



Clinical trial results:

MONO-INSTITUTIONAL PHASE II TRIAL ADDRESSING TOLERABILITY AND ACTIVITY OF R-CHOP CHEMOIMMUNOTHERAPY PRECEDED BY BLOOD-BRAIN BARRIER PERMEABILIZATION BY NGR-TUMOR NECROSIS FACTOR IN PATIENTS WITH RELAPSED OR REFRACTORY PRIMARY CENTRAL NERVOUS SYSTEM LYMPHOMA

Summary

EudraCT number	2014-001532-11
Trial protocol	IT
Global end of trial date	24 December 2024

Results information

Result version number	v1 (current)
This version publication date	12 February 2026
First version publication date	12 February 2026

Trial information

Trial identification

Sponsor protocol code	Ingrid
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	IRCCS Ospedale San Raffaele
Sponsor organisation address	Via Olgettina 60, Milan, Italy,
Public contact	Lymphoid malignancies Unit Data Ma, Ospedale San Raffaele, +39 0226433919, ferreri.andres@hsr.it
Scientific contact	Lymphoid malignancies Unit Data Ma, Ospedale San Raffaele, +39 0226433919, 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	03 August 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 August 2020
Global end of trial reached?	Yes
Global end of trial date	24 December 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

feasibility of chemo-immunotherapy with standard R-CHOP preceded by Ngr-TNF

Protection of trial subjects:

Common protection due to Clinical Trial participant:

- Pharmacovigilance
- Ethical Supervision
- Clinical peer reviewing

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 January 2016
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	Italy: 28
Worldwide total number of subjects	28
EEA total number of subjects	28

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)	23
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	28
Number of subjects completed	28

Period 1

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

Arms

Arm title	Treatment
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Arm description:

Outpatient (inpatient only if clinically indicated)

Patients will receive NGR-hTNF at dose of 0.8 mcg/sqm 1 hour before standard R-CHOP

(cyclophosphamide-doxorubicin-vincristine-prednisone-rituximab) regimen every 3 weeks for six courses

Day 1: Rituximab 375 mg/m² as IV infusion

NGR-hTNF 0.8 µg/m² as 1-hour infusion

Cyclophosphamide 750 mg/m² as IV bolus

Doxorubicin 50 mg/m² as IV bolus

Vincristine 1.4 mg/m² (max. 2 mg) as IV bolus

Days 2-6: Prednisone 75 mg/d oral

Any kind of consolidation treatment is allowed (i.e. WBRT, ASCT, maintenance using alkylating agents or oral immunodulatory drugs)

Arm type	Experimental
Investigational medicinal product name	NGR-hTNF
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Injection

Dosage and administration details:

dose of 0.8 mcg/sqm 1 hour before standard R-CHOP

Number of subjects in period 1	Treatment
Started	28
Completed	28

Baseline characteristics

Reporting groups

Reporting group title	Baseline
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Reporting group description: -

Reporting group values	Baseline	Total	
Number of subjects	28	28	
Age categorical			
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)	16	16	
From 65-84 years	12	12	
85 years and over	0	0	
Gender categorical			
Units: Subjects			
Female	14	14	
Male	14	14	

End points

End points reporting groups

Reporting group title	Treatment
Reporting group description:	
Outpatient (inpatient only if clinically indicated)	
Patients will receive NGR-hTNF at dose of 0.8 mcg/sqm 1 hour before standard R-CHOP (cyclophosphamide-doxorubicin-vincristine-prednisone-rituximab) regimen every 3 weeks for six courses	
Day 1: Rituximab 375 mg/m2 as IV infusion	
NGR-hTNF 0.8 µg/m2 as 1-hour infusion	
Cyclophosphamide 750 mg/m2 as IV bolus	
Doxorubicin 50 mg/m2 as IV bolus	
Vincristine 1.4 mg/m2 (max. 2 mg) as IV bolus	
Days 2-6: Prednisone 75 mg/d oral	
Any kind of consolidation treatment is allowed (i.e. WBRT, ASCT, maintenance using alkylating agents or oral immunodulatory drugs)	

Primary: ORR complete and partial responses based on IPCG response criteria

End point title	ORR complete and partial responses based on IPCG response criteria ^[1]
End point description:	
Overall response rate (ORR), defined as the proportion of patients achieving a complete response (CR) or partial response (PR) according to the IPCG response criteria, assessed at the end of treatment after completion of 6 cycles of R-CHOP chemo-immunotherapy preceded by NGR-hTNF and prior to any consolidative therapy.	
End point type	Primary
End point timeframe:	
ORR was evaluated after completion of 6 cycles of R-CHOP, before any consolidative 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: This is a single-arm, descriptive study. The two-stage Simon Minimax design will be used. The maximum overall response rate (complete and partial responses) considered of low interest will be 30% [17], and the minimum response rate considered of interest will be 50%; to demonstrate that difference, a total of 28 patients will be needed (one-sided test; type I error .10; power .9). No formal statistical comparison with a control group will be performed.

End point values	Treatment			
Subject group type	Reporting group			
Number of subjects analysed	28			
Units: %				
number (confidence interval 95%)	75 (59 to 91)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

from inclusion until 30 days after end of treatment

Adverse event reporting additional description:

Patients will be instructed by the investigator to report the occurrence of any AE. The investigator assesses and records all AEs observed during the AE reporting period.

AEs are coded with the NCI Common Terminology Criteria for Adverse Event

Assessment type	Systematic
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Dictionary used

Dictionary name	NCI-NCIC CTC
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Dictionary version	3
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Reporting groups

Reporting group title	Adverse event
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Reporting group description:

There were no cases of unexpected toxicity or interruptions because of toxicity, and no patient needed a reduction in dose of either NGR-hTNF or R-CHOP. Only 6 courses (4%) were delayed (cytopenia). Sixteen serious AEs were recorded in 12 patients: grade 1 to 2 seizures (3), grade 1 to 2 deep venous thrombosis (2), grade 3 infections (5), grade 3 syncope (2), grade 3 constipation, grade 4 febrile neutropenia, pulmonary aspergillosis, and grade 2 left ventricular function reduction.

Serious adverse events	Adverse event		
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 28 (42.86%)		
number of deaths (all causes)	22		
number of deaths resulting from adverse events	0		
Cardiac disorders			
left ventricular function reduction			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
seizures			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
deep venous thrombosis			

subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
syncope			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Febrile neutropenia			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
pulmonary aspergillosis			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
infections			
subjects affected / exposed	4 / 28 (14.29%)		
occurrences causally related to treatment / all	5 / 5		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Adverse event		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	28 / 28 (100.00%)		

General disorders and administration site conditions TNF infusion reactions subjects affected / exposed occurrences (all)	7 / 28 (25.00%) 9		
Blood and lymphatic system disorders Neutropenia subjects affected / exposed occurrences (all) Thrombocytopenia subjects affected / exposed occurrences (all) anemia subjects affected / exposed occurrences (all)	28 / 28 (100.00%) 83 28 / 28 (100.00%) 85 28 / 28 (100.00%) 100		
Gastrointestinal disorders Nausea and vomiting subjects affected / exposed occurrences (all)	3 / 28 (10.71%) 4		
Hepatobiliary disorders Hepatotoxicity subjects affected / exposed occurrences (all)	15 / 28 (53.57%) 32		
Infections and infestations Oral mucositis subjects affected / exposed occurrences (all)	3 / 28 (10.71%) 4		

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

None reported

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/32766857>