



Clinical trial results:

A Phase II study of oral JAK1/JAK2 inhibitor INC424 in adult patients with relapsed/refractory classical Hodgkin's lymphoma

Summary

EudraCT number	2012-004246-15
Trial protocol	BE
Global end of trial date	12 June 2018

Results information

Result version number	v1 (current)
This version publication date	22 September 2018
First version publication date	22 September 2018

Trial information

Trial identification

Sponsor protocol code	HIJAK
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01877005
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	LYSARC
Sponsor organisation address	Centre Hospitalier LYon Sud - secteur Sainte Eugénie - Pavillon 6D, Pierre Bénite, France, 69495
Public contact	Elise Gaire, Clinical Project Manager, LYSARC, 33 472669333, elise.gaire@lysarc.org
Scientific contact	Pr Franck Morschhauser Co-coordinating Investigator, LYSA, 33 320444290, franck.morschhauser@chru-lille.fr

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	30 July 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	12 June 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of oral JAK1/2 inhibitor ruxolitinib measured by overall response rate (ORR) by IWG criteria (Cheson 2007) occurring after 6 months of oral JAK1/2 inhibitor ruxolitinib treatment in patients with advanced HL for whom no treatment with proven efficacy is available

Protection of trial subjects:

Patients have been followed for safety (adverse event) during all study duration.

If a patient does not respond to study treatment, relapses or has progressive disease, each site was free to initiate further treatment according to local guidelines

Background therapy:

Not applicable

Evidence for comparator:

Not applicable

Actual start date of recruitment	01 July 2013
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	Belgium: 7
Country: Number of subjects enrolled	France: 26
Worldwide total number of subjects	33
EEA total number of subjects	33

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)	27

From 65 to 84 years	6
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

1st patient was included on 10/07/2013 and last patient on 16/12/2014.

33 patients were included

Pre-assignment

Screening details:

No patient created in eCRF was screen failed

Period 1

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

Arms

Arm title	Experimental
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Arm description:

Induction period: oral ruxolitinib will be given twice daily during 6 cycles of 28 days

Maintenance period: patients who achieve at least a SD (according Cheson 2007) at the end of cycle 6 and for whose a clinical benefit is observed according to the Investigator's opinion will be eligible for maintenance treatment by ruxolitinib (15mg or 20mg) twice daily every day of 28-day cycles. Treatment should be continued up to 2 years or until disease progression, intolerability and/or the investigator determine that further therapy is not in the patient's best interest (e.g., due to non-compliance, toxicity, etc.)

Dose regimen:

20 mg BID of ruxolitinib if platelets > 200 x 10⁹/L

15 mg BID of ruxolitinib if platelets count is between 75 to 200 x 10⁹/L (+ dose escalation allowed)

Arm type	Experimental
Investigational medicinal product name	Ruxolitinib
Investigational medicinal product code	INC424
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The induction treatment consists of 6 cycles of 28 days with ruxolitinib administrated every day continuously at the following dosage:

- Subjects with baseline platelet count > 200 x 10⁹/L will begin dosing at 20 mg BID

- Subjects with baseline platelet count between 75 and 200 x 10⁹/L will begin dosing at 15mg BID

Patients who achieve at least a SD (according Cheson 2007) at the end of cycle 6 and for whose a clinical benefit is observed according to the Investigator's opinion will be eligible for maintenance treatment by ruxolitinib (at the same posology for the induction period) twice daily every day of 28-day cycles. Treatment should be continued up to 2 years or until disease progression, intolerability and/or the

investigator determine that further therapy is not in the patient's best interest (e.g., due to noncompliance, toxicity etc.)

Ruxolitinib tablets will be administered orally twice daily (BID) approximately 12 hours apart, without regards to food.

Number of subjects in period 1	Experimental
Started	33
induction	33
maintenance	6
follow-up	32
Completed	2
Not completed	31
Adverse event, non-fatal	1
Lack of efficacy	30

Baseline characteristics

Reporting groups

Reporting group title	Overall trial
Reporting group description: -	

Reporting group values	Overall trial	Total	
Number of subjects	33	33	
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)	27	27	
From 65-84 years	6	6	
85 years and over	0	0	
Age continuous			
Units: years			
median	37		
full range (min-max)	19 to 80	-	
Gender categorical			
Units: Subjects			
Female	12	12	
Male	21	21	

End points

End points reporting groups

Reporting group title	Experimental
Reporting group description:	
Induction period: oral ruxolitinib will be given twice daily during 6 cycles of 28 days	
Maintenance period: patients who achieve at least a SD (according Cheson 2007) at the end of cycle 6 and for whose a clinical benefit is observed according to the Investigator's opinion will be eligible for maintenance treatment by ruxolitinib (15mg or 20mg) twice daily every day of 28-day cycles. Treatment should be continued up to 2 years or until disease progression, intolerability and/or the investigator determine that further therapy is not in the patient's best interest (e.g., due to non-compliance, toxicity, etc.)	
Dose regimen:	
20 mg BID of ruxolitinib if platelets > 200 x 10 ⁹ /L	
15 mg BID of ruxolitinib if platelets count is between 75 to 200 x 10 ⁹ /L (+ dose escalation allowed)	

Primary: Overall response at the end of treatment after 6 cycles of ruxolitinib during induction phase

End point title	Overall response at the end of treatment after 6 cycles of ruxolitinib during induction phase ^[1]
End point description:	
Overall response rate (CR+ PR) according to the Criteria for evaluation of response in Non-Hodgkin's lymphoma (Cheson, 2007).	
End point type	Primary
End point timeframe:	
At the end of treatment after 6 cycles of ruxolitinib during induction phase.	

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 statistical analysis is performed for the primary endpoint of the study as the overall response rate is only a percent calculation.

End point values	Experimental			
Subject group type	Reporting group			
Number of subjects analysed	32 ^[2]			
Units: percent				
number (confidence interval 90%)	9.4 (2.6 to 22.5)			

Notes:

[2] - Evaluable set: includes all enrolled patients who have received at least 28 days of study medication

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported from the date of informed consent signature to 30 days after last drug administration.

Adverse event reporting additional description:

Due to the expected toxicity of study treatment, were reported in eCRF:

- grade ≥ 3 toxicities
- grade ≥ 2 for infections
- toxicities of any intensity of grade related to a Serious Adverse Event

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	4

Reporting groups

Reporting group title	Safety set
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Reporting group description:

The safety set includes all patients who have received at least one dose of study medication

Serious adverse events	Safety set		
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 33 (15.15%)		
number of deaths (all causes)	14		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bowen's disease			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Subdural haematoma			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 1 / 33 (3.03%) 1 / 1 0 / 0		
Respiratory, thoracic and mediastinal disorders Pulmonary embolism subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 1 / 33 (3.03%) 1 / 1 0 / 0		
Musculoskeletal and connective tissue disorders Bone pain subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 1 / 33 (3.03%) 1 / 1 0 / 0		
Infections and infestations Device related sepsis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 1 / 33 (3.03%) 1 / 1 0 / 0		
Gastroenteritis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 1 / 33 (3.03%) 1 / 1 0 / 0		
Papilloma viral infection subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 1 / 33 (3.03%) 0 / 1 0 / 0		
Pneumocystis jirovecii pneumonia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 1 / 33 (3.03%) 1 / 1 0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Safety set		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 33 (45.45%)		
Investigations			
Investigations	Additional description: All AE from this SOC have been pooled		
subjects affected / exposed	4 / 33 (12.12%)		
occurrences (all)	6		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bowen's disease			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Subdural haematoma			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Nervous system disorders			
Nervous system disorders	Additional description: All AE from this SOC have been pooled		
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	2		
Blood and lymphatic system disorders			
Blood and lymphatic system disorders	Additional description: All AE from this SOC have been pooled		
subjects affected / exposed	5 / 33 (15.15%)		
occurrences (all)	14		
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			

Respiratory, thoracic and mediastinal disorders		Additional description: All AE from this SOC have been pooled	
subjects affected / exposed	2 / 33 (6.06%)		
occurrences (all)	3		
Musculoskeletal and connective tissue disorders			
Bone pain			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Infections and infestations			
Infections and infestations		Additional description: All AE from this SOC have been pooled	
subjects affected / exposed	10 / 33 (30.30%)		
occurrences (all)	15		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 August 2013	<ul style="list-style-type: none">• The addition in the biochemical analysis of the blood of two additional biological parameters (C-reactive protein and β2-microglobulin) and replacement of a parameter (measurement of the acid uric in place of urea), being essential for the assessment of patients before and during treatment• The addition of a recommendation to perform a lymph node biopsy to relapse before inclusion in the protocol• Clarification of concomitant treatments prohibited (reported inconsistency after the first set up): the authorization to take systemic steroids at a dose \leq 20mg (as prednisolone equivalent) in Annex 9 and page 21• A precision made on the realization of the tumoral evaluation visits for a better understanding: in Cycle 6 (end of induction) the evaluation should be carried out within 7 days before the end of induction to decide if the patient is responder to the treatment and continues the maintenance.• Same precision for maintenance cycles• A precision made on the time of realization of the samples for the biological study on biomarkers (page 25 and Appendix 8)• Update of the start and end dates of the study (page 3 and synopsis)• Modification of "Flow Chart" of the study: correction of an inconsistency and the addition of evaluation visits during maintenance period.
10 January 2014	<ul style="list-style-type: none">• Expansion of the maintenance phase to patients with stable disease and in which a clinical benefit is observed at the end of induction,• Modification of the study design (page 41 of the protocol) accordingly
25 July 2014	<ul style="list-style-type: none">• Modification of ruxolitinib packaging (from bottles of 60 tablets to wallets of 56 tablets)
28 May 2015	<ul style="list-style-type: none">• Addition of an anatomopathological study on biopsy samples already collected

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/29351986>