



Clinical trial results:

Phase II trial evaluating the efficacy and safety of carboplatin plus pemetrexed in Human Immunodeficiency Virus positive (HIV+) patients with stage III (not amenable to radiation or inoperable) or stage IV non-squamous Non Small Cell Lung Cancer

Summary

EudraCT number	2010-023676-48
Trial protocol	FR
Global end of trial date	03 July 2017

Results information

Result version number	v1 (current)
This version publication date	11 February 2023
First version publication date	11 February 2023

Trial information

Trial identification

Sponsor protocol code	IFCT-1001 CHIVA
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01296113
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 1.56.81.10.46, contact@ifct.fr
Scientific contact	Contact, IFCT, 33 1.56.81.10.46, 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 2017
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	03 July 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Disease control rate (DCR) (stable, partial and complete response) of at least 30% after 4 cycles (12 weeks).

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	25 May 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 61
Worldwide total number of subjects	61
EEA total number of subjects	61

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)	56
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Between May 2011 and July 2015, 61 patients were enrolled. 60 patients received at least one first-line Carboplatin-Pemetrexed cycle. The full planned induction regimen (four cycles) was completed in 38 patients (62.3%). Among the 38 four-cycle completers, 31 patients (50.8% of efficacy population) started pemetrexed-maintenance.

Pre-assignment

Screening details:

To be eligible, People Living with HIV (PLHIV) were diagnosed with histological or cytological confirmed non-squamous NSCLC, stage III–IV, and had no previous administration of chemotherapy, age between 18 and 75 years, an ECOG-PS 0–2, patients with symptomatic or asymptomatic brain metastases could be included without prior treatment.

Period 1

Period 1 title	Induction
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

Not blinded

Arms

Arm title	Carboplatin-Pemetrexed
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Arm description:

Patients received first-line intravenous chemotherapy with pemetrexed, 500 mg/m², bolus infused in 10 min, every 3 weeks, combined with carboplatin bolus infusion, with a target AUC5 on day 1 for a maximum of four cycles.

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

Dosage and administration details:

AUC5 every 3 weeks on day 1 for a maximum of four cycles

Investigational medicinal product name	Pemetrexed
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

pemetrexed every 3 week, 500 mg/m², bolus infused in 10 min, on day 1 for a maximum of four cycles.

Number of subjects in period 1	Carboplatin-Pemetrexed
Started	61
Completed	38
Not completed	23
not received treatment (death)	1
Lack of efficacy	22

Period 2

Period 2 title	Maintenance Pemetrexed
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

Not blinded

Arms

Arm title	Pemetrexed
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Arm description:

After the four-cycle induction, patients achieving disease control (partial responses or stable diseases) and ECOG-PS 2 were continued on pemetrexed.

Arm type	Experimental
Investigational medicinal product name	Pemetrexed
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

pemetrexed every 3 week, 500 mg/m, bolus infused in 10 min, on day 1 for a maximum of four cycles.

Number of subjects in period 2 ^[1]	Pemetrexed
Started	31
Completed	31

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: After the four-cycle induction, 7/38 patients didn't achieve disease control (partial response or stable) and were not allowed to continued on maintenance pemetrexed.

Baseline characteristics

Reporting groups

Reporting group title	Induction
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Reporting group description: -

Reporting group values	Induction	Total	
Number of subjects	61	61	
Age categorical			
Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		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)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous			
Units: years			
median	52.9		
full range (min-max)	36.6 to 67.5	-	
Gender categorical			
Units: Subjects			
Female	15	15	
Male	46	46	
HIV viral load			
Units: Subjects			
Undetectable	48	48	
Detectable	12	12	
Missing	1	1	
Antiretroviral therapy at study entry			
Units: Subjects			
Yes	58	58	
No	3	3	
ECOG performans status (PS)			
Units: Subjects			
PS 0	17	17	
PS 1	32	32	
PS 2	12	12	
Smocking status			
Units: Subjects			
Current	54	54	
Former	3	3	
Never	4	4	
Histology			

Units: Subjects			
Adenocarcinoma	56	56	
Sarcomatoïd	1	1	
Non-squamous cell predominant NSCLC	4	4	
Disease stage			
Units: Subjects			
III	6	6	
IV	55	55	
Brain metastasis			
Units: Subjects			
Symptomatic	9	9	
Asymptomatic	10	10	
No brain metastasis	42	42	
History of cancer			
Units: Subjects			
AIDS related	3	3	
Non-AIDS related	6	6	
No history of cancer	52	52	
History of AIDS-related infectio,			
Units: Subjects			
Yes	44	44	
No	17	17	
History of Hepatitis C			
Units: Subjects			
Yes	24	24	
No	37	37	
History of Hepatitis B			
Units: Subjects			
Yes	7	7	
No	54	54	
Comorbidity: arterial hypertension			
Units: Subjects			
Yes	10	10	
No	51	51	
Comorbidity: Dyslipidemia			
Units: Subjects			
Yes	7	7	
No	54	54	
Comorbidity: diabetes			
Units: Subjects			
Yes	3	3	
No	58	58	
Comorbidity: cardiopathy			
Units: Subjects			
Yes	8	8	
No	53	53	
Genetic status			
Units: Subjects			
Wild type	44	44	
KRAS mutation	7	7	

ALK mutation	2	2	
BRAF V600 mutation	2	2	
EGFR mutation L858R exon 21	1	1	
Missing	5	5	
CD4 count			
Units: cells/microlitre			
median	418.0		
full range (min-max)	18 to 1230	-	
Nadir CD4 count			
Units: cells/microlitre			
median	169.5		
full range (min-max)	1 to 822	-	
Duration of HIV infection			
Units: years			
median	20.7		
full range (min-max)	0.1 to 29	-	
Number of pack-year			
Units: Pack-years			
median	36		
full range (min-max)	6 to 120	-	
Median known duration of HIV infection			
Units: year			
median	20.7		
full range (min-max)	0.1 to 29	-	

End points

End points reporting groups

Reporting group title	Carboplatin-Pemetrexed
Reporting group description: Patients received first-line intravenous chemotherapy with pemetrexed, 500 mg/m ² , bolus infused in 10 min, every 3 weeks, combined with carboplatin bolus infusion, with a target AUC5 on day 1 for a maximum of four cycles.	
Reporting group title	Pemetrexed
Reporting group description: After the four-cycle induction, patients achieving disease control (partial responses or stable diseases) and ECOG-PS 2 were continued on pemetrexed.	

Primary: 12-week disease control rate

End point title	12-week disease control rate ^[1]
End point description: Number of patient with complete or partial responses and stable diseases at 12 weeks	
End point type	Primary
End point timeframe: After 4 cycles of induction chemotherapy (12 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	Carboplatin-Pemetrexed			
Subject group type	Reporting group			
Number of subjects analysed	61			
Units: Subjects	31			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS)
End point description: PFS was defined as the time between patient's inclusion and disease progression, relapse or death of any cause.	
End point type	Secondary
End point timeframe: 45.5 months (median follow-up)	

End point values	Carboplatin-Pemetrexed			
Subject group type	Reporting group			
Number of subjects analysed	61			
Units: months				
median (confidence interval 95%)	3.5 (2.7 to 4.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival (OS)

End point title	Overall survival (OS)
End point description: OS as the time between inclusion and death from any cause.	
End point type	Secondary
End point timeframe: 45.5 months (median follow-up)	

End point values	Carboplatin-Pemetrexed			
Subject group type	Reporting group			
Number of subjects analysed	61			
Units: months				
median (confidence interval 95%)	7.6 (5.7 to 12.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Best overall response at 12 weeks

End point title	Best overall response at 12 weeks
End point description:	
End point type	Secondary
End point timeframe: At 12 weeks	

End point values	Carboplatin-Pemetrexed			
Subject group type	Reporting group			
Number of subjects analysed	61			
Units: Subjects				
Partial response	13			
Stable disease	18			
Progressive disease	30			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of opportunistic infections

End point title	Number of opportunistic infections
End point description:	
End point type	Secondary
End point timeframe:	
45.5 months (median follow-up)	

End point values	Carboplatin-Pemetrexed	Pemetrexed		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60 ^[2]	31 ^[3]		
Units: Number of opportunistic infections	0	0		

Notes:

[2] - Safety population includes all patients who received at least one cycle of study chemotherapy (N=60)

[3] - Safety population includes all patients who received at least one cycle of maintenance (N=31).

Statistical analyses

No statistical analyses for this end point

Secondary: Death due to sepsis or infections

End point title	Death due to sepsis or infections
End point description:	
Number of death due to sepsis or infections.	
End point type	Secondary
End point timeframe:	
45.5 months (median follow-up)	

End point values	Carboplatin-Pemetrexed	Pemetrexed		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60 ^[4]	31 ^[5]		
Units: Number of death	2	0		

Notes:

[4] - Safety population includes all patients who received at least one cycle of study chemotherapy (N=60)

[5] - Safety population includes all patients who received at least one cycle of maintenance (N=31).

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Prognosis Analysis of PFS

End point title	Prognosis Analysis of PFS
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End point description:

End point type	Other pre-specified
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End point timeframe:

At 12 weeks

End point values	Carboplatin-Pemetrexed			
Subject group type	Reporting group			
Number of subjects analysed	61			
Units: Hazard ratio				
number (confidence interval 95%)				
Cancer history : yes	1.69 (0.79 to 3.60)			
PS 2	2.67 (1.31 to 5.43)			
Brain metastasis : yes	1.52 (0.86 to 2.67)			
History of AIDS : yes	1.07 (0.58 to 1.97)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Prognosis Analysis of OS

End point title	Prognosis Analysis of OS
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End point description:

End point type	Other pre-specified
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End point timeframe:

At 12 weeks

End point values	Carboplatin-Pemetrexed			
Subject group type	Reporting group			
Number of subjects analysed	61			
Units: Hazard ration				
number (confidence interval 95%)				
Cancer history : yes	1.56 (0.70 to 3.46)			
PS 2	4.44 (1.93 to 10.22)			
Brain metastasis : yes	1.75 (0.95 to 3.22)			
highly active antiretroviral therapy : yes	0.44 (0.09 to 2.23)			
History of AIDS : yes	1.06 (0.56 to 2.0)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: PFS according to PS at inclusion

End point title	PFS according to PS at inclusion
End point description:	
End point type	Other pre-specified
End point timeframe:	
45.5 months (median follow-up)	

End point values	Carboplatin-Pemetrexed			
Subject group type	Reporting group			
Number of subjects analysed	61			
Units: months				
median (confidence interval 95%)				
PS 0-1	4.3 (3.1 to 5.2)			
PS 2	1.7 (1.3 to 2.9)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: PFS according to brain metastasis at inclusion

End point title	PFS according to brain metastasis at inclusion
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End point description:

End point type	Other pre-specified
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End point timeframe:

45 months (median follow-up)

End point values	Carboplatin-Pemetrexed			
Subject group type	Reporting group			
Number of subjects analysed	61			
Units: months				
median (confidence interval 95%)				
Without brain metastasis	4.0 (2.9 to 5.3)			
With brain metastasis	2.6 (1.3 to 4.4)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: OS according to PS at inclusion

End point title	OS according to PS at inclusion
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End point description:

End point type	Other pre-specified
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End point timeframe:

45.5 months (median follow-up)

End point values	Carboplatin-Pemetrexed			
Subject group type	Reporting group			
Number of subjects analysed	61			
Units: months				
median (confidence interval 95%)				
PS 0-1	11.9 (6.4 to 14.3)			
PS 2	2.4 (0.7 to 5.4)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: OS According to brain metastasis at inclusion

End point title OS According to brain metastasis at inclusion

End point description:

End point type Other pre-specified

End point timeframe:

45.5 months (median follow-up)

End point values	Carboplatin-Pemetrexed			
Subject group type	Reporting group			
Number of subjects analysed	61			
Units: months				
median (confidence interval 95%)				
Without brain metastasis	11.9 (5.9 to 16.6)			
With brain metastasis	6.2 (1.9 to 8.8)			

Statistical analyses

No statistical analyses for this end point

Post-hoc: Risk factor of grade 3-4 haematologic toxicity of carboplatin-pemetrexed in patient treated with antiretroviral therapy

End point title Risk factor of grade 3-4 haematologic toxicity of carboplatin-pemetrexed in patient treated with antiretroviral therapy

End point description:

End point type Post-hoc

End point timeframe:

At 12 weeks

End point values	Carboplatin-Pemetrexed			
Subject group type	Reporting group			
Number of subjects analysed	58 ^[6]			
Units: % of subjects				
number (not applicable)				
Grade 3-4 hematologic toxicity if no AIDS-history	60.6			
Grade 3-4 hematologic toxicity if AIDS-history	39.4			

No gr 3-4 hematologic toxicity if no AIDS-history	84.0			
No gr 3-4 hematologic toxicity if AIDS-history	16.0			

Notes:

[6] - 58 patients treated with antiretroviral therapy at inclusion

Statistical analyses

No statistical analyses for this end point

Post-hoc: Quality of Life Evaluated With the Lung Cancer Symptom Scale (LCSS)

End point title	Quality of Life Evaluated With the Lung Cancer Symptom Scale (LCSS)
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End point description:

The quality of life was described by the sum of the score of all domains of LCSS questionnaire, at the end of each first-line chemotherapy cycle compared to the baseline value.

Declined : mean score increased by at least 10 points from baseline.

Improved : mean score decreased by at least 10 points from baseline.

End point type	Post-hoc
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End point timeframe:

At 12 weeks

End point values	Carboplatin-Pemetrexed			
Subject group type	Reporting group			
Number of subjects analysed	61			
Units: % of subjects				
number (not applicable)				
C1 vs baseline : declined	12.8			
C1 vs baseline : stable	71.8			
C1 vs baseline : improved	15.4			
C2 vs baseline : declined	9.4			
C2 vs baseline : stable	65.6			
C2 vs baseline : improved	25.0			
C3 vs baseline : declined	20.8			
C3 vs baseline : stable	50.0			
C3 vs baseline : improved	29.2			
C4 vs baseline : declined	12.2			
C4 vs baseline : stable	58.2			
C4 vs baseline : improved	29.2			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The adverse events have to be reported from inclusion to 30 day following the end of administration of study treatments.

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	18.0
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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	32 / 60 (53.33%)		
number of deaths (all causes)	55		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Progression of bronchial carcinoma			
subjects affected / exposed	4 / 60 (6.67%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 4		
Vascular disorders			
Hypovolaemic shock			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Superior vena cava syndrome			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Thromboembolism NOS			

subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Thrombosis			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Fever			
subjects affected / exposed	3 / 60 (5.00%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Reduced general condition			
subjects affected / exposed	6 / 60 (10.00%)		
occurrences causally related to treatment / all	2 / 6		
deaths causally related to treatment / all	0 / 3		
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bronchopneumopathy			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
COAD exacerbated			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Dyspnoea			
subjects affected / exposed	3 / 60 (5.00%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
Hemoptysis			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumopathy			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Productive cough			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Pulmonary embolism			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory distress			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory failure			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Hemoglobin decreased			
subjects affected / exposed	5 / 60 (8.33%)		
occurrences causally related to treatment / all	5 / 5		
deaths causally related to treatment / all	0 / 0		
Neutrophil count decreased			

subjects affected / exposed	2 / 60 (3.33%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Platelet count decreased			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Nervous system disorders			
Cerebral oedema management			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Confusion			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Headache			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Hemiparesis			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Neuropathic pain			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Aplasia bone marrow			
subjects affected / exposed	3 / 60 (5.00%)		
occurrences causally related to treatment / all	4 / 4		
deaths causally related to treatment / all	1 / 1		
Febrile aplasia			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Febrile neutropenia			
subjects affected / exposed	4 / 60 (6.67%)		
occurrences causally related to treatment / all	4 / 4		
deaths causally related to treatment / all	1 / 1		
Hemolysis			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Eye disorder			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Colitis			

subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Diarrhea			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Dysphagia			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorder			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Nausea			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 1		
Vomiting			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Rash			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			

Acute renal failure			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Fracture NOS			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Bronchitis			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	1 / 1		
Catheter related infection			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Catheter site infection			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Localized infection			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		

Septic shock			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Spastic bronchitis			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	4 / 60 (6.67%)		
occurrences causally related to treatment / all	2 / 5		
deaths causally related to treatment / all	0 / 3		

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	60 / 60 (100.00%)		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	9 / 60 (15.00%)		
occurrences (all)	27		
Aspartate aminotransferase increased			
subjects affected / exposed	10 / 60 (16.67%)		
occurrences (all)	25		
Blood alkaline phosphatase increased			
subjects affected / exposed	6 / 60 (10.00%)		
occurrences (all)	16		
Gamma-glutamyltransferase increased			
subjects affected / exposed	8 / 60 (13.33%)		
occurrences (all)	21		
Weight decreased			

subjects affected / exposed occurrences (all)	13 / 60 (21.67%) 31		
Vascular disorders Haemoptysis subjects affected / exposed occurrences (all)	4 / 60 (6.67%) 6		
Nervous system disorders Headache subjects affected / exposed occurrences (all) Paraesthesia subjects affected / exposed occurrences (all)	9 / 60 (15.00%) 19 3 / 60 (5.00%) 9		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) Febrile neutropenia subjects affected / exposed occurrences (all) Leukopenia subjects affected / exposed occurrences (all) Neutropenia subjects affected / exposed occurrences (all) Thrombocytopenia subjects affected / exposed occurrences (all)	54 / 60 (90.00%) 264 7 / 60 (11.67%) 8 3 / 60 (5.00%) 7 49 / 60 (81.67%) 186 43 / 60 (71.67%) 190		
General disorders and administration site conditions Abdominal pain subjects affected / exposed occurrences (all) Asthenia subjects affected / exposed occurrences (all)	8 / 60 (13.33%) 14 47 / 60 (78.33%) 173		

Chest pain			
subjects affected / exposed	9 / 60 (15.00%)		
occurrences (all)	18		
General physical health deterioration			
subjects affected / exposed	11 / 60 (18.33%)		
occurrences (all)	18		
Oedema peripheral			
subjects affected / exposed	9 / 60 (15.00%)		
occurrences (all)	21		
Pyrexia			
subjects affected / exposed	10 / 60 (16.67%)		
occurrences (all)	21		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	10 / 60 (16.67%)		
occurrences (all)	15		
Diarrhoea			
subjects affected / exposed	11 / 60 (18.33%)		
occurrences (all)	17		
Dysphagia			
subjects affected / exposed	4 / 60 (6.67%)		
occurrences (all)	9		
Nausea			
subjects affected / exposed	31 / 60 (51.67%)		
occurrences (all)	74		
Stomatitis			
subjects affected / exposed	5 / 60 (8.33%)		
occurrences (all)	6		
Vomiting			
subjects affected / exposed	20 / 60 (33.33%)		
occurrences (all)	41		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	17 / 60 (28.33%)		
occurrences (all)	36		
Dysphonia			

subjects affected / exposed occurrences (all)	3 / 60 (5.00%) 9		
Dyspnoea subjects affected / exposed occurrences (all)	25 / 60 (41.67%) 50		
Productive cough subjects affected / exposed occurrences (all)	5 / 60 (8.33%) 7		
Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all)	5 / 60 (8.33%) 22		
Rash subjects affected / exposed occurrences (all)	4 / 60 (6.67%) 6		
Renal and urinary disorders Renal failure subjects affected / exposed occurrences (all)	7 / 60 (11.67%) 27		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	4 / 60 (6.67%) 14		
Back pain subjects affected / exposed occurrences (all)	8 / 60 (13.33%) 15		
Bone pain subjects affected / exposed occurrences (all)	5 / 60 (8.33%) 8		
Musculoskeletal chest pain subjects affected / exposed occurrences (all)	6 / 60 (10.00%) 20		
Neck pain subjects affected / exposed occurrences (all)	3 / 60 (5.00%) 7		
Pain in extremity			

subjects affected / exposed occurrences (all)	3 / 60 (5.00%) 3		
Infections and infestations			
Catheter site infection			
subjects affected / exposed	5 / 60 (8.33%)		
occurrences (all)	7		
Lung infection			
subjects affected / exposed	4 / 60 (6.67%)		
occurrences (all)	6		
Oral candidiasis			
subjects affected / exposed	10 / 60 (16.67%)		
occurrences (all)	13		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	24 / 60 (40.00%)		
occurrences (all)	67		
Hypokalaemia			
subjects affected / exposed	3 / 60 (5.00%)		
occurrences (all)	5		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 May 2015	Modification was made in order to add growth factors to prevent febrile neutropenia.
13 June 2017	Modification was made in order to reduce the frequency of tumour evaluation after the 5th assessment and to extend the duration of the study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

The trial suffers from a bias related to the potential heterogeneity of patients living with HIV; however, the option of a restricted population of patients without PS 2 and without symptomatic brain metastases could have affected the recruitment.

Notes:

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/32444410>