Clinical trial results:
A Multinational, Randomized, Open-Label Phase III Study of Custirsen (TV-1011/OGX-011) In Combination With Docetaxel Versus Docetaxel As A Second-Line Treatment In Patients With Advanced or Metastatic (Stage IV) Non-Small Cell Lung Cancer

Summary

EudraCT number	2012-002447-14
Trial protocol	HU ES DE IT PL
Global end of trial date	17 November 2016

Results information

Result version number	v1 (current)
This version publication date	19 February 2017
First version publication date	19 February 2017

Trial information

Trial identification

Sponsor protocol code	TV1011-LC-303

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01630733
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	OncoGenex Technologies Inc.
Sponsor organisation address	19820 North Creek Parkway, Suite 201, Bothell, Washington, United States, 98011
Public contact	Chief Medical Officer , OncoGenex Technologies Inc., 001 425-686-1500,
Scientific contact	Chief Medical Officer , OncoGenex Technologies Inc., 001 425-686-1500,

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	17 November 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 November 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to compare overall survival of subjects randomized to receiving custirsen in combination with docetaxel with subjects randomized to receive docetaxel alone.

Protection of trial subjects:

Each subject was provided an informed consent form that was reviewed and approved by the site's governing Institutional Review Board (IRB), Research Ethics Board (REB) or Ethics Committee (EC). The Principal Investigator (or designee) provided potential subjects with a verbal description of the study, including but not limited to, study purpose and study procedures, risks and benefits and answered all subject questions prior to signing the form.

Background therapy:

Docetaxel 75 mg/m2 was administered as a 1 hr constant rate infusion on Day 1 of each 21-day treatment cycle

Evidence for comparator: -

Actual start date of recruitment	24 October 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 27
Country: Number of subjects enrolled	Germany: 43
Country: Number of subjects enrolled	Hungary: 57
Country: Number of subjects enrolled	Taiwan: 8
Country: Number of subjects enrolled	Thailand: 34
Country: Number of subjects enrolled	Ukraine: 118
Country: Number of subjects enrolled	United States: 69
Country: Number of subjects enrolled	Israel: 8
Country: Number of subjects enrolled	Italy: 58
Country: Number of subjects enrolled	Korea, Republic of: 20
Country: Number of subjects enrolled	New Zealand: 5
Country: Number of subjects enrolled	Poland: 77
Country: Number of subjects enrolled	Russian Federation: 77
Country: Number of subjects enrolled	Spain: 63
Worldwide total number of subjects	664
EEA total number of subjects	298

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)	377
From 65 to 84 years	285
85 years and over	2

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Screening evaluations occurred in a period of up to 28 days (+3 days) from the first screening evaluation to randomization.

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	Docetaxel

Arm description:

Docetaxel: 75 mg/m^2 intravenously (IV) over 1 hour on Day 1 of every 21-day cycle.

Treatment continued until disease progression, unacceptable toxicity, withdrawal of consent, or protocol-specified parameters to stop.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Custirsen + Docetaxel

Arm description:

Custirsen: Three loading doses of custirsen 640 mg IV over 2 hours administered in 5 to 9 days prior to Day 1 of Cycle 1, then custirsen 640 mg IV weekly every 21-day cycle. Docetaxel: 75 mg/m^2 IV over 1 hour on Day 1 of every 21-day cycle.

Treatment continued until disease progression, unacceptable toxicity, withdrawal of consent, or protocol-specified parameters to stop.

Arm type	Experimental
Investigational medicinal product name	Custirsen 20mg/ml concentrate for solution for infusion
Investigational medicinal product code	OGX-011/TV-1011
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Custirsen was added to 250 mL D5W or 0.9% normal saline solution. The dose was administered using either aperipheral or central indwelling catheter IV as an infusion over 2 hours.

Number of subjects in period 1	Docetaxel	Custirsen + Docetaxel
Started	332	332
Started	325	332
Entered Chemotherapy Period	325	320
Entered Off Treatment Follow-up	50 [1]	49 [2]

Entered Survival Follow-Up	222 [3]	234 [4]
Completed	229	237
Not completed	103	95
Consent withdrawn by subject	9	10
Not Specified	3	2
Study Terminated by Sponsor	85	80
Lost to follow-up	6	3

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Milestones represent the flow of subjects through the study.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Milestones represent the flow of subjects through the study.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Milestones represent the flow of subjects through the study.

[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Milestones represent the flow of subjects through the study.

Baseline characteristics

Reporting groups	
Reporting group title	Docetaxel

Reporting group description:

Docetaxel: 75 mg/m^2 intravenously (IV) over 1 hour on Day 1 of every 21-day cycle.

Treatment continued until disease progression, unacceptable toxicity, withdrawal of consent, or protocol-specified parameters to stop.

Reporting group title	Custirsen + Docetaxel

Reporting group description:

Custirsen: Three loading doses of custirsen 640 mg IV over 2 hours administered in 5 to 9 days prior to Day 1 of Cycle 1, then custirsen 640 mg IV weekly every 21-day cycle. Docetaxel: 75 mg/m^2 IV over 1 hour on Day 1 of every 21-day cycle.

Treatment continued until disease progression, unacceptable toxicity, withdrawal of consent, or protocol-specified parameters to stop.

Reporting group values	Docetaxel	Custirsen + Docetaxel	Total
Number of subjects	332	332	664
Age categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	63.1	62.2	
standard deviation	± 8.4	± 9.3	-
Gender categorical Units: Subjects			
Female	103	100	203
Male	229	232	461
Sex: Female, Male Units: Subjects			
Female	103	100	203
Male	229	232	461

End points

End points reporting groups

Reporting group title	Docetaxel

Reporting group description:

Docetaxel: 75 mg/m^2 intravenously (IV) over 1 hour on Day 1 of every 21-day cycle.

Treatment continued until disease progression, unacceptable toxicity, withdrawal of consent, or protocol-specified parameters to stop.

Reporting group title	Custirsen + Docetaxel

Reporting group description:

Custirsen: Three loading doses of custirsen 640 mg IV over 2 hours administered in 5 to 9 days prior to Day 1 of Cycle 1, then custirsen 640 mg IV weekly every 21-day cycle. Docetaxel: 75 mg/m^2 IV over 1 hour on Day 1 of every 21-day cycle.

Treatment continued until disease progression, unacceptable toxicity, withdrawal of consent, or protocol-specified parameters to stop.

Primary: Overall Survival: All Randomized Population

End point title	Overall Survival: All Randomized Population

End point description:

Overall survival time is defined as the number of days from the date of randomization until the date of death from any cause. Participants who did not achieve the event (death) at the time of the analysis or who dropped out before completing the survival follow-up period will be censored at the date they were last known to be alive (i.e., right censored). Partial or missing dates of death or last contact were imputed.

End point type	Primary

End point timeframe:

From randomization to death or last known date alive (up to 1269 days for Docetaxel arm and up to 1271 days for Docetaxel + Custirsen arm)

End point values	Docetaxel	Custirsen + Docetaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	332	332		
Units: days				
median (confidence interval 95%)	239 (197 to 276)	275 (219 to 329)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analyses control for stratification variables: Gender, Histology (Squamous, Non-Squamous), Best Overall Response to 1st-line platinum treatment, and Eastern Cooperative Oncology Group (ECOG) score.

Comparison groups	Docetaxel v Custirsen + Docetaxel

Number of subjects included in analysis	664
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.178
Method	one-sided Score test
Parameter estimate	Hazard ratio (HR)
Point estimate	0.915
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.758
upper limit	1.105

Primary: Overall Survival: Stratified by Histology - Squamous vs. Non-Squamous Tumor Histology

End point title	Overall Survival: Stratified by Histology - Squamous vs. Non-Squamous Tumor Histology

End point description:

Overall survival time is defined as the number of days from the date of randomization until the date of death from any cause. Participants who did not achieve the event (death) at the time of the analysis or who dropped out before completing the survival follow-up period will be censored at the date they were last known to be alive (i.e., right censored). Partial or missing dates of death or last contact were imputed. Non-squamous histology includes: adenocarcinoma, large-cell carcinoma, carcinoid tumor, and other.

