Clinical trial results:
Clofarabine salvage therapy in patients with relapsed or refractory AML
The BRIDGE Trial

Summary

EudraCT number	2010-022584-35
Trial protocol	DE
Global end of trial date	23 August 2013

Results information

Result version number	v1 (current)
This version publication date	01 September 2021
First version publication date	01 September 2021

Trial information

Trial identification

Sponsor protocol code	TUD-BRIDGE-046

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01295307
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Technische Universität Dresden
Sponsor organisation address	Mommsenstr. 9, Dresden, Germany,
Public contact	Head of Clinical Trials Unit, Universitätsklinikum Dresden, Med. Klinik und Poliklinik I, +49 351458-3775, christoph.roellig@uniklinikum-dresden.de
Scientific contact	Head of Clinical Trials Unit, Universitätsklinikum Dresden, Med. Klinik und Poliklinik I, +49 351458-3775, christoph.roellig@uniklinikum-dresden.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	09 September 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 August 2013
Global end of trial reached?	Yes
Global end of trial date	23 August 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To study the safety and efficacy of clofarabine salvage therapy prior to allogeneic HCT. (Rate of treatment success)

Protection of trial subjects:

In the responsibility of the investigator, subjects were closely monitored during this study.
Via the safety desk, the coordinating investigator on behalf of the sponsor reviewed all reported SAEs for reasonable suspected causal relationship to the investigational treatment and for expectedness in terms of nature and severity of an SAR in relation to the applicable clofarabine product information or investigator's brochure.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 December 2010
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	Germany: 84
Worldwide total number of subjects	84
EEA total number of subjects	84

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)	56
From 65 to 84 years	28
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Between March 2011 and May 2013, 84 pts with relapsed or refractory AML older than 40 years were enrolled.

Pre-assignment

Screening details:

Pretreatment evaluations were done to determine the patients eligibility for the study within 14 days prior to study inclusion.

Period 1

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

Arms

Arm title	CLARA

Arm description:

Pts were scheduled for at least one cycle of induction therapy with CLARA (clofarabine 30 mg/m2 and cytarabine 1 g/m2 days 1-5). Pts with a donor received HSCT in aplasia after first CLARA. In case of a prolonged donor search HSCT was performed as soon as possible. Consolidation therapy contained clofarabine 30 mg/m2 (1 hr IV infusion) days 1-4 followed 3 hours after the end of infusion by intermediate dose cytarabine 1 g/m2 (2 hrs IV infusion) days 1-4. The conditioning regimen consisted of clofarabine 30 mg/m2 day -6 to -3 and melphalan 140 mg/m2 on day -2. In pts with partially matched unrelated donors ATG (Genzyme) at a cumulative dose of 4.5 mg/kg was recommended.

Arm type	Experimental
Investigational medicinal product name	Clofarabine
Investigational medicinal product code	
Other name	CAS: 123318-82-1
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Induction: clofarabine 30 mg/m2 (1 hr IV infusion) days 1-5
Re-Induction: clofarabine 30 mg/m2 (1 hr IV infusion) days 1-5
Consolidation: clofarabine 30 mg/m2 (1 hr IV infusion) days 1-4
Conditioning: clofarabine 30 mg/m2 (1 hr IV infusion) days –6 to –3

Investigational medicinal product name	Cytarabine
Investigational medicinal product code	
Other name	CAS: 147-94-4
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Induction: cytarabine 1 g/m2 (2 hrs IV infusion) days 1-5
Re-Induction: cytarabine 1 g/m2 (2 hrs IV infusion) days 1-5
Consolidation: cytarabine 1 g/m2 (2 hrs IV infusion) days 1-4

Number of subjects in period 1	CLARA
Started	84
Completed	67
Not completed	17
Adverse event, serious fatal	13
Consent withdrawn by subject	1
Adverse event, non-fatal	3

Baseline characteristics

Reporting groups	
Reporting group title	overall trial
Reporting group description:	
Patients with relapsed or refractory AML older than 40 years	

Reporting group values	overall trial	Total	
Number of subjects	84	84	
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)	56	56	
From 65-84 years	28	28	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	33	33	
Male	51	51	

End points

End points reporting groups

Reporting group title	CLARA

Reporting group description:

Pts were scheduled for at least one cycle of induction therapy with CLARA (clofarabine 30 mg/m2 and cytarabine 1 g/m2 days 1-5). Pts with a donor received HSCT in aplasia after first CLARA. In case of a prolonged donor search HSCT was performed as soon as possible. Consolidation therapy contained clofarabine 30 mg/m2 (1 hr IV infusion) days 1-4 followed 3 hours after the end of infusion by intermediate dose cytarabine 1 g/m2 (2 hrs IV infusion) days 1-4. The conditioning regimen consisted of clofarabine 30 mg/m2 day -6 to -3 and melphalan 140 mg/m2 on day -2. In pts with partially matched unrelated donors ATG (Genzyme) at a cumulative dose of 4.5 mg/kg was recommended.

Primary: rate of treatment success

End point title	rate of treatment success[1]

End point description:

This rate was assessed in the intent-to-treat population. The rate of treatment success was analyzed in an optimal two-stage design according to Simon.

End point type	Primary

End point timeframe:

The primary endpoint, treatment success, was defined as complete remission (CR), CR with incomplete recovery (CRi) or CRchim (BM donor chimerism >95% and absolute neutrophil count >0.5/nL) on day 35 after HSCT.

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: More detailed description available (see online references)

End point values	CLARA			
Subject group type	Reporting group			
Number of subjects analysed	84			
Units: percent				
number (confidence interval 95%)				
rate of treatment success	61 (50 to 70)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Adverse events were reported after intake of the first dose of study medication.

Adverse event reporting additional description:

Adverse events of special interest of any grade
All adverse events CTCAE grade ≥3

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	13

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: More detailed description available (see online references)

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 November 2011	protocol amendment: The interval for investigations had been refined. Prompted by a report on preliminary results of CLARA chemotherapy the starting dose level has been reduced.

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/26283567

http://www.ncbi.nlm.nih.gov/pubmed/28527985