Clinical trial results:
A Phase 2, Open label Study to Assess the Efficacy and Safety of Tenalisib (RP6530), a Novel PI3K Dual / Inhibitor, in Patients with Relapsed/Refractory Chronic Lymphocytic Leukemia (CLL)

Summary

EudraCT number	2019-003622-25
Trial protocol	PL
Global end of trial date	02 October 2020

Results information

Result version number	v1 (current)
This version publication date	21 August 2021
First version publication date	21 August 2021
Summary attachment (see zip file)	Summary clinical report (Summary Clinical Report_RP6530-1901 V 1.0_Dated 22 April 21.pdf)

Trial information

Trial identification

Sponsor protocol code	RP6530-1901

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04204057
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Rhizen Pharmaceuticals AG
Sponsor organisation address	Steinentorstrasse 23,, Basel, India, 4051
Public contact	Ajit Nair / SVP & Head Clinical R&D, Rhizen Pharmaceuticals AG, +41 4033241041, kr@rhizen.com
Scientific contact	Ajit Nair / SVP & Head Clinical R&D, Rhizen Pharmaceuticals AG, 9703031098 4033241041, kr@rhizen.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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	22 April 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 October 2020
Global end of trial reached?	Yes
Global end of trial date	02 October 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the anti-tumor activity of Tenalisib as determined by the objective response rate (ORR) and duration of response (DoR)

Protection of trial subjects:

The DRC was constituted by the sponsor to review the safety and efficacy data. The committee consisted of PI of respective sites, sponsor representative, sponsor's medical expert, and a statistician. The DRC reviewed the efficacy and safety data at regular intervals to assess the safety and efficacy of the study drug and provided the recommendations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 November 2019
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	Poland: 9
Country: Number of subjects enrolled	Bulgaria: 3
Country: Number of subjects enrolled	Georgia: 9
Worldwide total number of subjects	21
EEA total number of subjects	12

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)	9

From 65 to 84 years	12
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This was a Phase II, open-label, Simon’s two-stage study design to evaluate the efficacy and safety of Tenalisib in 61 patients. Eligible patients were enrolled in order of their eligibility

Pre-assignment

Screening details:

All consented subjects who undergo at least one post-consent procedure were given a unique screening number that will be used to identify the subject for all procedures that occur prior to dosing or allocation. A total of 27 patients were screened in the study, of which 21 patients were eligible and received at least one dose of Tenalisib.

Period 1

Period 1 title	No (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

Non-randomized open-label study

Arms

Arm title	Single arm

Arm description:

Tenalisib (800 mg BID)

Arm type	Experimental
Investigational medicinal product name	Tenalisib
Investigational medicinal product code	RP6530
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Tenalisib (800 mg BID) daily in a 28-day cycle

Number of subjects in period 1	Single arm
Started	21
Completed	15
Not completed	6
Adverse event, serious fatal	1
Disease progression	3
Adverse event, non-fatal	2

Baseline characteristics

Reporting groups	
Reporting group title	No
Reporting group description:	
Patients who have treated with at least one dose of Tenalisib	

Reporting group values	No	Total	
Number of subjects	21	21	
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)	9	9	
From 65-84 years	12	12	
85 years and over	0	0	
Age continuous Units: years			
geometric mean	64.5		
standard deviation	± 8.7	-	
Gender categorical Units: Subjects			
Female	3	3	
Male	18	18	

Subject analysis sets	
Subject analysis set title	Safety analysis set
Subject analysis set type	Safety analysis
Subject analysis set description:	
A patient who have received at least one dose of study drug i.e. Tenalisib	

Reporting group values	Safety analysis set		
Number of subjects	21		
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)	9		
From 65-84 years	12		
85 years and over	0		
Age continuous			
Units: years			
geometric mean	64.5		
standard deviation	± 8.7		
Gender categorical			
Units: Subjects			
Female	3		
Male	18		

End points

End points reporting groups

Reporting group title	Single arm
Reporting group description: Tenalisib (800 mg BID)	
Subject analysis set title	Safety analysis set
Subject analysis set type	Safety analysis
Subject analysis set description: A patient who have received at least one dose of study drug i.e. Tenalisib	

Primary: overall response rate (ORR)

End point title	overall response rate (ORR)[1]
End point description: ORR is defined as the sum of complete response (CR) and partial response (PR) rates as defined by the iwCLL guideline for CLL (Hallek et al. 2018)	
End point type	Primary
End point timeframe: 8 months	

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: A priory hypothesis was set based on Simon-two-stage design that the response in the subjects in Part-1 is less than 8 then null hypotheses will be accepted and part-2 will not be initiated. Therefore, no additional statistics were performed to test this hypothesis.

End point values	Safety analysis set			
Subject group type	Subject analysis set			
Number of subjects analysed	21			
Units: Percentage				
number (not applicable)	33.3			

Statistical analyses

No statistical analyses for this end point

Primary: Duration of response (DoR)

End point title	Duration of response (DoR)[2]
End point description: DoR is defined as the interval from the first documentation of CR/PR to first documentation of definitive disease progression or death from any cause.	
End point type	Primary
End point timeframe: The DoR was calculated up to a predefined cut-off date (i.e. LPLV)	

Notes:

[2] - 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: A priory hypothesis was set based on Simon-two-stage design that the response in the subjects in Part-1 is less than 8 then null hypotheses will be accepted and part-2 will not be initiated.

Therefore, no additional statistics were performed to test this hypothesis.

End point values	Safety analysis set			
Subject group type	Subject analysis set			
Number of subjects analysed	21			
Units: days				
number (not applicable)	143			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: up-to a predefined cut-off date (i.e., up-to LPLV)	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	23.1
Reporting groups	
Reporting group title	Safety analysis set
Reporting group description: Patients who have treated at least one dose of study drug	

Serious adverse events	Safety analysis set		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 21 (14.29%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events	2		
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		

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

Non-serious adverse events	Safety analysis set		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 21 (71.43%)		
Investigations			
Alanine aminotransferase increased			

subjects affected / exposed	4 / 21 (19.05%)		
occurrences (all)	7		
Aspartate aminotransferase increased			
subjects affected / exposed	4 / 21 (19.05%)		
occurrences (all)	6		
Blood alkaline phosphatase increased			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	3		
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	6 / 21 (28.57%)		
occurrences (all)	10		
Neutropenia			
subjects affected / exposed	5 / 21 (23.81%)		
occurrences (all)	18		
Thrombocytopenia			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	3		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	2		
Infections and infestations			
Pneumonia			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	3		

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

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

After evaluating the anti-tumor effect in stage 1 by the DRC committee (fewer than 8 responses seen in stage 1), as per the Simon two-stage design of the study protocol, the study would be discontinued and stage 2 was not initiated.

Notes: