Clinical trial results:
Venetoclax, lenalidomide and rituximab in patients with relapsed/refractory mantle cell lymphoma.

Summary

EudraCT number	2017-001060-38
Trial protocol	SE NO DK FI
Global end of trial date	01 December 2024

Results information

Result version number	v1 (current)
This version publication date	29 June 2025
First version publication date	29 June 2025

Trial information

Trial identification

Sponsor protocol code	NLG-MCL7

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03505944
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Skåne University Hospital
Sponsor organisation address	Department of Oncology, Lund, Sweden, 221085
Public contact	Academic Clinical trial office, Nordic Lymphoma Group, Department of Hematology, Aarhus University Hospital, +45 7845 5855, a-cto@auh.rm.dk
Scientific contact	Academic Clinical trial office, Nordic Lymphoma Group, Department of Hematology, Aarhus University Hospital, +45 7845 5855, a-cto@auh.rm.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	24 November 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 November 2021
Global end of trial reached?	Yes
Global end of trial date	01 December 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to assess the overall response rate (ORR) at 6 months with lenalidomide-venetoclax and rituximab, in patients with relapsed or refractory mantle cell lymphoma, by use of an MRD driven strategy.

Protection of trial subjects:

The study was conducted according to the guidelines for Good Clinical Practice, issued by The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). The protocol was approved by the local, regional or national Ethical Review Boards according to the existing national and local regulatory requirements. The study was conducted in agreement with the declaration of Helsinki and the laws and the regulations of the respective countries.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 July 2018
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: 16
Country: Number of subjects enrolled	Sweden: 29
Country: Number of subjects enrolled	Denmark: 12
Country: Number of subjects enrolled	Finland: 2
Worldwide total number of subjects	59
EEA total number of subjects	59

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)	9
From 65 to 84 years	50
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Overall 59 patients were included in the trial. 15 Nordic sites contributed to the study. The first patient was included on 07-Jul-2018. The last
patient was included on 29-Apr-2021.

Pre-assignment

Screening details:

Patients were screened for the complete list of inclusion and exclusion criteria according to the protocol.

Period 1

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

Arms

Arm title	Treatment

Arm description:

Single arm study
Phase 1 tested dose groups A, B, C, Y
Phase 2 applied the dose schedule of phase 1 dose group Y

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

Dosage and administration details:

Phase 1 dose group A+B: 400 mg po daily (after ramp-up dosing of 20 mg, 50 mg, 100 mg, 200 mg, for one week each)
Phase 1 dose group C: 800 mg po daily (after ramp-up dosing of 20 mg, 50 mg, 100 mg, 200 mg, 400 mg, for one week each)
Phase 1 dose group C + Phase 2: 600 mg po daily (after ramp-up dosing of 20 mg, 50 mg, 100 mg, 200 mg, 400 mg, for one week each)

Investigational medicinal product name	lenalidomide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Phase 1 dose group A: 15 mg po days 1-21 in cycles of 28 days
Phase 1 dose group B+C: 20 mg po days 1-21 in cycles of 28 days
Phase 1 dose group Y + Phase 2: 15 mg po days 1-21 in cycles of 28 days

Number of subjects in period 1	Treatment
Started	59
Completed	42
Not completed	17
Adverse event, non-fatal	5
Lack of efficacy	12

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	59	59	
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)	9	9	
From 65-84 years	50	50	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	11	11	
Male	48	48	

End points

End points reporting groups

Reporting group title	Treatment

Reporting group description:

Single arm study
Phase 1 tested dose groups A, B, C, Y
Phase 2 applied the dose schedule of phase 1 dose group Y

Primary: Overall response rate

End point title	Overall response rate[1]

End point description:

The primary objective is to assess the overall response rate (ORR) at 6 months with lenalidomide-venetoclax and rituximab, in patients with relapsed or refractory mantle cell lymphoma, by use of an MRD driven strategy. ORR includes complete (CR) and partial remissions (PR).

End point type	Primary

End point timeframe:

6 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: The statistical analyses is described in the publication - see reference

End point values	Treatment			
Subject group type	Reporting group			
Number of subjects analysed	59			
Units: subjects	37			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs will be recorded from the time the subject signs informed consent to 28 days after the last dose of study drug.

Adverse event reporting additional description:

For grade 1-2 events, only the ones occurring in 10% or more of patients are reported. Haematological adverse events less than grade 3 were not reported.

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	4.03

Reporting groups

Reporting group title	Treatment

Reporting group description:

Single arm study
Phase 1 tested dose groups A, B, C, Y
Phase 2 applied the dose schedule of phase 1 dose group Y

Serious adverse events	Treatment		
Total subjects affected by serious adverse events			
subjects affected / exposed	30 / 59 (50.85%)		
number of deaths (all causes)	32		
number of deaths resulting from adverse events	4		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Second primary malignancy			
subjects affected / exposed	2 / 59 (3.39%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Vascular			
subjects affected / exposed	3 / 59 (5.08%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
neurological			
subjects affected / exposed	5 / 59 (8.47%)		
occurrences causally related to treatment / all	2 / 5		
deaths causally related to treatment / all	1 / 1		

General disorders and administration site conditions			
General disorders			
subjects affected / exposed	8 / 59 (13.56%)		
occurrences causally related to treatment / all	3 / 9		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Haematological			
subjects affected / exposed	4 / 59 (6.78%)		
occurrences causally related to treatment / all	3 / 5		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Blurred vision			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
gastrointestinal disorder			
subjects affected / exposed	2 / 59 (3.39%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Cystitis			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Infections			
subjects affected / exposed	16 / 59 (27.12%)		
occurrences causally related to treatment / all	13 / 25		
deaths causally related to treatment / all	3 / 3		

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

Non-serious adverse events	Treatment		
Total subjects affected by non-serious adverse events subjects affected / exposed	59 / 59 (100.00%)		
Cardiac disorders Cardiovascular disorders subjects affected / exposed occurrences (all)	12 / 59 (20.34%) 12		
Nervous system disorders Neurological subjects affected / exposed occurrences (all) CNS subjects affected / exposed occurrences (all)	21 / 59 (35.59%) 21 9 / 59 (15.25%) 9		
Blood and lymphatic system disorders Thrombocytopenia subjects affected / exposed occurrences (all) Anemia subjects affected / exposed occurrences (all) Neutropenia subjects affected / exposed occurrences (all)	21 / 59 (35.59%) 21 8 / 59 (13.56%) 8 52 / 59 (88.14%) 52		
Gastrointestinal disorders gastrointestinal disorder subjects affected / exposed occurrences (all)	35 / 59 (59.32%) 35		
Respiratory, thoracic and mediastinal disorders Respiratory subjects affected / exposed occurrences (all)	17 / 59 (28.81%) 17		
Hepatobiliary disorders Hepatic			

subjects affected / exposed occurrences (all)	8 / 59 (13.56%) 8		
Skin and subcutaneous tissue disorders Cutaneous subjects affected / exposed occurrences (all)	 31 / 59 (52.54%) 31		
Renal and urinary disorders Renal subjects affected / exposed occurrences (all)	 7 / 59 (11.86%) 7		
Musculoskeletal and connective tissue disorders Muscular subjects affected / exposed occurrences (all)	 14 / 59 (23.73%) 14		
Infections and infestations Infections subjects affected / exposed occurrences (all)	 23 / 59 (38.98%) 23		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 February 2019	Introduced Dose Group Y
08 February 2021	Removed cohort of 15 untreated patients

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/38113470