



Clinical trial results:

Immunochemotherapy in Primary Central Nervous System Lymphoma with Rituximab, HD-MTX, HD-Ara C, cyclophosphamide, ifosfamide, vincristine, vindesine, temozolomide and DepoCyt induction followed by maintenance treatment in elderly patients with temozolomide.

Summary

EudraCT number	2006-004772-12
Trial protocol	DK SE FI
Global end of trial date	13 July 2023

Results information

Result version number	v1 (current)
This version publication date	11 October 2023
First version publication date	11 October 2023
Summary attachment (see zip file)	Adverse Events (Adverse Event.pdf)

Trial information

Trial identification

Sponsor protocol code	NLGPCNSL
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01458730
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Nordic Lymphoma Group
Sponsor organisation address	Tage Hansens Gade 2, Aarhus, Denmark, 8000
Public contact	Elisa Pulczynski, Elisa Pulczynski, e.jacobsen@dadlnet.dk
Scientific contact	Elisa Pulczynski, Elisa Pulczynski, e.jacobsen@dadlnet.dk

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	06 September 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 July 2023
Global end of trial reached?	Yes
Global end of trial date	13 July 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

1. To investigate the efficacy and safety of a high-dose methotrexate-based induction polychemotherapy regimen combined with Rituximab and intraspinal DepoCyt followed by temozolomide maintenance treatment in newly diagnosed primary central nervous system lymphoma
2. To assess the long term outcome concerning neurotoxicity

Protection of trial subjects:

The study was monitored by the Good Clinical Practice Unit at Aarhus and Aalborg University Hospitals. And the study was conducted according to the Helsinki declaration.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 May 2007
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	Norway: 24
Country: Number of subjects enrolled	Sweden: 27
Country: Number of subjects enrolled	Denmark: 8
Country: Number of subjects enrolled	Finland: 7
Worldwide total number of subjects	66
EEA total number of subjects	66

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)	39
From 65 to 84 years	27
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The patients were recruited in clinic and the in- and exclusion criteria checked.

Pre-assignment

Screening details:

The patients were screened for in- and exclusion criteria.

Period 1

Period 1 title	Overall period (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

None

Arms

Are arms mutually exclusive?	Yes
Arm title	18-65 years

Arm description:

Patients in the age group 18-65 years

Arm type	Experimental
Investigational medicinal product name	Methotrexat
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Infusion

Dosage and administration details:

Patients aged 18-65 years will receive HD-MTX 5g/ m2 four cycles administered intravenously over three hours on weeks 1, 4, 10 and 13.

Investigational medicinal product name	Cytarabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Infusion

Dosage and administration details:

Patients aged 18-65 years received Cytarabine 1.5g/m2 two cycles administered intravenously over three hours every 12 hours for two days on weeks 7 and 16.

Investigational medicinal product name	Ifosfamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Infusion

Dosage and administration details:

Patients aged 18-65 years received ifosfamide 800 mg/m2 intravenously two cycles administered for four days during the weeks 1 and 10.

Investigational medicinal product name	Cyclophosphamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Infusion

Dosage and administration details:

Patients aged 18-65 years received cyclophosphamide 200 mg/m² intravenously two cycles administered for four days during the weeks 4 and 13.

Investigational medicinal product name	Vincristine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Injection

Dosage and administration details:

Patients aged 18-65 years received vincristine 2 mg intravenously administered once on week 4 and once on week 13

Investigational medicinal product name	Vindesine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Infusion

Dosage and administration details:

All patients received vindesine 5 mg intravenously administered once on week 7 and once on week 16

Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

All patients received dexamethasone orally 10 mg/m² for four days during the weeks 1, 4, 10 and 13 and 20 mg/m² for five days during the weeks 7 and 16

Investigational medicinal product name	DepoCyt
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Injection

Dosage and administration details:

All patients received DepoCyt 50 mg four treatments administered intraspinally on weeks 1, 4, 10 and 13

Investigational medicinal product name	Rituximab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Infusion

Dosage and administration details:

Rituximab (375mg/m²) was administered intravenously prior to the first HD-MTX infusion in case of CD20 + lymphoma

Arm title	66-75 years
Arm description:	
Patients in the age group 66-75 years	
Arm type	Experimental

Investigational medicinal product name	Methotrexat
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Infusion

Dosage and administration details:

Patients aged 66-75 years will receive HD-MTX 3g/m² four cycles administered intravenously over three hours on weeks 1, 4, 10 and 13.

Investigational medicinal product name	Cytarabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Infusion

Dosage and administration details:

Patients aged 66-75 years received Cytarabine 1g/m² two cycles administered intravenously over three hours every 12 hours for two days on weeks 7 and 16.

Investigational medicinal product name	Ifosfamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Infusion

Dosage and administration details:

Patients aged 66-75 years received ifosfamide 800mg/m² intravenously one cycle administered for four days during week 1.

Investigational medicinal product name	Vindesine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Infusion

Dosage and administration details:

All patients received vindesine 5 mg intravenously administered once on week 7 and once on week 16

Investigational medicinal product name	Temozolomide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Patients aged 66-75 years received temozolomide 150mg/m² orally for five days during the weeks 4, 10 and 13 and thereafter once a month for one year.

Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

All patients received dexamethasone orally 10 mg/m² for four days during the weeks 1, 4, 10 and 13 and 20 mg/m² for five days during the weeks 7 and 16

Investigational medicinal product name	DepoCyt
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion

Routes of administration	Injection
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Dosage and administration details:

All patients received DepoCyte 50 mg four treatments administered intraspinally on weeks 1, 4, 10 and 13

Investigational medicinal product name	Rituximab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Infusion

Dosage and administration details:

Rituximab (375mg/m²) was administered intravenously prior to the first HD-MTX infusion in case of CD20 + lymphoma

Number of subjects in period 1	18-65 years	66-75 years
Started	39	27
Completed	38	24
Not completed	1	3
Treatment related deaths	-	3
Treatment related deaths	1	-

Baseline characteristics

Reporting groups

Reporting group title	18-65 years
Reporting group description:	
Patients in the age group 18-65 years	
Reporting group title	66-75 years
Reporting group description:	
Patients in the age group 66-75 years	

Reporting group values	18-65 years	66-75 years	Total
Number of subjects	39	27	66
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	39	0	39
From 65-84 years	0	27	27
85 years and over	0	0	0
Gender categorical			
Units: Subjects			
Female	16	15	31
Male	23	12	35

End points

End points reporting groups

Reporting group title	18-65 years
Reporting group description: Patients in the age group 18-65 years	
Reporting group title	66-75 years
Reporting group description: Patients in the age group 66-75 years	

Primary: Overall survival - complete treatment and follow-up course

End point title	Overall survival - complete treatment and follow-up course ^[1]
End point description:	

End point type	Primary
End point timeframe: 10 years after completed therapy.	

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 article, linked under "More information"

End point values	18-65 years	66-75 years		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	27		
Units: percent				
number (not applicable)	14.1	22.7		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

Adverse events was observed at treatment sites

Adverse event reporting additional description:

There are 6 treatment cycles in the study. They are called: A1 – B1 – C1 – A2 – B2 and C2.
The toxicity (both haematological and infection-related) differs according to the different treatment cycles.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	None
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Dictionary version	1.0
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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: Adverse Events were not possible to report in the schemes, therefore reported in document, uploaded in the index

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 December 2006	Adding GCSF

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/25480497>