



Clinical trial results:

Phase II clinical study on the activity of salvage therapy with high doses of oral clarithromycin in patients with extranodal marginal zone relapsed or refractory lymphoma

Summary

EudraCT number	2011-004808-37
Trial protocol	IT
Global end of trial date	15 July 2013

Results information

Result version number	v1 (current)
This version publication date	20 December 2025
First version publication date	20 December 2025

Trial information

Trial identification

Sponsor protocol code	HD-K
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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 San Raffaele
Sponsor organisation address	Via Olgettina 60, Milano, Italy, 20132
Public contact	Unita' Operativa Linfomi, Fondazione San Raffaele del Monte Tabor, +39 0226437649, ferreri.andres@hsr.it
Scientific contact	Unita' Operativa Linfomi, Fondazione San Raffaele del Monte Tabor, +39 0226437649, 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	31 December 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 July 2013
Global end of trial reached?	Yes
Global end of trial date	15 July 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective is to evaluate the activity of oral clarithromycin high-dose (2 g/day) in patients with extranodal marginal zone relapsed / refractory lymphoma.

Protection of trial subjects:

The patient's confidentiality will be maintained and will not be made publicly available to the extent permitted by the applicable laws and regulations (Law n. 675/1996 and amendments) and Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (General Data Protection Regulation).

An identification number will be automatically attributed to each patient enrolled in the trial. This number will identify the patient and must be included on all case report forms. In order to avoid identification errors, date of birth will also be reported on forms.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 January 2012
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	Italy: 23
Worldwide total number of subjects	23
EEA total number of subjects	23

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)	5

From 65 to 84 years	17
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

From November 2011 to October 2013 , we enrolled 23 patients

Pre-assignment

Screening details:

Both male and female were included (>18 years), each with histological diagnosis of extragastric or gastric extranodal marginal zone B-cell lymphoma Helicobacter pylori-positive refractory to conventional antibiotic therapy or H. pylori-negative. Written informed consent.

Pre-assignment period milestones

Number of subjects started	23
Number of subjects completed	23

Period 1

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

Blinding implementation details:

Not applicable

Arms

Arm title	Clarithromycin
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Arm description:

The proposed strategy involves the administration of home antibiotic therapy with clarithromycin (Klacid®) in the form of 500 mg tablets to be taken orally. Clarithromycin is a macrolide antibiotic, commonly used in infections of the upper respiratory tract and community-acquired lung infections in immunocompetent hosts.

The therapy will be administered as follows: patients will take 4 500 mg tablets of clarithromycin, all together, once a day (every 24 hours), orally, for 14 days, followed by a 7-day interval. The tablets will be taken, away from meals, with plenty of water and in a sitting or standing position, never in bed or as the last activity of the day.

Arm type	Experimental
Investigational medicinal product name	clarithromycin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Buccal use

Dosage and administration details:

The therapy will be administered as follows: patients will take 4 500 mg tablets of clarithromycin, all together, once a day (every 24 hours), orally, for 14 days, followed by a 7-day interval. The tablets will be taken, away from meals, with plenty of water and in a sitting or standing position, never in bed or as the last activity of the day.

Number of subjects in period 1	Clarithromycin
Started	23
Completed	23

Baseline characteristics

Reporting groups

Reporting group title	HD-K treatment
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Reporting group description: -

Reporting group values	HD-K treatment	Total	
Number of subjects	23	23	
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)	5	5	
From 65-84 years	17	17	
85 years and over	1	1	
>18 years	0	0	
Age continuous			
Units: years			
median	70		
inter-quartile range (Q1-Q3)	47 to 88	-	
Gender categorical			
Units: Subjects			
Female	18	18	
Male	5	5	

End points

End points reporting groups

Reporting group title	Clarithromycin
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Reporting group description:

The proposed strategy involves the administration of home antibiotic therapy with clarithromycin (Klacid®) in the form of 500 mg tablets to be taken orally. Clarithromycin is a macrolide antibiotic, commonly used in infections of the upper respiratory tract and community-acquired lung infections in immunocompetent hosts.

The therapy will be administered as follows: patients will take 4 500 mg tablets of clarithromycin, all together, once a day (every 24 hours), orally, for 14 days, followed by a 7-day interval. The tablets will be taken, away from meals, with plenty of water and in a sitting or standing position, never in bed or as the last activity of the day.

Subject analysis set title	all patients treated with HD-K
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Subject analysis set type	Full analysis
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Subject analysis set description:

Full Analysis Set includes all patients who received at least one dose of HD-K and had at least one tumor response assessment. These patients are used to report baseline characteristics for the overall baseline period

Primary: overall response rate

End point title	overall response rate
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End point description:

End point type	Primary
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End point timeframe:

from the start of treatment until the post-treatment response assessment

End point values	Clarithromycin	all patients treated with HD-K		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	23	23		
Units: Subjects	12	12		

Statistical analyses

Statistical analysis title	Descriptive statistics
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Statistical analysis description:

This is a single-arm phase II trial using a Simon minimax two-stage design. There is no comparator arm. Analyses for ORR, PFS, OS, and safety are descriptive. The system requires two groups by default, but only one arm is present.

Comparison groups	Clarithromycin v all patients treated with HD-K
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Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05 ^[1]
Method	Simon minimax two-stage design
Parameter estimate	ORR=52%; 95%CI 32-72%
Confidence interval	
level	95 %
sides	1-sided
lower limit	32
upper limit	72
Variability estimate	Standard deviation

Notes:

[1] - The Simon minimax two-stage design was used. The maximum ORR considered of low interest was 40% (P0) [11] and the minimum ORR considered of interest was 70% (P1). The target enrollment ($\alpha = 0.05$; $\beta = 0.20$; two-sided) was estimated to be 21 patient

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All adverse events occurring from the first study-related procedure up to 30 days after the last dose of study drug

Assessment type	Non-systematic
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Dictionary used

Dictionary name	NCI-CTC AEs
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Dictionary version	4.3
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Reporting groups

Reporting group title	Adverse event
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Reporting group description:

Eighteen patients underwent treatment as scheduled; HD-K was interrupted in five patients due to nausea (n = 2) or progressive disease (n = 3); 79 (86%) of 92 planned courses were delivered. Tolerability was excellent; nausea was the commonest sideeffect, but it was manageable and did not require dose reduction, course each) were: grade-1 headache, grade-1 rash, grade-1 constipation, grade-2 joint pain. Diarrhea was not recorded. No hemogram and biochemical abnormalities were detected during or after HD-K. Electrocardiogram abnormalities (i.e. QT prolongation, arrhythmias), often reported during macrolides use, were not recorded.

Serious adverse events	Adverse event		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 23 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	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	5 / 23 (21.74%)		
General disorders and administration site conditions			
headache			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
joint pain			

subjects affected / exposed occurrences (all)	1 / 23 (4.35%) 1		
Immune system disorders rash subjects affected / exposed occurrences (all)	1 / 23 (4.35%) 1		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) constipation subjects affected / exposed occurrences (all)	2 / 23 (8.70%) 1 1 / 23 (4.35%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 April 2013	eliminate the possibility of administering statins in combination with clarithromycin due to evidence of an increased risk of rhabdomyolysis.

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/25935794>