Clinical trial results:
INTERNATIONAL MULTICENTER, OPEN-LABEL, PHASE 2 STUDY TO TREAT MOLECULAR RELAPSE OF PEDIATRIC ACUTE MYELOID LEUKEMIA WITH AZACITIDINE

Summary

EudraCT number	2017-003422-32
Trial protocol	DE AT NL SE BE DK
Global end of trial date	15 December 2023

Results information

Result version number	v1 (current)
This version publication date	15 May 2025
First version publication date	15 May 2025

Trial information

Trial identification

Sponsor protocol code	AMoRe2017

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	GPOH gGmbH
Sponsor organisation address	Holsterhauser Platz 2, Essen, Germany, 45147
Public contact	Katharina Waack-Buchholz, Pädiatrisches Forschungsnetzwerk gGmbH, 0049 020174949611, waack.katharina@gpoh-trials.org
Scientific contact	Dirk Reinhardt, Päd. Forschungsnetzwerk, 0049 02017494960, dirk.reinhardt@gpoh-trials.org

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	12 December 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	15 December 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the effect of azacitidine treatment in AML subjects at molecular relapse after CR1 with regard to molecular response prior to further treatment (reinduction / HSCT)

Protection of trial subjects:

Children and young adults with AML in molecular relapse after CR1 will be considered for participation in this study. The subject and/or guardian(s) (as appropriate by local law and regulations) will be provided with a written ICF and will be given the opportunity to ask any questions concerning the study. The ICF must be signed by the subject and/or guardian(s) (as appropriate by local law and regulations) prior to the subject participating in any study procedures. The ICF must be signed before performance of any study related activity.
Subjects who fail screening should be managed according to standard practice (including chemotherapy) in the responsible institution. For subjects who are rescreened, the ICF will need to be signed again, as well as all screening procedures repeated. Subjects will sign ICF and start the screening process at the following time points: Subjects will remain in the Screening Period for up to 10 days until the molecular relapse has been confirmed in PB and BM aspirate by the study reference laboratory. Once the molecular relapse has been confirmed, and provided that all other criteria for the study are satisfied, the subject will be enrolled.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 February 2018
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	Netherlands: 2
Country: Number of subjects enrolled	Austria: 3
Country: Number of subjects enrolled	Germany: 15
Worldwide total number of subjects	20
EEA total number of subjects	20

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)	2
Children (2-11 years)	11
Adolescents (12-17 years)	3
Adults (18-64 years)	4
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Dates of recruitment period: 03/2018 - 02/2023
Territories: Germany, The Netherlands, Austria
Total number of patients: 20

Pre-assignment

Screening details:

MRD sreening accoring to standard of care

Period 1

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

Blinding implementation details:

No blinding implemented.

Arms

Arm title	Azacitidine

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Azacitidine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous azacitidine 75 mg/m2, Days 1 to 7 of a 28-day cycle for up to 3 cycles initially.
In case of decline of MRD during azacitidine treatment additional cycles are allowed (maximum 6 cycles).

Number of subjects in period 1	Azacitidine
Started	20
Completed	19
Not completed	1
laboratory measurement error	1

Baseline characteristics

Reporting groups

Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	20	20	
Age categorical Units: Subjects			
3 months to <21 years	20	20	
Gender categorical Units: Subjects			
Female	9	9	
Male	11	11	

Subject analysis sets

Subject analysis set title	Full analysis
Subject analysis set type	Full analysis

Subject analysis set description:

All subjects eligible for the analysis of the primary and secondary endpoint.

Reporting group values	Full analysis		
Number of subjects	19		
Age categorical Units: Subjects			
3 months to <21 years	19		
Gender categorical Units: Subjects			
Female	9		
Male	10		

End points

End points reporting groups

Reporting group title	Azacitidine
Reporting group description: -	
Subject analysis set title	Full analysis
Subject analysis set type	Full analysis
Subject analysis set description:	
All subjects eligible for the analysis of the primary and secondary endpoint.	

Primary: To evaluate the effect of azacitidine treatment in AML subjects at molecular relapse after CR1 with regard to molecular response prior to further treatment (reinduction / HSCT)

End point title	To evaluate the effect of azacitidine treatment in AML subjects at molecular relapse after CR1 with regard to molecular response prior to further treatment (reinduction / HSCT)[1]
End point description:	
End point type	Primary
End point timeframe:	
During the recruitment period.	

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: Singel arm study: The statistical analysis for an endpoint is not mandatory.

End point values	Azacitidine			
Subject group type	Reporting group			
Number of subjects analysed	19[2]			
Units: totals				
Molecular stabilization	3			
Molecular progression	1			
Molecular improvement	5			
Hematological/clinical relapse	10			

Notes:

[2] - n = 1 drop-out due to measurement error, not eligible for analysis

Statistical analyses

No statistical analyses for this end point

Secondary: To assess the safety of azacitidine treatment in children and adolescents with a molecular relapse of AML. Disease free and overall survival post molecular relapse; quality of life

End point title	To assess the safety of azacitidine treatment in children and adolescents with a molecular relapse of AML. Disease free and overall survival post molecular relapse; quality of life
End point description:	
AE reports	
End point type	Secondary

End point timeframe:
Start of recruitment until 12/23.

End point values	Azacitidine			
Subject group type	Reporting group			
Number of subjects analysed	19[3]			
Units: totals				
AE Grade 1	78			
AE Grade 2	36			
AE Grade 3	29			
AE Grade 4	8			
AE Grade 5	0			

Notes:
[3] - n = 1 drop-out due to measurement error, not eligible for analysis

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Start at first patient in, ended 12/2023	
Assessment type	Systematic

Dictionary used	
Dictionary name	CTCAE Short Name
Dictionary version	5.0

Reporting groups	
Reporting group title	Subject eligible for analysis
Reporting group description: All subject that recieved at least one cycle of protocol treatment.	

Serious adverse events	Subject eligible for analysis		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 19 (15.79%)		
number of deaths (all causes)	4		
number of deaths resulting from adverse events	0		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Febrile Neutropenia			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Fever			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Flu like symptoms			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Subject eligible for analysis		
Total subjects affected by non-serious adverse events subjects affected / exposed	6 / 19 (31.58%)		
Cardiac disorders			
Tachycardia	Additional description: Garde 2		
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Bradycardia	Additional description: Grade 1		
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Hypotension	Additional description: Grade 1		
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
White blood cells decreased	Additional description: all grades		
subjects affected / exposed	3 / 19 (15.79%)		
occurrences (all)	13		
Anemia	Additional description: all grades		
subjects affected / exposed	2 / 19 (10.53%)		
occurrences (all)	16		
Platelet count decreased	Additional description: all grades		
subjects affected / exposed	3 / 19 (15.79%)		
occurrences (all)	22		
Lymphocyte count decreased	Additional description: Grade 1		
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Thrombocytopenia intermittend	Additional description: Grade 1		
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Hypernatremia	Additional description: Grade 1		

subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
LDH increased	Additional description: Grade 1		
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	2		
Low potassium	Additional description: Grade 2		
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
General disorders and administration site conditions			
Pain	Additional description: Grade 1 and 2		
subjects affected / exposed	6 / 19 (31.58%)		
occurrences (all)	8		
Edema	Additional description: Grade 1		
subjects affected / exposed	3 / 19 (15.79%)		
occurrences (all)	5		
Fall	Additional description: Grade 2		
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Allergic reaction to thrombocyte infusion	Additional description: Grade 3		
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Hematoma	Additional description: Grade 1		
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Reduced general condition	Additional description: Grade 1		
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Malaise	Additional description: Grade 1		
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Drowsiness	Additional description: Grade 1		
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Agitation	Additional description: Grade 1		

subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Gastrointestinal disorders			
Nausea	Additional description: all grades		
subjects affected / exposed	4 / 19 (21.05%)		
occurrences (all)	9		
Vomiting	Additional description: Grade 1		
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Diarrhea	Additional description: Grade 1		
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Flatulences intermitted	Additional description: Grade 2		
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Constipation	Additional description: Grade 1		
subjects affected / exposed	2 / 19 (10.53%)		
occurrences (all)	2		
Mucositis	Additional description: Grade 1		
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Gum bleeding	Additional description: Grade 2		
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Hepatobiliary disorders			
Blood bilirubin increased	Additional description: Grade 1		
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	2		
Aspartate aminotransferase increased	Additional description: Grade 1 and 2		
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	5		
Alanine aminotransferase increased	Additional description: Grade 2 and 3		
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders			

Rash	Additional description: Grade 1 and 3		
subjects affected / exposed	2 / 19 (10.53%)		
occurrences (all)	3		
Exanthema			
subjects affected / exposed	2 / 19 (10.53%)		
occurrences (all)	2		
Flaky skin	Additional description: Grade 1		
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Redness skin	Additional description: Grade 1		
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Warts	Additional description: Grade 1		
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Itching	Additional description: Grade 1		
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Renal and urinary disorders			
Creatinin increased	Additional description: Grade 1		
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
GTT increased	Additional description: Grade 1		
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	3		
Hyperuricemia	Additional description: Grade 1		
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	2		
Musculoskeletal and connective tissue disorders			
Myalgia	Additional description: Grade 1		
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Infections and infestations			
Febrile neutropenia	Additional description: Grade 3		
subjects affected / exposed	2 / 19 (10.53%)		
occurrences (all)	2		

Cough	Additional description: Grade 1 and 2		
subjects affected / exposed	2 / 19 (10.53%)		
occurrences (all)	6		
Lung infection	Additional description: Grade 3		
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Flu like symptoms	Additional description: Grade 2 and 3		
subjects affected / exposed	2 / 19 (10.53%)		
occurrences (all)	2		
Sore throat	Additional description: Grade 1		
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
CRP increased	Additional description: Grade 3		
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	4		
Herpes simplex labialis reactivation	Additional description: Grade 1		
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 February 2020	Substantial amendment included: - Contacts and contact details updated as appropriate - Inclusion criteria, methodology, study design, screening period, molecular progression: MRD Value removed - Treatment period: Dose corrected, Flowchart was also corrected - Pregancy (Harmonization international protocols) - Treatment Administration and Schedule (Harmonization international protocols) - Regulatory Considerations (Harmonization international protocols)

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported