Clinical trial results:
LGX818 in combination with MEK162 in refractory or relapsed multiple myeloma patients with BRAFV600E or BRAFV600K mutation

Summary

EudraCT number	2014-004597-42
Trial protocol	DE
Global end of trial date	30 January 2023

Results information

Result version number	v1 (current)
This version publication date	10 May 2024
First version publication date	10 May 2024

Trial information

Trial identification

Sponsor protocol code	BIRMA

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02834364
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Universtity Hospital Heidelberg
Sponsor organisation address	Im Neuenheimer Feld 672, Heidelberg, Germany, 69120
Public contact	Internal Medicine V, University Hospital Heidelberg, +49 6221564781, marc.raab@med.uni-heidelberg.de
Scientific contact	Internal Medicine V, University Hospital Heidelberg, +49 6221564781, marc.raab@med.uni-heidelberg.de

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	21 December 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 January 2023
Global end of trial reached?	Yes
Global end of trial date	30 January 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to demonstrate the therapeutic efficacy of LGX818/MEK162 to decrease myeloma tumour burden

Protection of trial subjects:

If, in the investigator’s opinion, continuation of the trial would be detrimental to the subject’s well-being, the trial participation would have been stopped.
Recommendations to modify dose in case of treatment-related adverse events were included in the protocol.
Specific measures were defined for management of hand foot skin reaction, nausea and vomiting, blood pressure management, management of opthalmological events, follow up evaluations for keratoacanthoma and/or squamous cell carcinoma.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 June 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	Germany: 12
Worldwide total number of subjects	12
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)	8
From 65 to 84 years	4

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were recruited at 4 different sites in Germany.

Pre-assignment

Screening details:

Patients with relapsed or refractory Multiple Myeloma after failure of at least two treatment regimens and with BRAFV600E/K mutation were examined for in- and exclusion criteria.

Period 1

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

Blinding implementation details:

In this single arm study no blinding was performed.

Arms

Arm title	Therapy

Arm description:

Patients with relaped or refractory Multiple Myeloma with BRAF V600E/K-mutation were treated with LGX818/MEK162

Arm type	Experimental
Investigational medicinal product name	Encorafenib
Investigational medicinal product code	L01EC03
Other name	LGY818, Braftovi
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

450 mg p.o.once daily

Investigational medicinal product name	Binimetinib
Investigational medicinal product code	L01EE03
Other name	MEK162, Mektovi
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

45 mg p.o. twice daily

Number of subjects in period 1	Therapy
Started	12
Completed	12

Baseline characteristics

End points

End points reporting groups

Reporting group title	Therapy

Reporting group description:

Patients with relaped or refractory Multiple Myeloma with BRAF V600E/K-mutation were treated with LGX818/MEK162

Primary: Overall Response Rate

End point title	Overall Response Rate[1]

End point description:

The primary objective of this study is to demonstrate the therapeutic efficacy of LGX818/MEK162 to decrease myeloma tumour burden. The overall response rate (ORR) is defined as the percentage of patients that achieved a minimal response (MR) or better within a time period of 1 year after start of study drug treatment. Best response will be used to calculate ORR.

End point type	Primary

End point timeframe:

Completion of at least one cycle of 28 days LGX818/MEK162

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: There was no control arm. A null hypothesis tested in the EP population was H0: ORR > 20% against the alternative H1: ORR > 20% using a one-sided binomial test with significance level 5%. For this analysis, missing response data would have been counted as non-responders. An effect estimate of 0.833 was calculated with a lower 95% confidence boudars 0f 0.592 (p=0.00).

End point values	Therapy			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: patients				
stable disease	2			
partial response	4			
very good partial response	3			
near complete response	2			
complete response	1			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
During therapy	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	26

Reporting groups	
Reporting group title	safety population

Reporting group description:

All patients were followed in weekly intervals during the first cycle, in cycle 2 week 2 and week 4, thereafter in 28 day intervals.

Serious adverse events	safety population		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 12 (16.67%)		
number of deaths (all causes)	7		
number of deaths resulting from adverse events	0		
Gastrointestinal disorders			
Dental caries			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Respiratory tract infection			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory infection			
subjects affected / exposed	1 / 12 (8.33%)		
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	safety population		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 12 (100.00%)		
Vascular disorders			
Vascular disorders			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	2		
General disorders and administration site conditions			
General disorders and administration site conditions			
subjects affected / exposed	7 / 12 (58.33%)		
occurrences (all)	9		
Reproductive system and breast disorders			
Reproductive system and breast disorders			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Respiratory, thoracic and mediastinal disorders			
subjects affected / exposed	6 / 12 (50.00%)		
occurrences (all)	7		
Psychiatric disorders			
Psychiatric disorders	Additional description: insomnia		
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Investigations			
Investigations			
subjects affected / exposed	12 / 12 (100.00%)		
occurrences (all)	39		
Injury, poisoning and procedural complications			
Injury, poisoning and procedural complications			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Cardiac disorders			
left ventricle failure			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		

Nervous system disorders Nevous system disorders subjects affected / exposed occurrences (all)	 4 / 12 (33.33%) 6		
Blood and lymphatic system disorders anaemia subjects affected / exposed occurrences (all) Bone marrow oedema subjects affected / exposed occurrences (all) Neutropenia subjects affected / exposed occurrences (all)	 8 / 12 (66.67%) 8 1 / 12 (8.33%) 1 1 / 12 (8.33%) 1		
Eye disorders Eye Disorders subjects affected / exposed occurrences (all)	 10 / 12 (83.33%) 17		
Gastrointestinal disorders Gastrointestinal disorders subjects affected / exposed occurrences (all)	 12 / 12 (100.00%) 23		
Skin and subcutaneous tissue disorders Skin and subcutaneous tissue disorders subjects affected / exposed occurrences (all)	 4 / 12 (33.33%) 4		
Musculoskeletal and connective tissue disorders Musculoskeletal and connective tissue disorders subjects affected / exposed occurrences (all)	 8 / 12 (66.67%) 15		
Infections and infestations Infections and infestations subjects affected / exposed occurrences (all)	 10 / 12 (83.33%) 26		
Metabolism and nutrition disorders			

Metabolism and nutrition disorders subjects affected / exposed occurrences (all)	9 / 12 (75.00%) 18		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 June 2017	The study timelines were extended, to have more time for recruitment. Additional saliva and blood samples were introduced.
16 April 2020	Sponsor Details updated Study timelines and total duration of study extended. Response assessment was clarified. Some responsibilities/contact data were updated.

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/36608320