Clinical trial results:
Combination Therapy Interferon Alpha + JAK1-2 Inhibitor in The Ph-Negative Chronic Myeloid Neoplasms

Summary

EudraCT number	2013-003295-12
Trial protocol	DK
Global end of trial date	29 May 2018

Results information

Result version number	v1 (current)
This version publication date	24 November 2021
First version publication date	24 November 2021

Trial information

Trial identification

Sponsor protocol code	15022013

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Zealand University Hospital, Department of Hematology
Sponsor organisation address	Sygehusvej 10 , Roskilde, Denmark, 4000
Public contact	Mads Emil Bjørn, Roskilde Hospital, 0045 26223678, hans.hasselbalch@dadlnet.dk
Scientific contact	Mads Emil Bjørn, Roskilde Hospital, 0045 26223678, hans.hasselbalch@dadlnet.dk

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	01 July 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 May 2018
Global end of trial reached?	Yes
Global end of trial date	29 May 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary Objectives
1. To describe the effect of combination therapy with IFN-alpha (Pegasys, PegIntron) and JAK1-2-inhibitor treatment (ruxolitinib) evaluated by hematological parameters (Hb, hematocrit, white blood cell count, platelet count, LDH, reduction in JAK2V617-mutation allele burden) and quality of life score, which indirectly will also reflect the remission of the IFN-alpha-induced side effects

Protection of trial subjects:

No specific measures were taken.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 June 2014
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy, Scientific research
Long term follow-up duration	3 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 51
Worldwide total number of subjects	51
EEA total number of subjects	51

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)	34

From 65 to 84 years	17
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruited by investigators in the out-patient clinic

Pre-assignment

Screening details:

Screened by investigators and study nurses in out-patient clinic

Period 1

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

Arms

Arm title	Intervention

Arm description: -

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

Dosage and administration details:

ruxolitinib (Jakavi®; Novartis, Basel, Switzerland) 5-20 mg BID orally depending on platelet count.

Investigational medicinal product name	Interferon alpha-2
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

PEG-IFNa2a [Pegasys®; Genentech (Roche), South San Francis-co, CA, USA] 45 µg/week or PEG-IFNa2b (PegIntron®; Merck Sharp & Dohme, Hertfordshire, UK) 35 µg/week subcutaneously

Number of subjects in period 1[1]	Intervention
Started	50
Completed	42
Not completed	8
Adverse event, non-fatal	5
Lack of efficacy	3

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: One patient died between enrollement and beginning the study medication.

Baseline characteristics

Reporting groups	
Reporting group title	Intervention

Reporting group description: -

Reporting group values	Intervention	Total	
Number of subjects	50	50	
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 Units: years			
median	58		
inter-quartile range (Q1-Q3)	49 to 67	-	
Gender categorical Units: Subjects			
Female	21	21	
Male	29	29	

End points

End points reporting groups

Reporting group title	Intervention

Reporting group description: -

Primary: Response

End point title	Response[1]

End point description:

The primary outcome was efficacy, based on hematologic parameters, quality of life measurements, and the JAK2 V617F burden. The 2013 European LeukemiaNet and International Working Group-Myeloproliferative Neoplasms Research and Treatment response criteria were used to assess efficacy.

End point type	Primary

End point timeframe:

2 years

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: The primary endpoint was presented as a frequency without statistical analysis

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	50			
Units: NA	18			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

2 years

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	3.0

Reporting groups

Reporting group title	intervention

Reporting group description: -

Serious adverse events	intervention		
Total subjects affected by serious adverse events			
subjects affected / exposed	21 / 50 (42.00%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Vascular disorders			
Phlebitis superficial			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Hypertension			
subjects affected / exposed	2 / 50 (4.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Angina pectoris			
subjects affected / exposed	2 / 50 (4.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Acute myocardial infarction			

subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Facial paralysis			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cerebellar artery occlusion			
subjects affected / exposed	2 / 50 (4.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
fever			
subjects affected / exposed	16 / 50 (32.00%)		
occurrences causally related to treatment / all	0 / 16		
deaths causally related to treatment / all	0 / 0		
Acute myeloid leukaemia			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Anaemia			
subjects affected / exposed	3 / 50 (6.00%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia			
subjects affected / exposed	2 / 50 (4.00%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Oral bleeding			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			

Gastrointestinal Bleeding			
subjects affected / exposed	3 / 50 (6.00%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	2 / 50 (4.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Dehydration			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal failure			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	2 / 50 (4.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia bacterial			
subjects affected / exposed	4 / 50 (8.00%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Influenza			

subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infection			
subjects affected / exposed	3 / 50 (6.00%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Herpes zoster			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Erysipelas			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	intervention		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	48 / 50 (96.00%)		
Cardiac disorders			
Palpitations			
subjects affected / exposed	5 / 50 (10.00%)		
occurrences (all)	5		
Hypertension			
subjects affected / exposed	5 / 50 (10.00%)		
occurrences (all)	7		
Nervous system disorders			
Neuropathy peripheral			
subjects affected / exposed	12 / 50 (24.00%)		
occurrences (all)	12		
Dizziness			
subjects affected / exposed	11 / 50 (22.00%)		
occurrences (all)	16		

Headache			
subjects affected / exposed	12 / 50 (24.00%)		
occurrences (all)	16		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	45 / 50 (90.00%)		
occurrences (all)	45		
Thrombocytopenia			
subjects affected / exposed	14 / 50 (28.00%)		
occurrences (all)	20		
Leukopenia			
subjects affected / exposed	23 / 50 (46.00%)		
occurrences (all)	40		
Lactate dehydrogenase increased			
subjects affected / exposed	17 / 50 (34.00%)		
occurrences (all)	17		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	24 / 50 (48.00%)		
occurrences (all)	24		
Night sweats			
subjects affected / exposed	14 / 50 (28.00%)		
occurrences (all)	17		
Influenza like illness			
subjects affected / exposed	15 / 50 (30.00%)		
occurrences (all)	23		
Fever			
subjects affected / exposed	9 / 50 (18.00%)		
occurrences (all)	15		
Local reaction			
subjects affected / exposed	10 / 50 (20.00%)		
occurrences (all)	19		
Gastrointestinal disorders			
Dyspepsia			
subjects affected / exposed	6 / 50 (12.00%)		
occurrences (all)	9		

Nausea subjects affected / exposed occurrences (all)	14 / 50 (28.00%) 23		
Abdominal pain subjects affected / exposed occurrences (all)	6 / 50 (12.00%) 6		
Weight gain poor subjects affected / exposed occurrences (all)	7 / 50 (14.00%) 7		
Respiratory, thoracic and mediastinal disorders Dyspnoea subjects affected / exposed occurrences (all)	8 / 50 (16.00%) 8		
Hepatobiliary disorders Alanine aminotransferase increased subjects affected / exposed occurrences (all)	7 / 50 (14.00%) 7		
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all)	20 / 50 (40.00%) 20		
Psychiatric disorders Mood altered subjects affected / exposed occurrences (all)	11 / 50 (22.00%) 11		
Musculoskeletal and connective tissue disorders Joint pain subjects affected / exposed occurrences (all)	21 / 50 (42.00%) 31		
Muscle discomfort subjects affected / exposed occurrences (all)	22 / 50 (44.00%) 35		
Infections and infestations Upper airway infection subjects affected / exposed occurrences (all)	23 / 50 (46.00%) 23		
Pneumonia bacterial			

subjects affected / exposed	3 / 50 (6.00%)		
occurrences (all)	3		
Urinary tract infection			
subjects affected / exposed	4 / 50 (8.00%)		
occurrences (all)	4		

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