



Clinical trial results:

Immunotherapy by Nivolumab after prior Chemotherapy for HIV+ patients with Advanced non-small cell lung cancer (NSCLC): IFCT-CHIVA2 phase IIa trial

Summary

EudraCT number	2016-003796-22
Trial protocol	FR
Global end of trial date	18 February 2021

Results information

Result version number	v1 (current)
This version publication date	22 October 2022
First version publication date	22 October 2022

Trial information

Trial identification

Sponsor protocol code	IFCT-1602
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03304093
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	IFCT
Sponsor organisation address	10 rue de la Grange-Batelière, Paris, France, 75009
Public contact	Contact, IFCT, 33 156811045, contact@ifct.fr
Scientific contact	Contact , IFCT, 33 156811045, contact@ifct.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	30 June 2020
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	18 February 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Efficacy of the anti-PD1 antibody (nivolumab) as measured by DCR.

Protection of trial subjects:

Algorithms for management of adverse events were provided in the protocol.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 December 2017
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	France: 16
Worldwide total number of subjects	16
EEA total number of subjects	16

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)	13
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Sixteen patients were enrolled between December 2017 and July 2019 in 7 centers.

Pre-assignment

Screening details:

Patients with combined (c)ART-controlled HIV-1 infection (VL <200 copies/mL), regardless of their CD4+ T-cell count, and histologically/cytologically proven NSCLC stage IIIB or IV at diagnosis or after relapse post-surgery were included. Patients had received at least one prior platinum-based doublet chemotherapy regimen

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	Nivolumab
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Arm description:

Nivolumab was administered intravenously over 30 minutes at 3 mg/kg every 2 weeks, until disease progression or limiting toxicity.

Arm type	Experimental
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 intravenously over 30 minutes at 3 mg/kg every 2 weeks, until disease progression or limiting toxicity.

Number of subjects in period 1	Nivolumab
Started	16
Completed	0
Not completed	16
Adverse event, serious fatal	4
Patient refusal	1
Adverse event, non-fatal	1
Lack of efficacy	10

Baseline characteristics

Reporting groups

Reporting group title	Overall trial (overall period)
Reporting group description: -	

Reporting group values	Overall trial (overall period)	Total	
Number of subjects	16	16	
Age categorical Units: Subjects			
Adults (18-64 years)	13	13	
From 65-84 years	3	3	
Age continuous Units: years			
median	58.4		
full range (min-max)	44.0 to 70.9	-	
Gender categorical Units: Subjects			
Female	2	2	
Male	14	14	
Smoking status Units: Subjects			
Yes	16	16	
No	0	0	
WHO performance status			
Measure Description: The WHO performance status (PS) classification categorizes patients as: 0: able to carry out all normal activity without restriction 1: restricted in strenuous activity but ambulatory and able to carry out light work 2 : ambulatory and capable of all self-care but unable to carry out any work activities; up and about more than 50% of waking hours 3: symptomatic and in a chair or in bed for greater than 50% of the day but not bedridden 4: completely disabled; cannot carry out any self-care; totally confined to bed or chair.			
Units: Subjects			
PS 0	5	5	
PS 1	7	7	
PS 2	4	4	
Histology Units: Subjects			
Adenocarcinoma	10	10	
Unspecified NSCLC	1	1	
Squamous cell carcinoma	5	5	
Stage Units: Subjects			
IIIB	1	1	
IVA	4	4	
IVB	11	11	
Cancer history Units: Subjects			
Yes, AIDS-related	1	1	
Yes, Non-AIDS-related	5	5	

No	10	10	
Infection history Units: Subjects			
Yes	11	11	
No	5	5	
Comorbidity Units: Subjects			
Yes	8	8	
No	7	7	
Unknown	1	1	
Significant pathology Units: Subjects			
Yes	10	10	
No	5	5	
Unknown	1	1	
EGFR baseline tumour mutation			
Measure Description: Genetic mutations were not tested in the patients with squamous cell carcinoma (n=5).			
Units: Subjects			
Yes	0	0	
No	9	9	
Not applicabe	5	5	
Not done	2	2	
KRAS baseline tumour mutation			
Measure Description: Genetic mutations were not tested in the patients with squamous cell carcinoma (n=5).			
Units: Subjects			
Yes	3	3	
No	7	7	
Not applicable	5	5	
Not done	1	1	
BRAF baseline tumour mutation			
Measure Description: Genetic mutations were not tested in the patients with squamous cell carcinoma (n=5).			
Units: Subjects			
Yes	1	1	
No	9	9	
Not applicable	5	5	
Not done	1	1	
HER2 baseline tumour mutation			
Measure Description: Genetic mutations were not tested in the patients with squamous cell carcinoma (n=5).			
Units: Subjects			
Yes	0	0	
No	6	6	
Not applicable	5	5	
Not done	5	5	
PI3KCA baseline tumour mutation			
Measure Description: Genetic mutations were not tested in the patients with squamous cell carcinoma (n=5).			
Units: Subjects			
Yes	0	0	

No	5	5	
Not determinated	1	1	
Not applicable	5	5	
Not done	5	5	
ALK baseline tumour mutation			
Measure Description: Genetic mutations were not tested in the patients with squamous cell carcinoma (n=5).			
Units: Subjects			
Yes	0	0	
No	11	11	
Not applicable	5	5	
ROS1 baseline tumour mutation			
Measure Description: Genetic mutations were not tested in the patients with squamous cell carcinoma (n=5).			
Units: Subjects			
Yes	0	0	
No	8	8	
Not determinated	1	1	
Not applicable	5	5	
Not done	2	2	
PD-L1			
Units: Subjects			
Less than 1%	9	9	
Between 1-49%	2	2	
50% or more	3	3	
Not available	2	2	
Smocking status			
Units: Pack Year			
median	40		
full range (min-max)	13 to 90	-	
Nadir CD4			
Units: mm3			
median	201.0		
full range (min-max)	32 to 534	-	
CD4 T cell count			
Units: mm3			
median	384.5		
full range (min-max)	187 to 778	-	
HIV viral load			
Units: copy/mL			
median	25		
full range (min-max)	0 to 44	-	

End points

End points reporting groups

Reporting group title	Nivolumab
Reporting group description:	
Nivolumab was administered intravenously over 30 minutes at 3 mg/kg every 2 weeks, until disease progression or limiting toxicity.	

Primary: Disease Control Rate

End point title	Disease Control Rate ^[1]
End point description:	
Patients who have achieved complete response (disappearance of all target lesions), partial response (at least a 30% decrease in the sum of diameters of target lesions since inclusion) and stable disease (between less than 30% decrease and less than 20% increase) as evaluated with Response Evaluation Criteria In Solid Tumors Criteria (RECIST v1.1).	
End point type	Primary
End point timeframe:	
8 weeks	
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: Not applicable as the study was single arm	

End point values	Nivolumab			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: % of participants				
number (confidence interval 95%)				
Disease control	62.5 (38.8 to 86.2)			
Progressive disease	31.3 (8.5 to 54.0)			
Not evaluable/Not done	6.3 (0.0 to 18.1)			

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 is defined as the time from the date of the first documented response (complete response (CR) or partial response (PR)) or disease stability (SD) to the earliest date of disease progression or death due to any cause. If a patient with a CR, PR or SD has neither progressed nor died at the time of the analysis cut-off, the patient will be censored at the date of last adequate tumour assessment.	
End point type	Secondary

End point timeframe:

Up to 1 year

End point values	Nivolumab			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: months				
median (full range (min-max))	3.52 (0.7 to 28.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Responses Rate According to Tissue PD-L1 Expression

End point title	Responses Rate According to Tissue PD-L1 Expression
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End point description:

End point type	Secondary
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End point timeframe:

8 weeks

End point values	Nivolumab			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: % of participants				
number (confidence interval 95%)				
PD-L1 positive - partial response	20.0 (0.0 to 55.1)			
PD-L1 positive - stable disease	80.0 (44.9 to 100.0)			
PD-L1 positive - progressive disease	0 (0 to 0)			
PD-L1 negative - partial response	11.1 (0.0 to 31.6)			
PD-L1 negative - stable disease	33.3 (2.5 to 64.1)			
PD-L1 negative - progressive disease	44.4 (12.0 to 76.9)			
PD-L1 negative - Not evaluable/Not done/missing	11.1 (0.0 to 31.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival

End point title	Progression Free Survival
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End point description:

Time between the date of inclusion and the first date of documented progression or death due to any cause, whichever occurs first. Subjects who die without a reported progression will be considered to have progressed on the date of their death.

Progression is defined using Response Evaluation Criteria In Solid Tumors Criteria(RECIST v1.1), as a 20% increase in the sum of the longest diameter of target lesions, taking as reference the smallest sum since inclusion or a unequivocal increase of a non-target lesion, or the appearance of new lesion(s).

End point type	Secondary
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End point timeframe:

Up to 1 year

End point values	Nivolumab			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: months				
median (confidence interval 95%)	3.4 (1.8 to 5.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

End point title	Overall Survival
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End point description:

Time elapsed between the date of inclusion and death. Subjects who did not die will be censored on the last date a subject was known to be alive.

End point type	Secondary
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End point timeframe:

Up to 1 year

End point values	Nivolumab			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: month				
median (confidence interval 95%)	10.9 (2.17 to 9999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Quality of Life Measured by LCSS Questionnaire

End point title	Quality of Life Measured by LCSS Questionnaire
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End point description:

Quality of life is assessed by Lung Cancer Symptom Scale (LCSS). Changes from baseline to the 9 items of the scale are classified into 3 categories: improvement (decrease of at least 1 point), deterioration (increase of at least 1 point) and stabilization.

End point type	Secondary
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End point timeframe:

After 2 cycles

End point values	Nivolumab			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: Participants				
Anorexia - improvement	2			
Anorexia - Stability	1			
Anorexia - Deterioration	8			
Fatigue - Improvement	0			
Fatigue - Stability	4			
Fatigue - Deterioration	7			
Cough - Improvement	4			
Cough - Stability	4			
Cough - Deterioration	3			
Dyspnea - Improvement	2			
Dyspnea - Stability	4			
Dyspnea - Deterioration	5			
Hemoptysis - Improvement	1			
Hemoptysis - Stability	10			
Hemoptysis - Deterioration	0			
Pain - Improvement	3			
Pain - Stability	4			
Pain - Deterioration	4			
Symptom distress - Improvement	5			
Symptom distress - Stability	2			
Symptom distress - Deterioration	4			
Activity level - Improvement	5			
Activity level - Stability	1			
Activity level - Deterioration	5			

Statistical analyses

No statistical analyses for this end point

Secondary: 6-month Overall Survival

End point title	6-month Overall Survival
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End point description:

End point type	Secondary
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End point timeframe:

6 months

End point values	Nivolumab			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: percent				
number (confidence interval 95%)	68.7 (40.5 to 85.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: 12-month survival rate

End point title	12-month survival rate
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End point description:

End point type	Secondary
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End point timeframe:

12 months

End point values	Nivolumab			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: percent				
number (confidence interval 95%)	48.1 (22.4 to 69.9)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected for a patient from the date of signature of inform consent form, during treatment period and until 100 days after the last dose of study treatment. Deaths were collected until data analysis.

Adverse event reporting additional description:

The maximal grade of adverse events was collected by cycle of treatment.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	21
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Reporting groups

Reporting group title	Safety population
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Reporting group description: -

Serious adverse events	Safety population		
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 16 (56.25%)		
number of deaths (all causes)	10		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant ascites			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Neoplasm progression			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Death			

subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
General physical health deterioration			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Pancreatitis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Haemoptysis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Hypoxia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Pemphigoid			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hypercalcaemia			

subjects affected / exposed	1 / 16 (6.25%)		
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	Safety population		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 16 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant ascites			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Neoplasm progression			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	4		
Pallor			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Peripheral coldness			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	10 / 16 (62.50%)		
occurrences (all)	46		
Chest pain			
subjects affected / exposed	4 / 16 (25.00%)		
occurrences (all)	10		
Pain			

subjects affected / exposed	3 / 16 (18.75%)		
occurrences (all)	3		
Fatigue			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Death			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Gait disturbance			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
General physical health deterioration			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Oedema peripheral			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Xerosis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Dyspnea			
subjects affected / exposed	8 / 16 (50.00%)		
occurrences (all)	17		
Cough			
subjects affected / exposed	6 / 16 (37.50%)		
occurrences (all)	15		
Haemoptysis			
subjects affected / exposed	3 / 16 (18.75%)		
occurrences (all)	4		
Productive cough			

subjects affected / exposed	3 / 16 (18.75%)		
occurrences (all)	4		
Chronic obstructive pulmonary disease			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Dysphonia			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	3		
Epistaxis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Hypoxia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Hyperhidrosis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Delirium			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Depression			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	3 / 16 (18.75%)		
occurrences (all)	8		
Weight decreased			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	4		
Blood alkaline phosphatase decreased			

subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Blood creatinine increased			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Breath sounds abnormal			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
CD4 lymphocytes decreased			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
CD8 lymphocytes increased			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Neutrophil count decreased			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Tlymphocyte count decreased			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Skin injury			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Cardiovascular insufficiency			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	2		
Tachycardia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Nervous system disorders			

Headache			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Paraesthesia			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	5		
Hypokinesia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Motor dysfunction			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Neuralgia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	4		
Sciatica			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	3		
Sensorimotor disorder			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	30		
Somnolence			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Tremor			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	4 / 16 (25.00%)		
occurrences (all)	18		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	8 / 16 (50.00%)		
occurrences (all)	11		
Constipation			

subjects affected / exposed	4 / 16 (25.00%)		
occurrences (all)	7		
Diarrhoea			
subjects affected / exposed	4 / 16 (25.00%)		
occurrences (all)	9		
Vomiting			
subjects affected / exposed	4 / 16 (25.00%)		
occurrences (all)	9		
Abdominal pain			
subjects affected / exposed	3 / 16 (18.75%)		
occurrences (all)	9		
Aphthous ulcer			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	6		
Ascites			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Dry mouth			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	2		
Pancreatitis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Rectal haemorrhage			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Stomatitis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	4 / 16 (25.00%)		
occurrences (all)	16		

Rash			
subjects affected / exposed	3 / 16 (18.75%)		
occurrences (all)	7		
Alopecia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	5		
Alopecia areata			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	2		
Madarosis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	2		
Onycholysis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	7		
Pemphigoid			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	12		
Skin exfoliation			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	3 / 16 (18.75%)		
occurrences (all)	3		
Hypothyroidism			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	20		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	5 / 16 (31.25%)		
occurrences (all)	15		
Back pain			
subjects affected / exposed	3 / 16 (18.75%)		
occurrences (all)	9		
Bone pain			

subjects affected / exposed	3 / 16 (18.75%)		
occurrences (all)	8		
Musculoskeletal chest pain			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	3		
Muscle spasms			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Myalgia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Pain in extremity			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	2		
Infections and infestations			
Folliculitis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	3 / 16 (18.75%)		
occurrences (all)	5		
Hypercalcaemia			
subjects affected / exposed	3 / 16 (18.75%)		
occurrences (all)	6		
Hyperkalaemia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Hypercreatinaemia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Hyperglycaemia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 February 2019	A substantial modification was done in order: - clarify which hospitalization were not to be reported as SAEs - increase inclusion duration

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
31 January 2020	Due to difficulties in recruiting patients with the rare HIV-NSCLC combination, the study independent data monitoring committee recommended that patient inclusion be stopped in January 2020.	-

Notes:

Limitations and caveats

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

Our study is limited by the small sample size, which was due to difficulties in recruiting patients with the rare HIV-NSCLC combination.

Notes:

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/34217967>