

**Clinical trial results:**

Open-label, dose-escalating trial to evaluate the tolerability, toxicity, safety, pharmacokinetics, pharmacodynamics and activity of volasertib added to the standard intensive salvage chemotherapy regimen with liposomal daunorubicine, fludarabine and cytarabine (DNX-FLA) followed by fludarabine and cytarabine (FLA) in children from 3 months to less than 18 years of age with acute myeloid leukaemia after failure of the front-line therapy

Summary

EudraCT number	2015-004625-14
Trial protocol	DE BE DK CZ FR NL IT
Global end of trial date	28 March 2016

Results information

Result version number	v1 (current)
This version publication date	30 September 2018
First version publication date	30 September 2018
Summary attachment (see zip file)	Statement (1230.28_Statement_Eudract.pdf)

Trial information**Trial identification**

Sponsor protocol code	01230.28
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Boehringer Ingelheim
Sponsor organisation address	Binger Strasse 173, Ingelheim am Rhein, Germany, 55216
Public contact	QRPE Processes and Systems Coordination, Clinical Trial Information Disclosure,, QRPE Processes and Systems Coordination, Clinical Trial Information Disclosure,, +1 8002430127, clintrriage.rdg@boehringer-ingelheim.com
Scientific contact	QRPE Processes and Systems Coordination, Clinical Trial Information Disclosure,, Boehringer Ingelheim, +1 8002430127, clintrriage.rdg@boehringer-ingelheim.com

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
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Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	28 March 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 March 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To define the MTD and/or dose to be used for further development by evaluation of DLT in course 1 and the safety of volasertib when added to standard intensive salvage chemotherapy with DNX-FLA in paediatric patients with AML after failure of first-line therapy

Protection of trial subjects:

99999 is "Not applicable" value or 0 participants, this trial was discontinued with no participants enrolled in the trial

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 March 2016
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	Netherlands: 99999
Worldwide total number of subjects	99999
EEA total number of subjects	99999

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)	99999
Adolescents (12-17 years)	0

Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

99999 is "Not applicable" value or 0 participants, this trial was discontinued with no participants enrolled in the trial

Pre-assignment

Screening details:

All subjects had to be screened for eligibility to participate in the trial. Subjects had to attend specialist sites which would then ensure that they (the subjects) met all inclusion/exclusion criteria. Subjects were not to be randomised to trial treatment if any one of the specific entry criteria were violated

Period 1

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

Blinding implementation details:

This is an open-label, dose-escalating trial

Arms

Arm title	Volasertib
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Arm description:

Patients were to be administered Volasertib when added to standard intensive salvage chemotherapy with DNX-FLA in paediatric patients with AML after failure of first-line therapy.

Arm type	Experimental
Investigational medicinal product name	Volasertib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Single Group Assignment Volasertib Added to the Standard Intensive Salvage Chemotherapy Regimen With Liposomal Daunorubicine, Fludarabine and Cytarabine (DNX-FLA) Followed by Fludarabine and Cytarabine (FLA)

Number of subjects in period 1	Volasertib
Started	99999
Completed	99999

Baseline characteristics

Reporting groups

Reporting group title	Volasertib
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Reporting group description:

Patients were to be administered Volasertib when added to standard intensive salvage chemotherapy with DNX-FLA in paediatric patients with AML after failure of first-line therapy.

Reporting group values	Volasertib	Total	
Number of subjects	99999	99999	
Age categorical			
Units: Subjects			

Age continuous			
99999 is "Not applicable" value or 0 participants, this trial was discontinued with no participants enrolled in the trial			
Units: years			
arithmetic mean	0		
standard deviation	± 0	-	
Gender categorical			
99999 is "Not applicable" value or 0 participants, this trial was discontinued with no participants enrolled in the trial			
Units: Subjects			
Female	99999	99999	
Male	0	0	

End points

End points reporting groups

Reporting group title	Volasertib
Reporting group description: Patients were to be administered Volasertib when added to standard intensive salvage chemotherapy with DNX-FLA in paediatric patients with AML after failure of first-line therapy.	

Primary: Determination of the maximal tolerated dose of volasertib or the recommended volasertib dose for further studies in combination with standard salvage therapy in paediatric patients with AML after failure of the front-line intensive chemotherapy regimen

End point title	Determination of the maximal tolerated dose of volasertib or the recommended volasertib dose for further studies in combination with standard salvage therapy in paediatric patients with AML after failure of the front-line intensive chemotherapy regimen ^[1]
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End point description:

99999 is "Not applicable" value or 0 participants, this trial was discontinued with no participants enrolled in the trial.

End point type	Primary
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End point timeframe:

4 weeks

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: No subjects were enrolled in the trial hence results are not available

End point values	Volasertib			
Subject group type	Reporting group			
Number of subjects analysed	99999 ^[2]			
Units: Not available				
number (not applicable)	99999			

Notes:

[2] - 99999 is "Not applicable" value or 0 participants, this trial was discontinued with no participants

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-leukaemic activity of volasertib in combination with standard salvage therapy

End point title	Anti-leukaemic activity of volasertib in combination with standard salvage therapy
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End point description:

99999 is "Not applicable" value or 0 participants, this trial was discontinued with no participants enrolled in the trial.

End point type	Secondary
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End point timeframe:

8 weeks

End point values	Volasertib			
Subject group type	Reporting group			
Number of subjects analysed	99999 ^[3]			
Units: not available				
number (not applicable)	99999			

Notes:

[3] - 99999 is "Not applicable" value or 0 participants, this trial was discontinued with no participants

Statistical analyses

No statistical analyses for this end point

Secondary: Event-free survival (EFS)

End point title	Event-free survival (EFS)
End point description: 99999 is "Not applicable" value or 0 participants, this trial was discontinued with no participants enrolled in the trial.	
End point type	Secondary
End point timeframe: up to 5 years	

End point values	Volasertib			
Subject group type	Reporting group			
Number of subjects analysed	99999 ^[4]			
Units: not available				
median (full range (min-max))	99999 (99999 to 99999)			

Notes:

[4] - 99999 is "Not applicable" value or 0 participants, this trial was discontinued with no participants

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival (OS)

End point title	Overall survival (OS)
End point description: 99999 is "Not applicable" value or 0 participants, this trial was discontinued with no participants enrolled in the trial.	
End point type	Secondary
End point timeframe: up to 5 years	

End point values	Volasertib			
Subject group type	Reporting group			
Number of subjects analysed	99999 ^[5]			
Units: not available				
median (full range (min-max))	99999 (99999 to 99999)			

Notes:

[5] - 99999 is "Not applicable" value or 0 participants, this trial was discontinued with no participants

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with clinically relevant lab value changes of calcium (hyperand/ or hypocalcaemia) as judged by the investigator and reported as adverse events (Common Terminology Criteria for Adverse Events (CTCAE) grade 3 or higher)

End point title	Number of patients with clinically relevant lab value changes of calcium (hyperand/ or hypocalcaemia) as judged by the investigator and reported as adverse events (Common Terminology Criteria for Adverse Events (CTCAE) grade 3 or higher)
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End point description:

99999 is "Not applicable" value or 0 participants, this trial was discontinued with no participants enrolled in the trial.

End point type	Secondary
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End point timeframe:

8 weeks

End point values	Volasertib			
Subject group type	Reporting group			
Number of subjects analysed	99999 ^[6]			
Units: not available				
number (not applicable)	99999			

Notes:

[6] - 99999 is "Not applicable" value or 0 participants, this trial was discontinued with no participants

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with changes in cardiac activity (prolonged QTc interval) reported as clinically relevant observations (i.e. Adverse Events)

End point title	Number of patients with changes in cardiac activity (prolonged QTc interval) reported as clinically relevant observations (i.e. Adverse Events)
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End point description:

99999 is "Not applicable" value or 0 participants, this trial was discontinued with no participants enrolled in the trial.

End point type Secondary

End point timeframe:

8 weeks

End point values	Volasertib			
Subject group type	Reporting group			
Number of subjects analysed	99999 ^[7]			
Units: not available				
number (not applicable)	99999			

Notes:

[7] - 99999 is "Not applicable" value or 0 participants, this trial was discontinued with no participants

Statistical analyses

No statistical analyses for this end point

Secondary: Predose concentration of volasertib before administration of second dose

End point title Predose concentration of volasertib before administration of second dose

End point description:

99999 is "Not applicable" value or 0 participants, this trial was discontinued with no participants enrolled in the trial.

End point type Secondary

End point timeframe:

8 weeks

End point values	Volasertib			
Subject group type	Reporting group			
Number of subjects analysed	99999 ^[8]			
Units: not available				
arithmetic mean (standard deviation)	99999 (\pm 99999)			

Notes:

[8] - 99999 is "Not applicable" value or 0 participants, this trial was discontinued with no participants

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the concentration-time curve of volasertib

End point title Area under the concentration-time curve of volasertib

End point description:

99999 is "Not applicable" value or 0 participants, this trial was discontinued with no participants enrolled in the trial.

End point type Secondary

End point timeframe:

8 weeks

End point values	Volasertib			
Subject group type	Reporting group			
Number of subjects analysed	99999 ^[9]			
Units: not available				
geometric mean (geometric coefficient of variation)	99999 (± 99999)			

Notes:

[9] - 99999 is "Not applicable" value or 0 participants, this trial was discontinued with no participants

Statistical analyses

No statistical analyses for this end point

Secondary: Terminal half-life of volasertib in plasma

End point title Terminal half-life of volasertib in plasma

End point description:

99999 is "Not applicable" value or 0 participants, this trial was discontinued with no participants enrolled in the trial.

End point type Secondary

End point timeframe:

8 weeks

End point values	Volasertib			
Subject group type	Reporting group			
Number of subjects analysed	99999 ^[10]			
Units: not available				
median (full range (min-max))	99999 (99999 to 99999)			

Notes:

[10] - 99999 is "Not applicable" value or 0 participants, this trial was discontinued with no participants

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum concentration of volasertib

End point title Maximum concentration of volasertib

End point description:

99999 is "Not applicable" value or 0 participants, this trial was discontinued with no participants enrolled in the trial.

End point type	Secondary
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End point timeframe:

8 weeks

End point values	Volasertib			
Subject group type	Reporting group			
Number of subjects analysed	99999 ^[11]			
Units: not available				
geometric mean (geometric coefficient of variation)	99999 (± 99999)			

Notes:

[11] - 99999 is "Not applicable" value or 0 participants, this trial was discontinued with no participants

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

All adverse events occurring during the course of the clinical trial (i.e., from signing the informed consent onwards through the observational phase) were to be collected

Adverse event reporting additional description:

99999 is "Not applicable" value or 0 participants, this trial was discontinued with no participants enrolled in the trial.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	0
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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: No subjects were enrolled in the trial hence results are not available

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