Clinical trial results:
A SECOND-LINE, SINGLE ARM, PHASE II CLINICAL STUDY WITH TREMELIMUMAB, A FULLY HUMANIZED ANTI-CTLA-4 MONOCLONAL ANTIBODY, AS MONOTHERAPY IN PATIENTS WITH UNRESECTABLE MALIGNANT MESOTHELIOMA

Summary

EudraCT number	2012-002762-12
Trial protocol	IT
Global end of trial date	20 January 2016

Results information

Result version number	v1 (current)
This version publication date	15 May 2021
First version publication date	15 May 2021

Trial information

Trial identification

Sponsor protocol code	MESOT-TREM-2012

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01655888
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Azienda Ospedaliera Universitaria Senese
Sponsor organisation address	Viale Bracci 14, Siena, Italy, 53100
Public contact	UOC Immunoterapia Oncologica, Azienda Ospedaliera Universitaria Senese, l.calabro@ao-siena.toscana.it
Scientific contact	UOC Immunoterapia Oncologica, Azienda Ospedaliera Universitaria Senese, l.calabro@ao-siena.toscana.it

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	26 March 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 March 2015
Global end of trial reached?	Yes
Global end of trial date	20 January 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the rate of objective clinical complete response (CR) or partial response (PR)

Protection of trial subjects:

nothing

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 July 2012
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	Italy: 29
Worldwide total number of subjects	29
EEA total number of subjects	29

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)	12
From 65 to 84 years	17
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Between July 30, 2012, and July 15, 2013, we enrolled 29 patients,
Enrollment ended on 15/july/2013

Pre-assignment

Screening details:

Eligible patient were: advanced mesothelioma (pleural or peritoneal) in progression disease after one platinum-based chemotherapy regimen.

Patient without Brain Metastasis or aoutoimmune disease and ECOG between 0 and 2

Need to have measurable disease per modified RECIST

Period 1

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

Blinding implementation details:

single arm

Arms

Arm title	tremelimumab arm

Arm description: -

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

Dosage and administration details:

10 mg/kg every 28 days

Number of subjects in period 1	tremelimumab arm
Started	29
Completed	29

Baseline characteristics

Reporting groups

Reporting group title	tremelimumab arm

Reporting group description: -

Reporting group values	tremelimumab arm	Total	
Number of subjects	29	29	
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)	12	12	
From 65-84 years	17	17	
85 years and over	0	0	
Age continuous			
Age at the start of treatment			
Units: years			
median	65		
full range (min-max)	42 to 78	-	
Gender categorical Units: Subjects			
Female	9	9	
Male	20	20	

Subject analysis sets

Subject analysis set title	primary analysis
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All patients were considered for the primary endpoint: immune related response
All patients were also considered for secondary endpoint: immune related disease control; immune related PSF; OS; toxicity

Reporting group values	primary analysis		
Number of subjects	29		
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)	12		
From 65-84 years	17		
85 years and over	0		
Age continuous			
Age at the start of treatment			
Units: years			
median	65		
full range (min-max)	42 to 78		
Gender categorical			
Units: Subjects			
Female			
Male			

End points

End points reporting groups

Reporting group title	tremelimumab arm
Reporting group description: -	
Subject analysis set title	primary analysis
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All patients were considered for the primary endpoint: immune related response
All patients were also considered for secondary endpoint: immune related disease control; immune related PSF; OS; toxicity

Primary: Objective tumor response

End point title	Objective tumor response

End point description:

End point type	Primary

End point timeframe:

To estimate objective responce rate (proportion of patients with best response of CR+PR) defined as the total number of patients with CR, PR, , divided by the the total number of treated patients

End point values	tremelimumab arm	primary analysis		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	29	29		
Units: number	29	29		

Statistical analyses

Statistical analysis title	Statistical analysis

Statistical analysis description:

The proportion of patients with immune related response was calculated as a ratio between the number of CR or PR and the number of patients included.
Immune-related progression-free survival, overall survival, and survival rates at specified timepoints with two-sided 95% CIs based on normal approximation were estimated with the Kaplan-Meier method. Median values of circulating cells were taken as the cutoff to divide patient in two subgroups.

Comparison groups	tremelimumab arm v primary analysis
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	< 0.05 [2]
Method	Based on 95% confidence interval
Parameter estimate	Based on 95% confidence interval
Point estimate	13.8

Confidence interval	
level	95 %
sides	2-sided
lower limit	3.9
upper limit	31.7
Variability estimate	Standard error of the mean

Notes:

[1] - Assuming a response rate of 5% or lower (null hypothesis) of no therapeutic interest (ie, a response rate below which the treatment would be deemed
inactive) and a target response rate of 17% (alternative hypothesis) to consider the study drug clinically active, an α error of 0·05, we calculated that a total of
29 evaluable patients would have 70% power to detect an effect. On this basis, at least four immune-related objective responses would need to be detected
to consider the drug active.

[2] - The Simon's two stage design was used.

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From the sign of ICF to 90 days from the last study treatment	
Assessment type	Systematic
Dictionary used	
Dictionary name	CTCAE
Dictionary version	3.0
Reporting groups	
Reporting group title	immune-related toxicity

Reporting group description: -

Serious adverse events	immune-related toxicity		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 29 (3.45%)		
number of deaths (all causes)	23		
number of deaths resulting from adverse events	0		
Gastrointestinal disorders			
diarrhea			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	immune-related toxicity		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	29 / 29 (100.00%)		
General disorders and administration site conditions			
fever			
subjects affected / exposed	12 / 29 (41.38%)		
occurrences (all)	29		
Gastrointestinal disorders			
gastrointestinal toxicity			
subjects affected / exposed	21 / 29 (72.41%)		
occurrences (all)	29		

Hepatobiliary disorders liver toxicities subjects affected / exposed occurrences (all)	 3 / 29 (10.34%) 29		
Skin and subcutaneous tissue disorders dermatological toxicities subjects affected / exposed occurrences (all)	 17 / 29 (58.62%) 29		
Musculoskeletal and connective tissue disorders general pain toxcities subjects affected / exposed occurrences (all)	 4 / 29 (13.79%) 29		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported