Clinical trial results:
Immunomodulation of pembrolizumab plus docetaxel for the treatment of r/m SCCHN after platinum failure

Summary

EudraCT number	2015-002325-18
Trial protocol	AT
Global end of trial date	27 November 2021

Results information

Result version number	v1 (current)
This version publication date	20 June 2024
First version publication date	20 June 2024

Trial information

Trial identification

Sponsor protocol code	PemDoc

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02718820
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	MedUniWien
Sponsor organisation address	Spitalgasse 23, Vienna, Austria, 1090
Public contact	Marika Rosner, MedUniWien, +43 14040044450, marika.rosner@meduniwien.ac.at
Scientific contact	Thorsten Füreder, MedUniWien, +43 14040044450, thorsten.fuereder@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	27 November 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 November 2021
Global end of trial reached?	Yes
Global end of trial date	27 November 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

• To evaluate the Overall Response Rate (CR/PR) rate and Progression Free Survival (PFS) in patients treated with pembrolizumab plus docetaxel for recurrent or metastatic (R/M) HNSCC after platinum-based first-line therapy
• To evaluate the safety of pembrolizumab in combination with docetaxel in subjects diagnosed with R/M HNSCC

Protection of trial subjects:

CT Thorax/Abdomen every 12 weeks

Background therapy:

antiemetics and dexamethason before and 3 days after administration of docetaxel

Evidence for comparator: -

Actual start date of recruitment	30 December 2015
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: 22
Worldwide total number of subjects	22
EEA total number of subjects	22

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)	13
From 65 to 84 years	9

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

22 patient were enrolled in this single-site at the University Hospital Vienna

Pre-assignment

Screening details:

22 patient were screened according to the inclusion and exclusion criteria

Period 1

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

Arms

Arm title	Treatment arm

Arm description:

There is only one arm

Arm type	Experimental
Investigational medicinal product name	Docetaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

75mg/m2 every 3 weeks

Investigational medicinal product name	Pembolizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

200mg every 3 weeks

Number of subjects in period 1	Treatment arm
Started	22
Completed	22

Baseline characteristics

Reporting groups

Reporting group title	Overall period

Reporting group description: -

Reporting group values	Overall period	Total	
Number of subjects	22	22	
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)	13	13	
From 65-84 years	9	9	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	4	4	
Male	18	18	

Subject analysis sets

Subject analysis set title	Overall trial
Subject analysis set type	Full analysis

Subject analysis set description:

Docetaxel 75mg/m2 plus pembrolizumab 200mg will be administered every 3 weeks intravenously for 6 cycles. Thereafter pembrolizumab 200mg every 3 weeks will be given as maintenance therapy until progression.

Docetaxel: Docetaxel 75mg/m2; q21

Pembrolizumab: Pembrolizumab 200mg, q21

Reporting group values	Overall trial		
Number of subjects	22		
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)	13		

From 65-84 years	9		
85 years and over	0		

Gender categorical Units: Subjects			
Female	4		
Male	18		

End points

End points reporting groups

Reporting group title	Treatment arm
Reporting group description:	
There is only one arm	
Subject analysis set title	Overall trial
Subject analysis set type	Full analysis
Subject analysis set description:	
Docetaxel 75mg/m2 plus pembrolizumab 200mg will be administered every 3 weeks intravenously for 6 cycles. Thereafter pembrolizumab 200mg every 3 weeks will be given as maintenance therapy until progression. Docetaxel: Docetaxel 75mg/m2; q21 Pembrolizumab: Pembrolizumab 200mg, q21	

Primary: objective tumor response

End point title	objective tumor response
End point description:	
End point type	Primary
End point timeframe:	
Baseline until end of treatment	

End point values	Treatment arm	Overall trial		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	22	22		
Units: mg/m2;q21				
median (confidence interval 95%)	22.7 (10.1 to 43.3)	22.7 (10.1 to 43.3)		

Statistical analyses

Statistical analysis title	Objective responses rate
Comparison groups	Treatment arm v Overall trial
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.05
Method	descriptive statistics

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Time the consent is signed through 90 days following cessation of treatment, or the initiation of new anti-cancer therapy, whichever is earlier.

Assessment type	Systematic

Dictionary used

Dictionary name	NCI CTCAE
Dictionary version	4.0

Reporting groups

Reporting group title	Treatment-related AEs

Reporting group description: -

Serious adverse events	Treatment-related AEs		
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 22 (31.82%)		
number of deaths (all causes)	14		
number of deaths resulting from adverse events	0		
Blood and lymphatic system disorders			
Neutropenic infection			
subjects affected / exposed	3 / 22 (13.64%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
emesis			
subjects affected / exposed	3 / 22 (13.64%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Infection			

subjects affected / exposed	2 / 22 (9.09%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Treatment-related AEs		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 22 (100.00%)		
Nervous system disorders			
Vertigo			
subjects affected / exposed	8 / 22 (36.36%)		
occurrences (all)	8		
Polyneuropathy			
subjects affected / exposed	9 / 22 (40.91%)		
occurrences (all)	9		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	14 / 22 (63.64%)		
occurrences (all)	14		
Blood and lymphatic system disorders			
Petechiae			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Anaemia			
subjects affected / exposed	4 / 22 (18.18%)		
occurrences (all)	4		
Neutropenia			
subjects affected / exposed	4 / 22 (18.18%)		
occurrences (all)	4		
Immune system disorders			
fever			
subjects affected / exposed	3 / 22 (13.64%)		
occurrences (all)	3		
Gastrointestinal disorders			

Diarrhoea subjects affected / exposed occurrences (all) emesis subjects affected / exposed occurrences (all)	 4 / 22 (18.18%) 4 2 / 22 (9.09%) 2		
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all) Mucositis subjects affected / exposed occurrences (all) Erythema subjects affected / exposed occurrences (all) Alopecia subjects affected / exposed occurrences (all) nail changes subjects affected / exposed occurrences (all)	 9 / 22 (40.91%) 9 9 / 22 (40.91%) 9 13 / 22 (59.09%) 13 5 / 22 (22.73%) 5 2 / 22 (9.09%) 2		
Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all)	 3 / 22 (13.64%) 3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 June 2021	Exploratory analysis of cytokine profile in HNSCC patients treated with docetaxel and pembrolizumab It has been published recently, that serum cytokine levels are altered in HNSCC patients and correlate with disease progression1. Apart from that, it there is growing evidence that not only cytokines such as interferon gamma but also soluble PD-L1 levels are of prognostic and predictive value in patients treated with CPI2,3. Based on this recent evidence we propose a retrospective exploratory analysis of the serum samples collected within the Pem-Doc study prior to publication in order to better understand the treatment responses. In particular we plan to measure the serum levels of interferon gamma; Interleukin 6, interleukin 17A, soluble PD-L1, major-histocompatibility-complex (MHC) class I-related chain genes A and B employing a ProcartaPlex 6-plex immunoassay. Soluble serum parameters will be quantified at baseline and at the initial restaging for patients with disease control and non-responders. Potential differences between paired data will be calculated using Wilcoxon signed-rank tests. Since this is a retrospective exploratory analysis of stored serum samples there will be no additional risks for the remaining patients. Next generation sequencing As already described in the protocol next generation sequencing will be performed. However, the Oncomine Comprehensive Assay v3 (Thermo Fisher Scientific, Waltham, MA, USA) instead of the Qiagen Comprehensive Cancer GeneRead DNAseq Targeted Panel will be used, since this assay is the one currently employed (for routine purposes as well) at the Department of Pathology due to superior performance.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported