



Clinical trial results:

A Randomized, Multicenter, Open-Label Phase Ib/II Study of RO5083945 in Combination With Cisplatin and Gemcitabine/Pemetrexed Versus Cisplatin and Gemcitabine/Pemetrexed in Patients With Advanced or Recurrent Non-Small Cell Lung Cancer Who Have not Received Prior Chemotherapy

Summary

EudraCT number	2010-018945-72
Trial protocol	DE GB BE
Global end of trial date	01 August 2013

Results information

Result version number	v1 (current)
This version publication date	02 March 2016
First version publication date	02 March 2016

Trial information

Trial identification

Sponsor protocol code	BP22349
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01185847
WHO universal trial number (UTN)	-

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	01 August 2013
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	01 August 2013
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and efficacy of RO5083945 in combination with standard chemotherapy in participants with advanced or recurrent NSCLC who have not received prior chemotherapy. In Part 1, participants received RO5083945 intravenously and standard chemotherapy (cisplatin plus either gemcitabine or pemetrexed) for up to 6 cycles of 3 weeks and then RO5083945 until disease progression, unacceptable toxicity, or withdrawal of consent. In Part 1, maximum tolerated dose (MTD) and recommended dose were established for Phase II. In Part 2, participants were randomized to receive either RO5083945 in combination with standard chemotherapy or chemotherapy alone for up to 6 cycles in non-squamous group only. In the absence of disease progression, participants receiving RO5083945 could continue treatment with RO5083945 as monotherapy.

Protection of trial subjects:

The investigator ensured that this study was conducted in full conformance with the principles of the "Declaration of Helsinki" or with the laws and regulations of the country in which the research was conducted, whichever afforded the greater protection to the individual. The study fully adhered to the principles outlined in "Guideline for Good Clinical Practice" International Conference on Harmonisation Tripartite Guideline (January 1997) or with local law if it afforded greater protection to the participant. For European Union/European Economic Area (EU/EEA) countries, the investigator ensured compliance with the EU Clinical Trial Directive (2001/20/ethics committee). In other countries where "Guideline for Good Clinical Practice" existed Roche and the investigators strictly ensured adherence to the stated provisions.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 November 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 6
Country: Number of subjects enrolled	Spain: 48
Country: Number of subjects enrolled	United Kingdom: 4
Country: Number of subjects enrolled	Belgium: 6
Country: Number of subjects enrolled	France: 5
Country: Number of subjects enrolled	Germany: 12
Country: Number of subjects enrolled	Italy: 12
Worldwide total number of subjects	93
EEA total number of subjects	93

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)	65
From 65 to 84 years	28
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants were classified into 2 histology groups, with squamous or non--squamous NSCLC and sequentially enrolled into 2 consecutive cohorts (Cohort 1: chemotherapy plus [+] 1000 milligram [mg] RO5083945 followed by RO5083945 monotherapy; Cohort 2: chemotherapy + 1400 mg RO5083945 followed by RO5083945 monotherapy).

Period 1

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

Arms

Are arms mutually exclusive?	No
Arm title	Squamous NSCLC Phase 1b Cohort 1a: RO5083945 + Chemotherapy

Arm description:

Chemotherapy (75 milligrams per square meter [mg/m²] cisplatin + 1250 mg/m² gemcitabine) and 1000 mg RO5083945 administered intravenously, every three weeks (q3w) for a maximum of 6 cycles (18 weeks) followed by 1000 mg RO5083945 monotherapy until disease progression, unacceptable toxicity, or withdrawal of consent.

Arm type	Experimental
Investigational medicinal product name	RO5083945
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Participants received 1000 mg RO5083945 intravenously, q3w until disease progression, unacceptable toxicity, or withdrawal of consent.

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

Dosage and administration details:

Participants received 75 mg/m² cisplatin intravenously q3w for a maximum of 6 cycles (18 weeks).

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

Dosage and administration details:

Participants received 1250 mg/m² gemcitabine intravenously q3w for a maximum of 6 cycles (18 weeks).

Arm title	Squamous NSCLC Phase 1b Cohort 1b: RO5083945 + Chemotherapy
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Arm description:

Chemotherapy (75 mg/m² cisplatin + 1000 mg/m² gemcitabine) and 1000 mg RO5083945

administered intravenously q3w for a maximum of 6 cycles (18 weeks), followed by 1000 mg RO5083945 monotherapy until disease progression, unacceptable toxicity, or withdrawal of consent.

Arm type	Experimental
Investigational medicinal product name	RO5083945
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Participants received 1000 mg RO5083945 intravenously q3w until disease progression, unacceptable toxicity, or withdrawal of consent.

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

Dosage and administration details:

Participants received 75 mg/m² cisplatin intravenously q3w for a maximum of 6 cycles (18 weeks).

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

Dosage and administration details:

Participants received 1000 mg/m² gemcitabine intravenously q3w for a maximum of 6 cycles (18 weeks).

Arm title	Squamous NSCLC Phase 1b Cohort 1c: Chemotherapy +RO5083945
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Arm description:

Chemotherapy (60 mg/m² cisplatin + 1000 mg/m² gemcitabine) and 1000 mg RO5083945 administered intravenously q3w for a maximum of 6 cycles (18 weeks), followed by 1000 mg RO5083945 monotherapy until disease progression, unacceptable toxicity, or withdrawal of consent.

Arm type	Experimental
Investigational medicinal product name	RO5083945
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Participants received 1000 mg RO5083945 intravenously, q3w until disease progression, unacceptable toxicity, or withdrawal of consent.

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

Dosage and administration details:

Participants received 60 mg/m² cisplatin intravenously q3w for a maximum of 6 cycles (18 weeks).

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

Dosage and administration details:

Participants received 1000 mg/m² gemcitabine intravenously q3w for a maximum of 6 cycles (18 weeks).

Arm title	Non-Squamous NSCLC Phase 1b Cohort 1: RO5083945 + Chemotherapy
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Arm description:

Chemotherapy (75 mg/m² cisplatin + 500 mg/m² pemetrexed) and 1000 mg RO5083945 administered intravenously q3w for a maximum of 6 cycles (18 weeks), followed by 1000 mg RO5083945 monotherapy until disease progression, unacceptable toxicity, or withdrawal of consent.

Arm type	Experimental
Investigational medicinal product name	RO5083945
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Participants received 1000 mg RO5083945 intravenously, q3w until disease progression, unacceptable toxicity, or withdrawal of consent.

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

Dosage and administration details:

Participants received 75 mg/m² cisplatin intravenously q3w for a maximum of 6 cycles (18 weeks).

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

Dosage and administration details:

Participants received 500 mg/m² pemetrexed intravenously q3w for a maximum of 6 cycles (18 weeks).

Arm title	Non-Squamous NSCLC Phase 1b Cohort 2: RO5083945 + Chemotherapy
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Arm description:

Chemotherapy (75 mg/m² cisplatin + 500 mg/m² pemetrexed) and 1400 mg RO5083945 administered intravenously q3w for a maximum of 6 cycles (18 weeks), followed by RO5083945 monotherapy until disease progression, unacceptable toxicity, or withdrawal of consent.

Arm type	Experimental
Investigational medicinal product name	RO5083945
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Participants received 1400 mg RO5083945 intravenously, q3w until disease progression, unacceptable toxicity, or withdrawal of consent.

Investigational medicinal product name	Cisplatin
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use
Dosage and administration details:	
Participants received 75 mg/m ² cisplatin intravenously q3w for a maximum of 6 cycles (18 weeks).	
Investigational medicinal product name	Pemetrexed
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use
Dosage and administration details:	
Participants received 500 mg/m ² pemetrexed intravenously q3w for a maximum of 6 cycles (18 weeks).	
Arm title	Non-Squamous NSCLC Phase 2 Arm A: RO5083945 + Chemotherapy
Arm description:	
Chemotherapy (75 mg/m ² cisplatin + 500 mg/m ² pemetrexed) and 1400 mg RO5083945 administered intravenously q3w for a maximum of 6 cycles (18 weeks), followed by 1400 mg RO5083945 monotherapy until disease progression, unacceptable toxicity, or withdrawal of consent.	
Arm type	Experimental
Investigational medicinal product name	RO5083945
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use
Dosage and administration details:	
Participants received 1400 mg RO5083945 intravenously, q3w until disease progression, unacceptable toxicity, or withdrawal of consent.	
Investigational medicinal product name	Cisplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use
Dosage and administration details:	
Participants received 75 mg/m ² cisplatin intravenously q3w for a maximum of 6 cycles (18 weeks).	
Investigational medicinal product name	Pemetrexed
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use
Dosage and administration details:	
Participants received 500 mg/m ² pemetrexed intravenously q3w for a maximum of 6 cycles (18 weeks).	
Arm title	Non-Squamous NSCLC Phase 2 Arm B: Chemotherapy
Arm description:	
Chemotherapy (75 mg/m ² cisplatin + 500 mg/m ² pemetrexed) administered intravenously q3w for a maximum of 6 cycles (18 weeks).	
Arm type	Active comparator
Investigational medicinal product name	Cisplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Participants received 75 mg/m² cisplatin intravenously q3w for a maximum of 6 cycles (18 weeks).

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

Dosage and administration details:

Participants received 500 mg/m² pemetrexed intravenously q3w for a maximum of 6 cycles (18 weeks).

Number of subjects in period 1	Squamous NSCLC Phase 1b Cohort 1a: RO5083945 + Chemotherapy	Squamous NSCLC Phase 1b Cohort 1b: RO5083945 + Chemotherapy	Squamous NSCLC Phase 1b Cohort 1c: Chemotherapy + RO5083945
Started	8	1	8
Completed	0	0	0
Not completed	8	1	8
Adverse event, serious fatal	-	1	-
Consent withdrawn by subject	-	-	1
Non-compliance of subject	-	-	-
Intercurrent illness	-	-	-
Adverse event, non-fatal	4	-	2
Unspecified	-	-	-
Progressive disease	4	-	4
Not received treatment	-	-	1

Number of subjects in period 1	Non-Squamous NSCLC Phase 1b Cohort 1: RO5083945 + Chemotherapy	Non-Squamous NSCLC Phase 1b Cohort 2: RO5083945 + Chemotherapy	Non-Squamous NSCLC Phase 2 Arm A: RO5083945 + Chemotherapy
Started	3	11	41
Completed	0	0	0
Not completed	3	11	41
Adverse event, serious fatal	-	-	1
Consent withdrawn by subject	-	-	4
Non-compliance of subject	-	-	2
Intercurrent illness	-	-	9
Adverse event, non-fatal	-	1	-
Unspecified	-	-	2
Progressive disease	3	10	23
Not received treatment	-	-	-

Number of subjects in period 1	Non-Squamous NSCLC Phase 1b Cohort 1: RO5083945 + Chemotherapy
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	Phase 2 Arm B: Chemotherapy
Started	21
Completed	13
Not completed	8
Adverse event, serious fatal	2
Consent withdrawn by subject	1
Non-compliance of subject	-
Intercurrent illness	-
Adverse event, non-fatal	-
Unspecified	-
Progressive disease	5
Not received treatment	-

Baseline characteristics

Reporting groups

Reporting group title	Squamous NSCLC Phase 1b Cohort 1a: RO5083945 + Chemotherapy
Reporting group description: Chemotherapy (75 milligrams per square meter [mg/m ²] cisplatin + 1250 mg/m ² gemcitabine) and 1000 mg RO5083945 administered intravenously, every three weeks (q3w) for a maximum of 6 cycles (18 weeks) followed by 1000 mg RO5083945 monotherapy until disease progression, unacceptable toxicity, or withdrawal of consent.	
Reporting group title	Squamous NSCLC Phase 1b Cohort 1b: RO5083945 + Chemotherapy
Reporting group description: Chemotherapy (75 mg/m ² cisplatin + 1000 mg/m ² gemcitabine) and 1000 mg RO5083945 administered intravenously q3w for a maximum of 6 cycles (18 weeks), followed by 1000 mg RO5083945 monotherapy until disease progression, unacceptable toxicity, or withdrawal of consent.	
Reporting group title	Squamous NSCLC Phase 1b Cohort 1c: Chemotherapy +RO5083945
Reporting group description: Chemotherapy (60 mg/m ² cisplatin + 1000 mg/m ² gemcitabine) and 1000 mg RO5083945 administered intravenously q3w for a maximum of 6 cycles (18 weeks), followed by 1000 mg RO5083945 monotherapy until disease progression, unacceptable toxicity, or withdrawal of consent.	
Reporting group title	Non-Squamous NSCLC Phase 1b Cohort 1: RO5083945 + Chemotherapy
Reporting group description: Chemotherapy (75 mg/m ² cisplatin + 500 mg/m ² pemetrexed) and 1000 mg RO5083945 administered intravenously q3w for a maximum of 6 cycles (18 weeks), followed by 1000 mg RO5083945 monotherapy until disease progression, unacceptable toxicity, or withdrawal of consent.	
Reporting group title	Non-Squamous NSCLC Phase 1b Cohort 2: RO5083945 + Chemotherapy
Reporting group description: Chemotherapy (75 mg/m ² cisplatin + 500 mg/m ² pemetrexed) and 1400 mg RO5083945 administered intravenously q3w for a maximum of 6 cycles (18 weeks), followed by RO5083945 monotherapy until disease progression, unacceptable toxicity, or withdrawal of consent.	
Reporting group title	Non-Squamous NSCLC Phase 2 Arm A: RO5083945 + Chemotherapy
Reporting group description: Chemotherapy (75 mg/m ² cisplatin + 500 mg/m ² pemetrexed) and 1400 mg RO5083945 administered intravenously q3w for a maximum of 6 cycles (18 weeks), followed by 1400 mg RO5083945 monotherapy until disease progression, unacceptable toxicity, or withdrawal of consent.	
Reporting group title	Non-Squamous NSCLC Phase 2 Arm B: Chemotherapy
Reporting group description: Chemotherapy (75 mg/m ² cisplatin + 500 mg/m ² pemetrexed) administered intravenously q3w for a maximum of 6 cycles (18 weeks).	

Reporting group values	Squamous NSCLC Phase 1b Cohort 1a: RO5083945 + Chemotherapy	Squamous NSCLC Phase 1b Cohort 1b: RO5083945 + Chemotherapy	Squamous NSCLC Phase 1b Cohort 1c: Chemotherapy +RO5083945
Number of subjects	8	1	8
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	63.5 ± 7.87	61 ± 0	63.5 ± 6.59
Gender categorical Units: Subjects			
Female	1	0	0
Male	7	1	8

Reporting group values	Non-Squamous NSCLC Phase 1b Cohort 1: RO5083945 + Chemotherapy	Non-Squamous NSCLC Phase 1b Cohort 2: RO5083945 + Chemotherapy	Non-Squamous NSCLC Phase 2 Arm A: RO5083945 + Chemotherapy
Number of subjects	3	11	41
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	55 ± 6.08	56.9 ± 10.6	56.3 ± 10.25
Gender categorical Units: Subjects			
Female	0	4	15
Male	3	7	26

Reporting group values	Non-Squamous NSCLC Phase 2 Arm B: Chemotherapy	Total	
Number of subjects	21	93	
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	58.7 ± 11.4	-	
Gender categorical Units: Subjects			
Female	3	23	
Male	18	70	

End points

End points reporting groups

Reporting group title	Squamous NSCLC Phase 1b Cohort 1a: RO5083945 + Chemotherapy
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Reporting group description:

Chemotherapy (75 milligrams per square meter [mg/m^2] cisplatin + 1250 mg/m^2 gemcitabine) and 1000 mg RO5083945 administered intravenously, every three weeks (q3w) for a maximum of 6 cycles (18 weeks) followed by 1000 mg RO5083945 monotherapy until disease progression, unacceptable toxicity, or withdrawal of consent.

Reporting group title	Squamous NSCLC Phase 1b Cohort 1b: RO5083945 + Chemotherapy
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Reporting group description:

Chemotherapy (75 mg/m^2 cisplatin + 1000 mg/m^2 gemcitabine) and 1000 mg RO5083945 administered intravenously q3w for a maximum of 6 cycles (18 weeks), followed by 1000 mg RO5083945 monotherapy until disease progression, unacceptable toxicity, or withdrawal of consent.

Reporting group title	Squamous NSCLC Phase 1b Cohort 1c: Chemotherapy + RO5083945
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Reporting group description:

Chemotherapy (60 mg/m^2 cisplatin + 1000 mg/m^2 gemcitabine) and 1000 mg RO5083945 administered intravenously q3w for a maximum of 6 cycles (18 weeks), followed by 1000 mg RO5083945 monotherapy until disease progression, unacceptable toxicity, or withdrawal of consent.

Reporting group title	Non-Squamous NSCLC Phase 1b Cohort 1: RO5083945 + Chemotherapy
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Reporting group description:

Chemotherapy (75 mg/m^2 cisplatin + 500 mg/m^2 pemetrexed) and 1000 mg RO5083945 administered intravenously q3w for a maximum of 6 cycles (18 weeks), followed by 1000 mg RO5083945 monotherapy until disease progression, unacceptable toxicity, or withdrawal of consent.

Reporting group title	Non-Squamous NSCLC Phase 1b Cohort 2: RO5083945 + Chemotherapy
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Reporting group description:

Chemotherapy (75 mg/m^2 cisplatin + 500 mg/m^2 pemetrexed) and 1400 mg RO5083945 administered intravenously q3w for a maximum of 6 cycles (18 weeks), followed by RO5083945 monotherapy until disease progression, unacceptable toxicity, or withdrawal of consent.

Reporting group title	Non-Squamous NSCLC Phase 2 Arm A: RO5083945 + Chemotherapy
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Reporting group description:

Chemotherapy (75 mg/m^2 cisplatin + 500 mg/m^2 pemetrexed) and 1400 mg RO5083945 administered intravenously q3w for a maximum of 6 cycles (18 weeks), followed by 1400 mg RO5083945 monotherapy until disease progression, unacceptable toxicity, or withdrawal of consent.

Reporting group title	Non-Squamous NSCLC Phase 2 Arm B: Chemotherapy
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Reporting group description:

Chemotherapy (75 mg/m^2 cisplatin + 500 mg/m^2 pemetrexed) administered intravenously q3w for a maximum of 6 cycles (18 weeks).

Primary: Progression-Free Survival (PFS) Assessed as per Response Evaluation Criteria in Solid Tumors (RECIST) Version 1.1

End point title	Progression-Free Survival (PFS) Assessed as per Response Evaluation Criteria in Solid Tumors (RECIST) Version 1.1 ^[1]
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End point description:

PFS was defined as the time between randomization and date of first documented disease progression (unequivocal appearance of new malignant lesions denotes) or death, whichever occurred first. Intent-to-Treat (ITT) Population defined as all randomized participants. Participants were assigned to the treatment group to which they were randomized.

End point type	Primary			
End point timeframe:				
Baseline and every 6 weeks thereafter until disease progression up to 33 months				
Notes:				
[1] - 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: The data was reported only for the non-squamous NSCLC Phase 2 Arm A (RO5083945 + chemotherapy) and Arm B (chemotherapy).				
End point values	Non-Squamous NSCLC Phase 2 Arm A: RO5083945 + Chemotherapy	Non-Squamous NSCLC Phase 2 Arm B: Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	21		
Units: months				
median (confidence interval 95%)	5.4 (4.1 to 6.5)	6 (3.7 to 8.4)		

Statistical analyses

Statistical analysis title	PFS
Comparison groups	Non-Squamous NSCLC Phase 2 Arm A: RO5083945 + Chemotherapy v Non-Squamous NSCLC Phase 2 Arm B: Chemotherapy
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7981
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.61
upper limit	1.92

Primary:

Percentage of Participants with Disease Progression or Death Assessed as per RECIST

End point title	Percentage of Participants with Disease Progression or Death Assessed as per RECIST Version 1.1 ^{[2][3]}
End point description:	
PFS was defined as the time between randomization and date of first documented disease progression (unequivocal appearance of new malignant lesions denotes) or death, whichever occurred first. ITT population.	
End point type	Primary
End point timeframe:	
Baseline and every 6 weeks thereafter until disease progression up to 33 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: No statistical analysis was planned for this endpoint.

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

Justification: The study was conducted in two phases. The endpoint was assessed in Phase 2 only, therefore the data for the Phase 1 arm group are not presented.

End point values	Non-Squamous NSC LC Phase 2 Arm A: RO5083945 + Chemotherapy	Non-Squamous NSC LC Phase 2 Arm B: Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	21		
Units: percentage of participants				
number (not applicable)	92.7	90.5		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Positive Human Anti-human Antibodies (HAHA) Values

End point title	Number of Participants With Positive Human Anti-human Antibodies (HAHA) Values ^[4]
End point description:	Levels of HAHA in serum were detected at baseline. Safety Population.
End point type	Primary
End point timeframe:	Predose on Day 1 of each cycle and on follow-up

Notes:

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

Justification: No statistical analysis was planned for this endpoint.

End point values	Squamous NSC LC Phase 1b Cohort 1a: RO5083945 + Chemotherapy	Squamous NSC LC Phase 1b Cohort 1b: RO5083945 + Chemotherapy	Squamous NSC LC Phase 1b Cohort 1c: Chemotherapy + RO5083945	Non-Squamous NSC LC Phase 1b Cohort 1: RO5083945 + Chemotherapy
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	1	7 ^[5]	3
Units: participants				
number (not applicable)	0	0	1	0

Notes:

[5] - Participants who received treatment were included in the analysis.

End point values	Non-Squamous NSC LC Phase 1b Cohort	Non-Squamous NSC LC Phase 2 Arm	Non-Squamous NSC LC Phase 2 Arm	
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	hort 2: RO5083945 + Chemotherapy	m A: RO5083945 + Chemotherapy	m B: Chemotherapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	41	21	
Units: participants				
number (not applicable)	1	6	1	

Statistical analyses

No statistical analyses for this end point

Primary: Pharmacokinetic (PK) Parameters of RO5083945, Cisplatin, Gemcitabine, and Pemetrexed

End point title	Pharmacokinetic (PK) Parameters of RO5083945, Cisplatin, Gemcitabine, and Pemetrexed ^[6]
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End point description:

PK parameters were not analyzed due to no further plans for clinical development of RO5083945.

End point type	Primary
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End point timeframe:

Multiple sampling Cycles 1-6 (18 weeks)

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: No statistical analysis was planned for this endpoint.

End point values	Squamous NSC LC Phase 1b Cohort 1a: RO5083945 + Chemotherapy	Squamous NSC LC Phase 1b Cohort 1b: RO5083945 + Chemotherapy	Squamous NSC LC Phase 1b Cohort 1c: Chemotherapy + RO5083945	Non-Squamous NSC LC Phase 1b Cohort 1: RO5083945 + Chemotherapy
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0 ^[7]	0 ^[8]	0 ^[9]	0 ^[10]
Units: micrograms per milliliter (mcg/L)				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[7] - PK parameters were not analyzed due to no further plans for clinical development of RO5083945.

[8] - PK parameters were not analyzed due to no further plans for clinical development of RO5083945.

[9] - PK parameters were not analyzed due to no further plans for clinical development of RO5083945.

[10] - PK parameters were not analyzed due to no further plans for clinical development of RO5083945.

End point values	Non-Squamous NSC LC Phase 1b Cohort 2: RO5083945 + Chemotherapy	Non-Squamous NSC LC Phase 2 Arm A: RO5083945 + Chemotherapy	Non-Squamous NSC LC Phase 2 Arm B: Chemotherapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0 ^[11]	0 ^[12]	0 ^[13]	
Units: micrograms per milliliter (mcg/L)				
arithmetic mean (standard deviation)	()	()	()	

Notes:

- [11] - PK parameters were not analyzed due to no further plans for clinical development of RO5083945.
[12] - PK parameters were not analyzed due to no further plans for clinical development of RO5083945.
[13] - PK parameters were not analyzed due to no further plans for clinical development of RO5083945.

Statistical analyses

No statistical analyses for this end point

Secondary:

Percentage of Participants with a Best Overall Response of Complete Response (CR) or Partial Response (PR)

End point title	Percentage of Participants with a Best Overall Response of Complete Response (CR) or Partial Response (PR) ^[14]
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End point description:

Best overall response was defined as CR or PR as assessed by investigator using RECIST version 1.1. CR: disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) having reduction in short axis to < 10 millimeter (mm); PR: at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters. Best Overall Response was not evaluated due to no further plans for clinical development of RO5083945.

End point type	Secondary
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End point timeframe:

Baseline and every 6 weeks thereafter up to 33 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: The study was conducted in two phases. The endpoint was assessed in Phase 2 only, therefore the data for the Phase 1 arm group are not presented.

End point values	Non-Squamous NSC LC Phase 2 Arm A: RO5083945 + Chemotherapy	Non-Squamous NSC LC Phase 2 Arm B: Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[15]	0 ^[16]		
Units: percentage of participants				
number (not applicable)				

Notes:

[15] - Best Overall Response was not evaluated due to no further plans for clinical development of RO508394

[16] - Best Overall Response was not evaluated due to no further plans for clinical development of RO508394

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response

End point title	Duration of Response ^[17]
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End point description:

Duration of response was defined as the time from when response (CR or PR) was first documented to first documented disease progression or death (whichever occurs first). Duration of response was not evaluated due to no further plans for clinical development of RO5083945.

End point type	Secondary			
End point timeframe:				
Baseline and every 6 weeks thereafter up to 33 months				
Notes:				
[17] - 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: The study was conducted in two phases. The endpoint was assessed in Phase 2 only, therefore the data for the Phase 1 arm group are not presented.				
End point values	Non-Squamous NSCLC Phase 2 Arm A: RO5083945 + Chemotherapy	Non-Squamous NSCLC Phase 2 Arm B: Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[18]	0 ^[19]		
Units: months				
median (confidence interval 95%)	(to)	(to)		

Notes:

[18] - Duration of response was not evaluated due to no further plans for clinical development of RO5083945

[19] - Duration of response was not evaluated due to no further plans for clinical development of RO5083945

Statistical analyses

No statistical analyses for this end point

Secondary:

Percentage of Participants With Stable Disease for at Least 6 Weeks, CR or PR

End point title	Percentage of Participants With Stable Disease for at Least 6 Weeks, CR or PR ^[20]
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End point description:

Stable Disease was defined as the condition which neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for progressive disease (PD). CR: disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to <10 mm; PR: at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters; PD: at least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study including baseline (nadir). In addition to the relative increase of 20%, the sum must also demonstrate an absolute increase of at least 5 mm. Stable Disease was not evaluated due to no further plans for clinical development of RO5083945.

End point type	Secondary
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End point timeframe:

Baseline and every 6 weeks thereafter up to 33 months

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: No statistical analysis was planned for this endpoint.

End point values	Non-Squamous NSC LC Phase 2 Arm A: RO5083945 + Chemotherapy	Non-Squamous NSC LC Phase 2 Arm B: Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[21]	0 ^[22]		

Units: percentage of participants				
number (not applicable)				

Notes:

[21] - Stable Disease was not evaluated due to no further plans for clinical development of RO5083945.

[22] - Stable Disease was not evaluated due to no further plans for clinical development of RO5083945.

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS) ^[23]
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End point description:

OS was defined as the time between randomization and date of death. Participants without an event will be censored at the last date known to be alive. OS was not evaluated due to no further plans for clinical development of RO5083945.

End point type	Secondary
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End point timeframe:

Baseline and every 6 weeks thereafter up to 33 months

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: The study was conducted in two phases. The endpoint was assessed in Phase 2 only, therefore the data for the Phase 1 arm group are not presented.

End point values	Non-Squamous NSC LC Phase 2 Arm A: RO5083945 + Chemotherapy	Non-Squamous NSC LC Phase 2 Arm B: Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[24]	0 ^[25]		
Units: percentage of participants				
number (not applicable)				

Notes:

[24] - OS was not evaluated due to no further plans for clinical development of RO5083945.

[25] - OS was not evaluated due to no further plans for clinical development of RO5083945.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From baseline up to 28 days after the last dose of study medication

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	15.0
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Reporting groups

Reporting group title	Squamous NSCLC Phase 1b Cohort 1a: RO5083945 + Chemotherapy
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Reporting group description:

Chemotherapy (75 mg/m² cisplatin + 1250 mg/m² gemcitabine) and 1000 mg RO5083945 administered intravenously, every three weeks (q3w) for a maximum of 6 cycles (18 weeks) followed by 1000 mg RO5083945 monotherapy until disease progression, unacceptable toxicity, or withdrawal of consent.

Reporting group title	Squamous NSCLC Phase 1b Cohort 1b: RO5083945 + Chemotherapy
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Reporting group description:

Chemotherapy (75 mg/m² cisplatin + 1000 mg/m² gemcitabine) and 1000 mg RO5083945 administered intravenously q3w for a maximum of 6 cycles (18 weeks), followed by 1000 mg RO5083945 monotherapy until disease progression, unacceptable toxicity, or withdrawal of consent.

Reporting group title	Squamous NSCLC Phase 1b Cohort 1c: Chemotherapy + RO5083945
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Reporting group description:

Chemotherapy (60 mg/m² cisplatin + 1000 mg/m² gemcitabine) and 1000 mg RO5083945 administered intravenously q3w for a maximum of 6 cycles (18 weeks), followed by 1000 mg RO5083945 monotherapy until disease progression, unacceptable toxicity, or withdrawal of consent.

Reporting group title	Non-Squamous NSCLC Phase 1b Cohort 1: RO5083945 + Chemotherapy
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Reporting group description:

Chemotherapy (75 mg/m² cisplatin + 500 mg/m² pemetrexed) and 1000 mg RO5083945 administered intravenously q3w for a maximum of 6 cycles (18 weeks), followed by 1000 mg RO5083945 monotherapy until disease progression, unacceptable toxicity, or withdrawal of consent.

Reporting group title	Non-Squamous NSCLC Phase 1b Cohort 2: RO5083945 + Chemotherapy
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Reporting group description:

Chemotherapy (75 mg/m² cisplatin + 500 mg/m² pemetrexed) and 1400 mg RO5083945 administered intravenously q3w for a maximum of 6 cycles (18 weeks), followed by RO5083945 monotherapy until disease progression, unacceptable toxicity, or withdrawal of consent.

Reporting group title	Non-Squamous NSCLC Phase 2 Arm A: RO5083945 + Chemotherapy
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Reporting group description:

Chemotherapy (75 mg/m² cisplatin + 500 mg/m² pemetrexed) and 1400 mg RO5083945 administered intravenously q3w for a maximum of 6 cycles (18 weeks), followed by 1400 mg RO5083945 monotherapy until disease progression, unacceptable toxicity, or withdrawal of consent.

Reporting group title	Non-Squamous NSCLC Phase 2 Arm B: Chemotherapy
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Reporting group description:

Chemotherapy (75 mg/m² cisplatin + 500 mg/m² pemetrexed) administered intravenously q3w for a maximum of 6 cycles (18 weeks).

Serious adverse events	Squamous NSCLC Phase 1b Cohort 1a: RO5083945 + Chemotherapy	Squamous NSCLC Phase 1b Cohort 1b: RO5083945 + Chemotherapy	Squamous NSCLC Phase 1b Cohort 1c: Chemotherapy + RO5083945
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 8 (75.00%)	1 / 1 (100.00%)	1 / 8 (12.50%)
number of deaths (all causes)	5	1	5
number of deaths resulting from adverse events			
Vascular disorders			
Superior vena cava syndrome			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
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			
Pyrexia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	0 / 8 (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
Chest pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
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 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
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 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			

subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
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 creatinine increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
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			
Infusion related reaction			
subjects affected / exposed	2 / 8 (25.00%)	0 / 1 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	2 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal fracture			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
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			
Bradycardia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
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			
Cerebral infarction			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	0 / 8 (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
Presyncope			

subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
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			
Neutropenia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	0 / 8 (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
Thrombocytopenia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
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			
Gastrointestinal inflammation			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
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 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
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 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatitis toxic			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
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			
Rash			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
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 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
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			
Sepsis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 1 (100.00%)	0 / 8 (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
Urinary tract infection			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	0 / 8 (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
Lung infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
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 necrotising			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative wound infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
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 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	0 / 8 (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
Hypocalcaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypomagnesaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cachexia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
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	Non-Squamous NSCLC Phase 1b Cohort 1: RO5083945 + Chemotherapy	Non-Squamous NSCLC Phase 1b Cohort 2: RO5083945 + Chemotherapy	Non-Squamous NSCLC Phase 2 Arm A: RO5083945 + Chemotherapy
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 3 (66.67%)	1 / 11 (9.09%)	16 / 41 (39.02%)
number of deaths (all causes)	2	9	28
number of deaths resulting from adverse events			
Vascular disorders			
Superior vena cava syndrome			

subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 41 (0.00%)
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			
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 11 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pulmonary embolism			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	2 / 41 (4.88%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 11 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood creatinine increased			

subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	2 / 41 (4.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Bradycardia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Neutropenia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastrointestinal inflammation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatitis toxic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Sepsis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 41 (0.00%)
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 / 3 (0.00%)	1 / 11 (9.09%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia necrotising			
subjects affected / exposed	1 / 3 (33.33%)	0 / 11 (0.00%)	0 / 41 (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
Postoperative wound infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypocalcaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypomagnesaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cachexia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 41 (0.00%)
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	Non-Squamous NSCLC Phase 2 Arm B: Chemotherapy		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 21 (14.29%)		
number of deaths (all causes)	16		
number of deaths resulting from adverse events			
Vascular disorders			
Superior vena cava syndrome			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Chest pain			

subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fatigue			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypoxia			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
Blood creatinine increased			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Spinal fracture			

subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Bradycardia			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Coronary artery disease			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Presyncope			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Leukopenia			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Gastrointestinal disorders			
Gastrointestinal inflammation			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nausea			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Hepatitis toxic			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Sepsis			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			

subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lung infection			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia necrotising			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Postoperative wound infection			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Upper respiratory tract infection			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypocalcaemia			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypomagnesaemia			

subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cachexia			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Squamous NSCLC Phase 1b Cohort 1a: RO5083945 + Chemotherapy	Squamous NSCLC Phase 1b Cohort 1b: RO5083945 + Chemotherapy	Squamous NSCLC Phase 1b Cohort 1c: Chemotherapy + RO5083945
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 8 (87.50%)	1 / 1 (100.00%)	5 / 8 (62.50%)
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	2	0	0
Hypotension			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Orthostatic hypotension			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	3 / 8 (37.50%)	0 / 1 (0.00%)	1 / 8 (12.50%)
occurrences (all)	4	0	1
Fatigue			
subjects affected / exposed	3 / 8 (37.50%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	3	0	0
Pyrexia			
subjects affected / exposed	3 / 8 (37.50%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	3	0	0
Oedema peripheral			

subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	2 / 8 (25.00%)
occurrences (all)	0	0	4
Chest pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Gait disturbance			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Xerosis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Mucosal inflammation			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Oedema			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Cough			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Productive cough			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Epistaxis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Dyspnoea Exertional			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Nasal dryness			

subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Dysphonia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Pulmonary embolism			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Anxiety			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Confusional state			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Investigations			
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Blood bilirubin increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Blood sodium decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Platelet count decreased			

subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	2	0	0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Urine output decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	3 / 8 (37.50%)	1 / 1 (100.00%)	1 / 8 (12.50%)
occurrences (all)	3	1	3
Fall			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Atrial flutter			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	1
Dizziness			

subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Sciatica			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Syncope			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Paraesthesia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Lethargy			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Trigeminal neuralgia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	5 / 8 (62.50%)	0 / 1 (0.00%)	2 / 8 (25.00%)
occurrences (all)	6	0	3
Anaemia			
subjects affected / exposed	2 / 8 (25.00%)	0 / 1 (0.00%)	2 / 8 (25.00%)
occurrences (all)	4	0	2
Thrombocytopenia			
subjects affected / exposed	3 / 8 (37.50%)	1 / 1 (100.00%)	2 / 8 (25.00%)
occurrences (all)	7	1	5
Leukopenia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Vertigo			

subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 1 (0.00%) 0	1 / 8 (12.50%) 1
Deafness subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 1 (0.00%) 0	0 / 8 (0.00%) 0
Hearing impaired subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 1 (0.00%) 0	1 / 8 (12.50%) 1
Ototoxicity subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 1 (0.00%) 0	0 / 8 (0.00%) 0
Tinnitus subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 1 (0.00%) 0	0 / 8 (0.00%) 0
Eye disorders Conjunctivitis subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 1 (0.00%) 0	0 / 8 (0.00%) 0
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 1 (0.00%) 0	0 / 8 (0.00%) 0
Nausea subjects affected / exposed occurrences (all)	4 / 8 (50.00%) 5	0 / 1 (0.00%) 0	1 / 8 (12.50%) 2
Diarrhoea subjects affected / exposed occurrences (all)	4 / 8 (50.00%) 6	0 / 1 (0.00%) 0	1 / 8 (12.50%) 1
Vomiting subjects affected / exposed occurrences (all)	3 / 8 (37.50%) 4	0 / 1 (0.00%) 0	1 / 8 (12.50%) 1
Stomatitis subjects affected / exposed occurrences (all)	3 / 8 (37.50%) 4	0 / 1 (0.00%) 0	0 / 8 (0.00%) 0
Constipation			

subjects affected / exposed	2 / 8 (25.00%)	0 / 1 (0.00%)	3 / 8 (37.50%)
occurrences (all)	2	0	5
Dyspepsia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Cheilitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Mouth ulceration			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal motility disorder			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Haemorrhoids			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Oral mucosal erythema			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Proctitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Odynophagia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	6 / 8 (75.00%)	0 / 1 (0.00%)	2 / 8 (25.00%)
occurrences (all)	11	0	2

Dry skin			
subjects affected / exposed	2 / 8 (25.00%)	0 / 1 (0.00%)	2 / 8 (25.00%)
occurrences (all)	2	0	2
Alopecia			
subjects affected / exposed	2 / 8 (25.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	2	0	0
Pruritus			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	1
Erythema			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	1
Exfoliative rash			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	2
Telangiectasia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Hypertrichosis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Hair colour changes			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Skin fissures			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Dermatitis acneiform			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			

Nocturia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Dysuria			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Oliguria			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Pain in extremity			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Bone pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Tendon pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Arthralgia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			

Paronychia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Oral fungal infection			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Candida infection			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Pharyngitis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Sinusitis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Tooth abscess			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Urinary tract infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Device related infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Furuncle			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Urethritis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0

Metabolism and nutrition disorders			
Hypomagnesaemia			
subjects affected / exposed	4 / 8 (50.00%)	0 / 1 (0.00%)	3 / 8 (37.50%)
occurrences (all)	4	0	4
Decreased appetite			
subjects affected / exposed	3 / 8 (37.50%)	0 / 1 (0.00%)	2 / 8 (25.00%)
occurrences (all)	4	0	3
Hypocalcaemia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	2 / 8 (25.00%)
occurrences (all)	1	0	2
Hypokalaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	3
Hypophosphataemia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	1
Hyperglycaemia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	1
Dehydration			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Hypoalbuminaemia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Electrolyte imbalance			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Fluid imbalance			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Non-Squamous NSCLC Phase 1b Cohort 1: RO5083945 + Chemotherapy	Non-Squamous NSCLC Phase 1b Cohort 2: RO5083945 + Chemotherapy	Non-Squamous NSCLC Phase 2 Arm A: RO5083945 + Chemotherapy
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	11 / 11 (100.00%)	41 / 41 (100.00%)

Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	2 / 41 (4.88%)
occurrences (all)	0	0	2
Hypotension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Orthostatic hypotension			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 3 (66.67%)	4 / 11 (36.36%)	13 / 41 (31.71%)
occurrences (all)	2	12	27
Fatigue			
subjects affected / exposed	1 / 3 (33.33%)	1 / 11 (9.09%)	13 / 41 (31.71%)
occurrences (all)	1	1	18
Pyrexia			
subjects affected / exposed	2 / 3 (66.67%)	1 / 11 (9.09%)	3 / 41 (7.32%)
occurrences (all)	2	1	4
Oedema peripheral			
subjects affected / exposed	1 / 3 (33.33%)	0 / 11 (0.00%)	5 / 41 (12.20%)
occurrences (all)	1	0	6
Chest pain			
subjects affected / exposed	3 / 3 (100.00%)	0 / 11 (0.00%)	2 / 41 (4.88%)
occurrences (all)	3	0	2
Gait disturbance			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Xerosis			
subjects affected / exposed	0 / 3 (0.00%)	2 / 11 (18.18%)	3 / 41 (7.32%)
occurrences (all)	0	3	3
Mucosal inflammation			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	1 / 41 (2.44%)
occurrences (all)	0	1	1
Oedema			

subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 11 (0.00%) 0	3 / 41 (7.32%) 4
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 3 (33.33%)	4 / 11 (36.36%)	5 / 41 (12.20%)
occurrences (all)	2	4	5
Cough			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	4 / 41 (9.76%)
occurrences (all)	0	1	4
Productive cough			
subjects affected / exposed	1 / 3 (33.33%)	2 / 11 (18.18%)	2 / 41 (4.88%)
occurrences (all)	1	2	5
Epistaxis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	4 / 41 (9.76%)
occurrences (all)	0	0	4
Dyspnoea Exertional			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 41 (2.44%)
occurrences (all)	0	0	1
Nasal dryness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 41 (2.44%)
occurrences (all)	0	0	1
Dysphonia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 11 (18.18%)	1 / 41 (2.44%)
occurrences (all)	0	2	1
Pulmonary embolism			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	1 / 41 (2.44%)
occurrences (all)	0	1	1
Oropharyngeal pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	1 / 41 (2.44%)
occurrences (all)	0	1	1
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 11 (18.18%)	2 / 41 (4.88%)
occurrences (all)	0	2	2
Anxiety			

subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 41 (2.44%)
occurrences (all)	0	0	1
Confusional state			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	2 / 41 (4.88%)
occurrences (all)	0	0	2
Investigations			
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 3 (33.33%)	1 / 11 (9.09%)	0 / 41 (0.00%)
occurrences (all)	1	1	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Blood bilirubin increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Blood sodium decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	1 / 41 (2.44%)
occurrences (all)	0	1	1
Urine output decreased			
subjects affected / exposed	1 / 3 (33.33%)	1 / 11 (9.09%)	0 / 41 (0.00%)
occurrences (all)	2	1	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Weight decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	5 / 41 (12.20%)
occurrences (all)	0	0	5
Injury, poisoning and procedural complications			

Infusion related reaction subjects affected / exposed occurrences (all)	2 / 3 (66.67%) 2	7 / 11 (63.64%) 8	19 / 41 (46.34%) 21
Fall subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 11 (9.09%) 1	0 / 41 (0.00%) 0
Cardiac disorders			
Sinus tachycardia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 11 (0.00%) 0	1 / 41 (2.44%) 1
Atrial flutter subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 11 (0.00%) 0	0 / 41 (0.00%) 0
Nervous system disorders			
Dysgeusia subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	2 / 11 (18.18%) 2	1 / 41 (2.44%) 1
Headache subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 11 (9.09%) 1	1 / 41 (2.44%) 1
Dizziness subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 11 (9.09%) 1	2 / 41 (4.88%) 2
Sciatica subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 11 (0.00%) 0	0 / 41 (0.00%) 0
Syncope subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 11 (0.00%) 0	0 / 41 (0.00%) 0
Paraesthesia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 11 (9.09%) 1	4 / 41 (9.76%) 7
Hypoaesthesia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 11 (9.09%) 1	0 / 41 (0.00%) 0
Lethargy			

subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Trigeminal neuralgia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 11 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	1 / 3 (33.33%)	4 / 11 (36.36%)	18 / 41 (43.90%)
occurrences (all)	1	8	30
Anaemia			
subjects affected / exposed	3 / 3 (100.00%)	5 / 11 (45.45%)	12 / 41 (29.27%)
occurrences (all)	4	5	13
Thrombocytopenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	6 / 41 (14.63%)
occurrences (all)	0	0	10
Leukopenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	2 / 41 (4.88%)
occurrences (all)	0	0	3
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 41 (2.44%)
occurrences (all)	0	0	1
Deafness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Hearing impaired			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Ototoxicity			
subjects affected / exposed	1 / 3 (33.33%)	2 / 11 (18.18%)	2 / 41 (4.88%)
occurrences (all)	2	2	2
Tinnitus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	3 / 41 (7.32%)
occurrences (all)	0	0	3
Eye disorders			

Conjunctivitis subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	3 / 11 (27.27%) 6	4 / 41 (9.76%) 7
Gastrointestinal disorders			
Abdominal pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 11 (0.00%) 0	2 / 41 (4.88%) 2
Nausea subjects affected / exposed occurrences (all)	2 / 3 (66.67%) 4	4 / 11 (36.36%) 8	22 / 41 (53.66%) 44
Diarrhoea subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	4 / 11 (36.36%) 6	16 / 41 (39.02%) 22
Vomiting subjects affected / exposed occurrences (all)	2 / 3 (66.67%) 4	3 / 11 (27.27%) 5	17 / 41 (41.46%) 29
Stomatitis subjects affected / exposed occurrences (all)	2 / 3 (66.67%) 3	5 / 11 (45.45%) 7	18 / 41 (43.90%) 28
Constipation subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	4 / 11 (36.36%) 4	8 / 41 (19.51%) 10
Dyspepsia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 11 (0.00%) 0	3 / 41 (7.32%) 3
Cheilitis subjects affected / exposed occurrences (all)	2 / 3 (66.67%) 5	0 / 11 (0.00%) 0	1 / 41 (2.44%) 1
Dry mouth subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 11 (0.00%) 0	1 / 41 (2.44%) 1
Mouth ulceration subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 11 (9.09%) 1	1 / 41 (2.44%) 4
Gastrointestinal motility disorder			

subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Haemorrhoids			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Oral mucosal erythema			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Proctitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Flatulence			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	3 / 41 (7.32%)
occurrences (all)	0	0	3
Odynophagia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	3 / 41 (7.32%)
occurrences (all)	0	0	4
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	3 / 3 (100.00%)	11 / 11 (100.00%)	28 / 41 (68.29%)
occurrences (all)	6	23	40
Dry skin			
subjects affected / exposed	1 / 3 (33.33%)	1 / 11 (9.09%)	9 / 41 (21.95%)
occurrences (all)	1	1	9
Alopecia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	6 / 41 (14.63%)
occurrences (all)	0	0	7
Pruritus			
subjects affected / exposed	1 / 3 (33.33%)	0 / 11 (0.00%)	5 / 41 (12.20%)
occurrences (all)	1	0	7
Erythema			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	3 / 41 (7.32%)
occurrences (all)	0	1	3
Palmar-plantar erythrodysesthesia syndrome			

subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 41 (2.44%)
occurrences (all)	0	0	1
Exfoliative rash			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Telangiectasia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Hypertrichosis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 11 (0.00%)	1 / 41 (2.44%)
occurrences (all)	1	0	1
Hair colour changes			
subjects affected / exposed	1 / 3 (33.33%)	0 / 11 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Skin fissures			
subjects affected / exposed	2 / 3 (66.67%)	5 / 11 (45.45%)	7 / 41 (17.07%)
occurrences (all)	2	12	15
Dermatitis acneiform			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	8 / 41 (19.51%)
occurrences (all)	0	0	8
Renal and urinary disorders			
Nocturia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	1 / 41 (2.44%)
occurrences (all)	0	1	1
Oliguria			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	2 / 11 (18.18%)	6 / 41 (14.63%)
occurrences (all)	0	2	7
Pain in extremity			

subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	2 / 41 (4.88%)
occurrences (all)	0	0	2
Bone pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 41 (2.44%)
occurrences (all)	0	0	1
Tendon pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Arthralgia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 11 (0.00%)	3 / 41 (7.32%)
occurrences (all)	1	0	4
Muscle spasms			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	3 / 41 (7.32%)
occurrences (all)	0	1	6
Musculoskeletal pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	1 / 41 (2.44%)
occurrences (all)	0	2	1
Myalgia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 11 (0.00%)	1 / 41 (2.44%)
occurrences (all)	1	0	1
Infections and infestations			
Paronychia			
subjects affected / exposed	0 / 3 (0.00%)	6 / 11 (54.55%)	8 / 41 (19.51%)
occurrences (all)	0	12	15
Nasopharyngitis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 11 (0.00%)	1 / 41 (2.44%)
occurrences (all)	1	0	1
Oral fungal infection			
subjects affected / exposed	1 / 3 (33.33%)	0 / 11 (0.00%)	0 / 41 (0.00%)
occurrences (all)	2	0	0
Candida infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0

Sinusitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Tooth abscess			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	1 / 3 (33.33%)	1 / 11 (9.09%)	0 / 41 (0.00%)
occurrences (all)	1	1	0
Oral candidiasis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Device related infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Furuncle			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Urethritis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Hypomagnesaemia			
subjects affected / exposed	2 / 3 (66.67%)	8 / 11 (72.73%)	25 / 41 (60.98%)
occurrences (all)	2	8	39
Decreased appetite			
subjects affected / exposed	1 / 3 (33.33%)	0 / 11 (0.00%)	18 / 41 (43.90%)
occurrences (all)	1	0	25
Hypocalcaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 11 (0.00%)	4 / 41 (9.76%)
occurrences (all)	1	0	4
Hypokalaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	3 / 41 (7.32%)
occurrences (all)	0	1	3
Hypophosphataemia			

subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	1 / 41 (2.44%)
occurrences (all)	0	1	1
Hyperglycaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Dehydration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 41 (2.44%)
occurrences (all)	0	0	1
Hypoalbuminaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 41 (2.44%)
occurrences (all)	0	0	1
Electrolyte imbalance			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Fluid imbalance			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Non-Squamous NSCLC Phase 2 Arm B: Chemotherapy		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 21 (90.48%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Hypotension			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Orthostatic hypotension			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	12 / 21 (57.14%)		
occurrences (all)	26		

Fatigue			
subjects affected / exposed	4 / 21 (19.05%)		
occurrences (all)	4		
Pyrexia			
subjects affected / exposed	6 / 21 (28.57%)		
occurrences (all)	9		
Oedema peripheral			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Chest pain			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Gait disturbance			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Xerosis			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Mucosal inflammation			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Oedema			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	3 / 21 (14.29%)		
occurrences (all)	4		
Cough			
subjects affected / exposed	3 / 21 (14.29%)		
occurrences (all)	5		
Productive cough			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Epistaxis			

subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Dyspnoea Exertional			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Nasal dryness			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Dysphonia			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	2		
Pulmonary embolism			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Oropharyngeal pain			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Anxiety			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	2		
Confusional state			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Investigations			
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Blood bilirubin increased			

subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Blood sodium decreased			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Platelet count decreased			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Alanine aminotransferase increased			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Urine output decreased			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Weight decreased			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	2		
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Fall			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Atrial flutter			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Nervous system disorders			

Dysgeusia			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	2		
Dizziness			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Sciatica			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Syncope			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Paraesthesia			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Hypoaesthesia			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Lethargy			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Trigeminal neuralgia			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	10 / 21 (47.62%)		
occurrences (all)	22		
Anaemia			
subjects affected / exposed	10 / 21 (47.62%)		
occurrences (all)	10		
Thrombocytopenia			

subjects affected / exposed	3 / 21 (14.29%)		
occurrences (all)	4		
Leukopenia			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Deafness			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Hearing impaired			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Ototoxicity			
subjects affected / exposed	4 / 21 (19.05%)		
occurrences (all)	4		
Tinnitus			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	2		
Eye disorders			
Conjunctivitis			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	11 / 21 (52.38%)		
occurrences (all)	29		
Diarrhoea			
subjects affected / exposed	6 / 21 (28.57%)		
occurrences (all)	9		
Vomiting			

subjects affected / exposed	5 / 21 (23.81%)		
occurrences (all)	6		
Stomatitis			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	2		
Constipation			
subjects affected / exposed	7 / 21 (33.33%)		
occurrences (all)	10		
Dyspepsia			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	2		
Cheilitis			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Dry mouth			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Mouth ulceration			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Gastrointestinal motility disorder			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Haemorrhoids			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Oral mucosal erythema			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Proctitis			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Flatulence			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Odynophagia			

subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	4 / 21 (19.05%)		
occurrences (all)	4		
Dry skin			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Alopecia			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	2		
Pruritus			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	2		
Erythema			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Exfoliative rash			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Telangiectasia			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Hypertrichosis			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Hair colour changes			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Skin fissures			

subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Dermatitis acneiform			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Nocturia			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Dysuria			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Oliguria			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	2		
Pain in extremity			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Bone pain			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Tendon pain			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Arthralgia			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Muscle spasms			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Musculoskeletal pain			

subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Myalgia			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Paronychia			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			
subjects affected / exposed	3 / 21 (14.29%)		
occurrences (all)	3		
Oral fungal infection			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	2		
Candida infection			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Pharyngitis			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Sinusitis			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Tooth abscess			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Urinary tract infection			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Oral candidiasis			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Device related infection			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		

Furuncle			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Urethritis			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Hypomagnesaemia			
subjects affected / exposed	4 / 21 (19.05%)		
occurrences (all)	4		
Decreased appetite			
subjects affected / exposed	7 / 21 (33.33%)		
occurrences (all)	9		
Hypocalcaemia			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Hypokalaemia			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Hypophosphataemia			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Hyperglycaemia			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Dehydration			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Hypoalbuminaemia			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Electrolyte imbalance			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Fluid imbalance			

subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 May 2010	<p>This amendment was done for including the following information:</p> <ul style="list-style-type: none">-- To allow the two formulations of RO5083945 (RO508-3945/F02 and RO5083945/F03) to be used in this study. Formulation RO508-3945/F02 was used in earlier clinical trials. Formulation RO5083945/F03 contained RO508-3945 derived from a modified drug substance processes, i.e. different manufacturing site, different fermentation scale using the same cell line and a slightly modified purification process.-- To include the preparation guidelines for both formulations.-- To clarify the wording for blood collection timepoints has been updated to clarify this for participants not receiving RO5083945 (i.e. Phase II, Arm B participants).-- Clarified the extension of blood pharmacodynamic (PD) parameters to permit residual sample material to be investigated to provide a more in-depth analysis of peripheral blood immunophenotype.
25 October 2010	<p>This amendment was done for including the following information: -</p> <ul style="list-style-type: none">- To update with new data from the BO21495 and BP22350 studies.- To clarify timepoints for participants in Arm B i.e. those not receiving RO5083945.-- To correct the typographical errors.- To clarify the treatment of epidermal growth factor receptor (EGFR)-related skin toxicity.- To limit analysis up to ITT and Safety populations which were deemed sufficient to gather preliminary evidence of superior activity and safety of RO5083945.
31 January 2011	<p>This amendment was done to include the following information:</p> <ul style="list-style-type: none">- To update the clinical section for the first 2 participants with squamous cell NSCLC treated in the Phase Ib part of study BP22349 both experienced Grade 3 infusion-related reaction (IRR) event and added premedication required to reduce the incidence of IRRs events.-- To update additional measures required for Phase 2 start to ensure the safety of squamous NSCLC participants.-- To collect additional blood sample to confirm the biology of the IRRs in terms of cytokine release (levels and types).-- Clarified that the recommended dose may be differ between histology groups.-- To collect the blood samples at a later cycle if if the drug administration schedule is altered due to toxicity or other reasons.-- To advice additional safety measures with early high dose oral supplementation for participants who developed hypomagnesemia.-- To include PK blood samples collection for Phase II participants at Cycle 4 Day 15 and Cycle 6 Day 1.- To update the guidelines for prophylactic measures for EGFR-inhibition-associated rash based on clinical experience with RO5083945.

26 August 2011	<p>This amendment was done to include the following information:</p> <ul style="list-style-type: none"> -- To correct inconsistency for tumour response criteria. - To add 2 additional PK samples for Phase Ib and 1 additional sample for Phase II to enable a better characterization of the PK profile of RO5083945 on Cycle 4, and to enable a better comparison of exposure parameters between Cycle 4 and Cycle 1. -- Clarified to avoid the collection of cytological samples for tumour biopsies. -- To include the need of prophylaxis treatment for EGFR-related skin toxicity. -- To include the information for interruption of infusion if participants developed IRRs. -- To extend time window for allowing more flexibility to perform the Safety Follow-Up Visit. -- To revise the hypomagnesaemia management guidelines. -- To clarify PK/PD sampling in Phase II as some PK/PD samplings were not applicable for participants in Arm B. -- To include the information regarding gemcitabine dose reduction. - To implement a safety run-in stage within Phase II to closely monitor the hematological profile and to mitigate the risk of potential unexpected toxicities. -- To provide clarification on storage conditions of RO5083945. -- To allow more flexibility for scheduling visits during treatment.
28 June 2012	<p>This amendment was done to reduce the dose of cisplatin from 75 mg/m² to 60 mg/m² as the first participant from the squamous histology group enrolled in the first cohort of RO5083945 1000 mg on Day 1 and Day 8 and then every two weeks, cisplatin 75 mg/m² q3w and the reduced dose of gemcitabine 1000 mg/m² Day 1 and Day 8 q3w died of sepsis (related to cisplatin as per investigator) in the presence of pancytopenia on Day 15 of Cycle 1.</p>
22 November 2012	<p>This amendment was done to include the initial results received from Phase II Study BP22349 in non-squamous NSCLC group. Based on these results the overall benefit risk ratio for the BP22349 Phase II in non-squamous was negative.</p>

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
21 December 2010	<p>In response to Grade 3 IRR events observed in the first 2 participants with squamous NSCLC treated in the Phase Ib part of study BP22349, recruitment of participants with squamous cell histology into study BP22349 was put on hold on 21 December 2010 in order to review the data and plan subsequent actions. A 2-step approach with intensified premedication was taken for squamous cancer NSCLC participants in the Phase Ib part of study BP22349 for the first infusion of RO5083945. In addition the same 2-step safety approach was taken if Grade 3 IRRs are seen in non-squamous participants in Phase Ib.</p>	08 March 2011

Notes:

Limitations and caveats

None reported