End point type	Primary

End point timeframe:

From randomization to death or last known date alive (up to 1331 days for Docetaxel arm and up to 1271 days for Docetaxel + Custirsen arm)

End point values	Docetaxel	Custirsen + Docetaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	332	332		
Units: days				
median (confidence interval 95%)				
Squamous	221 (162 to 267)	232 (202 to 318)		
Non-squamous	249 (198 to 357)	281 (229 to 368)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Squamous tumor histology. Analyses control for stratification variables: Gender, Histology (Squamous, Non-Squamous), Best Overall Response to 1st-line platinum treatment, and ECOG score.

Comparison groups	Docetaxel v Custirsen + Docetaxel

Number of subjects included in analysis	664
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.183
Method	one-sided Score test
Parameter estimate	Hazard ratio (HR)
Point estimate	0.876
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.656
upper limit	1.169

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Non-squamous tumor histology. Analyses control for stratification variables: Gender, Histology (Squamous, Non-Squamous), Best Overall Response to 1st-line platinum treatment, and ECOG score.	
Comparison groups	Docetaxel v Custirsen + Docetaxel
Number of subjects included in analysis	664
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.33
Method	one-sided Score test
Parameter estimate	Hazard ratio (HR)
Point estimate	0.946
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.737
upper limit	1.214

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose to last dose plus 30 days (31 to 941 days for docetaxel arm and 31 to 725 days for docetaxel + custirsen arm) until disease progression or death.

Adverse event reporting additional description:

Safety Analysis Set: Participants who received at least 1 dose of study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	12.1

Reporting groups

Reporting group title	Custirsen + Docetaxel

Reporting group description:

Custirsen: Three loading doses of custirsen 640 mg IV over 2 hours administered in 5 to 9 days prior to Day 1 of Cycle 1, then custirsen 640 mg IV weekly every 21-day cycle. Docetaxel: 75 mg/m^2 IV over 1 hour on Day 1 of every 21-day cycle.

Treatment continued until disease progression, unacceptable toxicity, withdrawal of consent, or protocol-specified parameters to stop.

Reporting group title	Docetaxel

Reporting group description:

Docetaxel: 75 mg/m^2 IV over 1 hour on Day 1 of every 21-day cycle.

Treatment continued until disease progression, unacceptable toxicity, withdrawal of consent, or protocol-specified parameters to stop.

Serious adverse events	Custirsen + Docetaxel	Docetaxel	
Total subjects affected by serious adverse events			
subjects affected / exposed	113 / 332 (34.04%)	97 / 325 (29.85%)	
number of deaths (all causes)	9	5	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to central nervous system			
subjects affected / exposed	3 / 332 (0.90%)	0 / 325 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Metastases to spine			
subjects affected / exposed	1 / 332 (0.30%)	0 / 325 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Tumour pain			
subjects affected / exposed	0 / 332 (0.00%)	1 / 325 (0.31%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	2 / 332 (0.60%)	1 / 325 (0.31%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	4 / 332 (1.20%)	0 / 325 (0.00%)	
occurrences causally related to treatment / all	1 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Superior vena cava syndrome			
subjects affected / exposed	1 / 332 (0.30%)	0 / 325 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	0 / 332 (0.00%)	1 / 325 (0.31%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Asthenia			
subjects affected / exposed	1 / 332 (0.30%)	1 / 325 (0.31%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	1 / 332 (0.30%)	0 / 325 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Fatigue			
subjects affected / exposed	4 / 332 (1.20%)	4 / 325 (1.23%)	
occurrences causally related to treatment / all	4 / 5	2 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	

General physical health deterioration			
subjects affected / exposed	4 / 332 (1.20%)	4 / 325 (1.23%)	
occurrences causally related to treatment / all	1 / 4	0 / 4	
deaths causally related to treatment / all	1 / 2	0 / 1	
Generalised oedema			
subjects affected / exposed	0 / 332 (0.00%)	1 / 325 (0.31%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multi-organ failure			
subjects affected / exposed	1 / 332 (0.30%)	0 / 325 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Influenza like illness			
subjects affected / exposed	1 / 332 (0.30%)	1 / 325 (0.31%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	0 / 332 (0.00%)	1 / 325 (0.31%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	1 / 332 (0.30%)	1 / 325 (0.31%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	7 / 332 (2.11%)	3 / 325 (0.92%)	
occurrences causally related to treatment / all	6 / 7	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden death			
subjects affected / exposed	1 / 332 (0.30%)	1 / 325 (0.31%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Systemic inflammatory response syndrome			

subjects affected / exposed	1 / 332 (0.30%)	0 / 325 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 332 (0.30%)	0 / 325 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Bronchial obstruction			
subjects affected / exposed	0 / 332 (0.00%)	1 / 325 (0.31%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory failure			
subjects affected / exposed	2 / 332 (0.60%)	1 / 325 (0.31%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Cough			
subjects affected / exposed	0 / 332 (0.00%)	1 / 325 (0.31%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	3 / 332 (0.90%)	1 / 325 (0.31%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	6 / 332 (1.81%)	13 / 325 (4.00%)	
occurrences causally related to treatment / all	0 / 8	2 / 14	
deaths causally related to treatment / all	0 / 0	0 / 1	
Epistaxis			
subjects affected / exposed	1 / 332 (0.30%)	0 / 325 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			

subjects affected / exposed	3 / 332 (0.90%)	3 / 325 (0.92%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			
subjects affected / exposed	0 / 332 (0.00%)	2 / 325 (0.62%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	4 / 332 (1.20%)	5 / 325 (1.54%)	
occurrences causally related to treatment / all	0 / 4	1 / 5	
deaths causally related to treatment / all	0 / 2	0 / 1	
Pneumonitis			
subjects affected / exposed	0 / 332 (0.00%)	1 / 325 (0.31%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	2 / 332 (0.60%)	1 / 325 (0.31%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Productive cough			
subjects affected / exposed	0 / 332 (0.00%)	1 / 325 (0.31%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	5 / 332 (1.51%)	1 / 325 (0.31%)	
occurrences causally related to treatment / all	2 / 5	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pulmonary haemorrhage			
subjects affected / exposed	1 / 332 (0.30%)	2 / 325 (0.62%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 2	
Pulmonary hypertension			

subjects affected / exposed	0 / 332 (0.00%)	1 / 325 (0.31%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pulmonary oedema			
subjects affected / exposed	0 / 332 (0.00%)	2 / 325 (0.62%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 2	
Respiratory distress			
subjects affected / exposed	2 / 332 (0.60%)	0 / 325 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	4 / 332 (1.20%)	4 / 325 (1.23%)	
occurrences causally related to treatment / all	1 / 4	2 / 5	
deaths causally related to treatment / all	0 / 1	0 / 3	
Psychiatric disorders			
Adjustment disorder			
subjects affected / exposed	1 / 332 (0.30%)	0 / 325 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Panic attack			
subjects affected / exposed	1 / 332 (0.30%)	0 / 325 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Influenza A virus test positive			
subjects affected / exposed	1 / 332 (0.30%)	0 / 325 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutrophil count decreased			
subjects affected / exposed	1 / 332 (0.30%)	0 / 325 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Platelet count decreased			

subjects affected / exposed	1 / 332 (0.30%)	0 / 325 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	1 / 332 (0.30%)	0 / 325 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury			
subjects affected / exposed	1 / 332 (0.30%)	0 / 325 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ilium fracture			
subjects affected / exposed	0 / 332 (0.00%)	1 / 325 (0.31%)	
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	1 / 332 (0.30%)	0 / 325 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Splenic rupture			
subjects affected / exposed	1 / 332 (0.30%)	0 / 325 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	1 / 332 (0.30%)	0 / 325 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	1 / 332 (0.30%)	0 / 325 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Atrial fibrillation			
subjects affected / exposed	1 / 332 (0.30%)	2 / 325 (0.62%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	0 / 332 (0.00%)	1 / 325 (0.31%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	0 / 332 (0.00%)	1 / 325 (0.31%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac failure			
subjects affected / exposed	2 / 332 (0.60%)	0 / 325 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure acute			
subjects affected / exposed	1 / 332 (0.30%)	1 / 325 (0.31%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Cardiac failure congestive			
subjects affected / exposed	1 / 332 (0.30%)	0 / 325 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac tamponade			
subjects affected / exposed	0 / 332 (0.00%)	1 / 325 (0.31%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiomyopathy			
subjects affected / exposed	0 / 332 (0.00%)	1 / 325 (0.31%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			

subjects affected / exposed	1 / 332 (0.30%)	0 / 325 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	1 / 332 (0.30%)	2 / 325 (0.62%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stress cardiomyopathy			
subjects affected / exposed	0 / 332 (0.00%)	1 / 325 (0.31%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	0 / 332 (0.00%)	1 / 325 (0.31%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Aphasia			
subjects affected / exposed	1 / 332 (0.30%)	0 / 325 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Altered state of consciousness			
subjects affected / exposed	1 / 332 (0.30%)	0 / 325 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Convulsion			
subjects affected / exposed	3 / 332 (0.90%)	0 / 325 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Dizziness			
subjects affected / exposed	0 / 332 (0.00%)	1 / 325 (0.31%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalopathy			

subjects affected / exposed	1 / 332 (0.30%)	0 / 325 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	1 / 332 (0.30%)	1 / 325 (0.31%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiparesis			
subjects affected / exposed	1 / 332 (0.30%)	0 / 325 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	3 / 332 (0.90%)	0 / 325 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Agranulocytosis			
subjects affected / exposed	1 / 332 (0.30%)	0 / 325 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia			
subjects affected / exposed	6 / 332 (1.81%)	3 / 325 (0.92%)	
occurrences causally related to treatment / all	6 / 7	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	13 / 332 (3.92%)	16 / 325 (4.92%)	
occurrences causally related to treatment / all	15 / 15	16 / 16	
deaths causally related to treatment / all	0 / 0	2 / 2	
Leukopenia			
subjects affected / exposed	1 / 332 (0.30%)	1 / 325 (0.31%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			

subjects affected / exposed	16 / 332 (4.82%)	2 / 325 (0.62%)	
occurrences causally related to treatment / all	21 / 21	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	0 / 332 (0.00%)	1 / 325 (0.31%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Thrombotic thrombocytopenic purpura			
subjects affected / exposed	1 / 332 (0.30%)	0 / 325 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 332 (0.60%)	3 / 325 (0.92%)	
occurrences causally related to treatment / all	2 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal haemorrhage			
subjects affected / exposed	0 / 332 (0.00%)	1 / 325 (0.31%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	1 / 332 (0.30%)	0 / 325 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	0 / 332 (0.00%)	1 / 325 (0.31%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	12 / 332 (3.61%)	3 / 325 (0.92%)	
occurrences causally related to treatment / all	12 / 12	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			

subjects affected / exposed	1 / 332 (0.30%)	0 / 325 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal inflammation			
subjects affected / exposed	0 / 332 (0.00%)	1 / 325 (0.31%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematemesis			
subjects affected / exposed	1 / 332 (0.30%)	0 / 325 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	0 / 332 (0.00%)	1 / 325 (0.31%)	
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 / 332 (0.30%)	1 / 325 (0.31%)	
occurrences causally related to treatment / all	3 / 3	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis			
subjects affected / exposed	1 / 332 (0.30%)	1 / 325 (0.31%)	
occurrences causally related to treatment / all	1 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal perforation			
subjects affected / exposed	0 / 332 (0.00%)	1 / 325 (0.31%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stomatitis			
subjects affected / exposed	2 / 332 (0.60%)	2 / 325 (0.62%)	
occurrences causally related to treatment / all	2 / 2	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			

subjects affected / exposed	3 / 332 (0.90%)	1 / 325 (0.31%)	
occurrences causally related to treatment / all	2 / 3	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Acute hepatic failure			
subjects affected / exposed	0 / 332 (0.00%)	1 / 325 (0.31%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Skin and subcutaneous tissue disorders			
Cutaneous vasculitis			
subjects affected / exposed	1 / 332 (0.30%)	0 / 325 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	1 / 332 (0.30%)	1 / 325 (0.31%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure acute			
subjects affected / exposed	0 / 332 (0.00%)	1 / 325 (0.31%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 332 (0.30%)	0 / 325 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	2 / 332 (0.60%)	0 / 325 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscular weakness			

subjects affected / exposed	0 / 332 (0.00%)	2 / 325 (0.62%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal pain			
subjects affected / exposed	1 / 332 (0.30%)	0 / 325 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bronchopneumonia			
subjects affected / exposed	0 / 332 (0.00%)	1 / 325 (0.31%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	0 / 332 (0.00%)	3 / 325 (0.92%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	1 / 332 (0.30%)	0 / 325 (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	1 / 332 (0.30%)	0 / 325 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis infectious			
subjects affected / exposed	1 / 332 (0.30%)	0 / 325 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	1 / 332 (0.30%)	0 / 325 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile infection			

subjects affected / exposed	2 / 332 (0.60%)	0 / 325 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	2 / 332 (0.60%)	0 / 325 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	1 / 332 (0.30%)	1 / 325 (0.31%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection bacterial			
subjects affected / exposed	1 / 332 (0.30%)	0 / 325 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection			
subjects affected / exposed	3 / 332 (0.90%)	1 / 325 (0.31%)	
occurrences causally related to treatment / all	1 / 3	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Neutropenic sepsis			
subjects affected / exposed	2 / 332 (0.60%)	0 / 325 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral infection			
subjects affected / exposed	0 / 332 (0.00%)	1 / 325 (0.31%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	0 / 332 (0.00%)	1 / 325 (0.31%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumocystis jiroveci pneumonia			

subjects affected / exposed	0 / 332 (0.00%)	1 / 325 (0.31%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatitis Escherichia coli			
subjects affected / exposed	0 / 332 (0.00%)	1 / 325 (0.31%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	9 / 332 (2.71%)	17 / 325 (5.23%)	
occurrences causally related to treatment / all	8 / 11	8 / 19	
deaths causally related to treatment / all	3 / 3	1 / 5	
Pyelonephritis			
subjects affected / exposed	1 / 332 (0.30%)	0 / 325 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary sepsis			
subjects affected / exposed	0 / 332 (0.00%)	1 / 325 (0.31%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	3 / 332 (0.90%)	1 / 325 (0.31%)	
occurrences causally related to treatment / all	1 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	2 / 332 (0.60%)	3 / 325 (0.92%)	
occurrences causally related to treatment / all	2 / 2	1 / 3	
deaths causally related to treatment / all	1 / 1	0 / 1	
Septic shock			
subjects affected / exposed	4 / 332 (1.20%)	0 / 325 (0.00%)	
occurrences causally related to treatment / all	2 / 4	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Upper respiratory tract infection			

subjects affected / exposed	4 / 332 (1.20%)	2 / 325 (0.62%)	
occurrences causally related to treatment / all	4 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 332 (0.30%)	0 / 325 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 332 (0.60%)	1 / 325 (0.31%)	
occurrences causally related to treatment / all	2 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	3 / 332 (0.90%)	3 / 325 (0.92%)	
occurrences causally related to treatment / all	3 / 3	2 / 3	
deaths causally related to treatment / all	0 / 0	1 / 1	
Hypercalcaemia			
subjects affected / exposed	0 / 332 (0.00%)	2 / 325 (0.62%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	0 / 332 (0.00%)	1 / 325 (0.31%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoalbuminaemia			
subjects affected / exposed	0 / 332 (0.00%)	1 / 325 (0.31%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	1 / 332 (0.30%)	1 / 325 (0.31%)	
occurrences causally related to treatment / all	2 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			

subjects affected / exposed	2 / 332 (0.60%)	0 / 325 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Custirsen + Docetaxel	Docetaxel	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	312 / 332 (93.98%)	296 / 325 (91.08%)	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	18 / 332 (5.42%)	6 / 325 (1.85%)	
occurrences (all)	32	7	
Aspartate aminotransferase increased			
subjects affected / exposed	19 / 332 (5.72%)	4 / 325 (1.23%)	
occurrences (all)	30	4	
Blood creatinine increased			
subjects affected / exposed	20 / 332 (6.02%)	11 / 325 (3.38%)	
occurrences (all)	30	13	
Weight decreased			
subjects affected / exposed	31 / 332 (9.34%)	29 / 325 (8.92%)	
occurrences (all)	36	33	
Nervous system disorders			
Dizziness			
subjects affected / exposed	22 / 332 (6.63%)	17 / 325 (5.23%)	
occurrences (all)	25	19	
Dysgeusia			
subjects affected / exposed	19 / 332 (5.72%)	19 / 325 (5.85%)	
occurrences (all)	20	20	
Headache			
subjects affected / exposed	29 / 332 (8.73%)	27 / 325 (8.31%)	
occurrences (all)	39	31	
Peripheral sensory neuropathy			
subjects affected / exposed	22 / 332 (6.63%)	17 / 325 (5.23%)	
occurrences (all)	33	18	

Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	87 / 332 (26.20%)	66 / 325 (20.31%)	
occurrences (all)	148	100	
Leukopenia			
subjects affected / exposed	16 / 332 (4.82%)	17 / 325 (5.23%)	
occurrences (all)	22	24	
Neutropenia			
subjects affected / exposed	58 / 332 (17.47%)	39 / 325 (12.00%)	
occurrences (all)	103	68	
Thrombocytopenia			
subjects affected / exposed	22 / 332 (6.63%)	3 / 325 (0.92%)	
occurrences (all)	34	4	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	66 / 332 (19.88%)	62 / 325 (19.08%)	
occurrences (all)	154	110	
Chills			
subjects affected / exposed	31 / 332 (9.34%)	9 / 325 (2.77%)	
occurrences (all)	46	10	
Fatigue			
subjects affected / exposed	81 / 332 (24.40%)	83 / 325 (25.54%)	
occurrences (all)	165	152	
Non-cardiac chest pain			
subjects affected / exposed	18 / 332 (5.42%)	14 / 325 (4.31%)	
occurrences (all)	22	16	
Oedema peripheral			
subjects affected / exposed	30 / 332 (9.04%)	31 / 325 (9.54%)	
occurrences (all)	40	48	
Pyrexia			
subjects affected / exposed	110 / 332 (33.13%)	38 / 325 (11.69%)	
occurrences (all)	172	53	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	19 / 332 (5.72%)	16 / 325 (4.92%)	
occurrences (all)	20	20	

Constipation			
subjects affected / exposed	39 / 332 (11.75%)	33 / 325 (10.15%)	
occurrences (all)	50	45	
Diarrhoea			
subjects affected / exposed	85 / 332 (25.60%)	74 / 325 (22.77%)	
occurrences (all)	136	117	
Nausea			
subjects affected / exposed	84 / 332 (25.30%)	70 / 325 (21.54%)	
occurrences (all)	139	98	
Stomatitis			
subjects affected / exposed	27 / 332 (8.13%)	22 / 325 (6.77%)	
occurrences (all)	37	40	
Vomiting			
subjects affected / exposed	47 / 332 (14.16%)	33 / 325 (10.15%)	
occurrences (all)	72	40	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	47 / 332 (14.16%)	46 / 325 (14.15%)	
occurrences (all)	53	50	
Dyspnoea			
subjects affected / exposed	56 / 332 (16.87%)	67 / 325 (20.62%)	
occurrences (all)	67	83	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	61 / 332 (18.37%)	72 / 325 (22.15%)	
occurrences (all)	65	84	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	15 / 332 (4.52%)	19 / 325 (5.85%)	
occurrences (all)	17	20	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	24 / 332 (7.23%)	16 / 325 (4.92%)	
occurrences (all)	34	22	
Back pain			

subjects affected / exposed	24 / 332 (7.23%)	19 / 325 (5.85%)	
occurrences (all)	32	25	
Bone pain			
subjects affected / exposed	7 / 332 (2.11%)	17 / 325 (5.23%)	
occurrences (all)	7	17	
Muscular weakness			
subjects affected / exposed	15 / 332 (4.52%)	19 / 325 (5.85%)	
occurrences (all)	20	24	
Myalgia			
subjects affected / exposed	28 / 332 (8.43%)	23 / 325 (7.08%)	
occurrences (all)	51	34	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	83 / 332 (25.00%)	71 / 325 (21.85%)	
occurrences (all)	116	87	
Hypokalaemia			
subjects affected / exposed	18 / 332 (5.42%)	12 / 325 (3.69%)	
occurrences (all)	24	13	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 August 2012	• Clarified exclusion criteria number 10 stating exclusion of patients with known hypersensitivity to taxanes. • Added clarification that worsening of bone pain requiring palliative radiation therapy will be considered clinical disease progression. • Corrected the permissible time window for hematology and serum biochemistry assesments on day 1 of each cycle to be consistent with other sections of the protocol. • Changed the dose modification relating to hematology toxicity to state that custirsen will not be held or modified. • Corrected the pharmacokinetic sampling procedure.
12 March 2013	• Added new exclusion criterion stating that patients with known and documented epidermal growth factor (EGFR) mutation who have not received an EGFR inhibitor must be excluded. • Revised pregnancy precautions for men of reproductive potential to use precautionary instruction as outlined in the docetaxel summary of product characteristics. • Revised diluents acceptable for custirsen formulation to include either 0.9% normal saline or 0.9% D5W. • Changed sample type for pregnancy testing (beta-human chorionic gonadotropin) for female subjects of childbearing potential from urine to serum. • Clarified terms for relationship of an adverse event to study drug by adding (not related) to No reasonable possibility and adding (related) to Reasonable possibility.
16 March 2015	• Changed sponsorship of study from Teva Pharmaceutical Industries, Ltd. to OncoGenex Technologies Inc. • Clarified 3 week delay in treatment timing for patient withdrawal. • Clarified that radiation therapy specifically for lung cancer could be reason for patient withdrawal. • Clarified Day 1 of each cycle is tied the day of docetaxel administration. • Clarified that a subject should have an "End of Treatment" assessment if more than 42 days between docetaxel administrations. • Clarified that either docetaxel or custirsen should be modified or held based on hematology toxicity for dose modification guidelines as outlined in protocol. • Changed SGOT (AST) Grade 1 and Grade 2 levels for dose modifications for hepatic toxicity (Grade 1 changed from <2.5x upper limit of normal [ULN] to <3.0xULN and Grade 2 from >2.5xULN to >3.0xULN). • Clarified that study period for serious adverse event reporting is from the subject's signature on the informed consent form until the end of the treatment visit (28 days following last dose). • Changed parameters based on revision of the primary objective hypothesized HR from 0.8 to 0.75 as follows: 850 death events to 508 death events required, recruitment period of 4 years to 3.1 years and sample size target of 1100 to 700. • Added that OS analysis will include comparison by histology (squamous, non-squamous) between subjects receiving docetaxel with or without custirsen.
13 September 2016	• Decreased the number of subjects to be enrolled from 700 to approximately 660 and referenced the revised Statistical Analysis Plan (Version 3.1) which covered details related to patient enrollment and target of 447 death events for final analysis.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported