Clinical trial results:
An Open Label Phase II Study of Tipifarnib in Advanced Squamous Non-small Cell Lung Cancer with HRAS mutations

Summary

EudraCT number	2017-004822-13
Trial protocol	ES
Global end of trial date	09 November 2022

Results information

Result version number	v1 (current)
This version publication date	01 November 2023
First version publication date	01 November 2023
Summary attachment (see zip file)	THOMAS_summary final report (THOMAS_summary final report_v.1.0_13Mar2023.pdf)

Trial information

Trial identification

Sponsor protocol code	GECP17/04

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03496766
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Fundación GECP
Sponsor organisation address	Avda. Meridiana 358, Barcelona, Spain, 08027
Public contact	Eva Pereira, Fundación GECP, +34 934302006, epereira@gecp.org
Scientific contact	Eva Pereira, Fundación GECP, +34 934302006, epereira@gecp.org

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	13 March 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 October 2022
Global end of trial reached?	Yes
Global end of trial date	09 November 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the antitumor activity in terms of objective response rate (ORR) of tipifarnib in subjects with locally advanced unresectable or metastatic, relapsed and/or refractory, squamous non-small cell lung cancer (SQ-NSCLC) with HRAS mutations. This objective will be evaluated in the treatment phase of the study.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 May 2018
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	Spain: 9
Worldwide total number of subjects	9
EEA total number of subjects	9

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	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Between July 2018 and July 2022, a total of 43 9 patients were enrolled in the study, no patient was finally considered as an inclusion error. Finally 9 patients from 7 different sites were considered for the analysis. The recruitment was closed prematurely to due to slow recruitment.

Pre-assignment

Screening details:

This Phase II study consists of 2 parts: 1) pre-screening phase and 2) treatment phase.
The pre-screening phase will investigate the presence of HRAS mutations in subjects with a histologically or cytologically confirmed diagnosis of squamous non-small cell lung cancer (SQ-NSCLC).

Period 1

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

Arms

Arm title	Experimental

Arm description: -

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

Dosage and administration details:

Tipifarnib will be administered with food at a starting dose of 600 mg, daily on days 1-7 and 15-21 of 28-day treatment cycles. In the absence of unmanageable toxicities, subjects may continue to receive tipifarnib treatment for up to 24 months in the absence of disease progression and unmanageable toxicity. Treatment may continue beyond 24 months if there is documented evidence of continued clinical benefit.

Number of subjects in period 1	Experimental
Started	9
Completed	9

Baseline characteristics

Reporting groups

Reporting group title	Overall study (overall period)

Reporting group description: -

Reporting group values	Overall study (overall period)	Total	
Number of subjects	9	9	
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			
arithmetic mean	68.8		
standard deviation	± 5.4	-	
Gender categorical Units: Subjects			
Female	1	1	
Male	8	8	
Race Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	0	0	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	0	
White	9	9	
More than one race	0	0	
Unknown or Not Reported	0	0	
Cigarette Smoking History Units: Subjects			
Never smoker (<= 100 cigarettes/ lifetime)	0	0	
Former smoker (>= 1 year)	5	5	
Active smoker	4	4	
Performance status Units: Subjects			
ECOG 0	0	0	
ECOG 1	9	9	
ECOG 2	0	0	

ECOG 3	0	0	
ECOG 4	0	0	
Clinical Stage at inclusion Units: Subjects			
IIIB-IIIC	1	1	
IVA	4	4	
IVB	4	4	
Prior Therapy Best Response Units: Subjects			
Partial Response	3	3	
Stable Disease	4	4	
Progression Disease	2	2	
Pulse rate Units: bpm			
arithmetic mean	88.8		
standard deviation	± 12.1	-	
Systolic Blood Pressure Units: mmHg			
arithmetic mean	121.8		
standard deviation	± 22.2	-	
Diastolic Blood Pressure Units: mmHg			
arithmetic mean	73.2		
standard deviation	± 10.4	-	

End points

End points reporting groups

Reporting group title	Experimental

Reporting group description: -

Primary: Overall response

End point title	Overall response[1]

End point description:

To determine the antitumor activity in terms of objective response rate (ORR) of tipifarnib in subjects with locally
advanced unresectable or metastatic, relapsed and/or refractory, squamous non-small cell lung cancer (SQ-NSCLC)
with HRAS mutations

End point type	Primary

End point timeframe:

From the first dose until progression disease, assessed from the first dose until the first assessment at week 6 from the
first dose.

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 recruitment was closed prematurely to due to slow recruitment, so there are no consistent data to achieve any relevant conclusion.
All 9 evaluable patients in the efficacy cohort started treatment and subsequently failed. Of the 9 patients included, 8 (88.9%) patients have a disease progression and 1 (11.1%) died before performing first tumor assessment evaluation.
2 patients out of the 8 evaluable patients achieved SD, the rest of patients progressed. Thus, objective response rate was 0%.

End point values	Experimental			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: Participants				
Stable Disease	2			
Progression Disease	4			
Not evaluated	3			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival

End point title	Progression Free Survival

End point description:

Defined as the time from the start date of treatment TMT as the origin of follow-up and the first progression or death as final date

End point type	Secondary

End point timeframe:

From the start of treatment until first progression or death.

End point values	Experimental			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: Months				
median (standard deviation)	8.6 (± 18.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

End point title	Overall Survival

End point description:

Defined as the length of time from either the date of diagnosis or the start of the treatment that patients diagnosed with
the disease are still alive.

End point type	Secondary

End point timeframe:

From the date of randomization until end of follow up.

End point values	Experimental			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: Months				
median (full range (min-max))	12.4 (9.7 to 21.7)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Any adverse event or breakdown occurring during the course of the study.
The investigator will have to collect all adverse events once they have signed informed consent, during treatment and 30 days after the last dose study treatment administration.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	12.1

Reporting groups

Reporting group title	As-treated population

Reporting group description: -

Serious adverse events	As-treated population		
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 9 (100.00%)		
number of deaths (all causes)	9		
number of deaths resulting from adverse events	0		
Vascular disorders			
Thromboembolic event			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Nervous system disorders			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Platelet count decreased			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Fatigue			

subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Dysnea			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
subjects affected / exposed	6 / 9 (66.67%)		
occurrences causally related to treatment / all	6 / 6		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Sepsis			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	As-treated population		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 9 (100.00%)		
Investigations			
Hyperglycaemia			
subjects affected / exposed	7 / 9 (77.78%)		
occurrences (all)	7		
Blood and lymphatic system disorders			
Anemia			

subjects affected / exposed occurrences (all)	9 / 9 (100.00%) 9		
General disorders and administration site conditions Confusional state subjects affected / exposed occurrences (all)	 1 / 9 (11.11%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 December 2019	Change in selection criteria and schedule of the study to improve study management.
04 February 2022	The sponsor change from GECP group to Fundation GECP.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
09 November 2022	The recruitment and study was closed prematurally due to slow recruitment.	-

Notes:

Limitations and caveats

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

The recruitment and study were closed prematurally due to slow recruitment.

Notes: