Clinical trial results:
An open-label, multicenter study of INC424 monotherapy or in combination with azacitidine for patients with post-myeloproliferative disorders (MPD) – AML or with CMML

Summary

EudraCT number	2014-000346-30
Trial protocol	DE
Global end of trial date	28 November 2018

Results information

Result version number	v1 (current)
This version publication date	23 September 2021
First version publication date	23 September 2021

Trial information

Trial identification

Sponsor protocol code	CINC424XDE04T

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	University of Leipzig
Sponsor organisation address	Ritterstrasse 26, Leipzig, Germany, D 04109
Public contact	Studiensekretariat Hämatologie, Universität Leipzig, 0049 34197 13 130,
Scientific contact	Studiensekretariat Hämatologie, Universität Leipzig, 0049 34197 13 130,

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	28 November 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 February 2018
Global end of trial reached?	Yes
Global end of trial date	28 November 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Phase I: Feasibility to administer INC424 alone or in combination with azacitidine on 4 patients.

Phase II: To collect efficacy data on AML secondary to MPN and on CMML either with INC424 alone or in combination with azacitidine.
This phase did not start because phase I was not successful.

Protection of trial subjects:

prophylactic use of fluoroquinolone and
oral antifungal during neutropenia is recommended,
broad-spectrum antibiotic if neutropenic fever occurs;
if fever persists despite the use of antibiotic, myeloid growth factor is applied at the descretion of the investigator.

Background therapy:

Standard administration of hydroxyurea

Evidence for comparator:

low evidence for treatment of newly diagnosed AML with azacitidine,
no evidence for combination treatment with azacitidine and ANC2424 of patients with post-myeloproliferative disorders.

Actual start date of recruitment	03 November 2014
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	Germany: 5
Worldwide total number of subjects	5
EEA total number of subjects	5

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)	3
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

FPI on January 15, 2015;
last patient in on March 27, 2017

Pre-assignment

Screening details:

Four patients with secondary AML and one patient with CMML were enrolled

Period 1

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

Arms

Arm title	Jakvida

Arm description:

INC 424 in monotherapy or in combination with azacitidine

Arm type	Experimental
Investigational medicinal product name	Jakavi
Investigational medicinal product code	Ruxolitinib
Other name	ANC 424
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

following the therapy scheme (Trial Protocol, figure 1)

Investigational medicinal product name	Vidaza
Investigational medicinal product code	Azacitidine
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

following the therapy scheme (Fig. 1 of the Trial Protocol)

Number of subjects in period 1	Jakvida
Started	5
Completed	2
Not completed	3
patient was transplanted	1
Lack of efficacy	2

Baseline characteristics

Reporting groups

Reporting group title	Phase I

Reporting group description: -

Reporting group values	Phase I	Total	
Number of subjects	5	5	
Age categorical Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		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)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous			
Patient age at inclusion			
Units: years			
median	63		
full range (min-max)	32 to 73	-	
Gender categorical			
Sex distribution			
Units: Subjects			
Female	4	4	
Male	1	1	
ECOG score Units: Subjects			
Grade 1	2	2	
Grade 2	2	2	
unknown	1	1	
BMI			
body mass index			
Units: kg/m²			
median	21.7		
full range (min-max)	19.3 to 31.3	-	

End points

End points reporting groups

Reporting group title	Jakvida
Reporting group description:	
INC 424 in monotherapy or in combination with azacitidine	
Subject analysis set title	FAS
Subject analysis set type	Full analysis
Subject analysis set description:	
Full analysis set	

Primary: Haematological response

End point title	Haematological response[1]
End point description:	
Response following the IWG response criteria for AML / myelofibrosis	
End point type	Primary
End point timeframe:	
84 days	

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: This is a single arm study. Confirmatory statistics is not applicable.

End point values	Jakvida			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: Patients				
Complete remission (CR)	0			
Complete remission with incomplete blood count rec	1			
Partial remission (PR)	1			
Relapse after CR or CRi	0			
Treatment failure	1			
Progressive Disease	1			
Clinical improvement	0			
Stable disease	0			
Not assessable	1			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Screening, baseline	
Adverse event reporting additional description:	
Toxicities are recorded after each treatment period	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups	
Reporting group title	Jakvida
Reporting group description:	
Treatment arm	

Serious adverse events	Jakvida		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 5 (60.00%)		
number of deaths (all causes)	5		
number of deaths resulting from adverse events	3		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm progression			
subjects affected / exposed	3 / 5 (60.00%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 3		
Leukaemia recurrent			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Respiratory, thoracic and mediastinal disorders			
Pneumonia			

subjects affected / exposed	1 / 5 (20.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Dyspnoea			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Infections and infestations			
Sepsis			
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 5 (60.00%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	3 / 3		
Gastrointestinal bacterial infection			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Septic shock			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Multiple organ dysfunction syndrome			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		

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

Non-serious adverse events	Jakvida		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 5 (100.00%)		
Investigations			
Alanine aminotransferase increased			

subjects affected / exposed	3 / 5 (60.00%)		
occurrences (all)	3		
Aspartate aminotransferase increased			
subjects affected / exposed	3 / 5 (60.00%)		
occurrences (all)	3		
creatinine increased			
subjects affected / exposed	5 / 5 (100.00%)		
occurrences (all)	5		
Alkaline phosphatase increased			
subjects affected / exposed	4 / 5 (80.00%)		
occurrences (all)	4		
Blood bilirubin increased			
subjects affected / exposed	4 / 5 (80.00%)		
occurrences (all)	4		
General disorders and administration site conditions			
Fever			
subjects affected / exposed	4 / 5 (80.00%)		
occurrences (all)	4		
lower leg edema			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Weight loss			
subjects affected / exposed	3 / 5 (60.00%)		
occurrences (all)	3		
Pain sternal	Additional description: after GMT		
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 5 (40.00%)		
occurrences (all)	2		
Nausea			

subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all)	3 / 5 (60.00%) 3 2 / 5 (40.00%) 2		
Respiratory, thoracic and mediastinal disorders Dyspnoea subjects affected / exposed occurrences (all)	 3 / 5 (60.00%) 3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 March 2017	Substantial changes: - The deputy of the coordinating investigator, one member of the DMC and the project manager at the ZKS Leipzig - KKS changed. - Description of the trial design was changed. - Due to prolonged patient recruitment, the expected trial duration is adapted.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study was terminated because of insufficient patient accrual.
The trial ended unscheduled in phase I with only 5 patients with incomplete courses.
Efficacy evaluation was not possible.

Notes: