



Clinical trial results: Multicentre pilot-study for the therapy of medulloblastoma of adults (NOA-07) Phase II

Summary

EudraCT number	2007-002560-10
Trial protocol	DE
Global end of trial date	12 October 2018

Results information

Result version number	v1 (current)
This version publication date	15 December 2022
First version publication date	15 December 2022
Summary attachment (see zip file)	NOA 07 DSUR 2018_Last (03_DSUR NOA07_10-2018_gesamt27_LAST English.pdf) NOA 07 short synopsis (German) (NOA07_KurzP_2.1 vom 25.04.2016.pdf) NOA 07_Publication of Results incl AE's SAE (NOA_07_Pub_Results_incl TOX.pdf)

Trial information

Trial identification

Sponsor protocol code	NOA-07
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01614132
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University Hospital Regensburg
Sponsor organisation address	Franz-Josef-Strauss-Allee 11, Regensburg, Germany, 93053
Public contact	Prof. Peter Hau, University of Regensburg Department Neurology, +49 9419448083, peter.hau@ukr.de
Scientific contact	Prof. Peter Hau, University of Regensburg Department Neurology, +49 9419448083, peter.hau@ukr.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	04 October 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 September 2018
Global end of trial reached?	Yes
Global end of trial date	12 October 2018
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main objective is the feasibility of the adjuvant chemotherapy which has gained the best results when combined with radiotherapy so far. The present protocol is primarily to determine the number of interruptions of the maintenance chemotherapy due to toxicity. In addition, the maximum number of cycles that are feasible shall be determined.

Primary outcome measure:

Tolerability of additional maintenance chemotherapy, which in combination with radiation has achieved the best therapeutic results to date.

Secondary outcome measures:

Secondary outcome measures relate to additional safety and efficacy parameters as well as evaluation of imaging, histologic, and molecular parameters and assessment of cognitive performance, quality of life, and social outcome.

Protection of trial subjects:

not applicable

Background therapy:

not applicable

Evidence for comparator:

Rationale of the study

Primary aim of the NOA-07 study was to evaluate the toxicity of adjuvant chemotherapy with cisplatin, lomustine and vincristine in adults > 18 years of age with medulloblastoma in a controlled prospective setting.

In children with medulloblastoma, the introduction of adjuvant chemotherapy with cisplatin, lomustine and vincristine led to a significant improvement of the overall survival to a 5-year OS rate of >80 % (Packer et al., 1994), (Packer et al., 1999).

In adults, less and heterogeneous data existed, showing survival times varying between 26%-83% with various regimes in retrospective series. The only available prospective observation concerning adjuvant chemotherapy with cisplatin, lomustine and vincristine derived from the HIT88/89/91 study: 46 adults (age 16-51 years, median 21 years) were treated within the protocol reaching overall a 5y-PFS of 63% (n=46) and a 5y-PFS of 71% in cases of M0-situation (n=18) - a result that appeared promising and required prospective randomised trials for further validation.

However, toxicity concerns were raised when dealing with intensive adjuvant chemotherapy. In children, up to 60% of patients require dose modification. In adults, very little was known about the toxicity of the combination therapy. It was not possible to simply transfer the results from children to adults due to differing age-dependent chemotherapy sensitivities.

Accordingly, the scope of the NOA-07 trial was to accurately evaluate toxicity of an adjuvant treatment with cisplatin, lomustine, vincristine in a phase II study before planning a phase III trial on the efficacy on adjuvant chemotherapy in adult medulloblastoma.

Actual start date of recruitment	01 January 2009
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 30
Worldwide total number of subjects	30
EEA total number of subjects	30

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)	30
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

First Patient in: 26.01.2009; Last Patient in: 29.04.2014-Germany

Pre-assignment

Screening details:

Medulloblastoma (+/- postoperative residual tumor, M0) or Medulloblastoma (+/- postoperative residual tumor, M1-3).

Age: completed 18 years of age

The diagnosis for this is made by the local pathologist, it must be confirmed immediately at study inclusion by reference histology

Period 1

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

Arms

Arm title	Single Arm
Arm description: -	
Arm type	test
Investigational medicinal product name	Vincristine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Injection

Dosage and administration details:

1.5mg/m² weekly, cap at 2.0mg during radiation (6 week period). followed by a maximum of 8 six-weekly cycles of 1.5mg/m² cap at 2.0mg days 1,8 and 15

Investigational medicinal product name	Cisplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

70.0mg/m² on Day 1 during a maximum of 8 six-weekly cycles

Investigational medicinal product name	Cecenu (Lomustin)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

75.0mg/m² on Day 1 during a maximum of 8 six-weekly cycles

Number of subjects in period 1	Single Arm
Started	30
Completed	30

Baseline characteristics

Reporting groups

Reporting group title	Overall Period
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Reporting group description: -

Reporting group values	Overall Period	Total	
Number of subjects	30	30	
Age categorical			
Age 18 and over			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age 18 and over	30	30	
Age continuous			
Units: years			
median	37.2		
full range (min-max)	21.7 to 53.7	-	
Gender categorical			
Units: Subjects			
Female	11	11	
Male	19	19	

End points

End points reporting groups

Reporting group title	Single Arm
Reporting group description: -	

Primary: rate of toxicity-related treatment terminations

End point title	rate of toxicity-related treatment terminations ^[1]
End point description:	

End point type	Primary
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End point timeframe:

after 4 chemotherapy cycles

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: In this single arm trial, no inferential statistics were done. The primary endpoint is solely descriptive regarding safety.

End point values	Single Arm			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: whole	25			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

Adverse Events were reported as soon as Patient signed informed consent. Adverse. During telephone calls. The first 10 weeks at least on a weekly basis after that Day 1, 8 and 15 on site in every cycle during entire trial period until resolved or end of FU

Adverse event reporting additional description:

See Table 4 on uploaded Publication. Adverse Events listed Grades 1-4. The main objective of the trial was to determine the number of interruptions due to toxicity.

Assessment type	Systematic
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Dictionary used

Dictionary name	CTCAE
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Dictionary version	3
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Frequency threshold for reporting non-serious adverse events: 5 %

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 attached document for results

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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.

Due to the small number of remaining evaluable patients, a meaningful evaluation of the PFS at the 5 year time point was no longer possible. The trial was terminated at the 3 year PFS time point instead.

Notes: