
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 / 15 (0.00%)	1 / 5 (20.00%)	0 / 18 (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
Musculoskeletal chest pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neck pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Trismus			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
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 infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
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 abscess			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
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 infectious			

subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
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 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epiglottitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
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 infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
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	2 / 15 (13.33%)	0 / 5 (0.00%)	4 / 18 (22.22%)
occurrences causally related to treatment / all	0 / 2	0 / 0	2 / 4
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 2
Post procedural infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Purulent discharge			

subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (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
Septic shock			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Superinfection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
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 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
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 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
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	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (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
Hypernatraemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
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 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypophosphataemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour lysis syndrome			
subjects affected / exposed	0 / 15 (0.00%)	1 / 5 (20.00%)	0 / 18 (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

Serious adverse events	Phase Ib@Disp. tablets@BYL719 300mg@+ CETU	Phase II@randomized@BYL 719 300mg + CETU	Phase II@randomized@CETU
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 6 (66.67%)	40 / 69 (57.97%)	15 / 35 (42.86%)
number of deaths (all causes)	2	14	8
number of deaths resulting from adverse events	0	4	1

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	2 / 69 (2.90%)	2 / 35 (5.71%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 1
Tumour necrosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Embolism			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	0 / 35 (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 / 6 (0.00%)	0 / 69 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
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			
Gastrostomy			

subjects affected / exposed	1 / 6 (16.67%)	1 / 69 (1.45%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	0 / 35 (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
Chills			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	0 / 35 (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
Fatigue			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	0 / 35 (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 / 6 (0.00%)	2 / 69 (2.90%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	0 / 35 (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
Pyrexia			
subjects affected / exposed	1 / 6 (16.67%)	4 / 69 (5.80%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
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 / 6 (0.00%)	0 / 69 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Respiratory, thoracic and mediastinal disorders			
Aspiration			
subjects affected / exposed	0 / 6 (0.00%)	2 / 69 (2.90%)	0 / 35 (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
Dyspnoea			
subjects affected / exposed	0 / 6 (0.00%)	3 / 69 (4.35%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Interstitial lung disease			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	0 / 35 (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
Laryngeal oedema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung infiltration			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	0 / 35 (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
Oropharyngeal pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	0 / 35 (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
Pleural effusion			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	0 / 35 (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 aspiration			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	0 / 35 (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
Pneumothorax			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	0 / 35 (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
Productive cough			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
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 air leakage			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	0 / 35 (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	0 / 6 (0.00%)	2 / 69 (2.90%)	0 / 35 (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
Pulmonary haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	0 / 35 (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
Respiratory distress			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Respiratory failure			

subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Stridor			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device dislocation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
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			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	0 / 35 (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
Injury, poisoning and procedural complications			
Feeding tube complication			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	0 / 35 (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
Pneumocephalus			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	0 / 35 (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 fracture			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Tracheal obstruction			

subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound secretion			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 6 (16.67%)	1 / 69 (1.45%)	0 / 35 (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
Myocardial infarction			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	0 / 35 (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
Myocardial ischaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulseless electrical activity			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	0 / 35 (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
Nervous system disorders			
Carotid artery perforation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cerebrovascular accident			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolic cerebral infarction			

subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Somnolence			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	0 / 35 (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	0 / 6 (0.00%)	1 / 69 (1.45%)	0 / 35 (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
Neutropenia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	0 / 35 (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
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	0 / 35 (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
Diarrhoea			
subjects affected / exposed	0 / 6 (0.00%)	2 / 69 (2.90%)	0 / 35 (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
Dysphagia			
subjects affected / exposed	0 / 6 (0.00%)	2 / 69 (2.90%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Enterocolitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine perforation			

subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mouth haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
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 / 6 (0.00%)	1 / 69 (1.45%)	0 / 35 (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
Oesophageal fistula			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal ulcer			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophagitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	0 / 35 (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
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	2 / 35 (5.71%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Vomiting			

subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	0 / 35 (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			
Erythema nodosum			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Swelling face			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
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 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ketonuria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
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 injury			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	0 / 35 (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
Bone pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Fistula			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	0 / 35 (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
Muscular weakness			
subjects affected / exposed	0 / 6 (0.00%)	3 / 69 (4.35%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	0 / 35 (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
Neck pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Trismus			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	0 / 35 (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
Infections and infestations			
Abdominal infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Brain abscess			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	0 / 35 (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
Cellulitis			
subjects affected / exposed	0 / 6 (0.00%)	2 / 69 (2.90%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Device related infection			

subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea infectious			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epiglottitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	0 / 35 (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
Lower respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Lung infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 6 (16.67%)	8 / 69 (11.59%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 1	1 / 9	0 / 1
deaths causally related to treatment / all	0 / 1	1 / 5	0 / 1
Post procedural infection			

subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Purulent discharge			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
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 / 6 (0.00%)	4 / 69 (5.80%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	1 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	1 / 3	0 / 0
Septic shock			
subjects affected / exposed	1 / 6 (16.67%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Superinfection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	0 / 35 (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
Upper respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	2 / 35 (5.71%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Wound infection			
subjects affected / exposed	0 / 6 (0.00%)	2 / 69 (2.90%)	0 / 35 (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
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	0 / 6 (0.00%)	3 / 69 (4.35%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Dehydration			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	0 / 35 (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
Hypercalcaemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	0 / 35 (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
Hyperglycaemia			
subjects affected / exposed	2 / 6 (33.33%)	7 / 69 (10.14%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	2 / 2	7 / 7	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Hypernatraemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 69 (0.00%)	0 / 35 (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
Hypokalaemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	0 / 35 (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
Hypophosphataemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Tumour lysis syndrome			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
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	Phase II@open label@BYL719 300mg + CETU	All@patients	

Total subjects affected by serious adverse events			
subjects affected / exposed	15 / 29 (51.72%)	99 / 178 (55.62%)	
number of deaths (all causes)	3	33	
number of deaths resulting from adverse events	1	9	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour haemorrhage			
subjects affected / exposed	1 / 29 (3.45%)	5 / 178 (2.81%)	
occurrences causally related to treatment / all	0 / 3	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 3	
Tumour necrosis			
subjects affected / exposed	1 / 29 (3.45%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour pain			
subjects affected / exposed	1 / 29 (3.45%)	2 / 178 (1.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	1 / 1	
Embolism			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	0 / 29 (0.00%)	2 / 178 (1.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	1 / 1	
Hypotension			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Surgical and medical procedures			
Gastrostomy			
subjects affected / exposed	0 / 29 (0.00%)	2 / 178 (1.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Chills			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Fatigue			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	0 / 29 (0.00%)	3 / 178 (1.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 2	
Pain			
subjects affected / exposed	1 / 29 (3.45%)	2 / 178 (1.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	0 / 29 (0.00%)	8 / 178 (4.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Anaphylactic reaction			

subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug hypersensitivity			
subjects affected / exposed	1 / 29 (3.45%)	2 / 178 (1.12%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	1 / 1	
Respiratory, thoracic and mediastinal disorders			
Aspiration			
subjects affected / exposed	0 / 29 (0.00%)	3 / 178 (1.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	1 / 29 (3.45%)	6 / 178 (3.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 3	
Interstitial lung disease			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Laryngeal oedema			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infiltration			
subjects affected / exposed	1 / 29 (3.45%)	2 / 178 (1.12%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oropharyngeal pain			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			

subjects affected / exposed	0 / 29 (0.00%)	2 / 178 (1.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumonia aspiration			
subjects affected / exposed	0 / 29 (0.00%)	2 / 178 (1.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	0 / 29 (0.00%)	2 / 178 (1.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumothorax			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Productive cough			
subjects affected / exposed	1 / 29 (3.45%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	1 / 1	1 / 1	
Pulmonary air leakage			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 29 (0.00%)	2 / 178 (1.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pulmonary haemorrhage			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Respiratory distress			

subjects affected / exposed	0 / 29 (0.00%)	3 / 178 (1.69%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Respiratory failure			
subjects affected / exposed	1 / 29 (3.45%)	3 / 178 (1.69%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 3	
Stridor			
subjects affected / exposed	1 / 29 (3.45%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Device dislocation			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Feeding tube complication			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumocephalus			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal fracture			

subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Tracheal obstruction			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Wound secretion			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 29 (0.00%)	2 / 178 (1.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial ischaemia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulseless electrical activity			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nervous system disorders			
Carotid artery perforation			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cerebrovascular accident			

subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolic cerebral infarction			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Somnolence			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 29 (3.45%)	2 / 178 (1.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Neutropenia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 29 (3.45%)	2 / 178 (1.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 29 (0.00%)	3 / 178 (1.69%)	
occurrences causally related to treatment / all	0 / 0	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	1 / 29 (3.45%)	5 / 178 (2.81%)	
occurrences causally related to treatment / all	0 / 1	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 1	
Enterocolitis			

subjects affected / exposed	1 / 29 (3.45%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine perforation			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mouth haemorrhage			
subjects affected / exposed	2 / 29 (6.90%)	2 / 178 (1.12%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	1 / 29 (3.45%)	2 / 178 (1.12%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal fistula			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal haemorrhage			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal ulcer			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Oesophagitis			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			

subjects affected / exposed	0 / 29 (0.00%)	2 / 178 (1.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Vomiting			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Erythema nodosum			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Swelling face			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ketonuria			
subjects affected / exposed	1 / 29 (3.45%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal injury			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Bone pain			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fistula			
subjects affected / exposed	1 / 29 (3.45%)	2 / 178 (1.12%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscular weakness			
subjects affected / exposed	0 / 29 (0.00%)	4 / 178 (2.25%)	
occurrences causally related to treatment / all	0 / 0	4 / 4	
deaths causally related to treatment / all	0 / 0	2 / 2	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neck pain			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Trismus			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal infection			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Brain abscess			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			

subjects affected / exposed	0 / 29 (0.00%)	3 / 178 (1.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Device related infection			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea infectious			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epiglottitis			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Lung infection			
subjects affected / exposed	2 / 29 (6.90%)	2 / 178 (1.12%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 1	
Osteomyelitis			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			

subjects affected / exposed	4 / 29 (13.79%)	20 / 178 (11.24%)	
occurrences causally related to treatment / all	2 / 4	5 / 21	
deaths causally related to treatment / all	0 / 0	1 / 10	
Post procedural infection			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Purulent discharge			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 29 (0.00%)	6 / 178 (3.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 6	
deaths causally related to treatment / all	0 / 0	1 / 3	
Septic shock			
subjects affected / exposed	0 / 29 (0.00%)	2 / 178 (1.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Superinfection			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Upper respiratory tract infection			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 29 (0.00%)	2 / 178 (1.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Wound infection			

subjects affected / exposed	0 / 29 (0.00%)	3 / 178 (1.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 2	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 29 (0.00%)	3 / 178 (1.69%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	1 / 1	
Dehydration			
subjects affected / exposed	1 / 29 (3.45%)	2 / 178 (1.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercalcaemia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hyperglycaemia			
subjects affected / exposed	5 / 29 (17.24%)	15 / 178 (8.43%)	
occurrences causally related to treatment / all	5 / 5	15 / 15	
deaths causally related to treatment / all	0 / 0	1 / 1	
Hypernatraemia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypophosphataemia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Tumour lysis syndrome			

subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	

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

Non-serious adverse events	Phase Ib@Oral tablets@BYL719 300mg@+ CETU	Phase Ib@Oral tablets@BYL719 400mg@+ CETU	Phase Ib@Oral suspension@BYL719 300mg@+ CETU
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 15 (100.00%)	5 / 5 (100.00%)	18 / 18 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Tumour haemorrhage			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Tumour necrosis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Tumour pain			
subjects affected / exposed	0 / 15 (0.00%)	1 / 5 (20.00%)	1 / 18 (5.56%)
occurrences (all)	0	1	1
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Embolism			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Flushing			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Haematoma			

subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Hypertension			
subjects affected / exposed	3 / 15 (20.00%)	1 / 5 (20.00%)	2 / 18 (11.11%)
occurrences (all)	3	1	3
Hypotension			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	2
Lymphoedema			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	2	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Chills			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	2
Cyst rupture			
subjects affected / exposed	0 / 15 (0.00%)	1 / 5 (20.00%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Face oedema			
subjects affected / exposed	1 / 15 (6.67%)	1 / 5 (20.00%)	0 / 18 (0.00%)
occurrences (all)	1	1	0
Facial pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Fatigue			
subjects affected / exposed	5 / 15 (33.33%)	2 / 5 (40.00%)	5 / 18 (27.78%)
occurrences (all)	5	2	5
Gait disturbance			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
General physical health deterioration			

subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Localised oedema			
subjects affected / exposed	0 / 15 (0.00%)	1 / 5 (20.00%)	1 / 18 (5.56%)
occurrences (all)	0	1	1
Malaise			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Mucosal dryness			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Oedema peripheral			
subjects affected / exposed	2 / 15 (13.33%)	1 / 5 (20.00%)	0 / 18 (0.00%)
occurrences (all)	2	1	0
Pyrexia			
subjects affected / exposed	3 / 15 (20.00%)	0 / 5 (0.00%)	5 / 18 (27.78%)
occurrences (all)	3	0	6
Secretion discharge			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Submandibular mass			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			

Aspiration			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Atelectasis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Cough			
subjects affected / exposed	2 / 15 (13.33%)	1 / 5 (20.00%)	4 / 18 (22.22%)
occurrences (all)	2	1	4
Dysphonia			
subjects affected / exposed	1 / 15 (6.67%)	1 / 5 (20.00%)	1 / 18 (5.56%)
occurrences (all)	1	1	1
Dyspnoea			
subjects affected / exposed	1 / 15 (6.67%)	2 / 5 (40.00%)	3 / 18 (16.67%)
occurrences (all)	1	2	3
Epistaxis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 5 (20.00%)	1 / 18 (5.56%)
occurrences (all)	0	1	3
Haemoptysis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Hypoxia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Lung disorder			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Nasal dryness			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Oropharyngeal pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	4 / 18 (22.22%)
occurrences (all)	1	0	4

Pharyngeal inflammation			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Pleural effusion			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	2 / 18 (11.11%)
occurrences (all)	0	0	2
Pneumonia aspiration			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Productive cough			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Pulmonary mass			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Pulmonary oedema			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Respiratory distress			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Rhinitis allergic			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Rhinorrhoea			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 15 (0.00%)	1 / 5 (20.00%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Anxiety			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Depression			

subjects affected / exposed	2 / 15 (13.33%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	2	0	1
Insomnia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Irritability			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Sleep disorder			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Amylase increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 15 (13.33%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	3	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 15 (6.67%)	2 / 5 (40.00%)	0 / 18 (0.00%)
occurrences (all)	1	2	0
Blood creatinine increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	2 / 18 (11.11%)
occurrences (all)	0	0	3
Blood glucose increased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Blood testosterone decreased			

subjects affected / exposed	2 / 15 (13.33%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	2	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	2
Electrocardiogram T wave abnormal			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Electrocardiogram T wave inversion			
subjects affected / exposed	0 / 15 (0.00%)	1 / 5 (20.00%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Glycosylated haemoglobin increased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Lipase increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Lymphocyte count decreased			
subjects affected / exposed	0 / 15 (0.00%)	1 / 5 (20.00%)	1 / 18 (5.56%)
occurrences (all)	0	2	1
Troponin increased			
subjects affected / exposed	0 / 15 (0.00%)	1 / 5 (20.00%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Weight decreased			
subjects affected / exposed	6 / 15 (40.00%)	2 / 5 (40.00%)	6 / 18 (33.33%)
occurrences (all)	6	2	6
Weight increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			

Feeding tube complication			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal stoma complication			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Infusion related reaction			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Limb injury			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Procedural pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Skin abrasion			
subjects affected / exposed	2 / 15 (13.33%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	2	0	0
Stoma site erythema			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Stoma site ulcer			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Tracheal obstruction			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Wound			
subjects affected / exposed	0 / 15 (0.00%)	1 / 5 (20.00%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Wound secretion			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Angina pectoris			

subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Atrial fibrillation			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Cardiac arrest			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	2
Cardiomegaly			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Palpitations			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Pericardial effusion			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Sinus bradycardia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Sinus tachycardia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Tachycardia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Nervous system disorders			
Aphasia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Dizziness			
subjects affected / exposed	2 / 15 (13.33%)	0 / 5 (0.00%)	2 / 18 (11.11%)
occurrences (all)	2	0	2
Dysaesthesia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0

Dysgeusia			
subjects affected / exposed	2 / 15 (13.33%)	0 / 5 (0.00%)	2 / 18 (11.11%)
occurrences (all)	2	0	2
Headache			
subjects affected / exposed	2 / 15 (13.33%)	0 / 5 (0.00%)	4 / 18 (22.22%)
occurrences (all)	3	0	6
Hemiparesis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Lethargy			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Paraesthesia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Parosmia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Peripheral motor neuropathy			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Presyncope			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Somnolence			
subjects affected / exposed	1 / 15 (6.67%)	1 / 5 (20.00%)	0 / 18 (0.00%)
occurrences (all)	1	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Lymph node pain			

subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Lymphadenopathy			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Thrombocytopenia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Tympanic membrane perforation			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Conjunctival hyperaemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Diplopia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Dry eye			
subjects affected / exposed	3 / 15 (20.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	3	0	0
Eye irritation			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Eye pain			
subjects affected / exposed	2 / 15 (13.33%)	1 / 5 (20.00%)	0 / 18 (0.00%)
occurrences (all)	2	1	0
Ocular hyperaemia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Vision blurred			
subjects affected / exposed	1 / 15 (6.67%)	1 / 5 (20.00%)	0 / 18 (0.00%)
occurrences (all)	1	1	0
Gastrointestinal disorders			

Abdominal discomfort			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Abdominal distension			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Abdominal pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Anal incontinence			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Ascites			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	2 / 15 (13.33%)	0 / 5 (0.00%)	4 / 18 (22.22%)
occurrences (all)	5	0	4
Dental caries			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Diarrhoea			
subjects affected / exposed	7 / 15 (46.67%)	2 / 5 (40.00%)	10 / 18 (55.56%)
occurrences (all)	13	4	20
Dry mouth			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Dyspepsia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Dysphagia			
subjects affected / exposed	3 / 15 (20.00%)	1 / 5 (20.00%)	1 / 18 (5.56%)
occurrences (all)	3	1	1

Gastritis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Gastritis erosive			
subjects affected / exposed	0 / 15 (0.00%)	1 / 5 (20.00%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 15 (13.33%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	2	0	0
Glossodynia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Haemorrhoids			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Melaena			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Mouth haemorrhage			
subjects affected / exposed	0 / 15 (0.00%)	1 / 5 (20.00%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Mouth ulceration			
subjects affected / exposed	2 / 15 (13.33%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	3	0	1
Nausea			
subjects affected / exposed	6 / 15 (40.00%)	1 / 5 (20.00%)	4 / 18 (22.22%)
occurrences (all)	6	1	4
Odynophagia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Oesophageal fistula			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	2 / 18 (11.11%)
occurrences (all)	0	0	2
Oesophageal ulcer			
subjects affected / exposed	0 / 15 (0.00%)	1 / 5 (20.00%)	0 / 18 (0.00%)
occurrences (all)	0	1	0

Oesophagitis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 5 (20.00%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Oral pain			
subjects affected / exposed	0 / 15 (0.00%)	1 / 5 (20.00%)	1 / 18 (5.56%)
occurrences (all)	0	1	1
Salivary gland mucocoele			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Stomatitis			
subjects affected / exposed	7 / 15 (46.67%)	2 / 5 (40.00%)	8 / 18 (44.44%)
occurrences (all)	8	2	10
Vomiting			
subjects affected / exposed	3 / 15 (20.00%)	1 / 5 (20.00%)	3 / 18 (16.67%)
occurrences (all)	3	3	3
Skin and subcutaneous tissue disorders			
Cold sweat			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Decubitus ulcer			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Dermal cyst			
subjects affected / exposed	0 / 15 (0.00%)	1 / 5 (20.00%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Dermatitis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Dermatitis acneiform			
subjects affected / exposed	7 / 15 (46.67%)	2 / 5 (40.00%)	4 / 18 (22.22%)
occurrences (all)	9	2	5
Dry skin			
subjects affected / exposed	4 / 15 (26.67%)	2 / 5 (40.00%)	2 / 18 (11.11%)
occurrences (all)	4	2	4
Erythema			

subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Erythema nodosum			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Papule			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	1 / 15 (6.67%)	1 / 5 (20.00%)	1 / 18 (5.56%)
occurrences (all)	2	1	1
Rash			
subjects affected / exposed	7 / 15 (46.67%)	0 / 5 (0.00%)	4 / 18 (22.22%)
occurrences (all)	9	0	4
Rash maculo-papular			
subjects affected / exposed	3 / 15 (20.00%)	0 / 5 (0.00%)	2 / 18 (11.11%)
occurrences (all)	5	0	4
Rash papular			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Skin discolouration			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Skin fissures			
subjects affected / exposed	4 / 15 (26.67%)	1 / 5 (20.00%)	2 / 18 (11.11%)
occurrences (all)	5	1	2
Skin striae			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Skin toxicity			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0

Skin ulcer			
subjects affected / exposed	3 / 15 (20.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	3	0	1
Urticaria			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 15 (0.00%)	1 / 5 (20.00%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Dysuria			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Renal failure			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Urinary incontinence			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Urinary retention			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 15 (13.33%)	1 / 5 (20.00%)	2 / 18 (11.11%)
occurrences (all)	3	1	2
Bone pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Muscle spasms			
subjects affected / exposed	0 / 15 (0.00%)	1 / 5 (20.00%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Muscular weakness			

subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 15 (0.00%)	1 / 5 (20.00%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal stiffness			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Myalgia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 5 (20.00%)	2 / 18 (11.11%)
occurrences (all)	0	1	2
Neck pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Pain in extremity			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Trismus			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Candida infection			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Cellulitis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Conjunctivitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Ear infection			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0

Folliculitis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Herpes virus infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Klebsiella sepsis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 5 (20.00%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Lung infection			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Nail infection			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	2	0	0
Oral candidiasis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Paronychia			
subjects affected / exposed	6 / 15 (40.00%)	1 / 5 (20.00%)	5 / 18 (27.78%)
occurrences (all)	6	1	5
Rash pustular			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Rhinitis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 5 (20.00%)	1 / 18 (5.56%)
occurrences (all)	0	1	1
Sinusitis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Skin infection			
subjects affected / exposed	2 / 15 (13.33%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	2	0	0

Stoma site infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Tooth infection			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	3	0	0
Viral infection			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Wound infection			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	6 / 15 (40.00%)	1 / 5 (20.00%)	4 / 18 (22.22%)
occurrences (all)	7	1	4
Dehydration			
subjects affected / exposed	0 / 15 (0.00%)	1 / 5 (20.00%)	0 / 18 (0.00%)
occurrences (all)	0	2	0
Glucose tolerance impaired			
subjects affected / exposed	0 / 15 (0.00%)	1 / 5 (20.00%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Hypercalcaemia			
subjects affected / exposed	1 / 15 (6.67%)	1 / 5 (20.00%)	3 / 18 (16.67%)
occurrences (all)	1	1	3
Hyperglycaemia			
subjects affected / exposed	8 / 15 (53.33%)	2 / 5 (40.00%)	10 / 18 (55.56%)
occurrences (all)	14	6	15
Hyperkalaemia			

subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Hypermagnesaemia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	2	0	0
Hypernatraemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Hyperosmolar state			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Hypertriglyceridaemia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Hyperuricaemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Hypoalbuminaemia			
subjects affected / exposed	2 / 15 (13.33%)	1 / 5 (20.00%)	1 / 18 (5.56%)
occurrences (all)	2	1	1
Hypocalcaemia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Hypoglycaemia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 5 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Hypokalaemia			
subjects affected / exposed	5 / 15 (33.33%)	0 / 5 (0.00%)	4 / 18 (22.22%)
occurrences (all)	14	0	6
Hypomagnesaemia			
subjects affected / exposed	8 / 15 (53.33%)	2 / 5 (40.00%)	6 / 18 (33.33%)
occurrences (all)	17	2	6
Hyponatraemia			
subjects affected / exposed	1 / 15 (6.67%)	1 / 5 (20.00%)	0 / 18 (0.00%)
occurrences (all)	1	1	0
Hypophagia			

subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Hypophosphataemia			
subjects affected / exposed	2 / 15 (13.33%)	1 / 5 (20.00%)	4 / 18 (22.22%)
occurrences (all)	2	3	6
Malnutrition			
subjects affected / exposed	0 / 15 (0.00%)	0 / 5 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1

Non-serious adverse events	Phase Ib@Disp. tablets@BYL719 300mg@+ CETU	Phase II@randomized@BYL 719 300mg + CETU	Phase II@randomized@CETU
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	69 / 69 (100.00%)	35 / 35 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Tumour haemorrhage			
subjects affected / exposed	1 / 6 (16.67%)	0 / 69 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Tumour necrosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Tumour pain			
subjects affected / exposed	3 / 6 (50.00%)	4 / 69 (5.80%)	2 / 35 (5.71%)
occurrences (all)	3	4	3
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Embolism			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Flushing			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Haematoma			

subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	0 / 6 (0.00%)	5 / 69 (7.25%)	3 / 35 (8.57%)
occurrences (all)	0	6	10
Hypotension			
subjects affected / exposed	0 / 6 (0.00%)	4 / 69 (5.80%)	3 / 35 (8.57%)
occurrences (all)	0	4	3
Lymphoedema			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 6 (16.67%)	4 / 69 (5.80%)	1 / 35 (2.86%)
occurrences (all)	1	5	1
Chills			
subjects affected / exposed	0 / 6 (0.00%)	3 / 69 (4.35%)	4 / 35 (11.43%)
occurrences (all)	0	3	4
Cyst rupture			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Face oedema			
subjects affected / exposed	0 / 6 (0.00%)	3 / 69 (4.35%)	1 / 35 (2.86%)
occurrences (all)	0	4	1
Facial pain			
subjects affected / exposed	0 / 6 (0.00%)	5 / 69 (7.25%)	2 / 35 (5.71%)
occurrences (all)	0	5	3
Fatigue			
subjects affected / exposed	0 / 6 (0.00%)	22 / 69 (31.88%)	8 / 35 (22.86%)
occurrences (all)	0	22	10
Gait disturbance			
subjects affected / exposed	1 / 6 (16.67%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
General physical health deterioration			

subjects affected / exposed	0 / 6 (0.00%)	2 / 69 (2.90%)	0 / 35 (0.00%)
occurrences (all)	0	2	0
Localised oedema			
subjects affected / exposed	1 / 6 (16.67%)	0 / 69 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Malaise			
subjects affected / exposed	1 / 6 (16.67%)	1 / 69 (1.45%)	0 / 35 (0.00%)
occurrences (all)	1	1	0
Mucosal dryness			
subjects affected / exposed	1 / 6 (16.67%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Oedema peripheral			
subjects affected / exposed	0 / 6 (0.00%)	4 / 69 (5.80%)	1 / 35 (2.86%)
occurrences (all)	0	5	2
Pyrexia			
subjects affected / exposed	2 / 6 (33.33%)	6 / 69 (8.70%)	3 / 35 (8.57%)
occurrences (all)	2	7	3
Secretion discharge			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Submandibular mass			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 6 (0.00%)	2 / 69 (2.90%)	2 / 35 (5.71%)
occurrences (all)	0	2	2
Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			

Aspiration			
subjects affected / exposed	0 / 6 (0.00%)	2 / 69 (2.90%)	0 / 35 (0.00%)
occurrences (all)	0	2	0
Atelectasis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	1 / 6 (16.67%)	15 / 69 (21.74%)	7 / 35 (20.00%)
occurrences (all)	1	20	9
Dysphonia			
subjects affected / exposed	0 / 6 (0.00%)	5 / 69 (7.25%)	0 / 35 (0.00%)
occurrences (all)	0	5	0
Dyspnoea			
subjects affected / exposed	1 / 6 (16.67%)	11 / 69 (15.94%)	5 / 35 (14.29%)
occurrences (all)	1	13	5
Epistaxis			
subjects affected / exposed	0 / 6 (0.00%)	3 / 69 (4.35%)	1 / 35 (2.86%)
occurrences (all)	0	3	2
Haemoptysis			
subjects affected / exposed	0 / 6 (0.00%)	3 / 69 (4.35%)	1 / 35 (2.86%)
occurrences (all)	0	3	1
Hypoxia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Lung disorder			
subjects affected / exposed	1 / 6 (16.67%)	1 / 69 (1.45%)	0 / 35 (0.00%)
occurrences (all)	1	1	0
Nasal congestion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Nasal dryness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Oropharyngeal pain			
subjects affected / exposed	0 / 6 (0.00%)	4 / 69 (5.80%)	3 / 35 (8.57%)
occurrences (all)	0	4	3

Pharyngeal inflammation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			
subjects affected / exposed	0 / 6 (0.00%)	2 / 69 (2.90%)	1 / 35 (2.86%)
occurrences (all)	0	2	1
Pneumonia aspiration			
subjects affected / exposed	1 / 6 (16.67%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Productive cough			
subjects affected / exposed	1 / 6 (16.67%)	5 / 69 (7.25%)	2 / 35 (5.71%)
occurrences (all)	1	5	2
Pulmonary mass			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Pulmonary oedema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Respiratory distress			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Rhinitis allergic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 6 (0.00%)	2 / 69 (2.90%)	3 / 35 (8.57%)
occurrences (all)	0	2	3
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	0 / 6 (0.00%)	5 / 69 (7.25%)	1 / 35 (2.86%)
occurrences (all)	0	6	2
Depression			

subjects affected / exposed	0 / 6 (0.00%)	5 / 69 (7.25%)	1 / 35 (2.86%)
occurrences (all)	0	5	1
Insomnia			
subjects affected / exposed	1 / 6 (16.67%)	6 / 69 (8.70%)	4 / 35 (11.43%)
occurrences (all)	1	6	4
Irritability			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Sleep disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 6 (16.67%)	3 / 69 (4.35%)	1 / 35 (2.86%)
occurrences (all)	1	5	1
Amylase increased			
subjects affected / exposed	0 / 6 (0.00%)	3 / 69 (4.35%)	2 / 35 (5.71%)
occurrences (all)	0	7	4
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 6 (16.67%)	3 / 69 (4.35%)	1 / 35 (2.86%)
occurrences (all)	1	4	1
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 6 (0.00%)	5 / 69 (7.25%)	3 / 35 (8.57%)
occurrences (all)	0	5	3
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	2 / 35 (5.71%)
occurrences (all)	0	1	2
Blood creatinine increased			
subjects affected / exposed	0 / 6 (0.00%)	7 / 69 (10.14%)	1 / 35 (2.86%)
occurrences (all)	0	15	1
Blood glucose increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Blood testosterone decreased			

subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 6 (0.00%)	4 / 69 (5.80%)	1 / 35 (2.86%)
occurrences (all)	0	7	1
Electrocardiogram T wave abnormal			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram T wave inversion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Glycosylated haemoglobin increased			
subjects affected / exposed	0 / 6 (0.00%)	2 / 69 (2.90%)	0 / 35 (0.00%)
occurrences (all)	0	2	0
Lipase increased			
subjects affected / exposed	0 / 6 (0.00%)	5 / 69 (7.25%)	3 / 35 (8.57%)
occurrences (all)	0	15	6
Lymphocyte count decreased			
subjects affected / exposed	0 / 6 (0.00%)	4 / 69 (5.80%)	1 / 35 (2.86%)
occurrences (all)	0	5	1
Troponin increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	3 / 6 (50.00%)	27 / 69 (39.13%)	7 / 35 (20.00%)
occurrences (all)	3	27	7
Weight increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	2 / 35 (5.71%)
occurrences (all)	0	0	3
Injury, poisoning and procedural complications			

Feeding tube complication			
subjects affected / exposed	1 / 6 (16.67%)	1 / 69 (1.45%)	0 / 35 (0.00%)
occurrences (all)	1	1	0
Gastrointestinal stoma complication			
subjects affected / exposed	1 / 6 (16.67%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Infusion related reaction			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	2 / 35 (5.71%)
occurrences (all)	0	1	2
Limb injury			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	2 / 35 (5.71%)
occurrences (all)	0	0	2
Skin abrasion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Stoma site erythema			
subjects affected / exposed	1 / 6 (16.67%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Stoma site ulcer			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Tracheal obstruction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Wound			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Wound secretion			
subjects affected / exposed	2 / 6 (33.33%)	2 / 69 (2.90%)	0 / 35 (0.00%)
occurrences (all)	3	3	0
Cardiac disorders			
Angina pectoris			

subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Atrial fibrillation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Cardiac arrest			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Cardiomegaly			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Palpitations			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Pericardial effusion			
subjects affected / exposed	1 / 6 (16.67%)	1 / 69 (1.45%)	0 / 35 (0.00%)
occurrences (all)	1	1	0
Sinus bradycardia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Sinus tachycardia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 69 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Nervous system disorders			
Aphasia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	1 / 6 (16.67%)	5 / 69 (7.25%)	1 / 35 (2.86%)
occurrences (all)	1	5	1
Dysaesthesia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0

Dysgeusia			
subjects affected / exposed	0 / 6 (0.00%)	2 / 69 (2.90%)	1 / 35 (2.86%)
occurrences (all)	0	2	1
Headache			
subjects affected / exposed	0 / 6 (0.00%)	7 / 69 (10.14%)	4 / 35 (11.43%)
occurrences (all)	0	7	4
Hemiparesis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Lethargy			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Paraesthesia			
subjects affected / exposed	0 / 6 (0.00%)	3 / 69 (4.35%)	1 / 35 (2.86%)
occurrences (all)	0	3	1
Parosmia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Peripheral motor neuropathy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 6 (0.00%)	3 / 69 (4.35%)	1 / 35 (2.86%)
occurrences (all)	0	3	1
Presyncope			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 6 (33.33%)	9 / 69 (13.04%)	6 / 35 (17.14%)
occurrences (all)	2	10	7
Lymph node pain			

subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Lymphadenopathy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Tympanic membrane perforation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Conjunctival hyperaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Diplopia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Dry eye			
subjects affected / exposed	0 / 6 (0.00%)	2 / 69 (2.90%)	2 / 35 (5.71%)
occurrences (all)	0	2	2
Eye irritation			
subjects affected / exposed	1 / 6 (16.67%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Eye pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Ocular hyperaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	0 / 6 (0.00%)	3 / 69 (4.35%)	0 / 35 (0.00%)
occurrences (all)	0	3	0
Gastrointestinal disorders			

Abdominal discomfort			
subjects affected / exposed	0 / 6 (0.00%)	2 / 69 (2.90%)	1 / 35 (2.86%)
occurrences (all)	0	2	1
Abdominal distension			
subjects affected / exposed	0 / 6 (0.00%)	3 / 69 (4.35%)	0 / 35 (0.00%)
occurrences (all)	0	3	0
Abdominal pain			
subjects affected / exposed	0 / 6 (0.00%)	3 / 69 (4.35%)	0 / 35 (0.00%)
occurrences (all)	0	3	0
Abdominal pain upper			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	2 / 35 (5.71%)
occurrences (all)	0	0	4
Anal incontinence			
subjects affected / exposed	1 / 6 (16.67%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Ascites			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Constipation			
subjects affected / exposed	3 / 6 (50.00%)	9 / 69 (13.04%)	7 / 35 (20.00%)
occurrences (all)	3	10	7
Dental caries			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Diarrhoea			
subjects affected / exposed	2 / 6 (33.33%)	29 / 69 (42.03%)	5 / 35 (14.29%)
occurrences (all)	5	43	6
Dry mouth			
subjects affected / exposed	0 / 6 (0.00%)	4 / 69 (5.80%)	3 / 35 (8.57%)
occurrences (all)	0	4	3
Dyspepsia			
subjects affected / exposed	1 / 6 (16.67%)	7 / 69 (10.14%)	1 / 35 (2.86%)
occurrences (all)	1	7	1
Dysphagia			
subjects affected / exposed	0 / 6 (0.00%)	13 / 69 (18.84%)	2 / 35 (5.71%)
occurrences (all)	0	14	3

Gastritis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Gastritis erosive			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 6 (16.67%)	6 / 69 (8.70%)	0 / 35 (0.00%)
occurrences (all)	1	6	0
Glossodynia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Haemorrhoids			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Melaena			
subjects affected / exposed	1 / 6 (16.67%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Mouth haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Mouth ulceration			
subjects affected / exposed	0 / 6 (0.00%)	2 / 69 (2.90%)	1 / 35 (2.86%)
occurrences (all)	0	3	1
Nausea			
subjects affected / exposed	1 / 6 (16.67%)	16 / 69 (23.19%)	4 / 35 (11.43%)
occurrences (all)	1	23	6
Odynophagia			
subjects affected / exposed	0 / 6 (0.00%)	4 / 69 (5.80%)	0 / 35 (0.00%)
occurrences (all)	0	4	0
Oesophageal fistula			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Oesophageal ulcer			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0

Oesophagitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Oral pain			
subjects affected / exposed	0 / 6 (0.00%)	4 / 69 (5.80%)	2 / 35 (5.71%)
occurrences (all)	0	5	3
Salivary gland mucocoele			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	1 / 6 (16.67%)	31 / 69 (44.93%)	6 / 35 (17.14%)
occurrences (all)	1	39	6
Vomiting			
subjects affected / exposed	2 / 6 (33.33%)	15 / 69 (21.74%)	2 / 35 (5.71%)
occurrences (all)	4	20	6
Skin and subcutaneous tissue disorders			
Cold sweat			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Decubitus ulcer			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	2 / 35 (5.71%)
occurrences (all)	0	1	2
Dermal cyst			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Dermatitis			
subjects affected / exposed	0 / 6 (0.00%)	2 / 69 (2.90%)	0 / 35 (0.00%)
occurrences (all)	0	2	0
Dermatitis acneiform			
subjects affected / exposed	0 / 6 (0.00%)	21 / 69 (30.43%)	8 / 35 (22.86%)
occurrences (all)	0	22	10
Dry skin			
subjects affected / exposed	1 / 6 (16.67%)	18 / 69 (26.09%)	6 / 35 (17.14%)
occurrences (all)	1	18	6
Erythema			

subjects affected / exposed	0 / 6 (0.00%)	2 / 69 (2.90%)	2 / 35 (5.71%)
occurrences (all)	0	2	2
Erythema nodosum			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 6 (0.00%)	3 / 69 (4.35%)	2 / 35 (5.71%)
occurrences (all)	0	3	2
Papule			
subjects affected / exposed	1 / 6 (16.67%)	2 / 69 (2.90%)	0 / 35 (0.00%)
occurrences (all)	1	3	0
Pruritus			
subjects affected / exposed	1 / 6 (16.67%)	11 / 69 (15.94%)	2 / 35 (5.71%)
occurrences (all)	2	13	2
Rash			
subjects affected / exposed	2 / 6 (33.33%)	26 / 69 (37.68%)	14 / 35 (40.00%)
occurrences (all)	2	28	16
Rash maculo-papular			
subjects affected / exposed	0 / 6 (0.00%)	11 / 69 (15.94%)	2 / 35 (5.71%)
occurrences (all)	0	15	2
Rash papular			
subjects affected / exposed	0 / 6 (0.00%)	2 / 69 (2.90%)	0 / 35 (0.00%)
occurrences (all)	0	2	0
Skin discolouration			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Skin fissures			
subjects affected / exposed	0 / 6 (0.00%)	12 / 69 (17.39%)	4 / 35 (11.43%)
occurrences (all)	0	20	5
Skin striae			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Skin toxicity			
subjects affected / exposed	1 / 6 (16.67%)	4 / 69 (5.80%)	3 / 35 (8.57%)
occurrences (all)	1	4	5

Skin ulcer			
subjects affected / exposed	0 / 6 (0.00%)	5 / 69 (7.25%)	0 / 35 (0.00%)
occurrences (all)	0	5	0
Urticaria			
subjects affected / exposed	0 / 6 (0.00%)	4 / 69 (5.80%)	0 / 35 (0.00%)
occurrences (all)	0	4	0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	2 / 35 (5.71%)
occurrences (all)	0	0	2
Pollakiuria			
subjects affected / exposed	1 / 6 (16.67%)	1 / 69 (1.45%)	0 / 35 (0.00%)
occurrences (all)	1	1	0
Renal failure			
subjects affected / exposed	1 / 6 (16.67%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Urinary incontinence			
subjects affected / exposed	1 / 6 (16.67%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Urinary retention			
subjects affected / exposed	1 / 6 (16.67%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 6 (0.00%)	5 / 69 (7.25%)	4 / 35 (11.43%)
occurrences (all)	0	6	4
Bone pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	2 / 35 (5.71%)
occurrences (all)	0	1	3
Muscle spasms			
subjects affected / exposed	0 / 6 (0.00%)	2 / 69 (2.90%)	0 / 35 (0.00%)
occurrences (all)	0	2	0
Muscular weakness			

subjects affected / exposed	0 / 6 (0.00%)	4 / 69 (5.80%)	2 / 35 (5.71%)
occurrences (all)	0	4	2
Musculoskeletal chest pain			
subjects affected / exposed	0 / 6 (0.00%)	2 / 69 (2.90%)	2 / 35 (5.71%)
occurrences (all)	0	2	2
Musculoskeletal pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	2 / 35 (5.71%)
occurrences (all)	0	1	2
Musculoskeletal stiffness			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Myalgia			
subjects affected / exposed	0 / 6 (0.00%)	4 / 69 (5.80%)	1 / 35 (2.86%)
occurrences (all)	0	4	1
Neck pain			
subjects affected / exposed	1 / 6 (16.67%)	6 / 69 (8.70%)	4 / 35 (11.43%)
occurrences (all)	1	7	4
Pain in extremity			
subjects affected / exposed	0 / 6 (0.00%)	4 / 69 (5.80%)	0 / 35 (0.00%)
occurrences (all)	0	7	0
Trismus			
subjects affected / exposed	0 / 6 (0.00%)	3 / 69 (4.35%)	1 / 35 (2.86%)
occurrences (all)	0	3	1
Infections and infestations			
Candida infection			
subjects affected / exposed	0 / 6 (0.00%)	3 / 69 (4.35%)	2 / 35 (5.71%)
occurrences (all)	0	3	2
Cellulitis			
subjects affected / exposed	0 / 6 (0.00%)	2 / 69 (2.90%)	2 / 35 (5.71%)
occurrences (all)	0	3	3
Conjunctivitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Ear infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	0 / 35 (0.00%)
occurrences (all)	0	1	0

Folliculitis			
subjects affected / exposed	0 / 6 (0.00%)	3 / 69 (4.35%)	5 / 35 (14.29%)
occurrences (all)	0	3	5
Herpes virus infection			
subjects affected / exposed	1 / 6 (16.67%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Herpes zoster			
subjects affected / exposed	1 / 6 (16.67%)	0 / 69 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Klebsiella sepsis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Lung infection			
subjects affected / exposed	0 / 6 (0.00%)	3 / 69 (4.35%)	0 / 35 (0.00%)
occurrences (all)	0	3	0
Nail infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Oral candidiasis			
subjects affected / exposed	0 / 6 (0.00%)	4 / 69 (5.80%)	1 / 35 (2.86%)
occurrences (all)	0	4	1
Paronychia			
subjects affected / exposed	1 / 6 (16.67%)	15 / 69 (21.74%)	6 / 35 (17.14%)
occurrences (all)	1	18	11
Rash pustular			
subjects affected / exposed	0 / 6 (0.00%)	3 / 69 (4.35%)	1 / 35 (2.86%)
occurrences (all)	0	3	1
Rhinitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Sinusitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Skin infection			
subjects affected / exposed	0 / 6 (0.00%)	2 / 69 (2.90%)	0 / 35 (0.00%)
occurrences (all)	0	2	0

Stoma site infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Tooth infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Urinary tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Viral infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Wound infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 6 (16.67%)	26 / 69 (37.68%)	5 / 35 (14.29%)
occurrences (all)	1	28	5
Dehydration			
subjects affected / exposed	3 / 6 (50.00%)	5 / 69 (7.25%)	1 / 35 (2.86%)
occurrences (all)	3	6	1
Glucose tolerance impaired			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Hypercalcaemia			
subjects affected / exposed	1 / 6 (16.67%)	4 / 69 (5.80%)	1 / 35 (2.86%)
occurrences (all)	1	5	1
Hyperglycaemia			
subjects affected / exposed	5 / 6 (83.33%)	42 / 69 (60.87%)	5 / 35 (14.29%)
occurrences (all)	9	103	5
Hyperkalaemia			

subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Hypermagnesaemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Hypernatraemia			
subjects affected / exposed	2 / 6 (33.33%)	1 / 69 (1.45%)	0 / 35 (0.00%)
occurrences (all)	2	1	0
Hyperosmolar state			
subjects affected / exposed	1 / 6 (16.67%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Hypertriglyceridaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	2
Hyperuricaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Hypoalbuminaemia			
subjects affected / exposed	0 / 6 (0.00%)	5 / 69 (7.25%)	4 / 35 (11.43%)
occurrences (all)	0	6	4
Hypocalcaemia			
subjects affected / exposed	0 / 6 (0.00%)	5 / 69 (7.25%)	2 / 35 (5.71%)
occurrences (all)	0	8	2
Hypoglycaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 69 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	1 / 6 (16.67%)	13 / 69 (18.84%)	3 / 35 (8.57%)
occurrences (all)	1	26	4
Hypomagnesaemia			
subjects affected / exposed	1 / 6 (16.67%)	18 / 69 (26.09%)	8 / 35 (22.86%)
occurrences (all)	1	33	14
Hyponatraemia			
subjects affected / exposed	0 / 6 (0.00%)	7 / 69 (10.14%)	3 / 35 (8.57%)
occurrences (all)	0	8	3
Hypophagia			

subjects affected / exposed	0 / 6 (0.00%)	3 / 69 (4.35%)	0 / 35 (0.00%)
occurrences (all)	0	3	0
Hypophosphataemia			
subjects affected / exposed	1 / 6 (16.67%)	5 / 69 (7.25%)	5 / 35 (14.29%)
occurrences (all)	1	7	10
Malnutrition			
subjects affected / exposed	0 / 6 (0.00%)	1 / 69 (1.45%)	0 / 35 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	Phase II@open label@BYL719 300mg + CETU	All@patients	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	29 / 29 (100.00%)	177 / 178 (99.44%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	2 / 29 (6.90%)	3 / 178 (1.69%)	
occurrences (all)	2	3	
Tumour haemorrhage			
subjects affected / exposed	0 / 29 (0.00%)	2 / 178 (1.12%)	
occurrences (all)	0	2	
Tumour necrosis			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Tumour pain			
subjects affected / exposed	2 / 29 (6.90%)	13 / 178 (7.30%)	
occurrences (all)	2	14	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 29 (3.45%)	2 / 178 (1.12%)	
occurrences (all)	1	2	
Embolism			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Flushing			
subjects affected / exposed	1 / 29 (3.45%)	2 / 178 (1.12%)	
occurrences (all)	1	2	
Haematoma			

subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Hypertension			
subjects affected / exposed	4 / 29 (13.79%)	18 / 178 (10.11%)	
occurrences (all)	4	27	
Hypotension			
subjects affected / exposed	1 / 29 (3.45%)	9 / 178 (5.06%)	
occurrences (all)	1	10	
Lymphoedema			
subjects affected / exposed	0 / 29 (0.00%)	3 / 178 (1.69%)	
occurrences (all)	0	4	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	3 / 29 (10.34%)	11 / 178 (6.18%)	
occurrences (all)	3	12	
Chills			
subjects affected / exposed	1 / 29 (3.45%)	10 / 178 (5.62%)	
occurrences (all)	1	11	
Cyst rupture			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Face oedema			
subjects affected / exposed	1 / 29 (3.45%)	7 / 178 (3.93%)	
occurrences (all)	1	8	
Facial pain			
subjects affected / exposed	0 / 29 (0.00%)	8 / 178 (4.49%)	
occurrences (all)	0	9	
Fatigue			
subjects affected / exposed	14 / 29 (48.28%)	56 / 178 (31.46%)	
occurrences (all)	17	61	
Gait disturbance			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
General physical health deterioration			

subjects affected / exposed	0 / 29 (0.00%)	3 / 178 (1.69%)	
occurrences (all)	0	3	
Localised oedema			
subjects affected / exposed	2 / 29 (6.90%)	6 / 178 (3.37%)	
occurrences (all)	2	6	
Malaise			
subjects affected / exposed	0 / 29 (0.00%)	2 / 178 (1.12%)	
occurrences (all)	0	2	
Mucosal dryness			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Non-cardiac chest pain			
subjects affected / exposed	2 / 29 (6.90%)	4 / 178 (2.25%)	
occurrences (all)	2	4	
Oedema peripheral			
subjects affected / exposed	3 / 29 (10.34%)	11 / 178 (6.18%)	
occurrences (all)	3	13	
Pyrexia			
subjects affected / exposed	3 / 29 (10.34%)	22 / 178 (12.36%)	
occurrences (all)	3	24	
Secretion discharge			
subjects affected / exposed	1 / 29 (3.45%)	2 / 178 (1.12%)	
occurrences (all)	1	2	
Submandibular mass			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	1 / 29 (3.45%)	6 / 178 (3.37%)	
occurrences (all)	1	6	
Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			

Aspiration				
subjects affected / exposed	0 / 29 (0.00%)	3 / 178 (1.69%)		
occurrences (all)	0	3		
Atelectasis				
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)		
occurrences (all)	0	1		
Cough				
subjects affected / exposed	6 / 29 (20.69%)	36 / 178 (20.22%)		
occurrences (all)	6	43		
Dysphonia				
subjects affected / exposed	4 / 29 (13.79%)	12 / 178 (6.74%)		
occurrences (all)	4	12		
Dyspnoea				
subjects affected / exposed	3 / 29 (10.34%)	26 / 178 (14.61%)		
occurrences (all)	3	28		
Epistaxis				
subjects affected / exposed	1 / 29 (3.45%)	7 / 178 (3.93%)		
occurrences (all)	2	11		
Haemoptysis				
subjects affected / exposed	1 / 29 (3.45%)	6 / 178 (3.37%)		
occurrences (all)	1	6		
Hypoxia				
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)		
occurrences (all)	0	1		
Lung disorder				
subjects affected / exposed	0 / 29 (0.00%)	2 / 178 (1.12%)		
occurrences (all)	0	2		
Nasal congestion				
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)		
occurrences (all)	0	1		
Nasal dryness				
subjects affected / exposed	0 / 29 (0.00%)	2 / 178 (1.12%)		
occurrences (all)	0	2		
Oropharyngeal pain				
subjects affected / exposed	1 / 29 (3.45%)	13 / 178 (7.30%)		
occurrences (all)	1	13		

Pharyngeal inflammation			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Pleural effusion			
subjects affected / exposed	0 / 29 (0.00%)	5 / 178 (2.81%)	
occurrences (all)	0	5	
Pneumonia aspiration			
subjects affected / exposed	0 / 29 (0.00%)	2 / 178 (1.12%)	
occurrences (all)	0	2	
Productive cough			
subjects affected / exposed	1 / 29 (3.45%)	10 / 178 (5.62%)	
occurrences (all)	1	10	
Pulmonary mass			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Pulmonary oedema			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Respiratory distress			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Rhinitis allergic			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Rhinorrhoea			
subjects affected / exposed	0 / 29 (0.00%)	6 / 178 (3.37%)	
occurrences (all)	0	6	
Psychiatric disorders			
Agitation			
subjects affected / exposed	1 / 29 (3.45%)	2 / 178 (1.12%)	
occurrences (all)	1	2	
Anxiety			
subjects affected / exposed	2 / 29 (6.90%)	10 / 178 (5.62%)	
occurrences (all)	3	13	
Depression			

subjects affected / exposed	1 / 29 (3.45%)	10 / 178 (5.62%)	
occurrences (all)	1	10	
Insomnia			
subjects affected / exposed	1 / 29 (3.45%)	13 / 178 (7.30%)	
occurrences (all)	1	13	
Irritability			
subjects affected / exposed	2 / 29 (6.90%)	4 / 178 (2.25%)	
occurrences (all)	2	4	
Sleep disorder			
subjects affected / exposed	2 / 29 (6.90%)	2 / 178 (1.12%)	
occurrences (all)	2	2	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 29 (0.00%)	6 / 178 (3.37%)	
occurrences (all)	0	8	
Amylase increased			
subjects affected / exposed	1 / 29 (3.45%)	6 / 178 (3.37%)	
occurrences (all)	2	13	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 29 (0.00%)	7 / 178 (3.93%)	
occurrences (all)	0	9	
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 29 (3.45%)	10 / 178 (5.62%)	
occurrences (all)	1	10	
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 29 (3.45%)	7 / 178 (3.93%)	
occurrences (all)	1	7	
Blood creatinine increased			
subjects affected / exposed	1 / 29 (3.45%)	11 / 178 (6.18%)	
occurrences (all)	1	20	
Blood glucose increased			
subjects affected / exposed	0 / 29 (0.00%)	2 / 178 (1.12%)	
occurrences (all)	0	2	
Blood testosterone decreased			

subjects affected / exposed	2 / 29 (6.90%)	4 / 178 (2.25%)	
occurrences (all)	3	5	
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 29 (0.00%)	7 / 178 (3.93%)	
occurrences (all)	0	11	
Electrocardiogram T wave abnormal			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Electrocardiogram T wave inversion			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Glycosylated haemoglobin increased			
subjects affected / exposed	0 / 29 (0.00%)	3 / 178 (1.69%)	
occurrences (all)	0	3	
Lipase increased			
subjects affected / exposed	1 / 29 (3.45%)	10 / 178 (5.62%)	
occurrences (all)	1	23	
Lymphocyte count decreased			
subjects affected / exposed	2 / 29 (6.90%)	9 / 178 (5.06%)	
occurrences (all)	2	11	
Troponin increased			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Weight decreased			
subjects affected / exposed	11 / 29 (37.93%)	62 / 178 (34.83%)	
occurrences (all)	11	62	
Weight increased			
subjects affected / exposed	0 / 29 (0.00%)	2 / 178 (1.12%)	
occurrences (all)	0	3	
Injury, poisoning and procedural complications			

Feeding tube complication			
subjects affected / exposed	0 / 29 (0.00%)	2 / 178 (1.12%)	
occurrences (all)	0	2	
Gastrointestinal stoma complication			
subjects affected / exposed	1 / 29 (3.45%)	2 / 178 (1.12%)	
occurrences (all)	1	2	
Infusion related reaction			
subjects affected / exposed	0 / 29 (0.00%)	3 / 178 (1.69%)	
occurrences (all)	0	3	
Limb injury			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Procedural pain			
subjects affected / exposed	0 / 29 (0.00%)	2 / 178 (1.12%)	
occurrences (all)	0	2	
Skin abrasion			
subjects affected / exposed	0 / 29 (0.00%)	2 / 178 (1.12%)	
occurrences (all)	0	2	
Stoma site erythema			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Stoma site ulcer			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Tracheal obstruction			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Wound			
subjects affected / exposed	0 / 29 (0.00%)	2 / 178 (1.12%)	
occurrences (all)	0	2	
Wound secretion			
subjects affected / exposed	0 / 29 (0.00%)	4 / 178 (2.25%)	
occurrences (all)	0	6	
Cardiac disorders			
Angina pectoris			

subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Atrial fibrillation			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Cardiac arrest			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	2	
Cardiomegaly			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Palpitations			
subjects affected / exposed	1 / 29 (3.45%)	2 / 178 (1.12%)	
occurrences (all)	1	2	
Pericardial effusion			
subjects affected / exposed	0 / 29 (0.00%)	2 / 178 (1.12%)	
occurrences (all)	0	2	
Sinus bradycardia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Sinus tachycardia			
subjects affected / exposed	1 / 29 (3.45%)	2 / 178 (1.12%)	
occurrences (all)	1	2	
Tachycardia			
subjects affected / exposed	2 / 29 (6.90%)	5 / 178 (2.81%)	
occurrences (all)	2	5	
Nervous system disorders			
Aphasia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Dizziness			
subjects affected / exposed	5 / 29 (17.24%)	16 / 178 (8.99%)	
occurrences (all)	5	16	
Dysaesthesia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	

Dysgeusia			
subjects affected / exposed	4 / 29 (13.79%)	11 / 178 (6.18%)	
occurrences (all)	4	11	
Headache			
subjects affected / exposed	3 / 29 (10.34%)	20 / 178 (11.24%)	
occurrences (all)	3	23	
Hemiparesis			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Lethargy			
subjects affected / exposed	0 / 29 (0.00%)	2 / 178 (1.12%)	
occurrences (all)	0	2	
Paraesthesia			
subjects affected / exposed	0 / 29 (0.00%)	5 / 178 (2.81%)	
occurrences (all)	0	5	
Parosmia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Peripheral motor neuropathy			
subjects affected / exposed	1 / 29 (3.45%)	2 / 178 (1.12%)	
occurrences (all)	1	2	
Peripheral sensory neuropathy			
subjects affected / exposed	3 / 29 (10.34%)	8 / 178 (4.49%)	
occurrences (all)	3	8	
Presyncope			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Somnolence			
subjects affected / exposed	1 / 29 (3.45%)	5 / 178 (2.81%)	
occurrences (all)	1	5	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	7 / 29 (24.14%)	25 / 178 (14.04%)	
occurrences (all)	9	29	
Lymph node pain			

subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Lymphadenopathy			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Thrombocytopenia			
subjects affected / exposed	1 / 29 (3.45%)	2 / 178 (1.12%)	
occurrences (all)	1	2	
Ear and labyrinth disorders			
Tympanic membrane perforation			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Eye disorders			
Conjunctival hyperaemia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Diplopia			
subjects affected / exposed	0 / 29 (0.00%)	2 / 178 (1.12%)	
occurrences (all)	0	2	
Dry eye			
subjects affected / exposed	1 / 29 (3.45%)	8 / 178 (4.49%)	
occurrences (all)	1	8	
Eye irritation			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Eye pain			
subjects affected / exposed	0 / 29 (0.00%)	3 / 178 (1.69%)	
occurrences (all)	0	3	
Ocular hyperaemia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Vision blurred			
subjects affected / exposed	2 / 29 (6.90%)	7 / 178 (3.93%)	
occurrences (all)	2	7	
Gastrointestinal disorders			

Abdominal discomfort			
subjects affected / exposed	1 / 29 (3.45%)	5 / 178 (2.81%)	
occurrences (all)	1	5	
Abdominal distension			
subjects affected / exposed	0 / 29 (0.00%)	4 / 178 (2.25%)	
occurrences (all)	0	4	
Abdominal pain			
subjects affected / exposed	2 / 29 (6.90%)	6 / 178 (3.37%)	
occurrences (all)	2	6	
Abdominal pain upper			
subjects affected / exposed	1 / 29 (3.45%)	4 / 178 (2.25%)	
occurrences (all)	1	6	
Anal incontinence			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Ascites			
subjects affected / exposed	0 / 29 (0.00%)	2 / 178 (1.12%)	
occurrences (all)	0	2	
Constipation			
subjects affected / exposed	5 / 29 (17.24%)	30 / 178 (16.85%)	
occurrences (all)	6	35	
Dental caries			
subjects affected / exposed	0 / 29 (0.00%)	2 / 178 (1.12%)	
occurrences (all)	0	2	
Diarrhoea			
subjects affected / exposed	13 / 29 (44.83%)	68 / 178 (38.20%)	
occurrences (all)	17	108	
Dry mouth			
subjects affected / exposed	3 / 29 (10.34%)	11 / 178 (6.18%)	
occurrences (all)	3	11	
Dyspepsia			
subjects affected / exposed	3 / 29 (10.34%)	13 / 178 (7.30%)	
occurrences (all)	3	13	
Dysphagia			
subjects affected / exposed	5 / 29 (17.24%)	25 / 178 (14.04%)	
occurrences (all)	5	27	

Gastritis			
subjects affected / exposed	0 / 29 (0.00%)	2 / 178 (1.12%)	
occurrences (all)	0	2	
Gastritis erosive			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 29 (0.00%)	9 / 178 (5.06%)	
occurrences (all)	0	9	
Glossodynia			
subjects affected / exposed	3 / 29 (10.34%)	4 / 178 (2.25%)	
occurrences (all)	3	4	
Haemorrhoids			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Melaena			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Mouth haemorrhage			
subjects affected / exposed	0 / 29 (0.00%)	2 / 178 (1.12%)	
occurrences (all)	0	2	
Mouth ulceration			
subjects affected / exposed	0 / 29 (0.00%)	6 / 178 (3.37%)	
occurrences (all)	0	8	
Nausea			
subjects affected / exposed	11 / 29 (37.93%)	43 / 178 (24.16%)	
occurrences (all)	18	59	
Odynophagia			
subjects affected / exposed	1 / 29 (3.45%)	5 / 178 (2.81%)	
occurrences (all)	1	5	
Oesophageal fistula			
subjects affected / exposed	0 / 29 (0.00%)	2 / 178 (1.12%)	
occurrences (all)	0	2	
Oesophageal ulcer			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	

Oesophagitis			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Oral pain			
subjects affected / exposed	1 / 29 (3.45%)	9 / 178 (5.06%)	
occurrences (all)	1	11	
Salivary gland mucocoele			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Stomatitis			
subjects affected / exposed	12 / 29 (41.38%)	67 / 178 (37.64%)	
occurrences (all)	15	81	
Vomiting			
subjects affected / exposed	6 / 29 (20.69%)	32 / 178 (17.98%)	
occurrences (all)	16	55	
Skin and subcutaneous tissue disorders			
Cold sweat			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Decubitus ulcer			
subjects affected / exposed	0 / 29 (0.00%)	3 / 178 (1.69%)	
occurrences (all)	0	3	
Dermal cyst			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Dermatitis			
subjects affected / exposed	0 / 29 (0.00%)	3 / 178 (1.69%)	
occurrences (all)	0	3	
Dermatitis acneiform			
subjects affected / exposed	5 / 29 (17.24%)	47 / 178 (26.40%)	
occurrences (all)	11	59	
Dry skin			
subjects affected / exposed	10 / 29 (34.48%)	43 / 178 (24.16%)	
occurrences (all)	11	46	
Erythema			

subjects affected / exposed	4 / 29 (13.79%)	8 / 178 (4.49%)	
occurrences (all)	4	8	
Erythema nodosum			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 29 (0.00%)	5 / 178 (2.81%)	
occurrences (all)	0	5	
Papule			
subjects affected / exposed	0 / 29 (0.00%)	3 / 178 (1.69%)	
occurrences (all)	0	4	
Pruritus			
subjects affected / exposed	1 / 29 (3.45%)	18 / 178 (10.11%)	
occurrences (all)	1	22	
Rash			
subjects affected / exposed	7 / 29 (24.14%)	60 / 178 (33.71%)	
occurrences (all)	9	68	
Rash maculo-papular			
subjects affected / exposed	3 / 29 (10.34%)	21 / 178 (11.80%)	
occurrences (all)	3	29	
Rash papular			
subjects affected / exposed	1 / 29 (3.45%)	4 / 178 (2.25%)	
occurrences (all)	1	4	
Skin discolouration			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Skin fissures			
subjects affected / exposed	7 / 29 (24.14%)	30 / 178 (16.85%)	
occurrences (all)	8	41	
Skin striae			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Skin toxicity			
subjects affected / exposed	2 / 29 (6.90%)	10 / 178 (5.62%)	
occurrences (all)	2	12	

Skin ulcer			
subjects affected / exposed	2 / 29 (6.90%)	11 / 178 (6.18%)	
occurrences (all)	3	12	
Urticaria			
subjects affected / exposed	0 / 29 (0.00%)	4 / 178 (2.25%)	
occurrences (all)	0	4	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Dysuria			
subjects affected / exposed	0 / 29 (0.00%)	2 / 178 (1.12%)	
occurrences (all)	0	2	
Pollakiuria			
subjects affected / exposed	0 / 29 (0.00%)	2 / 178 (1.12%)	
occurrences (all)	0	2	
Renal failure			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Urinary incontinence			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Urinary retention			
subjects affected / exposed	1 / 29 (3.45%)	2 / 178 (1.12%)	
occurrences (all)	1	2	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 29 (3.45%)	15 / 178 (8.43%)	
occurrences (all)	3	19	
Bone pain			
subjects affected / exposed	0 / 29 (0.00%)	4 / 178 (2.25%)	
occurrences (all)	0	5	
Muscle spasms			
subjects affected / exposed	1 / 29 (3.45%)	4 / 178 (2.25%)	
occurrences (all)	1	4	
Muscular weakness			

subjects affected / exposed	0 / 29 (0.00%)	6 / 178 (3.37%)	
occurrences (all)	0	6	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 29 (0.00%)	5 / 178 (2.81%)	
occurrences (all)	0	5	
Musculoskeletal pain			
subjects affected / exposed	2 / 29 (6.90%)	5 / 178 (2.81%)	
occurrences (all)	2	5	
Musculoskeletal stiffness			
subjects affected / exposed	0 / 29 (0.00%)	2 / 178 (1.12%)	
occurrences (all)	0	2	
Myalgia			
subjects affected / exposed	2 / 29 (6.90%)	10 / 178 (5.62%)	
occurrences (all)	2	10	
Neck pain			
subjects affected / exposed	3 / 29 (10.34%)	15 / 178 (8.43%)	
occurrences (all)	4	17	
Pain in extremity			
subjects affected / exposed	2 / 29 (6.90%)	7 / 178 (3.93%)	
occurrences (all)	3	11	
Trismus			
subjects affected / exposed	2 / 29 (6.90%)	6 / 178 (3.37%)	
occurrences (all)	2	6	
Infections and infestations			
Candida infection			
subjects affected / exposed	0 / 29 (0.00%)	6 / 178 (3.37%)	
occurrences (all)	0	6	
Cellulitis			
subjects affected / exposed	1 / 29 (3.45%)	6 / 178 (3.37%)	
occurrences (all)	1	8	
Conjunctivitis			
subjects affected / exposed	0 / 29 (0.00%)	2 / 178 (1.12%)	
occurrences (all)	0	2	
Ear infection			
subjects affected / exposed	0 / 29 (0.00%)	2 / 178 (1.12%)	
occurrences (all)	0	2	

Folliculitis			
subjects affected / exposed	2 / 29 (6.90%)	12 / 178 (6.74%)	
occurrences (all)	2	12	
Herpes virus infection			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Herpes zoster			
subjects affected / exposed	1 / 29 (3.45%)	3 / 178 (1.69%)	
occurrences (all)	1	3	
Klebsiella sepsis			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Lung infection			
subjects affected / exposed	1 / 29 (3.45%)	6 / 178 (3.37%)	
occurrences (all)	1	6	
Nail infection			
subjects affected / exposed	2 / 29 (6.90%)	4 / 178 (2.25%)	
occurrences (all)	2	5	
Oral candidiasis			
subjects affected / exposed	0 / 29 (0.00%)	5 / 178 (2.81%)	
occurrences (all)	0	5	
Paronychia			
subjects affected / exposed	9 / 29 (31.03%)	43 / 178 (24.16%)	
occurrences (all)	11	53	
Rash pustular			
subjects affected / exposed	0 / 29 (0.00%)	6 / 178 (3.37%)	
occurrences (all)	0	6	
Rhinitis			
subjects affected / exposed	0 / 29 (0.00%)	3 / 178 (1.69%)	
occurrences (all)	0	3	
Sinusitis			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Skin infection			
subjects affected / exposed	0 / 29 (0.00%)	4 / 178 (2.25%)	
occurrences (all)	0	4	

Stoma site infection			
subjects affected / exposed	1 / 29 (3.45%)	3 / 178 (1.69%)	
occurrences (all)	1	3	
Tooth infection			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Upper respiratory tract infection			
subjects affected / exposed	2 / 29 (6.90%)	4 / 178 (2.25%)	
occurrences (all)	2	4	
Urinary tract infection			
subjects affected / exposed	2 / 29 (6.90%)	3 / 178 (1.69%)	
occurrences (all)	2	5	
Viral infection			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Wound infection			
subjects affected / exposed	2 / 29 (6.90%)	4 / 178 (2.25%)	
occurrences (all)	2	4	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	10 / 29 (34.48%)	53 / 178 (29.78%)	
occurrences (all)	10	56	
Dehydration			
subjects affected / exposed	3 / 29 (10.34%)	13 / 178 (7.30%)	
occurrences (all)	3	15	
Glucose tolerance impaired			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Hypercalcaemia			
subjects affected / exposed	1 / 29 (3.45%)	12 / 178 (6.74%)	
occurrences (all)	1	13	
Hyperglycaemia			
subjects affected / exposed	16 / 29 (55.17%)	88 / 178 (49.44%)	
occurrences (all)	30	182	
Hyperkalaemia			

subjects affected / exposed	1 / 29 (3.45%)	3 / 178 (1.69%)	
occurrences (all)	1	3	
Hypermagnesaemia			
subjects affected / exposed	0 / 29 (0.00%)	2 / 178 (1.12%)	
occurrences (all)	0	3	
Hypernatraemia			
subjects affected / exposed	0 / 29 (0.00%)	4 / 178 (2.25%)	
occurrences (all)	0	4	
Hyperosmolar state			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Hypertriglyceridaemia			
subjects affected / exposed	0 / 29 (0.00%)	2 / 178 (1.12%)	
occurrences (all)	0	3	
Hyperuricaemia			
subjects affected / exposed	0 / 29 (0.00%)	2 / 178 (1.12%)	
occurrences (all)	0	2	
Hypoalbuminaemia			
subjects affected / exposed	2 / 29 (6.90%)	15 / 178 (8.43%)	
occurrences (all)	2	16	
Hypocalcaemia			
subjects affected / exposed	1 / 29 (3.45%)	10 / 178 (5.62%)	
occurrences (all)	1	13	
Hypoglycaemia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Hypokalaemia			
subjects affected / exposed	8 / 29 (27.59%)	34 / 178 (19.10%)	
occurrences (all)	14	65	
Hypomagnesaemia			
subjects affected / exposed	12 / 29 (41.38%)	55 / 178 (30.90%)	
occurrences (all)	16	89	
Hyponatraemia			
subjects affected / exposed	3 / 29 (10.34%)	15 / 178 (8.43%)	
occurrences (all)	3	16	
Hypophagia			

subjects affected / exposed	0 / 29 (0.00%)	4 / 178 (2.25%)	
occurrences (all)	0	4	
Hypophosphataemia			
subjects affected / exposed	2 / 29 (6.90%)	20 / 178 (11.24%)	
occurrences (all)	2	31	
Malnutrition			
subjects affected / exposed	0 / 29 (0.00%)	2 / 178 (1.12%)	
occurrences (all)	0	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 March 2013	To facilitate enrollment in the Phase Ib portion of the protocol, patients who had received prior cetuximab or other EGFR-targeted antibodies treatments for recurrent or metastatic diseases were allowed to be included in the Phase Ib part of the study. A new arm (Arm B) was added to the Phase Ib part to explore a drinkable suspension (prepared from crushed BYL719 tablets) as an alternative method of administration of BYL719 in patients with swallowing dysfunction who were unable to swallow the BYL719 whole tablets. If the MTD/RP2D of Arm A and Arm B were same, then the administration of BYL719 as a drinkable suspension in patients with swallowing dysfunction may be allowed during the Phase II part of the study.
20 May 2013	Introduced the requirement of risk assessment and safety monitoring for the potential development of tumor lysis syndrome (TLS) in all patients treated in the study due to an event of death due to TLS. These changes were implemented immediately following the event with an Urgent Safety Measure.
24 October 2013	The patient population for the Phase II part of the study was expanded to include two additional clinical settings to test the efficacy of the combination of BYL719 and cetuximab in patients who have developed resistance to cetuximab. The first additional setting was to assess the activity of the combination in the Arm 2 cross-over population where patients who were platinum resistant (or intolerant/ineligible) and cetuximab naïve received single agent cetuximab as the first treatment on this study. At disease progression and thus development of resistance to single agent cetuximab, these patients had the option to cross-over to combination therapy with BYL719 and cetuximab to determine if the combination has efficacy in the setting of resistance to single agent cetuximab. The second additional setting was to assess the activity of BYL719 and cetuximab in the second line setting after disease progression following first line therapy with both platinum and cetuximab.
07 April 2014	A dose level of 250 mg BYL719 once daily was added as the first dose reduction level for the patients enrolled in the study. The second dose reduction was defined at 200 mgBYL719 once daily instead of 150 mg. Guidelines for the management of pneumonitis were added. In addition, ongoing monitoring of the safety and efficacy data during Phase II was described.
24 July 2014	Introduced a new formulation of BYL719 as a dispersible tablet for administration via gastrostomy tube (G or PEG tube) in a third Arm of the Phase Ib. Modified inclusion criteria to enroll patients in Phase II Arm 3 with stable grade 2 or less cetuximab-related skin toxicity.
02 June 2015	Introduced a mandatory baseline chest high-resolution computed tomography (CT) scan for safety purposes for all the newly enrolled patients to confirm no relevant pulmonary complications were present before starting study treatment.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Recruitment of new patients who were resistant to both platinum & cetuximab into Arm 3 was halted due to slow enrollment. The study was terminated early and health authorities were informed.

Notes: