Clinical trial results:
A Phase 1b/2 Randomized Study of MEDI-575 in Combination With Carboplatin Plus Paclitaxel Versus Carboplatin Plus Paclitaxel Alone in Adult Subjects With Previously Untreated, Advanced Non-Small Cell Lung Cancer

Summary

EudraCT number	2010-023854-35
Trial protocol	DE HU BG
Global end of trial date	04 September 2013

Results information

Result version number	v2 (current)
This version publication date	20 December 2020
First version publication date	23 June 2016
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	CD-ON-MEDI-575-1031

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01268059
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	MedImmune, LLC
Sponsor organisation address	One MedImmune Way, Gaithersburg, United States, 20878
Public contact	Mohammed Dar, MD, Vice President & Head, Clinical Development, Oncology, MedImmune, LLC, +1 301-398-0000, information.center@astrazeneca.com
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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	04 September 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	04 September 2013
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

For phase 1b, main objective was evaluation of the safety profile of MEDI-575 when used in combination with carboplatin/paclitaxel in participants with previously untreated, advanced non-small cell lung cancer (NSCLC). For phase 2, main objective was evaluation of progression-free survival of subjects following treatment with MEDI-575 when used in combination with paclitaxel/carboplatin versus paclitaxel/carboplatin alone in participants with previously untreated, advanced NSCLC.

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and the International Conference on Harmonization guideline E6: Good Clinical Practice. Participating participant signed informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 December 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	United States: 64
Country: Number of subjects enrolled	France: 3
Country: Number of subjects enrolled	Poland: 5
Country: Number of subjects enrolled	Canada: 12
Country: Number of subjects enrolled	Hungary: 1
Country: Number of subjects enrolled	Japan: 14
Worldwide total number of subjects	99
EEA total number of subjects	9

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)	50
From 65 to 84 years	49
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Overall, 99 participants were enrolled in study, (4 participants, all from North America sites, were enrolled in Phase 1b and 95 participants in Phase 2 of study). Of 95 participants, 14 were from Japan, 81 were from North American and European Union (EU) sites. End of study is 14 months from last participant enrolled, or sponsor stopped study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Carboplatin/Paclitaxel (C/P): North America/EU Population

Arm description:

Carboplatin/paclitaxel regimen (carboplatin area under the plasma concentration-time curve [AUC] of 6 milligram per milliliter into minute [mg/mL*min], and paclitaxel 200 milligram per square meter [mg/m^2]) administered as an intravenous (IV) infusion once every 21 days on Day 1, for a total of 6 doses (cycles) or until unacceptable toxicity, disease progression, or other reasons for participant withdrawal.

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

Dosage and administration details:

Carboplatin 6 milligram per milliliter into minute [mg/mL*min] once every 21 days on Day 1, for a total of 6 doses (cycles).

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

Dosage and administration details:

Paclitaxel 200 milligram per square meter [mg/m^2] once every 21 days on Day 1, for a total of 6 doses (cycles).

Arm title	C/P + MEDI-575 (C/P/M): North America/EU Population

Arm description:

Carboplatin/paclitaxel regimen (carboplatin AUC = 6 mg/mL*min, and paclitaxel 200 mg/m^2) followed by MEDI-575 at a dose of 25 milligram per kilogram (mg/kg) administered as an IV infusion once every 21 days on Day 1 for a total of 6 cycles. Participants who achieved stable disease or better at the completion of carboplatin/paclitaxel therapy and did not demonstrate toxicity to MEDI-575, MEDI-575 alone was continued until unacceptable toxicity, disease progression, initiation of alternative anticancer therapy, or other reasons for participant withdrawal.

Arm type	Experimental

Investigational medicinal product name	MEDI-575
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intracavernous use

Dosage and administration details:

MEDI-575 at a dose of 25 milligram per kilogram (mg/kg) once every 21 days on Day 1 for a total of 6 cycles.

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

Dosage and administration details:

Carboplatin 6 milligram per milliliter into minute [mg/mL*min] once every 21 days on Day 1, for a total of 6 doses (cycles).

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

Dosage and administration details:

Paclitaxel 200 milligram per square meter [mg/m^2] once every 21 days on Day 1, for a total of 6 doses (cycles).

Arm title	Carboplatin/Paclitaxel (C/P): Japan Population

Arm description:

Carboplatin/paclitaxel regimen (carboplatin AUC = 6 mg/mL*min, and paclitaxel 200 mg/m^2) administered as an IV infusion once every 21 days on Day 1, for a total of 6 doses (cycles) or until unacceptable toxicity, disease progression, or other reasons for participant withdrawal.

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

Dosage and administration details:

Carboplatin 6 milligram per milliliter into minute [mg/mL*min] once every 21 days on Day 1, for a total of 6 doses (cycles).

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

Dosage and administration details:

Paclitaxel 200 milligram per square meter [mg/m^2] once every 21 days on Day 1, for a total of 6 doses (cycles).

Arm title	C/P + MEDI-575 (C/P/M): Japan Population

Arm description:

Carboplatin/paclitaxel regimen (carboplatin AUC = 6 mg/mL*min, and paclitaxel 200 mg/m^2) followed by MEDI-575 at a dose of 25 milligram per kilogram (mg/kg) administered as an IV infusion once every 21 days on Day 1 for a total of 6 cycles. Participants who achieved stable disease or better at the completion of carboplatin/paclitaxel therapy and did not demonstrate toxicity to MEDI-575, MEDI-575 alone was continued until unacceptable toxicity, disease progression, initiation of alternative anticancer therapy, or other reasons for participant withdrawal.

Arm type	Experimental

Investigational medicinal product name	MEDI-575
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intracavernous use

Dosage and administration details:

MEDI-575 at a dose of 25 milligram per kilogram (mg/kg) once every 21 days on Day 1 for a total of 6 cycles.

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

Dosage and administration details:

Carboplatin 6 milligram per milliliter into minute [mg/mL*min] once every 21 days on Day 1, for a total of 6 doses (cycles).

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

Dosage and administration details:

Paclitaxel 200 milligram per square meter [mg/m^2] once every 21 days on Day 1, for a total of 6 doses (cycles).

Number of subjects in period 1	Carboplatin/Paclitaxel (C/P): North America/EU Population	C/P + MEDI-575 (C/P/M): North America/EU Population	Carboplatin/Paclitaxel (C/P): Japan Population
Started	40	45	6
Completed	12	10	3
Not completed	28	35	3
Consent withdrawn by subject	7	4	-
Death	20	30	3
Progression of disease	1	-	-
Lost to follow-up	-	1	-

Number of subjects in period 1	C/P + MEDI-575 (C/P/M): Japan Population
Started	8
Completed	3
Not completed	5
Consent withdrawn by subject	-
Death	5
Progression of disease	-
Lost to follow-up	-

Baseline characteristics

Reporting groups	
Reporting group title	Carboplatin/Paclitaxel (C/P): North America/EU Population
Reporting group description:	
Carboplatin/paclitaxel regimen (carboplatin area under the plasma concentration-time curve [AUC] of 6 milligram per milliliter into minute [mg/mL*min], and paclitaxel 200 milligram per square meter [mg/m^2]) administered as an intravenous (IV) infusion once every 21 days on Day 1, for a total of 6 doses (cycles) or until unacceptable toxicity, disease progression, or other reasons for participant withdrawal.	
Reporting group title	C/P + MEDI-575 (C/P/M): North America/EU Population
Reporting group description:	
Carboplatin/paclitaxel regimen (carboplatin AUC = 6 mg/mL*min, and paclitaxel 200 mg/m^2) followed by MEDI-575 at a dose of 25 milligram per kilogram (mg/kg) administered as an IV infusion once every 21 days on Day 1 for a total of 6 cycles. Participants who achieved stable disease or better at the completion of carboplatin/paclitaxel therapy and did not demonstrate toxicity to MEDI-575, MEDI-575 alone was continued until unacceptable toxicity, disease progression, initiation of alternative anticancer therapy, or other reasons for participant withdrawal.	
Reporting group title	Carboplatin/Paclitaxel (C/P): Japan Population
Reporting group description:	
Carboplatin/paclitaxel regimen (carboplatin AUC = 6 mg/mL*min, and paclitaxel 200 mg/m^2) administered as an IV infusion once every 21 days on Day 1, for a total of 6 doses (cycles) or until unacceptable toxicity, disease progression, or other reasons for participant withdrawal.	
Reporting group title	C/P + MEDI-575 (C/P/M): Japan Population
Reporting group description:	
Carboplatin/paclitaxel regimen (carboplatin AUC = 6 mg/mL*min, and paclitaxel 200 mg/m^2) followed by MEDI-575 at a dose of 25 milligram per kilogram (mg/kg) administered as an IV infusion once every 21 days on Day 1 for a total of 6 cycles. Participants who achieved stable disease or better at the completion of carboplatin/paclitaxel therapy and did not demonstrate toxicity to MEDI-575, MEDI-575 alone was continued until unacceptable toxicity, disease progression, initiation of alternative anticancer therapy, or other reasons for participant withdrawal.	

Reporting group values	Carboplatin/Paclitaxel (C/P): North America/EU Population	C/P + MEDI-575 (C/P/M): North America/EU Population	Carboplatin/Paclitaxel (C/P): Japan Population
Number of subjects	40	45	6
Age categorical Units: Subjects			
less than or equal to (<=) 70 years	35	32	6
greater than (>) 70 years	5	13	0
Age continuous Units: years			
arithmetic mean	64.0	65.1	57.5
standard deviation	± 6.6	± 8.2	± 13.9
Gender, Male/Female Units: participants			
Female	17	17	2
Male	23	28	4
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	1	6
Native Hawaiian or Other Pacific Islander	0	0	0

Black or African American	3	5	0
White	37	39	0
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1	2	0
Not Hispanic or Latino	39	43	6
Unknown or Not Reported	0	0	0

Reporting group values	C/P + MEDI-575 (C/P/M): Japan Population	Total	
Number of subjects	8	99	
Age categorical Units: Subjects			
less than or equal to (<=) 70 years	6	79	
greater than (>) 70 years	2	20	
Age continuous Units: years			
arithmetic mean	65.9		
standard deviation	± 6.0	-	
Gender, Male/Female Units: participants			
Female	2	38	
Male	6	61	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	8	15	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	8	
White	0	76	
More than one race	0	0	
Unknown or Not Reported	0	0	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	3	
Not Hispanic or Latino	8	96	
Unknown or Not Reported	0	0	

End points reporting groups

Reporting group title	Carboplatin/Paclitaxel (C/P): North America/EU Population

Reporting group description:

Carboplatin/paclitaxel regimen (carboplatin area under the plasma concentration-time curve [AUC] of 6 milligram per milliliter into minute [mg/mL*min], and paclitaxel 200 milligram per square meter [mg/m^2]) administered as an intravenous (IV) infusion once every 21 days on Day 1, for a total of 6 doses (cycles) or until unacceptable toxicity, disease progression, or other reasons for participant withdrawal.

Reporting group title	C/P + MEDI-575 (C/P/M): North America/EU Population

Reporting group description:

Carboplatin/paclitaxel regimen (carboplatin AUC = 6 mg/mL*min, and paclitaxel 200 mg/m^2) followed by MEDI-575 at a dose of 25 milligram per kilogram (mg/kg) administered as an IV infusion once every 21 days on Day 1 for a total of 6 cycles. Participants who achieved stable disease or better at the completion of carboplatin/paclitaxel therapy and did not demonstrate toxicity to MEDI-575, MEDI-575 alone was continued until unacceptable toxicity, disease progression, initiation of alternative anticancer therapy, or other reasons for participant withdrawal.

Reporting group title	Carboplatin/Paclitaxel (C/P): Japan Population

Reporting group description:

Carboplatin/paclitaxel regimen (carboplatin AUC = 6 mg/mL*min, and paclitaxel 200 mg/m^2) administered as an IV infusion once every 21 days on Day 1, for a total of 6 doses (cycles) or until unacceptable toxicity, disease progression, or other reasons for participant withdrawal.

Reporting group title	C/P + MEDI-575 (C/P/M): Japan Population

Reporting group description:

Carboplatin/paclitaxel regimen (carboplatin AUC = 6 mg/mL*min, and paclitaxel 200 mg/m^2) followed by MEDI-575 at a dose of 25 milligram per kilogram (mg/kg) administered as an IV infusion once every 21 days on Day 1 for a total of 6 cycles. Participants who achieved stable disease or better at the completion of carboplatin/paclitaxel therapy and did not demonstrate toxicity to MEDI-575, MEDI-575 alone was continued until unacceptable toxicity, disease progression, initiation of alternative anticancer therapy, or other reasons for participant withdrawal.

Subject analysis set title	Carboplatin/Paclitaxel (Total)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Carboplatin/paclitaxel regimen (carboplatin area under the plasma concentration-time curve [AUC] of 6 milligram per milliliter into minute [mg/mL*min], and paclitaxel 200 milligram per square meter [mg/m^2]) administered as an intravenous (IV) infusion once every 21 days on Day 1, for a total of 6 doses (cycles) or until unacceptable toxicity, disease progression, or other reasons for participant withdrawal.

Subject analysis set title	Carboplatin/Paclitaxel + MEDI-575 (Total)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Carboplatin/paclitaxel regimen (carboplatin AUC = 6 mg/mL*min, and paclitaxel 200 mg/m^2) followed by MEDI-575 at a dose of 25 milligram per kilogram (mg/kg) administered as an IV infusion once every 21 days on Day 1 for a total of 6 cycles. Participants who achieved stable disease or better at the completion of carboplatin/paclitaxel therapy and did not demonstrate toxicity to MEDI-575, MEDI-575 alone was continued until unacceptable toxicity, disease progression, initiation of alternative anticancer therapy, or other reasons for participant withdrawal.

Subject analysis set title	Carboplatin/Paclitaxel + MEDI-575 - Phase 1b
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Carboplatin/paclitaxel regimen (carboplatin AUC = 6 mg/mL*min, and paclitaxel 200 mg/m^2) followed by MEDI-575 at a dose of 25 milligram per kilogram (mg/kg) administered as an IV infusion once every 21 days on Day 1 for a total of 6 cycles. Participants who achieved stable disease or better at the completion of carboplatin/paclitaxel therapy and did not demonstrate toxicity to MEDI-575, MEDI-575 alone was continued until unacceptable toxicity, disease progression, initiation of alternative anticancer therapy, or other reasons for participant withdrawal.

Subject analysis set title	Carboplatin/Paclitaxel + MEDI-575 - Phase 2
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Carboplatin/paclitaxel regimen (carboplatin AUC = 6 mg/mL*min, and paclitaxel 200 mg/m^2) followed by MEDI-575 at a dose of 25 milligram per kilogram (mg/kg) administered as an IV infusion once every 21 days on Day 1 for a total of 6 cycles. Participants who achieved stable disease or better at the completion of carboplatin/paclitaxel therapy and did not demonstrate toxicity to MEDI-575, MEDI-575 alone was continued until unacceptable toxicity, disease progression, initiation of alternative anticancer therapy, or other reasons for participant withdrawal.

Subject analysis set title	Carboplatin/Paclitaxel - Phase 2
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Carboplatin/paclitaxel regimen (carboplatin area under the plasma concentration-time curve [AUC] of 6 milligram per milliliter into minute [mg/mL*min], and paclitaxel 200 milligram per square meter [mg/m^2]) administered as an intravenous (IV) infusion once every 21 days on Day 1, for a total of 6 doses (cycles) or until unacceptable toxicity, disease progression, or other reasons for participant withdrawal.

Primary: Number of Participants With Dose Limiting Toxicities (DLT): Phase 1b

End point title	Number of Participants With Dose Limiting Toxicities (DLT): Phase 1b[1]

End point description:

A DLT was defined as: 1. Any treatment-related Grade 3 or higher non-hematologic toxicity that occurred during the DLT assessment period with the following exceptions: a. Grade 3 fever (in the absence of neutropenia) defined as more than (>) 40.0 degree Celcius (> 104.0 degree Fahrenheit) that resolved to normal or baseline within 24 hours of treatment and was not considered a serious adverse event (SAE); or b. Grade 3 rigors/chills that responded to optimal therapy. 2. Any treatment-related Grade 3 or higher hematologic toxicity. The evaluable population for dose determination included all participants who were in Phase 1b, received at least 1 full cycle of MEDI-575 and completed the safety follow-up through the DLT evaluation period or participants who experienced any DLT.

End point type	Primary

End point timeframe:

From Day 1 to Day 21 of first cycle

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: Statistical analysis was not applicable since there were no inferential statistics, only descriptive statistics were performed for this end point. As listed in the table, there were 4 subjects dosed and analyzed and 0 experienced a DLT.

End point values	Carboplatin/Paclitaxel + MEDI-575 - Phase 1b			
Subject group type	Subject analysis set			
Number of subjects analysed	4			
Units: participants	0			

Statistical analyses

No statistical analyses for this end point

Primary: Progression Free-Survival (PFS)

End point title	Progression Free-Survival (PFS)[2]

End point description:

Progression-free survival defined as the time from randomization (randomization referred to the date of treatment assignment) to disease progression (defined according to Response Evaluation Criteria for Solid Tumors [RECIST] guidelines) or death due to any cause, whichever occurs first. Participants without progression or death at the time of analysis were censored at their last date of tumor

evaluation. PFS was assessed only in North America/European Union (EU) participants. The Intent-to-Treat (ITT) North America/EU population included all North America/EU participants who were randomized into Phase 2 portion of the study.

End point type	Primary

End point timeframe:

From randomization until the end of study (14 months from last participant enrolled or sponsor stopped the study), assessed at every 6 weeks until disease progression and every 3 months until the end of the study (approximately 3 years)

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	Carboplatin/Paclitaxel (C/P): North America/EU Population	C/P + MEDI-575 (C/P/M): North America/EU Population		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	27		
Units: months				
median (confidence interval 95%)	5.5 (4.7 to 6.5)	4.6 (3.9 to 5.5)		

Statistical analyses

Statistical analysis title	PFS

Statistical analysis description:

Progression-free Survival (ITT Phase 2 North America/EU Population) for Carboplatin/Paclitaxel + MEDI-575 versus Carboplatin/Paclitaxel

Comparison groups	Carboplatin/Paclitaxel (C/P): North America/EU Population v C/P + MEDI-575 (C/P/M): North America/EU Population
Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	= 0.027 [4]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	2.205
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.1
upper limit	4.5

Notes:

[3] - Hazard ratio and its 95 percent (%) confidence interval (CIs) were calculated using the Cox proportional hazard model stratified by histology, disease stage, and Eastern Cooperative Oncology Group (ECOG) performance status.
[4] - The 2-sided p-value was calculated using the log-rank test stratified by histology, disease stage, and ECOG performance status.

Secondary: Best Overall Response

End point title	Best Overall Response

End point description:

Best overall response of a participant was defined as the best tumor response [Complete Response (CR), Partial Response (PR), Stable Disease (SD), or Progressive Disease (PD)] observed during the trial period assessed according to the RECIST version 1.1 criteria. The participant's best overall response assignment depended on the findings of both target and non-target disease and also on the appearance of new lesions. CR was defined as disappearance of tumor lesions, PR was defined as a decrease of at least 30 percent (%) in the sum of diameters of target lesion, SD was defined as steady state of disease, and PD was defined as an increase of at least 20% in the sum of diameters of target lesions. The ITT North America/EU population included all North America/EU participants who were randomized into Phase 2 portion of the study. The ITT Japanese population included all Japanese participants who were randomized into the Phase 2 portion of the study.

End point type	Secondary

End point timeframe:

From initiation of treatment until the end of study (14 months from last participant enrolled or sponsor stopped the study), assessed at every 6 weeks until disease progression and every 3 months until the end of the study (approximately 3 years)

End point values	Carboplatin/Paclitaxel (C/P): North America/EU Population	C/P + MEDI-575 (C/P/M): North America/EU Population	Carboplatin/Paclitaxel (C/P): Japan Population	C/P + MEDI-575 (C/P/M): Japan Population
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	41	6	8
Units: participants				
Complete response	1	0	0	0
Partial response	12	19	2	1
Stable disease	19	12	3	5
Progressive disease	1	5	1	1
Unknown	7	5	0	1

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate (ORR)

End point title	Objective Response Rate (ORR)

End point description:

The ORR defined as the percentage of participants with confirmed CR or confirmed PR according to RECIST guidelines. Confirmed responses were those that persist on repeat imaging or assessment greater than or equal to (>=) 4 weeks after the initial documentation of response. The ITT North America/EU population included all North America/EU participants who were randomized into Phase 2 portion of the study. The ITT Japanese population included all Japanese participants who were randomized into the Phase 2 portion of the study.

End point type	Secondary

End point timeframe:

From initiation of treatment until the end of study (14 months from last participant enrolled or sponsor stopped the study), assessed at every 6 weeks until disease progression and every 3 months until the end of the study (approximately 3 years)

End point values	Carboplatin/Paclitaxel (C/P): North America/EU Population	C/P + MEDI-575 (C/P/M): North America/EU Population	Carboplatin/Paclitaxel (C/P): Japan Population	C/P + MEDI-575 (C/P/M): Japan Population
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	41	6	8
Units: percentage of participants				
number (confidence interval 95%)	22.5 (10.8 to 38.5)	31.7 (18.1 to 48.1)	33.3 (4.3 to 77.7)	12.5 (0.3 to 52.7)

Statistical analyses

Statistical analysis title	ORR (North America/EU)

Statistical analysis description:

Objective Response Rate Comparision for Carboplatin/Paclitaxel + MEDI-575 versus Carboplatin/Paclitaxel.

Comparison groups	Carboplatin/Paclitaxel (C/P): North America/EU Population v C/P + MEDI-575 (C/P/M): North America/EU Population
Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.487 [5]
Method	Cochran-Mantel-Haenszel

Notes:

[5] - The 2-sided p-value was calculated by adjusting for the stratification factors histology, disease stage, and Eastern Cooperative Oncology Group (ECOG) performance status.

Statistical analysis title	ORR (Japan)

Statistical analysis description:

Treatment effect Carboplatin/Paclitaxel + MEDI-575 versus Carboplatin/Paclitaxel.

Comparison groups	Carboplatin/Paclitaxel (C/P): Japan Population v C/P + MEDI-575 (C/P/M): Japan Population
Number of subjects included in analysis	14
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.386 [6]
Method	Cochran-Mantel-Haenszel

Notes:

[6] - The 2-sided p-value was calculated by adjusting for the stratification factors histology, disease stage, and ECOG performance status.

Secondary: Time to Response (TTR)

End point title	Time to Response (TTR)

End point description:

TTR was measured from randomization to the first documentation of objective response and assessed only in participants who achieved objective response. The ORR defined as the percentage of participants with confirmed CR or confirmed PR according to RECIST guidelines. Confirmed responses were those that persist on repeat imaging or assessment >=4 weeks after the initial documentation of response. The ITT North America/EU population included all North America/EU participants who were randomized into Phase 2 portion of the study. The ITT Japanese population included all Japanese participants who were randomized into the Phase 2 portion of the study. Participants who achieved OR were analyzed for this outcome measure. In the below table 0.9999 and 99999 indicates that the 95% confidence interval was not estimated because only 1 participant had OR in the specified arm.

End point type	Secondary

End point timeframe:

From initiation of treatment until the end of study (14 months from last participant enrolled or sponsor stopped the study), assessed at every 6 weeks until disease progression and every 3 months until the end of the study (approximately 3 years)

End point values	Carboplatin/Paclitaxel (C/P): North America/EU Population	C/P + MEDI-575 (C/P/M): North America/EU Population	Carboplatin/Paclitaxel (C/P): Japan Population	C/P + MEDI-575 (C/P/M): Japan Population
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	13	2	1
Units: months				
median (confidence interval 95%)	1.4 (1.2 to 2.7)	1.4 (1.3 to 1.6)	2.2 (1.4 to 3.1)	2.8 (0.9999 to 99999)

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DR)

End point title	Duration of Response (DR)

End point description:

The DR defined as the duration from the first documentation of objective response to the first documented disease progression. Participants without progression at the time of analysis were censored at their last date of tumor evaluation. The ITT North America/EU population included all North America/EU participants who were randomized into Phase 2 portion of the study. The ITT Japanese population included all Japanese participants who were randomized into the Phase 2 portion of the study. Participants who achieved OR were analyzed for this outcome measure. In the below table 0.9999 and 99999 indicates the 95% confidence interval was not estimated because only 1 participants had OR in the specified arm.

End point type	Secondary

End point timeframe:

From initiation of treatment until the end of study (14 months from last participant enrolled or sponsor stopped the study), assessed at every 6 weeks until disease progression and every 3 months until the end of the study (approximately 3 years)

End point values	Carboplatin/Paclitaxel (C/P): North America/EU Population	C/P + MEDI-575 (C/P/M): North America/EU Population	Carboplatin/Paclitaxel (C/P): Japan Population	C/P + MEDI-575 (C/P/M): Japan Population
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	13	2	1
Units: months				
median (confidence interval 95%)	3.3 (1.3 to 4.6)	4.2 (3.7 to 5.0)	4.9 (3.5 to 6.3)	2.1 (0.9999 to 99999)

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Progression (TTP)

End point title	Time to Progression (TTP)

End point description:

The TTP was measured from randomization until the documentation of disease progression. Disease progression defined according to RECIST v 1.1 guidelines. Participants without progression at the time of analysis were censored at their last date of tumor evaluation. The ITT North America/EU population included all North America/EU participants who were randomized into Phase 2 portion of the study. The ITT Japanese population included all Japanese participants who were randomized into the Phase 2 portion of the study. The TTP was analyzed for only those participants who had disease progression.

End point type	Secondary

End point timeframe:

From initiation of treatment until the end of study (14 months from last participant enrolled or sponsor stopped the study), assessed at every 6 weeks until disease progression and every 3 months until the end of the study (approximately 3 years)

End point values	Carboplatin/Paclitaxel (C/P): North America/EU Population	C/P + MEDI-575 (C/P/M): North America/EU Population	Carboplatin/Paclitaxel (C/P): Japan Population	C/P + MEDI-575 (C/P/M): Japan Population
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	23	5	6
Units: months				
number (confidence interval 95%)	6.4 (4.9 to 10.3)	4.6 (3.9 to 6.4)	6.5 (1.4 to 10.7)	4.6 (1.3 to 15.0)

Statistical analyses

Statistical analysis title	TTP (North America/EU)
Comparison groups	Carboplatin/Paclitaxel (C/P): North America/EU Population v C/P + MEDI-575 (C/P/M): North America/EU Population
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Hazard ratio (HR)
Point estimate	3.017

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.2
upper limit	7.4

Statistical analysis title	TTP (Japan)
Comparison groups	Carboplatin/Paclitaxel (C/P): Japan Population v C/P + MEDI-575 (C/P/M): Japan Population
Number of subjects included in analysis	11
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Hazard ratio (HR)
Point estimate	1.134
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	4.3

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

Overall survival defined as the time from randomization until death due to any cause. Participants who were still alive at the time of analysis were censored at their last date of last contact. In the below table 99999 indicates that median and confidence interval were not determined as an insufficient number of participants had the event. The ITT North America/EU population included all North America/EU participants who were randomized into Phase 2 portion of the study. The ITT Japanese population included all Japanese participants who were randomized into the Phase 2 portion of the study.

End point type	Secondary

End point timeframe:

From initiation of treatment until the end of study (14 months from last participant enrolled or sponsor stopped the study), assessed at every 6 weeks until disease progression and every 3 months until the end of the study (approximately 3 years)

End point values	Carboplatin/Paclitaxel (C/P): North America/EU Population	C/P + MEDI-575 (C/P/M): North America/EU Population	Carboplatin/Paclitaxel (C/P): Japan Population	C/P + MEDI-575 (C/P/M): Japan Population
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	27	3	5
Units: months				
number (confidence interval 95%)	11.8 (8.2 to 99999)	10.0 (6.4 to 11.6)	99999 (4.3 to 99999)	11.5 (2.3 to 99999)

Statistical analyses

Statistical analysis title	OS (North America/EU)
Comparison groups	Carboplatin/Paclitaxel (C/P): North America/EU Population v C/P + MEDI-575 (C/P/M): North America/EU Population
Number of subjects included in analysis	47
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Hazard ratio (HR)
Point estimate	1.315
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	2.4

Statistical analysis title	OS (Japan)
Comparison groups	Carboplatin/Paclitaxel (C/P): Japan Population v C/P + MEDI-575 (C/P/M): Japan Population
Number of subjects included in analysis	8
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Hazard ratio (HR)
Point estimate	2.083
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	10.8

Secondary: Number of Participants With Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point title	Number of Participants With Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point description:

An adverse event (AE) was any untoward medical occurrence in a participant who received study drug without regard to possibility of causal relationship. A serious adverse event (SAE) was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. The safety population included all participants who received at least one dose of study drug.

End point type	Secondary

End point timeframe:

From signing of informed consent form until 90 days post the last dose treatment (approximately 3 years)

End point values	Carboplatin/Paclitaxel (Total)	Carboplatin/Paclitaxel + MEDI-575 (Total)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	43	53		
Units: participants				
Any AE	42	53		
Any SAE	17	25		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Abnormalities in Laboratory Investigations Reported as Adverse Events (AEs) or Serious Adverse Events (SAEs)

End point title	Number of Participants With Abnormalities in Laboratory Investigations Reported as Adverse Events (AEs) or Serious Adverse Events (SAEs)

End point description:

Laboratory investigations included hematology, coagulation, serum chemistry and urinalysis parameters. Participants with abnormalities in these laboratory investigations recorded as AEs or SAEs were reported. The safety population included all participants who received at least one dose of study drug.

End point type	Secondary

End point timeframe:

From signing of informed consent form until 90 days post the last dose treatment (approximately 3 years)

End point values	Carboplatin/Paclitaxel (Total)	Carboplatin/Paclitaxel + MEDI-575 (Total)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	43	53		
Units: participants				
Anaemia	15	25		
Febrile neutropenia	3	6		
Idiopathic thrombocytopenic purpura	0	1		
Leukopenia	2	6		
Lymphadenopathy	0	2		
Lymphopenia	2	1		
Neutropenia	7	13		
Thrombocytopenia	3	10		

Activated partial thromboplastin time prolonged	0	1		
Haemoglobin decreased	1	5		
Lymphocyte count decreased	0	1		
Neutrophil count decreased	5	14		
Platelet count decreased	5	9		
White blood cell count decreased	4	10		
Alanine aminotransferase increased	2	5		
Aspartate aminotransferase increased	3	4		
Blood alkaline phosphatase increased	2	2		
Blood bilirubin increased	2	0		
Blood creatinine increased	1	3		
Blood magnesium decreased	0	1		
Gamma-glutamyl transferase increased	0	1		
Electrolyte imbalance	1	0		
Hypercholesterolaemia	1	0		
Hyperglycaemia	5	7		
Hypertriglyceridaemia	2	1		
Hypoalbuminaemia	3	7		
Hypocalcaemia	3	6		
Hypoglycaemia	1	1		
Hypokalemia	8	12		
Hypomagnesaemia	10	20		
Hyponatraemia	4	8		
Hypophosphataemia	2	4		
Iron deficiency	0	1		
Vitamin B12 deficiency	0	1		
Urine analysis abnormal	0	1		
Specific gravity urine increased	0	1		
Haematuria	1	1		
Proteinuria	1	1		
Pyelocaliectasis	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Electrocardiogram (ECG) Abnormalities Reported as AEs

End point title	Number of Participants With Electrocardiogram (ECG) Abnormalities Reported as AEs

End point description:

The 12-lead ECG data were performed and obtained in triplicate that is 3 ECGs obtained within a 5 minute time period. Number of participants with ECG abnormalities were reported and recorded as AEs. The safety population included all participants who received at least one dose of study drug.

End point type	Secondary

End point timeframe:

From signing of informed consent form until 90 days post the last dose treatment (approximately 3 years)

End point values	Carboplatin/Paclitaxel (Total)	Carboplatin/Paclitaxel + MEDI-575 (Total)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	43	53		
Units: participants				
Atrial fibrillation	0	1		
Atrial flutter	0	1		
Atrioventricular block first degree	0	1		
Myocardial infarction	1	0		
Tachycardia	2	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Serum Concentration (Cmax) for MEDI-575 After First Dose

End point title	Maximum Observed Serum Concentration (Cmax) for MEDI-575 After First Dose

End point description:

The Cmax refers to the highest measured drug concentration after a single dose which is obtained by collecting a series of blood samples and average of measuring the concentrations of drug in each sample. Participants who were treated with MEDI-575 and for whom serum concentrations were available for PK data analyses.

End point type	Secondary

End point timeframe:

Day 1 (pre-infusion and end of infusion), Day 2 (24 hours post Day 1 infusion), Day 8, and Day 15

End point values	Carboplatin/Paclitaxel + MEDI-575 - Phase 1b	Carboplatin/Paclitaxel + MEDI-575 - Phase 2		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	4	44		
Units: microgram per milliliter				
arithmetic mean (standard deviation)	589.3 (± 175.6)	628.9 (± 441.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time of Maximal Observed Concentration (Tmax) for MEDI-575 After First Dose

End point title	Time of Maximal Observed Concentration (Tmax) for MEDI-575 After First Dose

End point description:

The tmax refers to the time after dosing when a drug attains its highest measurable concentration (Cmax). It is obtained by collecting a series of blood samples at various times after dosing, and average of measuring them for drug content. Participants who were treated with MEDI-575 and for whom serum concentrations were available for PK data analyses.

End point type	Secondary

End point timeframe:

Day 1 (pre-infusion and end of infusion), Day 2 (24 hours post Day 1 infusion), Day 8, and Day 15

End point values	Carboplatin/Paclitaxel + MEDI-575 - Phase 1b	Carboplatin/Paclitaxel + MEDI-575 - Phase 2		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	4	44		
Units: day				
arithmetic mean (standard deviation)	0.044 (± 0.002)	0.046 (± 0.009)		

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Concentration-Time Curve Over the Dosing Interval (AUCtau) for MEDI-575 After First Dose

End point title	Area Under the Concentration-Time Curve Over the Dosing Interval (AUCtau) for MEDI-575 After First Dose

End point description:

The AUC is a measure of systemic drug exposure, which is obtained by collecting a series of blood samples and average of measuring the concentrations of drug in each sample. AUCtau defined as area under the plasma concentration time profile from time zero to the end of the dosing interval (tau). Participants who were treated with MEDI-575 and for whom serum concentrations were available for PK data analyses.

End point type	Secondary

End point timeframe:

Day 1 (pre-infusion and end of infusion), Day 2 (24 hours post Day 1 infusion), Day 8, and Day 15

End point values	Carboplatin/Paclitaxel + MEDI-575 - Phase 1b	Carboplatin/Paclitaxel + MEDI-575 - Phase 2		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	3	40		
Units: microgram*day per milliliter				

arithmetic mean (standard deviation)	3550 (± 496.1)	4803 (± 1948)		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Serum Concentration at Steady State (Cmax,ss) for MEDI-575 After First Dose

End point title	Maximum Serum Concentration at Steady State (Cmax,ss) for MEDI-575 After First Dose

End point description:

Maximum serum concentration at steady state for MEDI-575 after first dose was calculated. Participants who were treated with MEDI-575 and for whom serum concentrations were available for PK data analyses.

End point type	Secondary

End point timeframe:

Cycle 1 (pre-infusion and end of infusion on Day 1, Day 2, Day 8, and Day 15); Day 1 of Cycles 2 to 4 (pre-infusion and end of infusion)

End point values	Carboplatin/Paclitaxel + MEDI-575 - Phase 1b	Carboplatin/Paclitaxel + MEDI-575 - Phase 2		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2	27		
Units: microgram per milliliter				
arithmetic mean (standard deviation)	2997 (± 2588)	619.7 (± 160.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Maximum Serum Concentration at Steady State (Tmax,ss) for MEDI-575 After First Dose

End point title	Time to Maximum Serum Concentration at Steady State (Tmax,ss) for MEDI-575 After First Dose

End point description:

Time to maximum serum concentration at steady state for MEDI-575 after first dose was calculated. Participants who were treated with MEDI-575 and for whom serum concentrations were available for PK data analyses.

End point type	Secondary

End point timeframe:

Cycle 1 (pre-infusion and end of infusion on Day 1, Day 2, Day 8, and Day 15); Day 1 of Cycles 2 to 4 (pre-infusion and end of infusion)

End point values	Carboplatin/Paclitaxel + MEDI-575 - Phase 1b	Carboplatin/Paclitaxel + MEDI-575 - Phase 2		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2	27		
Units: day				
arithmetic mean (standard deviation)	0.042 (± 0.000)	0.049 (± 0.017)		

Statistical analyses

No statistical analyses for this end point

Secondary: Trough Serum Concentration at Steady State (Ctrough,ss) for MEDI-575 After First Dose

End point title	Trough Serum Concentration at Steady State (Ctrough,ss) for MEDI-575 After First Dose

End point description:

Trough serum concentration at steady state for MEDI-575 after first dose was calculated. Participants who were treated with MEDI-575 and for whom serum concentrations were available for PK data analyses.

End point type	Secondary

End point timeframe:

Cycle 1 (pre-infusion and end of infusion on Day 1, Day 2, Day 8, and Day 15); Day 1 of Cycles 2 to 4 (pre-infusion and end of infusion)

End point values	Carboplatin/Paclitaxel + MEDI-575 - Phase 1b	Carboplatin/Paclitaxel + MEDI-575 - Phase 2		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2	28		
Units: microgram per milliliter				
arithmetic mean (standard deviation)	375 (± 155)	168 (± 75.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Positive Anti-MEDI-575 Antibodies

End point title	Percentage of Participants With Positive Anti-MEDI-575 Antibodies

End point description:

Immunogenicity assessment included determination of anti-drug (MEDI-575) antibodies in serum samples. The evaluable population included all participants who were treated with MEDI-575 and for whom at least one serum sample for immunogenicity testing was available.

End point type	Secondary

End point timeframe:

Day 1 (prior to infusion) of Cycles 1 to 7 (21-day cycle), end of treatment, 30 and 60 days after the last dose (approximately 3 years)

End point values	Carboplatin/Paclitaxel + MEDI-575 - Phase 1b	Carboplatin/Paclitaxel + MEDI-575 - Phase 2		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	4	49		
Units: percentage of participants				
number (not applicable)	25.0	26.5		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Platelet-derived Growth Factor Receptor Alpha (PDGFRα) Expression in Tumor Cells of Archived Tumor Samples

End point title	Number of Participants With Platelet-derived Growth Factor Receptor Alpha (PDGFRα) Expression in Tumor Cells of Archived Tumor Samples

End point description:

The immunohistochemical expression of PDGFRα in tumor cells in archived formalin-fixed paraffin-embedded tissue samples collected at baseline are reported. The transmembrane receptor tyrosine kinase PDGFRα plays an important role in human carcinogenesis, both as a direct target on tumor cells and also as a mediator of stromal support for cancer cell growth. The data of positive-staining tumor cells are reported in 3 categories: intensity (1+ [weak expression, staining in <5 % of tumor cells]; 2+ [moderate expression, staining in >= 5 % of tumor cells]; and 3+ [strong expression, staining in >5 % of the tumor cells]), localization (membranous, cytoplasmic, or nuclear), and frequency (rare, occasional, or frequent). Evaluable populations for PDGFRα expression included all randomized participants who had formalin-fixed paraffin-embedded samples available at baseline and had positive-staining for tumor cells.

End point type	Secondary

End point timeframe:

Baseline (Screening [Days -28 to -1])

End point values	Carboplatin/Paclitaxel + MEDI-575 - Phase 1b	Carboplatin/Paclitaxel + MEDI-575 - Phase 2	Carboplatin/Paclitaxel - Phase 2	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	1	5	3	
Units: Participants				

number (not applicable)				
Intensity: 1+	1	2	3	
Intensity: 2+	0	2	0	
Intensity: 3+	0	1	0	
Localization: cytoplasmic	0	3	2	
Localization: membranous	0	2	0	
Localization: nuclear	1	0	1	
Frequency: rare	1	3	1	
Frequency: occasional	0	0	1	
Frequency: frequent	0	2	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With PDGFRα Expression in Stromal Cells of Archived Tumor Samples

End point title	Number of Participants With PDGFRα Expression in Stromal Cells of Archived Tumor Samples

End point description:

The immunohistochemical expression of PDGFRα in stromal cells in archived formalin-fixed paraffin-embedded tissue samples collected at baseline are reported. The transmembrane receptor tyrosine kinase PDGFRα plays an important role in human carcinogenesis, both as a direct target on tumor cells and also as a mediator of stromal support for cancer cell growth. The data of positive-staining stromal cells are reported in 3 categories: intensity (1+ [weak expression, staining in <5 % of tumor cells]; 2+ [moderate expression, staining in >= 5 % of tumor cells]; and 3+ [strong expression, staining in >5 % of the tumor cells]), localization (membranous, cytoplasmic, or nuclear), and frequency (rare, occasional, or frequent). Evaluable populations for PDGFRα expression included all randomized participants who had formalin-fixed paraffin-embedded samples available at baseline and had positive-staining for tumor cells.

End point type	Secondary

End point timeframe:

Baseline (Screening [Days -28 to -1])

End point values	Carboplatin/Paclitaxel + MEDI-575 - Phase 1b	Carboplatin/Paclitaxel + MEDI-575 - Phase 2	Carboplatin/Paclitaxel - Phase 2	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	3	16	10	
Units: Participants				
Intensity: 1+	2	3	3	
Intensity: 2+	1	10	5	
Intensity: 3+	0	3	2	
Localization: cytoplasmic	3	15	10	
Localization: membranous	0	1	0	
Localization: nuclear	0	0	0	
Frequency: rare	0	3	1	
Frequency: occasional	1	4	3	
Frequency: frequent	2	9	6	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From signing of informed consent form until 90 days post the last dose treatment (approximately 3 years)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups

Reporting group title	Carboplatin/Paclitaxel (Total)

Reporting group description:

Carboplatin/paclitaxel regimen (carboplatin area under the plasma concentration-time curve [AUC] of 6 milligram per milliliter into minute [mg/mL*min], and paclitaxel 200 milligram per square meter [mg/m^2]) administered as an intravenous (IV) infusion once every 21 days on Day 1, for a total of 6 doses (cycles) or until unacceptable toxicity, disease progression, or other reasons for participant withdrawal.

Reporting group title	Carboplatin/Paclitaxel + MEDI-575 (Total)

Reporting group description:

Carboplatin/paclitaxel regimen (carboplatin AUC = 6 mg/mL*min, and paclitaxel 200 mg/m^2) followed by MEDI-575 at a dose of 25 milligram per kilogram (mg/kg) administered as an IV infusion once every 21 days on Day 1 for a total of 6 cycles. Participants who achieved stable disease or better at the completion of carboplatin/paclitaxel therapy and did not demonstrate toxicity to MEDI-575, MEDI-575 alone was continued until unacceptable toxicity, disease progression, initiation of alternative anticancer therapy, or other reasons for participant withdrawal.

Serious adverse events	Carboplatin/Paclitaxel (Total)	Carboplatin/Paclitaxel + MEDI-575 (Total)	
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 43 (39.53%)	25 / 53 (47.17%)	
number of deaths (all causes)	23	35	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	1 / 43 (2.33%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung cancer metastatic			
subjects affected / exposed	1 / 43 (2.33%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm malignant			

subjects affected / exposed	1 / 43 (2.33%)	2 / 53 (3.77%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-small cell lung cancer			
subjects affected / exposed	3 / 43 (6.98%)	2 / 53 (3.77%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 43 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	0 / 43 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 43 (2.33%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	0 / 43 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Bronchopleural fistula			
subjects affected / exposed	1 / 43 (2.33%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			

subjects affected / exposed	1 / 43 (2.33%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	1 / 43 (2.33%)	2 / 53 (3.77%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary cavitation			
subjects affected / exposed	0 / 43 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary haemorrhage			
subjects affected / exposed	0 / 43 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory distress			
subjects affected / exposed	1 / 43 (2.33%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 43 (0.00%)	2 / 53 (3.77%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental status changes			
subjects affected / exposed	1 / 43 (2.33%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 43 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Femur fracture			
subjects affected / exposed	0 / 43 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infusion related reaction			
subjects affected / exposed	0 / 43 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 43 (2.33%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	0 / 43 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	1 / 43 (2.33%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia			
subjects affected / exposed	0 / 43 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Convulsion			
subjects affected / exposed	1 / 43 (2.33%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Somnolence			
subjects affected / exposed	0 / 43 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Syncope			
subjects affected / exposed	0 / 43 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	0 / 43 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 43 (2.33%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	3 / 43 (6.98%)	4 / 53 (7.55%)	
occurrences causally related to treatment / all	0 / 3	2 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	1 / 43 (2.33%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 43 (2.33%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	1 / 43 (2.33%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	1 / 43 (2.33%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 43 (0.00%)	2 / 53 (3.77%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine perforation			
subjects affected / exposed	0 / 43 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	1 / 43 (2.33%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	0 / 43 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 43 (2.33%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	1 / 43 (2.33%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Muscular weakness			
subjects affected / exposed	0 / 43 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abscess limb			

subjects affected / exposed	1 / 43 (2.33%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal abscess			
subjects affected / exposed	0 / 43 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	1 / 43 (2.33%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	0 / 43 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	0 / 43 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 43 (2.33%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infectious pleural effusion			
subjects affected / exposed	1 / 43 (2.33%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lobar pneumonia			
subjects affected / exposed	0 / 43 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericolic abscess			

subjects affected / exposed	0 / 43 (0.00%)	2 / 53 (3.77%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	3 / 43 (6.98%)	3 / 53 (5.66%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pyelonephritis			
subjects affected / exposed	0 / 43 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 43 (2.33%)	2 / 53 (3.77%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Urinary tract infection			
subjects affected / exposed	0 / 43 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 43 (2.33%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	1 / 43 (2.33%)	4 / 53 (7.55%)	
occurrences causally related to treatment / all	0 / 1	2 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electrolyte imbalance			
subjects affected / exposed	1 / 43 (2.33%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Failure to thrive			

subjects affected / exposed	0 / 43 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Carboplatin/Paclitaxel (Total)	Carboplatin/Paclitaxel + MEDI-575 (Total)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	41 / 43 (95.35%)	53 / 53 (100.00%)	
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 43 (2.33%)	7 / 53 (13.21%)	
occurrences (all)	1	7	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 43 (2.33%)	10 / 53 (18.87%)	
occurrences (all)	4	15	
Fatigue			
subjects affected / exposed	23 / 43 (53.49%)	31 / 53 (58.49%)	
occurrences (all)	35	54	
Mucosal inflammation			
subjects affected / exposed	1 / 43 (2.33%)	4 / 53 (7.55%)	
occurrences (all)	1	4	
Non-cardiac chest pain			
subjects affected / exposed	3 / 43 (6.98%)	2 / 53 (3.77%)	
occurrences (all)	3	2	
Oedema peripheral			
subjects affected / exposed	0 / 43 (0.00%)	10 / 53 (18.87%)	
occurrences (all)	0	12	
Pain			
subjects affected / exposed	3 / 43 (6.98%)	4 / 53 (7.55%)	
occurrences (all)	3	4	
Pyrexia			
subjects affected / exposed	4 / 43 (9.30%)	7 / 53 (13.21%)	
occurrences (all)	4	12	

Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	6 / 43 (13.95%)	10 / 53 (18.87%)	
occurrences (all)	6	10	
Dyspnoea			
subjects affected / exposed	6 / 43 (13.95%)	11 / 53 (20.75%)	
occurrences (all)	6	18	
Haemoptysis			
subjects affected / exposed	1 / 43 (2.33%)	5 / 53 (9.43%)	
occurrences (all)	1	6	
Hiccups			
subjects affected / exposed	3 / 43 (6.98%)	5 / 53 (9.43%)	
occurrences (all)	3	7	
Productive cough			
subjects affected / exposed	4 / 43 (9.30%)	3 / 53 (5.66%)	
occurrences (all)	6	5	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	2 / 43 (4.65%)	5 / 53 (9.43%)	
occurrences (all)	2	6	
Confusional state			
subjects affected / exposed	1 / 43 (2.33%)	6 / 53 (11.32%)	
occurrences (all)	1	10	
Insomnia			
subjects affected / exposed	3 / 43 (6.98%)	9 / 53 (16.98%)	
occurrences (all)	3	10	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 43 (4.65%)	5 / 53 (9.43%)	
occurrences (all)	3	6	
Aspartate aminotransferase increased			
subjects affected / exposed	3 / 43 (6.98%)	4 / 53 (7.55%)	
occurrences (all)	3	9	
Haemoglobin decreased			
subjects affected / exposed	1 / 43 (2.33%)	5 / 53 (9.43%)	
occurrences (all)	1	5	

Neutrophil count decreased			
subjects affected / exposed	5 / 43 (11.63%)	14 / 53 (26.42%)	
occurrences (all)	6	29	
Platelet count decreased			
subjects affected / exposed	5 / 43 (11.63%)	9 / 53 (16.98%)	
occurrences (all)	13	22	
Weight decreased			
subjects affected / exposed	3 / 43 (6.98%)	14 / 53 (26.42%)	
occurrences (all)	3	17	
White blood cell count decreased			
subjects affected / exposed	4 / 43 (9.30%)	10 / 53 (18.87%)	
occurrences (all)	5	23	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 43 (2.33%)	8 / 53 (15.09%)	
occurrences (all)	1	8	
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 43 (6.98%)	6 / 53 (11.32%)	
occurrences (all)	4	7	
Dysgeusia			
subjects affected / exposed	1 / 43 (2.33%)	12 / 53 (22.64%)	
occurrences (all)	1	12	
Headache			
subjects affected / exposed	4 / 43 (9.30%)	7 / 53 (13.21%)	
occurrences (all)	4	9	
Neuropathy peripheral			
subjects affected / exposed	11 / 43 (25.58%)	18 / 53 (33.96%)	
occurrences (all)	16	44	
Paraesthesia			
subjects affected / exposed	1 / 43 (2.33%)	5 / 53 (9.43%)	
occurrences (all)	1	6	
Peripheral sensory neuropathy			
subjects affected / exposed	13 / 43 (30.23%)	14 / 53 (26.42%)	
occurrences (all)	21	24	
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	14 / 43 (32.56%)	24 / 53 (45.28%)	
occurrences (all)	28	73	
Leukopenia			
subjects affected / exposed	2 / 43 (4.65%)	6 / 53 (11.32%)	
occurrences (all)	6	23	
Neutropenia			
subjects affected / exposed	6 / 43 (13.95%)	12 / 53 (22.64%)	
occurrences (all)	9	37	
Thrombocytopenia			
subjects affected / exposed	3 / 43 (6.98%)	10 / 53 (18.87%)	
occurrences (all)	3	46	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 43 (4.65%)	10 / 53 (18.87%)	
occurrences (all)	2	12	
Constipation			
subjects affected / exposed	13 / 43 (30.23%)	13 / 53 (24.53%)	
occurrences (all)	16	16	
Diarrhoea			
subjects affected / exposed	8 / 43 (18.60%)	24 / 53 (45.28%)	
occurrences (all)	11	49	
Dyspepsia			
subjects affected / exposed	4 / 43 (9.30%)	7 / 53 (13.21%)	
occurrences (all)	4	7	
Nausea			
subjects affected / exposed	22 / 43 (51.16%)	27 / 53 (50.94%)	
occurrences (all)	30	41	
Stomatitis			
subjects affected / exposed	3 / 43 (6.98%)	3 / 53 (5.66%)	
occurrences (all)	5	4	
Vomiting			
subjects affected / exposed	8 / 43 (18.60%)	14 / 53 (26.42%)	
occurrences (all)	11	18	
Skin and subcutaneous tissue disorders			

Alopecia			
subjects affected / exposed	21 / 43 (48.84%)	29 / 53 (54.72%)	
occurrences (all)	27	38	
Rash			
subjects affected / exposed	4 / 43 (9.30%)	5 / 53 (9.43%)	
occurrences (all)	4	5	
Rash maculo-papular			
subjects affected / exposed	2 / 43 (4.65%)	3 / 53 (5.66%)	
occurrences (all)	2	4	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 43 (4.65%)	11 / 53 (20.75%)	
occurrences (all)	2	18	
Arthralgia			
subjects affected / exposed	13 / 43 (30.23%)	22 / 53 (41.51%)	
occurrences (all)	22	35	
Bone pain			
subjects affected / exposed	4 / 43 (9.30%)	3 / 53 (5.66%)	
occurrences (all)	4	5	
Musculoskeletal chest pain			
subjects affected / exposed	3 / 43 (6.98%)	2 / 53 (3.77%)	
occurrences (all)	3	2	
Myalgia			
subjects affected / exposed	14 / 43 (32.56%)	17 / 53 (32.08%)	
occurrences (all)	25	33	
Pain in extremity			
subjects affected / exposed	6 / 43 (13.95%)	8 / 53 (15.09%)	
occurrences (all)	6	8	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	9 / 43 (20.93%)	4 / 53 (7.55%)	
occurrences (all)	11	5	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	11 / 43 (25.58%)	27 / 53 (50.94%)	
occurrences (all)	22	50	

Dehydration			
subjects affected / exposed	6 / 43 (13.95%)	7 / 53 (13.21%)	
occurrences (all)	7	10	
Hyperglycaemia			
subjects affected / exposed	5 / 43 (11.63%)	7 / 53 (13.21%)	
occurrences (all)	7	12	
Hypoalbuminaemia			
subjects affected / exposed	3 / 43 (6.98%)	7 / 53 (13.21%)	
occurrences (all)	4	9	
Hypocalcaemia			
subjects affected / exposed	3 / 43 (6.98%)	6 / 53 (11.32%)	
occurrences (all)	4	9	
Hypokalaemia			
subjects affected / exposed	8 / 43 (18.60%)	12 / 53 (22.64%)	
occurrences (all)	9	19	
Hypomagnesaemia			
subjects affected / exposed	10 / 43 (23.26%)	20 / 53 (37.74%)	
occurrences (all)	14	42	
Hyponatraemia			
subjects affected / exposed	4 / 43 (9.30%)	8 / 53 (15.09%)	
occurrences (all)	4	11	
Hypophosphataemia			
subjects affected / exposed	2 / 43 (4.65%)	4 / 53 (7.55%)	
occurrences (all)	2	4	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 December 2010	The protocol was amended for the modification of sample size and defining cohorts, participating sites were increased in Japanese sites, randomization criteria in North America/EU cohort and Japanese cohort were defined, clarification was provided for a cap on squamous cell histology and if subject experiences dose-limiting toxicity (DLT) due to MEDI-575 in the first 21-day cycle were provided, safety reporting procedures in Japan were added, inclusion and exclusion criteria were revised, information regarding the potential for a drug-drug interaction with CYP2C8 and CYP3A4 inhibitors and inducers (per the approved labeling for paclitaxel) was added, , updated population analysis definitions, clarifications for the administration of carboplatin/paclitaxel and MEDI-575 and analyses methods for objective response rate (ORR) and change in tumor size were included and confirmed that primary endpoint of progression-free survival (PFS) would only be in the North America/EU cohort.
10 February 2012	The protocol was amended for the modification of inclusion and withdrawal criteria, treatment administration, storage, and handling details were added, Preparation of Investigational Product at the site was updated (once prepared, MEDI-575 had to be used within 6 hours or discarded as it does not contain a preservative), Safety follow-up post last dose was increased from 60 to 90 days, and Data Safety Monitoring Board was added.
09 May 2012	The protocol was amended to remove primary endpoint of progression-free survival (PFS) as reference to a blinded central review of imaging data, NSCLC histology was removed as a stratification factor, MEDI-575 serum concentration and ADA assessments were removed from the 3-month post last treatment visit, Subgroup analysis for each NSCLC histology type was changed to be performed for each of the antitumor activity endpoints (PFS, ORR, DR, TTP, TTR, and OS) and Inclusion Criterion was revised.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
13 July 2012	Sponsor voluntarily suspended enrollment into this study based on safety issues observed across multiple studies in the MEDI-575 program and no suggestion of improved efficacy versus the control group in this specific study. MedImmune's Safety Monitoring Committee (SMC) recommended that the trial not be re-opened to enrollment. Subjects were continued to be followed until 04Sep2013 at which time the study was closed.	-

Notes:

Limitations and caveats

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

In conjunction with the overall risk-benefit assessment, study was terminated prematurely due to safety concerns. Change in tumor size outcome measure was not analyzed as per changed planned analysis due to premature termination of the study.

Notes: