# Clinical trial results:
# EuroNet-Paediatric Hodgkin's Lymphoma Group

# First international Inter-Group Study for nodular lymphocyte-predominant Hodgkin's Lymphoma in Children and Adolescents

## Summary

| | |
|---|---|
| EudraCT number | 2007-004092-19 |
| Trial protocol | DE CZ AT NL GB FR |
| Global end of trial date | 31 December 2023 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 19 December 2025 |
| First version publication date | 19 December 2025 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | EuroNet-PHL-LP1 |

**Additional study identifiers**

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

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Martin-Luther-University Halle-Wittenberg |
| Sponsor organisation address | Magdeburger Str. 27, Halle/Saale, Germany, |
| Public contact | Zentrum für Kinderheilkunde und Jugendmedizin, Universitätsklinikum Giessen udn Marburg GmbH, Standort Giessen, 0049 641 985-43420, dieter.koerholz@paediat.med.uni-giessen.de |
| Scientific contact | Zentrum für Kinderheilkunde und Jugendmedizin, Universitätsklinikum Giessen udn Marburg GmbH, Standort Giessen, 0049 641 985-43420, dieter.koerholz@paediat.med.uni-giessen.de |

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 | 10 February 2025 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 31 December 2023 |
| Global end of trial reached? | Yes |
| Global end of trial date | 31 December 2023 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

Building on the experience of the European PHL study groups since 1978, first line therapy for childhood nodular lymphocyte-predominant Hodgkin’s lymphoma shall be further optimised to avoid over-treatment and decrease long-term complications.

Surgery alone for patients with stage IA disease and complete resection.

Low intensity chemotherapy with CVP (Cyclophosphamide, Vincristine and Prednisolone (or Prednisone)) for patients with stage IA and incomplete resection or stage IIA disease

Patients with complete resection group:
Statistically estimate the five year event free survival rate with meaningful precision and show it is above 50%.
Patients with residual disease receiving 3 CVP:
Statistically estimate the 5 year Event free survival rate in all patients receiving CVP chemotherapy.

Protection of trial subjects:

Patients were monitored by the medical staff with regard to safety

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 01 November 2009 |
| 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 | Netherlands: 16 |
| Country: Number of subjects enrolled | United Kingdom: 61 |
| Country: Number of subjects enrolled | Austria: 13 |
| Country: Number of subjects enrolled | Czechia: 7 |
| Country: Number of subjects enrolled | France: 41 |
| Country: Number of subjects enrolled | Germany: 66 |
| Country: Number of subjects enrolled | Italy: 22 |
| Country: Number of subjects enrolled | Switzerland: 11 |
| Country: Number of subjects enrolled | United States: 10 |
| Worldwide total number of subjects | 247 |
| EEA total number of subjects | 165 |

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) | 118 |
| Adolescents (12-17 years) | 129 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Within this clinical trial, 270 patients were recruited in nine participating countries with 92 active trial sites. Three patients withdrew before start of treatment, leaving 267 for analysis. The list of active trial centres that have been recruiting study patients is attached to this report.

### Pre-assignment

Screening details:

After local staging and registration patients central review staging has been performed. Follwoing this, patienst ha sbeen assigned to the 3 substudies.

### Period 1

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

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Surgery only - watch and wait |

Arm description:

The study population of substudy 1 comprises all chemotherapy naive stage IA/IIA patients that either were already in complete resection after the diagnostic biopsy or in whom additional surgery was successful.

6 patients Relapse after surgery alone have been assigned to CVP

| | |
|---|---|
| Arm type | No intervention |

No investigational medicinal product assigned in this arm

| | |
|---|---|
| **Arm title** | CVP with partially PET-based RA |

Arm description:

The study population of substudy 2 comprises all all chemotherapy naive stage IA/IIA patients with residual disease in
whom additional surgery was not successful or deemed unfeasible. Patients who relapsed within the substudy 1 were
allowed to enter substudy 2 with a second registration.
The definition of good response in the CVP substudy was initially partially based on PET:
Patients have a good response if they are
• in overall CR or
• CRu and all initially involved regions are
• PET-negative or
• PET-unclear and either in local CR or undetectable

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Cyclophosphamide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Day 1
By slow bolus into established i.v. line or by intravenous infusion over 1 hour.
By i.v. infusion in Glucose 5%, Sodium chloride 0.9% or Glucose/saline.
Dosage: 500 mg/m²

| | |
|---|---|
| Investigational medicinal product name | Prednisone/Prednisolone |
| Investigational medicinal product code | |
| Other name | |

| | |
|---|---|
| Pharmaceutical forms | Infusion, Tablet |
| Routes of administration | Intravenous use, Oral use |

Dosage and administration details:

Day 1-8
40 mg/m²/day
Prednisone (Tablet); Prednisolone (infusion)

| | |
|---|---|
| Investigational medicinal product name | Vinblastine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion, Injection |
| Routes of administration | Intravenous bolus use , Intravenous use |

Dosage and administration details:

Day 1 and day 8
By bolus injection or into the tubing of a fast running intravenous infusion.
Dosage: 6 mg/m² i.v., capping dose 10 mg (single dose); used only as a substitute if acute vincristine toxicity occurs

| | |
|---|---|
| **Arm title** | CVP without PET RA |

Arm description:

The apparently low response rate detected in an interim analysis may have been a matter of definition and due to the application of overly strict response criteria (using PET). Most CRu patients with still visible FDG-PET uptake would have had a low relapse rate even without additional treatment, as suggested by data from a publication. Based on these interim results, a change in strategy was decided upon and PET-based RA was abandoned.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Cyclophosphamide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Day 1
By slow bolus into established i.v. line or by intravenous infusion over 1 hour.
By i.v. infusion in Glucose 5%, Sodium chloride 0.9% or Glucose/saline.
Dosage: 500 mg/m²

| | |
|---|---|
| Investigational medicinal product name | Prednisone/Prednisolone |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion, Tablet |
| Routes of administration | Intravenous use, Oral use |

Dosage and administration details:

Day 1-8
40 mg/m²/day
Prednisone (Tablet); Prednisolone (infusion)

| | |
|---|---|
| Investigational medicinal product name | Vinblastine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion, Injection |
| Routes of administration | Intravenous bolus use , Intravenous use |

Dosage and administration details:

Day 1 and day 8
By bolus injection or into the tubing of a fast running intravenous infusion.
Dosage: 6 mg/m² i.v., capping dose 10 mg (single dose); used only as a substitute if acute vincristine toxicity occurs

| **Number of subjects in period 1** | Surgery only - watch and wait | CVP with partially PET-based RA | CVP without PET RA |
|---|---|---|---|
| Started | 87 | 82 | 78 |
| Completed | 87 | 82 | 78 |

## Baseline characteristics

## End points

### End points reporting groups

| Reporting group title | Surgery only - watch and wait |
|---|---|

Reporting group description:

The study population of substudy 1 comprises all chemotherapy naive stage IA/IIA patients that either were already in complete resection after the diagnostic biopsy or in whom additional surgery was successful.

6 patients Relapse after surgery alone have been assigned to CVP

| Reporting group title | CVP with partially PET-based RA |
|---|---|

Reporting group description:

The study population of substudy 2 comprises all all chemotherapy naive stage IA/IIA patients with residual disease in
whom additional surgery was not successful or deemed unfeasible. Patients who relapsed within the substudy 1 were
allowed to enter substudy 2 with a second registration.
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• in overall CR or
• CRu and all initially involved regions are
• PET-negative or
• PET-unclear and either in local CR or undetectable

| Reporting group title | CVP without PET RA |
|---|---|

Reporting group description:

The apparently low response rate detected in an interim analysis may have been a matter of definition and due to the application of overly strict response criteria (using PET). Most CRu patients with still visible FDG-PET uptake would have had a low relapse rate even without additional treatment, as suggested by data from a publication. Based on these interim results, a change in strategy was decided upon and PET-based RA was abandoned.

### Primary: Primary: EFS

| End point title | Primary: EFS[1] |
|---|---|

End point description:

EFS as defined by time from registration until the first of the following events:
• Additional treatment for Hodgkin’s Lymphoma
• progression/relapse of disease
• occurrence of a secondary
• death by any cause

| End point type | Primary |
|---|---|

End point timeframe:

60 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: See uploaded Trial Report (*pdf)

| End point values | Surgery only - watch and wait | CVP with partially PET-based RA | CVP without PET RA | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 87 | 82 | 78 | |
| Units: Whole | | | | |
| number (not applicable) | 79.5 | 56.4 | 64.7 | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information[1]

Timeframe for reporting adverse events:

Reporting of adverse events is restricted to events occurring within 3 months after the end of the study treatment.

| | |
|---|---|
| Assessment type | Systematic |

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 28.0 |

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: See uploaded Trial Report (*pdf)

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 06 November 2009 | Minor; Clarification of study medication in the protocol synopsis (typing error); Change of contact information |
| 29 June 2011 | Minor; Updating contact information; Mentioning the investigational medical products in the protocol synopsis; Adjustment of data to effective trial start in Germany; Clarification of further follow-up in patients without good response, after they go off protocol; Clarification of what are the IMPs and determination of body surface area; Deletion of the chemotherapy drug monographs section from protocol; clarifications in language |
| 22 December 2011 | Minor: Clarification for logistics of central review and data storage of CT/MRI images and FDG-PET data sets in central review board; clarification of contact details |
| 04 November 2014 | Based on the interim results, change in strategy after the trial enrolment stops in Germany in October 2014. Starting in November 2014 the trial will continue for another four years in all participating countries, except Germany (for insurance reasons), applying new response criteria (CR/CRu by CT/MRI as described in the EuroNet-PHL-LP1 protocol) similar to those used in Shankar 2012.<br>Set-up German specific investigation of gene expression profile. |
| 26 August 2015 | Minor: Patients being enrolled onto the trial in all participating countries, except for France, were asked to agree to central clinical review of staging and response assessment.<br>Change of contact data. |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported