Clinical trial results:
A ROLLOVER PROTOCOL FOR PATIENTS WHO RECEIVED TREMELIMUMAB (CP-675,206) IN OTHER PROTOCOLS

Summary

EudraCT number	2008-000989-23
Trial protocol	GB IT
Global end of trial date	27 October 2023

Results information

Result version number	v1 (current)
This version publication date	06 September 2024
First version publication date	06 September 2024

Trial information

Trial identification

Sponsor protocol code	D4881C00024

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00378482
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca Clinical Study Information Center
Sponsor organisation address	Milbourn Science Park, Royston, United Kingdom, SG8 6EE
Public contact	Global Clinical Lead, AstraZeneca Clinical Study Information Center, +1 8772409479, information.center@astrazeneca.com
Scientific contact	Global Clinical Lead, AstraZeneca Clinical Study Information Center, +1 8772409479, information.center@astrazeneca.com

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	18 June 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 October 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To allow access to tremelimumab for subjects who received tremelimumab in other trials.

Protection of trial subjects:

This study was performed in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with International Council for Harmonization /Good Clinical Practice and applicable regulatory requirements and the AstraZeneca policy on Bioethics.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 March 2008
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: 1
Country: Number of subjects enrolled	United States: 35
Country: Number of subjects enrolled	United Kingdom: 2
Worldwide total number of subjects	38
EEA total number of subjects	1

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)	24
From 65 to 84 years	14

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

First subject enrolled: 05 Mar 2007;
Data Cut-off: 18 Jun 2020.
This was a multicenter study conducted at 11 study centers in 3 countries (the United Kingdom, the United States of America and Italy).

Pre-assignment

Screening details:

Total Consented/screened 38 subjects (1 of which was dead before enter any treatment), so total entered treatment 37 subjects
Subjects were assigned to treatment if they met all inclusion. 32 subjects withdrawn from this study. 6 subjects completed the study.
Final Efficacy/Safety analysis 37 subjects.

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	Tremelimumab 15mg/kg

Arm description:

All Patients

Arm type	NA
Investigational medicinal product name	TREMELIMUMAB
Investigational medicinal product code	MEDI1123
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

15 mg/kg milligram(s)/kilogram

Number of subjects in period 1	Tremelimumab 15mg/kg
Started	38
Completed	6
Not completed	32
Adverse event, serious fatal	1
Consent withdrawn by subject	4
Physician decision	9
Adverse event, non-fatal	9
Lost to follow-up	1
Lack of efficacy	8

Baseline characteristics

Reporting groups	
Reporting group title	Tremelimumab 15mg/kg
Reporting group description:	
All Patients	

Reporting group values	Tremelimumab 15mg/kg	Total	
Number of subjects	38	38	
Age Categorical Units: Participants			
<=18 years	0	0	
Between 18 and 65 years	24	24	
>=65 years	14	14	
Sex: Female, Male Units: Participants			
Female	11	11	
Male	27	27	
Race (NIH/OMB) 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	38	38	
More than one race	0	0	
Unknown or Not Reported	0	0	

End points

End points reporting groups	
Reporting group title	Tremelimumab 15mg/kg
Reporting group description: All Patients	
Subject analysis set title	All Patients
Subject analysis set type	Intention-to-treat
Subject analysis set description: All Patients enrolled	

Primary: Safety Endpoints: • Serious adverse events • Grade 3 or 4 tremelimumab-related adverse events • Immune-mediated adverse events • Hypersensitivity reactions to tremelimumab.	
End point title	Safety Endpoints: • Serious adverse events • Grade 3 or 4 tremelimumab-related adverse events • Immune-mediated adverse events • Hypersensitivity reactions to tremelimumab.
End point description:	
End point type	Primary
End point timeframe: as long as required	

End point values	Tremelimumab 15mg/kg	All Patients		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	37	37		
Units: Participants	37	37		

Statistical analyses

Statistical analysis title	Summaries of safety data
Statistical analysis description: No quantification or analysis performed for this outcome	
Comparison groups	Tremelimumab 15mg/kg v All Patients
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0
Method	N/A

Primary: Efficacy Endpoints: • Tumor status: alive with disease (AWD) or no evidence of disease (NED) • Survival	
End point title	Efficacy Endpoints: • Tumor status: alive with disease (AWD)

	or no evidence of disease (NED) • Survival

End point description:

End point type	Primary

End point timeframe:

End of study per participant

End point values	Tremelimumab 15mg/kg	All Patients		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	37	37		
Units: Participants				
No evidence of disease	19	19		
Evidence of disease	17	17		
Indeterminate	1	1		

Statistical analyses

Statistical analysis title	Summary of tumor status

Statistical analysis description:

Single-arm, no statistical testing performed

Comparison groups	Tremelimumab 15mg/kg v All Patients
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0
Method	N/A

Secondary: Disease Free Survival

End point title	Disease Free Survival

End point description:

Time from the first dose of study drug to the earliest date of evidence of disease (based on tumor status assessment) or death, whichever occurred first

End point type	Secondary

End point timeframe:

Varied per participant

End point values	Tremelimumab 15mg/kg	All Patients		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	37	37		
Units: Days				
median (confidence interval 95%)	3.0 (2.9 to 11.8)	3.0 (2.9 to 11.8)		

Statistical analyses

Statistical analysis title	Summary of Disease-Free Survival
Statistical analysis description: Single-arm study with no statistical testing	
Comparison groups	Tremelimumab 15mg/kg v All Patients
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0
Method	N/A
Parameter estimate	N/A

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 13 years, 3 months	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.0
Reporting groups	
Reporting group title	Tremelimumab 15mg/kg
Reporting group description: All Patients	

Serious adverse events	Tremelimumab 15mg/kg		
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 37 (10.81%)		
number of deaths (all causes)	11		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Prostate cancer			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Medical Device Complication			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Diarrhea			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis			

subjects affected / exposed	1 / 37 (2.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pulmonary Granuloma			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Sepsis			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary Tract Infection			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Tremelimumab 15mg/kg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 37 (13.51%)		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	4 / 37 (10.81%)		
occurrences (all)	12		
Pruritus			
subjects affected / exposed	3 / 37 (8.11%)		
occurrences (all)	3		
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	2 / 37 (5.41%)		
occurrences (all)	2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 December 2019	Incorporate the 2012 Protocol Administrative change (dated 05 April 2012) which included a change in Sponsor, compound name, and study number. Align the Protocol with the current tremelimumab Investigator's Brochure (IB) specifically in relation to safety. Update the toxicity management in the clinical protocol in line with updates being made across the clinical program, and introduce Dosing Modification and Toxicity Management Guidelines (TMG), which is provided as an Annex to the clinical protocol.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported