Clinical trial results:
Open-Label Phase Ib/II, Multicenter Study of the Combination of RO5479599 With Carboplatin and Paclitaxel in Patients With Advanced or Metastatic Non-Small Cell Lung Cancer (NSCLC) of Squamous Histology who Have not Received Prior Chemotherapy or Targeted Therapy for NSCLC

Summary

EudraCT number	2014-001498-15
Trial protocol	DK ES NL GB
Global end of trial date	14 March 2016

Results information

Result version number	v1 (current)
This version publication date	24 November 2016
First version publication date	24 November 2016

Trial information

Trial identification

Sponsor protocol code	BP29360

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02204345
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 Ltd., 41 61 6878333, global.trial_information@roche.com
Scientific contact	Roche Trial Information Hotline, F.Hoffmann-La Roche Ltd., 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	14 March 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 March 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

This was an open-label, single -arm, multicenter, Phase Ib/II study to evaluate the safety, tolerability, and efficacy (as measured by the objective response rate [ORR]) of RO5479599 in combination with carboplatin and paclitaxel.

Protection of trial subjects:

This study was conducted in full conformance with the International Conference on Harmonisation (ICH) E6 guideline for Good Clinical Practice and the principles of the Declaration of Helsinki, or the laws and regulations of the country in which the research was conducted, whichever affords the greater protection to the individual. The study complied with the requirements of the ICH E2A guideline (Clinical Safety Data Management: Definitions and Standards for Expedited Reporting).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 October 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 1
Country: Number of subjects enrolled	Spain: 10
Country: Number of subjects enrolled	Denmark: 1
Worldwide total number of subjects	12
EEA total number of subjects	11

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)	4

From 65 to 84 years	8
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Twelve participants were enrolled in the safety run-in phase and received treatment with RO5479599 in combination with carboplatin and paclitaxel.

Period 1

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

Arms

Arm title	RO5479599+Carboplatin+Paclitaxel

Arm description:

RO5479599 800 milligrams (mg) was administered in the Safety Run-In Phase by intravenous infusion once every 3 weeks (q3w) on Day 1 of 3-weekly cycles (each cycle of 21 days) in combination with carboplatin (to produce an area under the curve [AUC] of 6 mg/milliliter [mL]*minute) and paclitaxel 200 mg per square meter (mg/m^2) by intravenous infusion q3w for 4 to 6 cycles. Thereafter, RO5479599 was continued as a monotherapy (carboplatin and paclitaxel could be continued at the investigator’s discretion) until disease progression, death, unacceptable toxicity, withdrawal of consent, or study termination by sponsor, whichever occurred first.

Arm type	Experimental
Investigational medicinal product name	RO5479599
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

RO5479599 was administered as an IV infusion q3w until disease progression, death, unacceptable toxicity or withdrawal of consent

Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Carboplatin by intravenous infusion q3w for 4 to 6 cycles and thereafter as per investigator's discretion.

Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Paclitaxel by intravenous infusion q3w for 4 to 6 cycles and thereafter as per investigator's discretion.

Number of subjects in period 1	RO5479599+Carboplatin+Paclitaxel
Started	12
Completed	0
Not completed	12
Physician decision	1
Adverse Event	1
Progressive Disease	9
Unspecified	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall Study

Reporting group description:

RO5479599 800 mg was administered in the Safety Run-In Phase by intravenous infusion q3w on Day 1 of 3-weekly cycles (each cycle of 21 days) in combination with carboplatin (to produce an AUC of 6 mg/mL*minute and paclitaxel 200 mg/m^2 by intravenous infusion q3w for 4 to 6 cycles. Thereafter, RO5479599 was continued as a monotherapy (carboplatin and paclitaxel could be continued at the investigator's discretion) until disease progression, death, unacceptable toxicity, withdrawal of consent, or study termination by sponsor, whichever occurred first.

Reporting group values	Overall Study	Total	
Number of subjects	12	12	
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	 66 ± 6.6	 -	
Gender categorical Units: Subjects			
Female	2	2	
Male	10	10	

End points

End points reporting groups

Reporting group title	RO5479599+Carboplatin+Paclitaxel

Reporting group description:

RO5479599 800 milligrams (mg) was administered in the Safety Run-In Phase by intravenous infusion once every 3 weeks (q3w) on Day 1 of 3-weekly cycles (each cycle of 21 days) in combination with carboplatin (to produce an area under the curve [AUC] of 6 mg/milliliter [mL]*minute) and paclitaxel 200 mg per square meter (mg/m^2) by intravenous infusion q3w for 4 to 6 cycles. Thereafter, RO5479599 was continued as a monotherapy (carboplatin and paclitaxel could be continued at the investigator's discretion) until disease progression, death, unacceptable toxicity, withdrawal of consent, or study termination by sponsor, whichever occurred first.

Primary: Percentage of Participants With Objective Response as Assessed by Investigator Using Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v1.1)

End point title	Percentage of Participants With Objective Response as Assessed by Investigator Using Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v1.1)[1]

End point description:

Objective response is defined as a CR or PR as determined by the Investigator using RECIST v1.1 on 2 consecutive occasions at least 4 weeks apart. Participants were evaluated for tumor response for target lesions and assessed by computed tomography (CT) or magnetic resonance imaging (MRI). CR was defined as complete disappearance of all target lesions and non-target disease, with the exception of nodal disease. All nodes, both target and non-target, must decrease to normal (short axis less than [<] 10 millimeter [mm]). No new lesions. PR was defined as greater than or equal (>=) 30% decrease from baseline in the sum of diameters of target lesions. The short axis was used in the sum for target nodes, while the longest diameter was used in the sum for all other target lesions. No unequivocal progression of non-target disease. No new lesions; Efficacy analysis population: all participants enrolled in the study who received at least 1 dose of study treatment in the safety run-in phase.

End point type	Primary

End point timeframe:

Baseline until disease progression, death, unacceptable toxicity, or withdrawal of consent, whichever occurred first (assessed every 6 weeks from baseline [Cycle 1 Day 1] [Cycle length = 21 days] up to Day 342)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The study was of an explorative nature; therefore only descriptive and exploratory statistical methods were applied, and no statistical hypothesis testing was carried out.

End point values	RO5479599+Carboplatin+Paclitaxel			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Percentage of participants				
number (confidence interval 90%)	25 (4.44 to 45.56)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Disease Progression as Assessed Using RECIST v1.1

End point title	Percentage of Participants With Disease Progression as Assessed Using RECIST v1.1

End point description:

Disease Progression (PD): at least 20% increase in the sum of diameters of target lesions compared to the smallest sum of diameters on-study and absolute increase of at least 5 mm, progression of existing non-target lesions, or presence of new lesions. Efficacy analysis population.

End point type	Secondary

End point timeframe:

Baseline until disease progression, death, unacceptable toxicity, or withdrawal of consent, whichever occurred first (assessed every 6 weeks from baseline [Cycle 1 Day 1] [Cycle length = 21 days] up to Day 342)

End point values	RO5479599+Carboplatin+Paclitaxel			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Percentage of participants				
number (not applicable)	83.3			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free Survival (PFS) as Assessed Using RECIST v1.1

End point title	Progression-free Survival (PFS) as Assessed Using RECIST v1.1

End point description:

PFS is defined as the time from the first dose of study treatment to disease progression or death, whichever occurs first. Participants who do not progress or die while being followed were censored on the date of the last valid tumor assessment. Participants without post-baseline tumor assessments were conservatively censored on the date of first study medication, that is, PFS was assigned a value of 1 day and was censored in the analysis. PD: at least 20% increase in the sum of diameters of target lesions compared to the smallest sum of diameters on-study and absolute increase of at least 5 mm, progression of existing non-target lesions, or presence of new lesions. PFS was estimated using Kaplan-Meier method. Efficacy analysis population.

End point type	Secondary

End point timeframe:

Baseline until disease progression, death, unacceptable toxicity, or withdrawal of consent, whichever occurred first (assessed every 6 weeks from baseline [Cycle 1 Day 1] [Cycle length = 21 days] up to Day 342)

End point values	RO5479599+Carboplatin+Paclitaxel			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Days				
median (confidence interval 95%)	122 (81 to 217)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

OS is defined as the time from the first dose of study medication to death. Participants who do not die while being followed up were censored on the date of last contact. OS was estimated using Kaplan-Meier method. Efficacy analysis population. Median and corresponding 95% confidence interval (CI) could not be estimated due to higher number (>50%) of censored participants and have been reported as 99999.

End point type	Secondary

End point timeframe:

Baseline until disease progression, death, unacceptable toxicity, or withdrawal of consent, whichever occurred first (assessed every 6 weeks from baseline [Cycle 1 Day 1] [Cycle length = 21 days] up to Day 342)

End point values	RO5479599+Carboplatin+Paclitaxel			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Days				
median (confidence interval 95%)	99999 (99999 to 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Disease Control as Assessed by Investigator Using RECIST v1.1

End point title	Percentage of Participants With Disease Control as Assessed by Investigator Using RECIST v1.1

End point description:

Disease control was defined as having a best overall response of CR, PR, or stable disease (SD) according to RECIST v1.1. CR: complete disappearance of all target lesions and non-target disease (except nodal disease). All nodes, must decrease to normal (short axis<10 mm). No new lesions. PR:>=30% decrease under baseline of the sum of diameters of all target lesions. The short axis was used in the sum for target nodes, while the longest diameter was used in the sum for all other target

No unequivocal progression of non-target disease. No new lesions. SD: neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking as reference the smallest sum diameters while on study. PD: at least 20% increase in the sum of diameters of target lesions compared to the smallest sum of diameters on-study and absolute increase of at least 5 mm, progression of existing non-target lesions, or presence of new lesions. Efficacy analysis population.

End point type	Secondary

End point timeframe:

Baseline until disease progression, death, unacceptable toxicity, or withdrawal of consent, whichever occurred first (assessed every 6 weeks from baseline [Cycle 1 Day 1] [Cycle length = 21 days] up to Day 342)

End point values	RO5479599+Carboplatin+Paclitaxel			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Percentage of participants				
number (confidence interval 90%)	91.7 (78.54 to 100)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Curve From Time Zero to Last Quantifiable Concentration [AUC (0-t)] of RO5479599

End point title	Area Under the Curve From Time Zero to Last Quantifiable Concentration [AUC (0-t)] of RO5479599

End point description:

AUC (0-t)= Area under the plasma concentration versus time curve from time zero (pre-dose) to time of last quantifiable concentration (0-t).

End point type	Secondary

End point timeframe:

Pre-dose (Hour 0) and at end of infusion (infusion duration=approximately 2 hours) on Day 1 of each cycle (cycle length = 21 days) up to end of treatment (EOT, Day 314); 3-6, 24, 72, 168, 264, 336, 432, 480 hours post-dose on Day 1 of Cycle 1,4;at Day 342

End point values	RO5479599+Carboplatin+Paclitaxel			
Subject group type	Reporting group			
Number of subjects analysed	0[2]			
Units: mg/mL*minute				
arithmetic mean (standard deviation)	()			

Notes:

[2] - No data is reported since the PK data was not analyzed due to early termination of the study.

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Plasma Concentration (Cmax) of RO5479599

End point title	Maximum Observed Plasma Concentration (Cmax) of RO5479599

End point description:

End point type	Secondary

End point timeframe:

Pre-dose (Hour 0) and at end of infusion (infusion duration=approximately 2 hours) on Day 1 of each cycle (cycle length = 21 days) up to end of treatment (EOT, Day 314); 3-6, 24, 72, 168, 264, 336, 432, 480 hours post-dose on Day 1 of Cycle 1,4;at Day 342

End point values	RO5479599+Carboplatin+Paclitaxel			
Subject group type	Reporting group			
Number of subjects analysed	0[3]			
Units: mg/mL				
arithmetic mean (standard deviation)	()			

Notes:

[3] - No data is reported since the PK data was not analyzed due to early termination of the study.

Statistical analyses

No statistical analyses for this end point

Secondary: Trough Concentration (Ctrough) of RO5479599

End point title	Trough Concentration (Ctrough) of RO5479599

End point description:

End point type	Secondary

End point timeframe:

Pre-dose (Hour 0) on Day 1 of each cycle (cycle length = 21 days) up to EOT (Day 314)

End point values	RO5479599+Carboplatin+Paclitaxel			
Subject group type	Reporting group			
Number of subjects analysed	0[4]			
Units: mg/mL				
arithmetic mean (standard deviation)	()			

Notes:

[4] - No data is reported since the PK data was not analyzed due to early termination of the study.

Statistical analyses

No statistical analyses for this end point

Secondary: Total clearance (CL) of RO5479599

End point title	Total clearance (CL) of RO5479599

End point description:

Clearence was estimated as dose divided by the area under plasma concentration-time curve from time zero to infinity where the dose is the of amount RO5479599 actually administered.

End point type	Secondary

End point timeframe:

Pre-dose (Hour 0) and at end of infusion (infusion duration=approximately 2 hours) on Day 1 of each cycle (cycle length = 21 days) up to end of treatment (EOT, Day 314); 3-6, 24, 72, 168, 264, 336, 432, 480 hours post-dose on Day 1 of Cycle 1,4;at Day 342

End point values	RO5479599+Carboplatin+Paclitaxel			
Subject group type	Reporting group			
Number of subjects analysed	0[5]			
Units: Liter/hour (L/hr)				
geometric mean (standard deviation)	()			

Notes:

[5] - No data is reported since the PK data was not analyzed due to early termination of the study.

Statistical analyses

No statistical analyses for this end point

Secondary: Volume of Distribution at Steady State (Vss) of RO5479599

End point title	Volume of Distribution at Steady State (Vss) of RO5479599

End point description:

Volume of distribution is defined as the theoretical volume in which the total amount of drug would need to be uniformly distributed to produce the desired blood concentration of a drug. Vss is the apparent volume of distribution at steady-state.

End point type	Secondary

End point timeframe:

Pre-dose (Hour 0) and at end of infusion (infusion duration=approximately 2 hours) on Day 1 of each cycle (cycle length = 21 days) up to end of treatment (EOT, Day 314); 3-6, 24, 72, 168, 264, 336, 432, 480 hours post-dose on Day 1 of Cycle 1,4;at Day 342

End point values	RO5479599+Carboplatin+Paclitaxel			
Subject group type	Reporting group			
Number of subjects analysed	0[6]			
Units: Liter				
geometric mean (standard deviation)	()			

Notes:

[6] - No data is reported since the PK data was not analyzed due to early termination of the study.

Statistical analyses

No statistical analyses for this end point

Secondary: Accumulation Ratio (Rac) of RO5479599

End point title	Accumulation Ratio (Rac) of RO5479599

End point description:

Rac was calculated as, Rac obtained from Area Under the Concentration Time Curve (AUC, Day 342) from time 0-t divided by AUC from time 0-t (Day 1).

End point type	Secondary

End point timeframe:

Pre-dose (Hour 0) and at end of infusion (infusion duration=approximately 2 hours) on Day 1 of each cycle (cycle length = 21 days) up to end of treatment (EOT, Day 314); 3-6, 24, 72, 168, 264, 336, 432, 480 hours post-dose on Day 1 of Cycle 1,4;at Day 342

End point values	RO5479599+Carboplatin+Paclitaxel			
Subject group type	Reporting group			
Number of subjects analysed	0[7]			
Units: Ratio				
geometric mean (standard deviation)	()			

Notes:

[7] - No data is reported since the PK data was not analyzed due to early termination of the study.

Statistical analyses

No statistical analyses for this end point

Secondary: Terminal Elimination Half-life (t 1/2) of RO5479599

End point title	Terminal Elimination Half-life (t 1/2) of RO5479599

End point description:

Plasma terminal half-life is the time measured for the plasma concentration to decrease by one half.

End point type	Secondary

End point timeframe:

Pre-dose (Hour 0) and at end of infusion (infusion duration=approximately 2 hours) on Day 1 of each cycle (cycle length = 21 days) up to end of treatment (EOT, Day 314); 3-6, 24, 72, 168, 264, 336, 432, 480 hours post-dose on Day 1 of Cycle 1,4;at Day 342

End point values	RO5479599+Carboplatin+Paclitaxel			
Subject group type	Reporting group			
Number of subjects analysed	0[8]			
Units: Hour				
arithmetic mean (standard deviation)	()			

Notes:

[8] - No data is reported since the PK data was not analyzed due to early termination of the study.

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration of RO5479599 at the Time of Tumor Progression (Cprog)

End point title	Concentration of RO5479599 at the Time of Tumor Progression (Cprog)

End point description:

PD: at least 20% increase in the sum of diameters of target lesions compared to the smallest sum of diameters on-study and absolute increase of at least 5 mm, progression of existing non-target lesions, or presence of new lesions.

End point type	Secondary

End point timeframe:

At tumor progression (any time between Baseline and Day 342)

End point values	RO5479599+Carboplatin+Paclitaxel			
Subject group type	Reporting group			
Number of subjects analysed	0[9]			
Units: mg/mL				
arithmetic mean (standard deviation)	()			

Notes:

[9] - No data is reported since the PK data was not analyzed due to early termination of the study.

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration of RO5479599 at the Time of Tumor Response (CR or PR)

End point title	Concentration of RO5479599 at the Time of Tumor Response (CR or PR)

End point description:

CR: complete disappearance of all target lesions and non-target disease (except nodal disease). All nodes, must decrease to normal(short axis <10 mm). No new lesions. PR:>=30% decrease under baseline of the sum of diameters of all target lesions. The short axis was used in the sum for target nodes,while the longest diameter was used in the sum for all other target lesions. No unequivocal progression of non-target disease. No new lesions.

End point type	Secondary

End point timeframe:

At the time of tumor response (anytime between baseline and Day 342)

End point values	RO5479599+Carboplatin+Paclitaxel			
Subject group type	Reporting group			
Number of subjects analysed	0[10]			
Units: mg/mL				
arithmetic mean (standard deviation)	()			

Notes:

[10] - No data is reported since the PK data was not analyzed due to early termination of the study.

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration of RO5479599 at the Time of Toxicity

End point title	Concentration of RO5479599 at the Time of Toxicity

End point description:

The National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE) version 4.3 was used to grade toxicity. NCI-CTCAE: Grade 1: mild; asymptomatic or mild symptoms, clinical or diagnostic observations only, or intervention not indicated; Grade 2: moderate; minimal, local, or non-invasive intervention indicated or limiting age-appropriate instrumental activities of daily living; Grade 3: severe or medically significant, but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; or limiting self-care activities of daily living; Grade 4: Life-threatening consequences or urgent intervention indicated; Grade 5: Death related to toxicity.

End point type	Secondary

End point timeframe:

At the time of toxicity (anytime between baseline and Day 342)

End point values	RO5479599+Carboplatin+Paclitaxel			
Subject group type	Reporting group			
Number of subjects analysed	0[11]			
Units: mg/mL				
arithmetic mean (standard deviation)	()			

Notes:

[11] - No data is reported since the PK data was not analyzed due to early termination of the study.

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration of RO5479599 at the Time of Infusion-related Reactions (IRRs) or Hypersensitivity Reaction

End point title	Concentration of RO5479599 at the Time of Infusion-related Reactions (IRRs) or Hypersensitivity Reaction

End point description:

IRR was monitored until complete resolution of the symptoms and treated as clinically indicated.

End point type	Secondary

End point timeframe:

At the time of IRRs or Hypersensitivity Reaction (anytime between baseline and Day 342)

End point values	RO5479599+Carboplatin+Paclitaxel			
Subject group type	Reporting group			
Number of subjects analysed	0[12]			
Units: mg/mL				
arithmetic mean (standard deviation)	()			

Notes:

[12] - No data is reported since the PK data was not analyzed due to early termination of the study.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Died

End point title	Percentage of Participants Who Died

End point description:

Safety analysis population included all participants who have received at least 1 dose of the study treatment, whether prematurely withdrawn from the study or not.

End point type	Secondary

End point timeframe:

Baseline up to Day 342

End point values	RO5479599+Carboplatin+Paclitaxel			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Percentage of participants				
number (not applicable)	16.3			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Baseline up to Day 342	
Adverse event reporting additional description:	
Safety analysis population.	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups	
Reporting group title	RO5479599+Carboplatin+Paclitaxel

Reporting group description:

RO5479599 800 mg was administered in the Safety Run-In Phase by intravenous infusion q3w on Day 1 of 3-weekly cycles (each cycle of 21 days) in combination with carboplatin (to produce an AUC of 6 mg/mL*minute and paclitaxel 200 mg/m^2 by intravenous infusion q3w for 4 to 6 cycles. Thereafter, RO5479599 was continued as a monotherapy (carboplatin and paclitaxel could be continued at the investigator's discretion) until disease progression, death, unacceptable toxicity, withdrawal of consent, or study termination by sponsor, whichever occurred first.

Serious adverse events	RO5479599+Carboplatin+Paclitaxel		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 12 (25.00%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Infected Neoplasm			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Loss of consciousness			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			

subjects affected / exposed	1 / 12 (8.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Respiratory tract infection			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	RO5479599+Carboplatin+Paclitaxel		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 12 (100.00%)		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	8 / 12 (66.67%)		
occurrences (all)	13		
Fatigue			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	3		
General physical health deterioration			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Mucosal inflammation			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	2		
Oedema peripheral			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Reproductive system and breast disorders			

Vulval ulceration			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	3		
Haemoptysis			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Hiccups			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Nasal inflammation			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Pharyngeal inflammation			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Pleuritic pain			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Pneumonitis			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Insomnia			
subjects affected / exposed	3 / 12 (25.00%)		
occurrences (all)	3		
Investigations			
Neutrophil count decreased			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		

Platelet count decreased subjects affected / exposed occurrences (all)	3 / 12 (25.00%) 3		
Weight decreased subjects affected / exposed occurrences (all)	3 / 12 (25.00%) 3		
Injury, poisoning and procedural complications Infusion related reaction subjects affected / exposed occurrences (all)	4 / 12 (33.33%) 5		
Nervous system disorders Dyskinesia subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Headache subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Neurotoxicity subjects affected / exposed occurrences (all)	5 / 12 (41.67%) 7		
Peripheral sensory neuropathy subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	3 / 12 (25.00%) 5		
Neutropenia subjects affected / exposed occurrences (all)	2 / 12 (16.67%) 3		
Thrombocytopenia subjects affected / exposed occurrences (all)	2 / 12 (16.67%) 6		
Eye disorders Entropion			

subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Abdominal pain			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		
Abdominal pain upper			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		
Colitis			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Constipation			
subjects affected / exposed	3 / 12 (25.00%)		
occurrences (all)	5		
Diarrhoea			
subjects affected / exposed	9 / 12 (75.00%)		
occurrences (all)	21		
Dyspepsia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Haemorrhoids			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Hypoaesthesia oral			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	4 / 12 (33.33%)		
occurrences (all)	5		
Stomatitis			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		

Vomiting			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	4		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	3 / 12 (25.00%)		
occurrences (all)	4		
Dry skin			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Rash			
subjects affected / exposed	3 / 12 (25.00%)		
occurrences (all)	3		
Rash maculo-papular			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	2		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Back pain			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Groin pain			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Musculoskeletal chest pain			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Musculoskeletal pain			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	3		
Pain in extremity			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		
Infections and infestations			

Respiratory tract infection subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all)	2 / 12 (16.67%) 2 1 / 12 (8.33%) 1		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all) Hypomagnesaemia subjects affected / exposed occurrences (all)	3 / 12 (25.00%) 3 2 / 12 (16.67%) 5		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 September 2014	Inclusion criteria related to tumor biopsies and contraceptive methods was clarified.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

The study was prematurely terminated due to a strategic decision taken by the Sponsor to stop further development of RO5479599.

Notes: