Clinical trial results:
A phase II study evaluating the efficacy and the safety of first-line chemotherapy combined with TG4010 and nivolumab in patients with advanced non-squamous Non-Small-Cell Lung Cancer (NSCLC)

Summary

EudraCT number	2016-005115-41
Trial protocol	BE HU DK
Global end of trial date	02 November 2020

Results information

Result version number	v1 (current)
This version publication date	11 November 2021
First version publication date	11 November 2021

Trial information

Trial identification

Sponsor protocol code	TG4010.24

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02823990
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Transgene S.A.
Sponsor organisation address	400 boulevard Gonthier d'Andernach - Parc d'innovation – CS80166, Illkirch-Graffenstaden, France, 67405
Public contact	Medical Affairs Secretariat, Transgene S.A., +33 388 27 91 55, clinical.trials@transgene.fr
Scientific contact	Medical Affairs Secretariat, Transgene S.A., +33 388 27 91 55, clinical.trials@transgene.fr

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	26 February 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 November 2019
Global end of trial reached?	Yes
Global end of trial date	02 November 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the anti-tumor activity in terms of objective response rate (ORR) by using RECIST 1.1 in chemotherapy-naïve and immunotherapy-naïve advanced, non-squamous NSCLC subjects with PD-L1 membrane staining on <50% of tumor cells receiving first-line chemotherapy (pemetrexed + carboplatin or cisplatin followed by pemetrexed maintenance therapy) plus TG4010 and nivolumab.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 January 2018
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: 6
Country: Number of subjects enrolled	Belgium: 6
Country: Number of subjects enrolled	France: 26
Country: Number of subjects enrolled	Hungary: 6
Worldwide total number of subjects	44
EEA total number of subjects	38

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)	28
From 65 to 84 years	16
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment was initiated on 05 January 2018 and ended on 02 May 2019.

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	44
Number of subjects completed	44

Period 1

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

Arms

Arm title	TG4010,Nivo,Chemo

Arm description: -

Arm type	Experimental
Investigational medicinal product name	TG4010
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Patients received subcutaneous injections of TG4010 at the dose of 1 x 10E8 PFU weekly for 6 weeks and then once every 3 weeks until disease progression or death or premature discontinuation due to any reason

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

Dosage and administration details:

Nivolumab was administered as an IV infusion over at least 30 minutes at a dose of 360 mg once every 3 weeks until disease progression or death or premature discontinuation due to any reason or for a maximum of 24 months whichever occurs first.

Number of subjects in period 1	TG4010,Nivo,Chemo
Started	44
Completed	40
Not completed	4
Adverse event, serious fatal	2
Adverse event, non-fatal	2

Baseline characteristics

Reporting groups

Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	44	44	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	28	28	
From 65-84 years	16	16	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	17	17	
Male	27	27	
ECOG Units: Subjects			
00	21	21	
01	23	23	
PD-L1 percentage of stained cells			
Method Dako PD-L1 IHC 22C3 pharmDx assay kit			
Units: Subjects			
<1	22	22	
1 - <50	22	22	
≥50	0	0	
Body Mass Index (BMI) Units: kg/m²			
median	24.4		
full range (min-max)	15 to 37	-	

Subject analysis sets

Subject analysis set title	Full analysis set (FAS)
Subject analysis set type	Full analysis

Subject analysis set description:

All subjects included and who received any component of the study treatment were included in the FAS. Any subject who was assigned a subject number but did not receive any study treatment was not included in the FAS.
To be noted that in the study, all included subjects (N=44) received at least one administration of each treatment, thus the FAS is the same as the Safety Analysis Set.

Subject analysis set title	Evaluable Patients' Population (EPP)
Subject analysis set type	Per protocol

Subject analysis set description:

Evaluable Patients’ Population for tumor response (EPP): consists of all subjects without major protocol deviation and have at least one baseline and one post-baseline evaluable CT-scan after study treatment start except early disease progression and death due to lung cancer. The evaluable patients’ population was the primary population for efficacy analyses.

Reporting group values	Full analysis set (FAS)	Evaluable Patients' Population (EPP)	
Number of subjects	44	40	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	28	26	
From 65-84 years	16	14	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	17	14	
Male	27	26	
ECOG Units: Subjects			
00	21	19	
01	23	21	
PD-L1 percentage of stained cells			
Method Dako PD-L1 IHC 22C3 pharmDx assay kit			
Units: Subjects			
<1	22	20	
1 - <50	22	20	
≥50	0	0	
Body Mass Index (BMI) Units: kg/m²			
median	24.4	24.6	
full range (min-max)	15 to 37	15 to 37	

End points

End points reporting groups

Reporting group title	TG4010,Nivo,Chemo
Reporting group description: -	
Subject analysis set title	Full analysis set (FAS)
Subject analysis set type	Full analysis

Subject analysis set description:

All subjects included and who received any component of the study treatment were included in the FAS. Any subject who was assigned a subject number but did not receive any study treatment was not included in the FAS.
To be noted that in the study, all included subjects (N=44) received at least one administration of each treatment, thus the FAS is the same as the Safety Analysis Set.

Subject analysis set title	Evaluable Patients' Population (EPP)
Subject analysis set type	Per protocol

Subject analysis set description:

Evaluable Patients' Population for tumor response (EPP): consists of all subjects without major protocol deviation and have at least one baseline and one post-baseline evaluable CT-scan after study treatment start except early disease progression and death due to lung cancer. The evaluable patients' population was the primary population for efficacy analyses.

Primary: Overall Response rate

End point title	Overall Response rate[1]

End point description:

Percentage of subjects whose best overall response is complete response or partial response using RECIST 1.1. confirmed by a second scan no less than 4 weeks after the criteria for response are first met.
Complete response: disappearance of all lesions and no new lesions.
Partial response: decrease of at least 30% in the sum of the diameters of measurable lesions taking as reference the baseline sum of diameters, no progression of non-measurable lesions and no new lesions.

End point type	Primary

End point timeframe:

15 months

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Single arm study: no comparative test was performed.

End point values	TG4010,Nivo,Chemo	Evaluable Patients' Population (EPP)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	40	40		
Units: Percentage				
number (confidence interval 90%)				
Responders	32.5 (20.4 to 46.6)	32.5 (20.4 to 46.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response

End point title	Duration of Response

End point description:

Duration of Response (DoR): applies only to subjects with complete response or partial response. The start date was the date of first documented response (complete response or partial response) and the end date was the date of first documented disease progression. If no progression has been observed at the cut-off date of analysis or at the date when a subsequent cancer therapy was started, duration of response was censored at the date of the last evaluable tumor assessment.

End point type	Secondary

End point timeframe:

28 months

End point values	TG4010,Nivo,Chemo	Evaluable Patients' Population (EPP)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	13	13		
Units: weeks				
median (inter-quartile range (Q1-Q3))	74.9 (19.4 to 92.6)	74.9 (19.4 to 92.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS)

End point description:

Progression Free Survival (PFS): time from the date of first study treatment administration to the date of first documented tumor progression or death due to any cause, whichever occurs first. If a subject has not had a PFS event at the cut-off date for analysis or at the date when a subsequent cancer therapy (other than those planned as study treatment in the protocol) is started, PFS will be censored at the date of last evaluable tumor assessment before the cut-off date or start of subsequent therapy.

End point type	Secondary

End point timeframe:

28 months

End point values	TG4010,Nivo,Chemo	Evaluable Patients' Population (EPP)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	40	40		
Units: months				

median (inter-quartile range (Q1-Q3))	5.7 (1.5 to 11.1)	5.7 (1.5 to 11.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Disease Control Rate (DCR)

End point title	Disease Control Rate (DCR)

End point description:

Percentage of subjects whose best overall response is either complete response, partial response or stable disease.

End point type	Secondary

End point timeframe:

15 months

End point values	TG4010,Nivo,Chemo	Evaluable Patients' Population (EPP)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	40	40		
Units: Percentage of subjects				
number (confidence interval 90%)	75.0 (61.3 to 85.8)	75.0 (61.3 to 85.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS) at 1 year

End point title	Overall Survival (OS) at 1 year

End point description:

Percentage of participants alive 1 year after treatment start. Analyzed with standard Kaplan-Meier methodology. A 12-month survival rate is calculated since the upper limit of 95% confidence interval for overall survival was not reached by the end of the study period.

End point type	Secondary

End point timeframe:

12 months

End point values	Evaluable Patients' Population (EPP)			
Subject group type	Subject analysis set			
Number of subjects analysed	40			
Units: Percentage of subjects				
number (confidence interval 95%)	57.5 (40.8 to 71.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Assessment of Safety

End point title	Assessment of Safety

End point description:

The assessment of safety of the combination was based mainly on the frequency of adverse events, serious adverse events, adverse events of special interest (Injection site reaction, fatigue, pyrexia, infusion-related reactions and diarrhea), immune-mediated adverse events and laboratories abnormalities.

End point type	Secondary

End point timeframe:

28 months

End point values	TG4010,Nivo,Chemo	Full analysis set (FAS)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	44	44		
Units: Percentage of subjects				
Adverse events	100	100		
Serious adverse events	64	64		
Adverse events of special interest	84	84		
Immune-mediated adverse events	32	32		
Grade 3/4 laboratories abnormalities	70	70		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Collection of AEs / serious AEs starts from the date of signature of the informed consent form up to the safety follow-up visits (100 days after the last administration of any study treatment administration). Timeframe was approximately 28 months.

Adverse event reporting additional description:

Any new untoward medical occurrence or worsening of a preexisting medical condition in a clinical investigation patient administered study treatment and that does not necessarily have a causal relationship with this treatment.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups

Reporting group title	TG4010, Nivo, Chemo

Reporting group description: -

Serious adverse events	TG4010, Nivo, Chemo		
Total subjects affected by serious adverse events			
subjects affected / exposed	28 / 44 (63.64%)		
number of deaths (all causes)	28		
number of deaths resulting from adverse events	15		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain	Additional description: Cancer pain		
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Deep vein thrombosis	Additional description: Deep vein thrombosis		
subjects affected / exposed	2 / 44 (4.55%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Condition aggravated	Additional description: Condition aggravated		
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Fatigue	Additional description: Fatigue		
subjects affected / exposed	2 / 44 (4.55%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
General physical health deterioration	Additional description: General physical health deterioration		
subjects affected / exposed	9 / 44 (20.45%)		
occurrences causally related to treatment / all	0 / 9		
deaths causally related to treatment / all	0 / 8		
Immune system disorders			
Anaphylactic reaction	Additional description: Anaphylactic reaction		
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Prostatitis	Additional description: Prostatitis		
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure	Additional description: Acute respiratory failure		
subjects affected / exposed	2 / 44 (4.55%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		
Dyspnoea	Additional description: Dyspnoea		
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism	Additional description: Pulmonary embolism		
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary haemorrhage	Additional description: Pulmonary haemorrhage		

subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory distress	Additional description: Respiratory distress		
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Investigations			
Blood creatinine increased	Additional description: Blood creatinine increased		
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cerebral infarction	Additional description: Cerebral infarction		
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cerebral ischaemia	Additional description: Cerebral ischaemia		
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Headache	Additional description: Headache		
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ischaemic stroke	Additional description: Ischaemic stroke		
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Loss of consciousness	Additional description: Loss of consciousness		
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neuropathy peripheral	Additional description: Neuropathy peripheral		

subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Transient ischaemic attack	Additional description: Transient ischaemic attack		
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Febrile neutropenia	Additional description: Febrile neutropenia		
subjects affected / exposed	2 / 44 (4.55%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia	Additional description: Thrombocytopenia		
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain	Additional description: Abdominal pain		
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Autoimmune colitis	Additional description: Autoimmune colitis		
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Colitis ulcerative	Additional description: Colitis ulcerative		
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Diarrhoea	Additional description: Diarrhoea		
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Duodenitis	Additional description: Duodenitis		

subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pancreatitis	Additional description: Pancreatitis		
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Vomiting	Additional description: Vomiting		
subjects affected / exposed	3 / 44 (6.82%)		
occurrences causally related to treatment / all	2 / 3		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholangitis acute	Additional description: Cholangitis acute		
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Rash	Additional description: Rash		
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury	Additional description: Acute kidney injury		
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Bartholinitis	Additional description: Bartholinitis		
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Brain abscess	Additional description: Brain abscess		

subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cellulitis	Additional description: Cellulitis		
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diverticulitis	Additional description: Diverticulitis		
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Febrile infection	Additional description: Febrile infection		
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia	Additional description: Pneumonia		
subjects affected / exposed	2 / 44 (4.55%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Septic shock	Additional description: Septic shock		
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Metabolism and nutrition disorders			
Dehydration	Additional description: Dehydration		
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypercalcaemia	Additional description: Hypercalcaemia		
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hyperglycaemia	Additional description: Hyperglycaemia		

subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	TG4010, Nivo, Chemo		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	43 / 44 (97.73%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain	Additional description: Cancer pain		
subjects affected / exposed	4 / 44 (9.09%)		
occurrences (all)	4		
Vascular disorders			
Flushing	Additional description: Flushing		
subjects affected / exposed	3 / 44 (6.82%)		
occurrences (all)	4		
General disorders and administration site conditions			
Asthenia	Additional description: Asthenia		
subjects affected / exposed	3 / 44 (6.82%)		
occurrences (all)	3		
Fatigue	Additional description: Fatigue		
subjects affected / exposed	29 / 44 (65.91%)		
occurrences (all)	39		
Injection site erythema	Additional description: Injection site erythema		
subjects affected / exposed	5 / 44 (11.36%)		
occurrences (all)	6		
Injection site pain	Additional description: Injection site pain		
subjects affected / exposed	5 / 44 (11.36%)		
occurrences (all)	5		
Injection site reaction	Additional description: Injection site reaction		
subjects affected / exposed	6 / 44 (13.64%)		
occurrences (all)	6		
Oedema peripheral	Additional description: Oedema peripheral		

subjects affected / exposed	9 / 44 (20.45%)		
occurrences (all)	11		
Pyrexia	Additional description: Pyrexia		
subjects affected / exposed	5 / 44 (11.36%)		
occurrences (all)	7		
Respiratory, thoracic and mediastinal disorders			
Cough	Additional description: Cough		
subjects affected / exposed	12 / 44 (27.27%)		
occurrences (all)	13		
Dyspnoea	Additional description: Dyspnoea		
subjects affected / exposed	13 / 44 (29.55%)		
occurrences (all)	14		
Epistaxis	Additional description: Epistaxis		
subjects affected / exposed	4 / 44 (9.09%)		
occurrences (all)	5		
Productive cough	Additional description: Productive cough		
subjects affected / exposed	3 / 44 (6.82%)		
occurrences (all)	3		
Investigations			
Alanine aminotransferase increased	Additional description: Alanine aminotransferase increased		
subjects affected / exposed	4 / 44 (9.09%)		
occurrences (all)	4		
Aspartate aminotransferase increased	Additional description: Aspartate aminotransferase increased		
subjects affected / exposed	5 / 44 (11.36%)		
occurrences (all)	5		
Blood creatinine increased	Additional description: Blood creatinine increased		
subjects affected / exposed	7 / 44 (15.91%)		
occurrences (all)	7		
Lipase increased	Additional description: Lipase increased		
subjects affected / exposed	3 / 44 (6.82%)		
occurrences (all)	3		
Weight decreased	Additional description: Weight decreased		
subjects affected / exposed	8 / 44 (18.18%)		
occurrences (all)	8		
Injury, poisoning and procedural complications			

Infusion related reaction	Additional description: Infusion related reaction		
subjects affected / exposed	3 / 44 (6.82%)		
occurrences (all)	3		
Nervous system disorders			
Dizziness	Additional description: Dizziness		
subjects affected / exposed	4 / 44 (9.09%)		
occurrences (all)	4		
Dysgeusia	Additional description: Dysgeusia		
subjects affected / exposed	8 / 44 (18.18%)		
occurrences (all)	8		
Headache	Additional description: Headache		
subjects affected / exposed	9 / 44 (20.45%)		
occurrences (all)	9		
Paraesthesia	Additional description: Paraesthesia		
subjects affected / exposed	8 / 44 (18.18%)		
occurrences (all)	8		
Blood and lymphatic system disorders			
Anaemia	Additional description: Anaemia		
subjects affected / exposed	24 / 44 (54.55%)		
occurrences (all)	43		
Leukopenia	Additional description: Leukopenia		
subjects affected / exposed	5 / 44 (11.36%)		
occurrences (all)	5		
Neutropenia	Additional description: Neutropenia		
subjects affected / exposed	14 / 44 (31.82%)		
occurrences (all)	21		
Thrombocytopenia	Additional description: Thrombocytopenia		
subjects affected / exposed	13 / 44 (29.55%)		
occurrences (all)	20		
Eye disorders			
Lacrimation increased	Additional description: Lacrimation increased		
subjects affected / exposed	3 / 44 (6.82%)		
occurrences (all)	3		
Gastrointestinal disorders			
Abdominal pain	Additional description: Abdominal pain		
subjects affected / exposed	4 / 44 (9.09%)		
occurrences (all)	5		

Constipation	Additional description: Constipation		
subjects affected / exposed	16 / 44 (36.36%)		
occurrences (all)	17		
Diarrhoea	Additional description: Diarrhoea		
subjects affected / exposed	17 / 44 (38.64%)		
occurrences (all)	23		
Dry mouth	Additional description: Dry mouth		
subjects affected / exposed	3 / 44 (6.82%)		
occurrences (all)	3		
Gastrooesophageal reflux disease	Additional description: Gastrooesophageal reflux disease		
subjects affected / exposed	3 / 44 (6.82%)		
occurrences (all)	3		
Nausea	Additional description: Nausea		
subjects affected / exposed	26 / 44 (59.09%)		
occurrences (all)	31		
Stomatitis	Additional description: Stomatitis		
subjects affected / exposed	7 / 44 (15.91%)		
occurrences (all)	8		
Vomiting	Additional description: Vomiting		
subjects affected / exposed	8 / 44 (18.18%)		
occurrences (all)	10		
Skin and subcutaneous tissue disorders			
Alopecia	Additional description: Alopecia		
subjects affected / exposed	3 / 44 (6.82%)		
occurrences (all)	3		
Dry skin	Additional description: Dry skin		
subjects affected / exposed	7 / 44 (15.91%)		
occurrences (all)	7		
Pruritus	Additional description: Pruritus		
subjects affected / exposed	4 / 44 (9.09%)		
occurrences (all)	4		
Rash	Additional description: Rash		
subjects affected / exposed	7 / 44 (15.91%)		
occurrences (all)	9		
Endocrine disorders			

Hypothyroidism	Additional description: Hypothyroidism		
subjects affected / exposed	4 / 44 (9.09%)		
occurrences (all)	4		
Musculoskeletal and connective tissue disorders			
Myalgia	Additional description: Myalgia		
subjects affected / exposed	6 / 44 (13.64%)		
occurrences (all)	6		
Pain in extremity	Additional description: Pain in extremity		
subjects affected / exposed	5 / 44 (11.36%)		
occurrences (all)	5		
Infections and infestations			
Conjunctivitis	Additional description: Conjunctivitis		
subjects affected / exposed	5 / 44 (11.36%)		
occurrences (all)	5		
Metabolism and nutrition disorders			
Decreased appetite	Additional description: Decreased appetite		
subjects affected / exposed	13 / 44 (29.55%)		
occurrences (all)	15		
Hypokalaemia	Additional description: Hypokalaemia		
subjects affected / exposed	9 / 44 (20.45%)		
occurrences (all)	13		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 April 2018	The amendment objective was to i) implement changes demanded by the French and Danish Health Authorities : modification of an inclusion criterion to specify that patients with stage IIIB must not be eligible to radiotherapy and of an exclusion criterion to exclude patients with stage IIIB eligible to radiotherapy, strengthen the monitoring of pulmonary and cardiac toxicity possibly associated with nivolumab and/or pemetrexed, align the protocol with SmPC for dose reduction in case of haematologic or non-haematologic toxicity with pemetrexed + cisplatin and treatment modifications of nivolumab, addition of uric acid measurement as part of biochemistry analyses for surveillance of tumor lysis syndrome, implement the highly effective contraceptive methods in accordance with CTFG recommendation, ii) implement new data available from the nivolumab investigator brochure.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported