Clinical trial results:
Phase II trial on safety and activity of intensive short-term chemoimmunotherapy in HIV-positive patients with Burkitt's lymphoma.

Summary

EudraCT number	2011-003487-75
Trial protocol	IT
Global end of trial date	24 October 2019

Results information

Result version number	v1 (current)
This version publication date	01 November 2022
First version publication date	01 November 2022
Summary attachment (see zip file)	carmen trial pubblication (CARMEN trial - BJH 2020.pdf)

Trial information

Trial identification

Sponsor protocol code	CARMEN

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01516593
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	IRCCS OSPEDALE SAN RAFFAELE
Sponsor organisation address	VIA OLGETTINA 60, MILAN, Italy,
Public contact	Oncologia, U. D. Tumori Linfoidi, Fondazione Centro San Raffaele del Monte Tabor, +39 02 26437649, ferreri.andres@hsr.it
Scientific contact	Oncologia, U. D. Tumori Linfoidi, Fondazione Centro San Raffaele del Monte Tabor, +39 02 26437649, ferreri.andres@hsr.it

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	01 August 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 August 2019
Global end of trial reached?	Yes
Global end of trial date	24 October 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the activity in terms of complete remission rate (defined according to Cheson's criteria) at the end of the induction phase of the investigational intensive chemotherapy in HIV+ patients with Burkitt's lymphoma.

Protection of trial subjects:

NA

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 October 2011
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	3 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Italy: 20
Worldwide total number of subjects	20
EEA total number of subjects	20

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)	20
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Twenty patients (median age 42, range 26–58; 16 males) were recruited at seven centres between May 2012 and December 2015. The trial was ended after accrual completion, and the database lock for the primary analysis was August 1, 2019.

Pre-assignment

Screening details:

Targeted population: HIV-positive patients affected by Burkitt's Lymphoma aged between 18-60 years old, with organ functionality adequate to receive high-dose chemotherapy.

Period 1

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

Arms

Arm title	induction and consolidation

Arm description:

The phase includes administration of the following drugs:
- Methylprednisolone; Cyclophosphamide; Vincristine (VCR); Rituximab; Methotrexate (MTX); etoposide (VP-16) 250 mg/m2 q12h; MTX with leucovorin rescue therapy; Doxorubicin (ADM);
At the end of induction phase, initial sites of disease should be fully re-examined and, in selected cases assessed by surgical biopsy.
- Patients in complete remission (CR) after induction phase will be referred to consolidation phase, followed by bulky site irradiation.
- Patients in partial response (PR) after induction will be referred to consolidation phase followed by FEAM conditioning regimen supported by autologous stem-cell transplant (ASCT) and bulky irradiation.
- Patients with stable disease (SD) after or with progressive disease (PD) during/after induction will be referred to intensification phase, followed by FEAM conditioning regimen supported by autologous stem cell transplant (ASCT) and bulky irradiation.

Arm type	single arm
Investigational medicinal product name	rituximab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Infusion

Dosage and administration details:

375 mg/m2

Investigational medicinal product name	cyclophosophamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Infusion

Dosage and administration details:

500 mg/(m2 over 1h infusion

Investigational medicinal product name	doxorubicin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for concentrate for solution for infusion

Routes of administration	Infusion
Dosage and administration details: 50 mg/m2 i.v. bolus	
Investigational medicinal product name	vincristine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Infusion
Dosage and administration details: 2mg total dose i.v. bolus	
Investigational medicinal product name	methylprednisolone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for concentrate for solution for infusion
Routes of administration	Infusion
Dosage and administration details: 0.5 - 1 mg/kg/d i.v.	
Investigational medicinal product name	Cytarabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for concentrate for solution for infusion
Routes of administration	Infusion
Dosage and administration details: 2g/m2 in 3-h infusion, twice a day (every 12h)	
Investigational medicinal product name	etoposide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for concentrate for solution for infusion
Routes of administration	Infusion
Dosage and administration details: 250mg/m2 every 12h	
Investigational medicinal product name	methotrexate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for concentrate for solution for infusion
Routes of administration	Infusion
Dosage and administration details: 12mg	

Number of subjects in period 1	induction and consolidation
Started	20
Completed	20

Baseline characteristics

Reporting groups	
Reporting group title	Overll Trial

Reporting group description: -

Reporting group values	Overll Trial	Total	
Number of subjects	20	20	
Age categorical			
twenty patients (median age 42, range 26-58; 16 males) were recruited at seven centres between May 2012 and December 2015.			
Units: Subjects			
Adults (18-64 years)	20	20	
Age continuous			
Units: years			
median	42		
full range (min-max)	26 to 58	-	
Gender categorical			
Units: Subjects			
Female	4	4	
Male	16	16	

End points

End points reporting groups

Reporting group title	induction and consolidation

Reporting group description:

The phase includes administration of the following drugs:
- Methylprednisolone; Cyclophosphamide; Vincristine (VCR); Rituximab; Methotrexate (MTX); etoposide (VP-16) 250 mg/m2 q12h; MTX with leucovorin rescue therapy; Doxorubicin (ADM);
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Primary: CRR AFTER INDUCTION CHEMOIMMUNOTHERAPY

End point title	CRR AFTER INDUCTION CHEMOIMMUNOTHERAPY[1]

End point description:

CRR according to investigator assessment was used as supportive evidence.

End point type	Primary

End point timeframe:

60 days

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: The primary endpoint was CRR after induction chemoimmunotherapy. CRR according to investigator assessment was used as supportive evidence. The two-stage Simon optimal design was used to test the null hypothesis that the true CRR after the induction phase is 40% (considered unacceptable) as opposed to the alternative hypothesis of 70% (considered of interest). It's a single arm study and no comparison group was evaluated.

End point values	induction and consolidation			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: decimal number	20			

Statistical analyses

No statistical analyses for this end point

Secondary: toxicity and activity of the whole programme

End point title	toxicity and activity of the whole programme

End point description:

toxicity, activity of the whole programme, progression-free survival (PFS) and OS were the seconday end-points.

End point type	Secondary

End point timeframe:

60 days

End point values	induction and consolidation			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: DECIMAL NUMBER	20			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: 5years	
Assessment type	Systematic

Dictionary used	
Dictionary name	CTCAE
Dictionary version	5

Frequency threshold for reporting non-serious adverse events: 0 %

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: no non-serious adverse events were recorded.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 January 2013	administrative reaison.
08 May 2018	The amendment introduces the centralized pathological review of patient tumor biopsy samples collected prior to entry into the study. The aim is to reclassify tumors according to the new WHO nomenclature of 2016 and to assess whether there is a correlation with the clinical response.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/33090470