



Clinical trial results:

A double-blind, placebo-controlled, randomized, multi-center phase II trial to assess the efficacy of Sorafenib added to standard primary therapy in patients with newly diagnosed AML 60 years of age

Summary

EudraCT number	2008-004968-40
Trial protocol	DE
Global end of trial date	25 September 2014

Results information

Result version number	v1 (current)
This version publication date	09 September 2021
First version publication date	09 September 2021

Trial information

Trial identification

Sponsor protocol code	TUD-SORAML-034
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00893373
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Technische Universität Dresden
Sponsor organisation address	MommSENstr. 9, Dresden, Germany,
Public contact	MK1, Klinische Studien, Universitätsklinikum Dresden, 0049 03514583775, christoph.roellig@uniklinikum-dresden.de
Scientific contact	MK1, Klinische Studien, Universitätsklinikum Dresden, 0049 03514583775, 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	20 August 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 September 2014
Global end of trial reached?	Yes
Global end of trial date	25 September 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

to compare the median Event Free Survival (EFS) of AML patients in the age of ≥ 18 and ≤ 60 years between the Sorafenib and the control group

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 sorafenib product information or investigator's brochure.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 March 2009
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	78 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 276
Worldwide total number of subjects	276
EEA total number of subjects	276

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)	276

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients aged 18 to 60 years with newly diagnosed de-novo or secondary acute myeloid leukaemia according to WHO criteria, with a clinical performance score of 0–2 and adequate renal and liver function, were eligible for inclusion. Between March 27, 2009, and Nov 28, 2011, 276 patients were enrolled and randomised

Pre-assignment

Screening details:

Pretreatment evaluations were done to determine the patients eligibility for the study within 10 days prio to the first course of induction therapy.

Period 1

Period 1 title	overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm V (Sorafenib)
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Sorafenib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

double induction: sorafenib 800mg/day (2 tablets twice a day) from day 10 continuously until day 19
alternative induction therapy - HAM (in the case of insufficient response to induction therapy I):
sorafenib 800mg/day (2 tablets twice a day) from day 10 continuously until day 19
three cycles of consolidation: sorafenib 800mg/day (2 tablets twice a day) from day 8 continuously until
3 days before first day of next chemotherapy course
Maintenance: sorafenib 800mg/day (2 tablets twice a day)
started on day 8 of the last consolidation cycle; Maintenance therapy was administered continuously until one year after start of maintenance therapy.

Arm title	Arm P (Placebo)
Arm description: -	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

double induction: Placebo (2 tablets twice a day) from day 10 continuously until day 19
alternative induction therapy - HAM (in the case of insufficient response to induction therapy I): Placebo
(2 tablets twice a day) from day 10 continuously until day 19
three cycles of consolidation: Placebo (2 tablets twice a day) from day 8 continuously until 3 days before
first day of next chemotherapy course
Maintenance: Placebo (2 tablets twice a day)
started on day 8 of the last consolidation cycle; Maintenance therapy was administered continuously until

I one year after start of maintenance therapy.

Number of subjects in period 1	Arm V (Sorafenib)	Arm P (Placebo)
Started	138	138
Completed	134	133
Not completed	4	5
Consent withdrawn by subject	2	1
Adverse event, non-fatal	1	2
second malignancy	-	1
no AML	1	1

Baseline characteristics

Reporting groups

Reporting group title	Arm V (Sorafenib)
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Reporting group description: -

Reporting group title	Arm P (Placebo)
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Reporting group description: -

Reporting group values	Arm V (Sorafenib)	Arm P (Placebo)	Total
Number of subjects	138	138	276
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	138	138	276
From 65-84 years	0	0	0
85 years and over	0	0	0
Gender categorical			
Units: Subjects			
Female	66	71	137
Male	72	67	139

End points

End points reporting groups

Reporting group title	Arm V (Sorafenib)
Reporting group description: -	
Reporting group title	Arm P (Placebo)
Reporting group description: -	

Primary: event-free survival

End point title	event-free survival ^[1]
End point description:	

End point type	Primary
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End point timeframe:

The primary endpoint was event-free survival, with an event defined as either primary treatment failure or relapse or death, assessed in all randomised patients who received at least one dose of study treatment.

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: further information can be found in the publication (see online references)

End point values	Arm V (Sorafenib)	Arm P (Placebo)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	134	133		
Units: months				
median (confidence interval 95%)	21 (9 to 32)	9 (4 to 15)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

AEs and SAEs had to be recorded from the time the informed consent is signed, up to and including 30 days following last administration of study drug.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	12.0

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: further information can be found in the publication (see online references)

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/26549589>

<http://www.ncbi.nlm.nih.gov/pubmed/33603142>