Clinical trial results:
Expression/DNA methylation of cancer testis antigens may predict response to pembrolizumab in pretreated NSCLC patients

Summary

EudraCT number	2017-000689-30
Trial protocol	AT
Global end of trial date	01 June 2022

Results information

Result version number	v1 (current)
This version publication date	03 July 2024
First version publication date	03 July 2024

Trial information

Trial identification

Sponsor protocol code	Pem-NSCLC

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Medical University of Vienna
Sponsor organisation address	Währinger Gürtel 18-20, Wien, Austria, 1090
Public contact	Sabine Zoechbauer-Mueller, Med. Univ. Wien, +43 14040073783, sabine.zoechbauer-mueller@meduniwien.ac.at
Scientific contact	Sabine Zoechbauer-Mueller, Med. Univ. Wien, +43 14040073783, sabine.zoechbauer-mueller@meduniwien.ac.at

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	06 October 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 June 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The objectives of this study are to determine DNA methylation as well as expression of CTAs in lung adenocarcinoma patients whose tumor cells do express PD-L1 (≥ 1%) as well as in patients whose tumor cells do not express PD-L1. These results will be compared with the outcome of the patients after treatment with the combination of chemotherapy and pembrolizumab. In addition, expression of selected CTAs will be investigated in serum samples from these patients.
We hypothesize that in lung adenocarcinomas expression of CTAs may be upregulated by loss of DNA methylation which may result in an enhanced immune response and finally in an enhanced tumor response and in a better clinical outcome of some patients.

Protection of trial subjects:

Confidentiality of Data
The investigator affirms that information furnished to the investigator will be maintained in confidence, and such information will be divulged to the institutional review board, ethics review committee (IRB/ERC) or similar or expert committee; affiliated institution and employees, only under an appropriate understanding of confidentiality with such board or committee, affiliated institution and employees. Data generated by this trial will be considered confidential by the investigator, except to the extent that it is included in a publication as provided in the Publications section of this protocol.

Confidentiality of Subject Records
The investigator agrees that IRB/ERC, or regulatory authority representatives may consult and/or copy trial documents in order to verify worksheet/case report form data. By signing the consent form, the subject agrees to this process. If trial documents will be photocopied during the process of verifying worksheet/case report form information, the subject will be identified by unique code only; full names/initials will be masked prior to transmission to the Sponsor.
The investigator agrees to treat all subject data used and disclosed in connection with this trial in accordance with all applicable privacy laws, rules and regulations.

Confidentiality of Investigator Information
The investigator recognizes that certain personal identifying information with respect to the investigator, and all subinvestigators and trial site personnel, may be used and disclosed for trial management purposes, as part of a regulatory submissions, and as required by law. This information may include:
1. name, address, telephone number and e-mail address;
2. hospital or clinic address and telephone number;
3. curriculum vitae or other summary of qualifications and credentials; and
4. other professional documentation.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 June 2018
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	Austria: 11
Worldwide total number of subjects	11
EEA total number of subjects	11

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)	3
From 65 to 84 years	8
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients with advanced lung adenocarcinoma, without an EGFR mutation or ALK translocation, pretreated with at least 1 platin-based chemotherapy regimen and with by a CT scan documented tumor progression will be included.

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	40[1]
Number of subjects completed	11

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Protocol deviation: 29

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: From the 40 pre-assigned patients only 11 could finally be recruited due to protocol deviations.

Period 1

Period 1 title	Sample collection (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

In this single-center, phase II, single-arm, open-label study in total 42 patients (21 with ≥ 1% expression of the Programmed Death ligand 1 [PD-L1] on tumor cells and 21 without PD-L1 expression on tumor cells) with advanced NSCLC (adenocarcinoma), without an EGFR mutation or ALK translocation, pretreated with at least 1 platin-based chemotherapy regimen and with by a computertomography (CT) scan documented tumor progression were planned to be included.

Arms

Arm title	Study

Arm description:

In this single-center, phase II, single-arm, open-label study in total 42 patients (21 with ≥ 1% expression of the Programmed Death ligand 1 [PD-L1] on tumor cells and 21 without PD-L1 expression on tumor cells) with advanced NSCLC (adenocarcinoma), without an EGFR mutation or ALK translocation, pretreated with at least 1 platin-based chemotherapy regimen and with by a computertomography (CT) scan documented tumor progression were planned to be included.

Arm type	Active comparator
Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	MK-3475
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

2 mg/kg Q3W or 200 mg Q3W

Number of subjects in period 1	Study
Started	11
Completed	11

Baseline characteristics

Reporting groups	
Reporting group title	Sample collection

Reporting group description: -

Reporting group values	Sample collection	Total	
Number of subjects	11	11	
Age categorical Units: Subjects			
Adults (18-64 years)	3	3	
From 65-84 years	8	8	
Gender categorical Units: Subjects			
Female	6	6	
Male	5	5	
PD-L1 expression			
≥ 1% PD-L1 expression on tumor cells versus without PD-L1 expression on tumor cells			
Units: Subjects			
PD-L1 pos	7	7	
PD-L1 neg	4	4	

End points

End points reporting groups

Reporting group title	Study

Reporting group description:

In this single-center, phase II, single-arm, open-label study in total 42 patients (21 with ≥ 1% expression of the Programmed Death ligand 1 [PD-L1] on tumor cells and 21 without PD-L1 expression on tumor cells) with advanced NSCLC (adenocarcinoma), without an EGFR mutation or ALK translocation, pretreated with at least 1 platin-based chemotherapy regimen and with by a computertomography (CT) scan documented tumor progression were planned to be included.

Primary: CTA methylation

End point title	CTA methylation[1]

End point description:

End point type	Primary

End point timeframe:

2018-2022

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 study was prematurely stopped and no statistical analysis was calculated.

End point values	Study			
Subject group type	Reporting group			
Number of subjects analysed	0[2]			
Units: percent				
number (not applicable)				

Notes:

[2] - The study was prematurely stopped.

Statistical analyses

No statistical analyses for this end point

Secondary: Treatment response

End point title	Treatment response

End point description:

End point type	Secondary

End point timeframe:

2018-2022

End point values	Study			
Subject group type	Reporting group			
Number of subjects analysed	0[3]			
Units: Subjects				
number (not applicable)				
Stable disease Progressive disease Partial remission NA				

Notes:

[3] - The study was prematurely stopped.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

2018-2022

Adverse event reporting additional description:

No adverse event reached the 5% threshold.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21

Reporting groups

Reporting group title	Study

Reporting group description:

No adverse event reached the 5% threshold.

Serious adverse events	Study		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 11 (0.00%)		
number of deaths (all causes)	6		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Study		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 11 (0.00%)		

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: No adverse event reached the 5% threshold.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 July 2019	We initially planned to include with chemotherapy pretreated patients with advanced lung adenocarcinoma who received pembrolizumab monotherapy after tumor progression. Since the approval of pembrolizumab monotherapy and the combination of pembrolizumab/platin/pemetrexed by the EMA for the first-line treatment of NSCLC patients with adenocarcinoma subtype the vast majority of patients already receives pembrolizumab in the first line setting. Thus, the number of patients meeting our initial inclusion criteria drastically decreased and we decided to change the study cohort to untreated patients who will receive the EMA approved combination of pembrolizumab/platin/pemetrexed. This change of the project plan was communicated with and approved by Merck, the ethics committee of the Medical University of Vienna and the Austrian Agency for Health and Food Safety.

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.

Challenges were: ineligibility/unwillingness of patients for a tumor re-biopsy; tumor necrosis; SARS-CoV-2 pandemia.

Notes: