



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 | Overall 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 | cyclophosphamide |
| 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/m ² 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/m ² 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/m ² 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);
- 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.

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 secondary 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 reason. |
| 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>