Clinical trial results:
Survival, quality of life and self-reported outcomes of elderly patients with advanced non-small cell lung cancer (NSCLC), treated with pembrolizumab (MK-3475) in the first line setting

Summary

EudraCT number	2016-004353-32
Trial protocol	ES
Global end of trial date	28 April 2023

Results information

Result version number	v1 (current)
This version publication date	21 September 2023
First version publication date	21 September 2023
Summary attachment (see zip file)	Lung Cancer Publication of PEBEL study (PIIS0169500223008565.pdf)

Trial information

Trial identification

Sponsor protocol code	GECP16/06

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03293680
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Fundación GECP
Sponsor organisation address	Avenida Meridiana, 358, 6a planta, Barcelona, Spain, 08027
Public contact	Eva Pereira, Fundación GECP, 34 93 4302006, epereira@gecp.org
Scientific contact	Eva Pereira, Fundación GECP, 34 93 4302006, 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	14 July 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 April 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the efficacy, in terms of overall survival at one year, of first-line treatment with Pembrolizumab (MK-3475) in elderly patients with advanced NSCLC expressing PD-L1.

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	01 October 2017
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: 74
Worldwide total number of subjects	74
EEA total number of subjects	74

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)	0
From 65 to 84 years	47
85 years and over	27

Subject disposition

Recruitment

Recruitment details:

A total of 83 patients were recruited between February 2018 and November 2019 (the last patient included finished treatment in November 2021) at ten sites in Spain, and 82 patients received treatment. Of these, 74 patients were finally analysed since eight were inclusion errors

Pre-assignment

Screening details:

Patients with histological or cytological documented stage IIIB or IV squamous and non-squamous NSCLC previously untreated. EGFR and ALK have to be wild-type. Patients must be aged 70 years or more, on day of signing informed consent. Measurable disease (at least 1 lesion) based on RECIST criteria v1.1. PD-L1 expression ≥ 1%. Have a ECOG 0 or 1.

Period 1

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

Blinding implementation details:

Not blinded

Arms

Arm title	Experimental

Arm description:

Each subject received 200 mg of intravenous pembrolizumab every three weeks, continued for a maximum of two years or until disease progression, unacceptable toxicity, or patient-consent withdrawal.
Pembrolizumab treatment was allowed to continue beyond progression, and up to a maximum of 24 months, if the investigator considered that the clinical benefit to the patient persisted.

Arm type	Experimental
Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	MK-3475
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Each subject received 200 mg of intravenous pembrolizumab every three weeks for a maximum of two years.

Number of subjects in period 1	Experimental
Started	74
Completed	74

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	74	74	
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	78.1		
standard deviation	± 5.50	-	
Gender categorical Units: Subjects			
Female	10	10	
Male	64	64	
Race Units: Subjects			
Caucasian	74	74	
Smoking history Units: Subjects			
Never	11	11	
Former smoker	51	51	
Current smoker	12	12	
ECOG performance Status at diagnosis Units: Subjects			
ECOG 0	18	18	
ECOG 1	56	56	
Histology Units: Subjects			
Adenocarcinoma	32	32	
Squamous	33	33	
Large cell carcinoma	2	2	
Aden squamous	1	1	
Not otherwise specified / Undifferentiated	6	6	

Current cancer stage Units: Subjects			
IIIB	6	6	
IV	68	68	
Previous antineoplastic treatments Units: Subjects			
Radiotherapy	24	24	
Surgery	9	9	
Adjuvant chemotherapy	6	6	
Concurrent chemoradiotherapy	5	5	
Neo-adjuvant chemotherapy	2	2	
No previous treatment	28	28	
PD-L1 Units: Subjects			
1–19%	16	16	
20–49%	23	23	
≥50%	35	35	

End points

End points reporting groups

Reporting group title	Experimental

Reporting group description:

Each subject received 200 mg of intravenous pembrolizumab every three weeks, continued for a maximum of two years or until disease progression, unacceptable toxicity, or patient-consent withdrawal.
Pembrolizumab treatment was allowed to continue beyond progression, and up to a maximum of 24 months, if the investigator considered that the clinical benefit to the patient persisted.

Primary: Overall Survival

End point title	Overall Survival[1]

End point description:

End point type	Primary

End point timeframe:

From the initiation of treatment until end of follow up

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: We assessed OS, PFS, and DSS with the Kaplan-Meier product-limit method, using the log-rank test to compare curves for independent groups. We calculated two-sided
P -values and set the statistical significance level at P ≤ 0.05. We carried out all analyses using R 4.1.2 for Microsoft Windows.

End point values	Experimental			
Subject group type	Reporting group			
Number of subjects analysed	74			
Units: month				
median (confidence interval 95%)	19.2 (11.3 to 25.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Best response

End point title	Best response

End point description:

End point type	Secondary

End point timeframe:

From the initiation of study until end of follow up.

End point values	Experimental			
Subject group type	Reporting group			
Number of subjects analysed	74			
Units: Participant				
Complete response	0			
Partial Response	29			
Stable Disease	20			
Progression Disease	16			
Inevaluable for response, symptomatic impairment	9			

Statistical analyses

No statistical analyses for this end point

Secondary: OS for patients with a PD-L1 under 50%

End point title	OS for patients with a PD-L1 under 50%

End point description:

End point type	Secondary

End point timeframe:

From the initiation of treatment until end of follow up

End point values	Experimental			
Subject group type	Reporting group			
Number of subjects analysed	49			
Units: month				
median (confidence interval 95%)	16.5 (6.8 to 24.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: OS for patients with a PD-L1 than or equal to 50%

End point title	OS for patients with a PD-L1 than or equal to 50%

End point description:

End point type	Secondary

End point timeframe:

From the initiation of treatment until end of follow up.

End point values	Experimental			
Subject group type	Reporting group			
Number of subjects analysed	35			
Units: month				
median (confidence interval 95%)	23.3 (14.8 to 36)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival

End point title	Progression Free Survival

End point description:

End point type	Secondary

End point timeframe:

From the initiation of treatment until end of follow up

End point values	Experimental			
Subject group type	Reporting group			
Number of subjects analysed	74			
Units: month				
median (confidence interval 95%)	6.1 (4.6 to 8.4)			

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 90 days after the last administration of Pembrolizumab.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	12.0

Reporting groups

Reporting group title	As-treated population

Reporting group description:

The as-treated population included all patients who received at least one dose of a trial treatment.

Serious adverse events	As-treated population		
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 74 (13.51%)		
number of deaths (all causes)	36		
number of deaths resulting from adverse events	10		
General disorders and administration site conditions			
Death			
subjects affected / exposed	10 / 74 (13.51%)		
occurrences causally related to treatment / all	0 / 10		
deaths causally related to treatment / all	0 / 10		

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	59 / 74 (79.73%)		
Investigations			
Platelet count decreased			
subjects affected / exposed	6 / 74 (8.11%)		
occurrences (all)	6		
Increased creatinine level			

subjects affected / exposed occurrences (all)	5 / 74 (6.76%) 5		
Blood and lymphatic system disorders Anemia subjects affected / exposed occurrences (all)	 4 / 74 (5.41%) 4		
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	 23 / 74 (31.08%) 23		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	 14 / 74 (18.92%) 14		
Respiratory, thoracic and mediastinal disorders Pneumonitis subjects affected / exposed occurrences (all)	 6 / 74 (8.11%) 6		
Skin and subcutaneous tissue disorders Dry skin subjects affected / exposed occurrences (all) Pruritus subjects affected / exposed occurrences (all) Rash subjects affected / exposed occurrences (all)	 12 / 74 (16.22%) 12 19 / 74 (25.68%) 19 11 / 74 (14.86%) 11		
Endocrine disorders Hyperthyroidism subjects affected / exposed occurrences (all) Hypothyroidism subjects affected / exposed occurrences (all)	 9 / 74 (12.16%) 9 7 / 74 (9.46%) 7		
Metabolism and nutrition disorders			

Anorexia subjects affected / exposed occurrences (all)	12 / 74 (16.22%) 12		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 July 2018	Amendment due to the new IB IMP version of the study, the protocol is reviewed and editorial changes are made to some of its points to clarify procedures. The study schedule is also modified after making these clarifications in the protocol. The geriatric scales are updated and detected errors are corrected The procedures for sending samples and the type of samples sent are reviewed with the central laboratory, and it is added that sending cell blocks is allowed.
22 January 2019	Change of Sponsor: The Spanish Lung Cancer Group (GECP), sponsor of the PEBEL study, has recently established the GECP Foundation.

Notes:

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.

Age-specific issues for complete the study relative to older cancer patients.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/37557022