Clinical trial results:
A phase II study to investigate the activity and safety of anti-PD-L1 antibody (Durvalumab) In ADvancEd pretreated malignant pleural Mesothelioma - DIADEM Study

Summary

EudraCT number	2016-000617-67
Trial protocol	IT
Global end of trial date	27 November 2020

Results information

Result version number	v1 (current)
This version publication date	21 October 2022
First version publication date	21 October 2022

Trial information

Trial identification

Sponsor protocol code	IRFMN-MPM-7109

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Istituto di Ricerche Farmacologiche Mario Negri IRCCS
Sponsor organisation address	Via Mario Negri 2, Milan, Italy, 20156
Public contact	Eliana Rulli, Istituto di Ricerche Farmacologiche Mario Negri IRCCS , 02 0239014645, eliana.rulli@marionegri.it
Scientific contact	Eliana Rulli, Istituto di Ricerche Farmacologiche Mario Negri IRCCS, 02 0239014645, eliana.rulli@marionegri.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	24 May 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 November 2020
Global end of trial reached?	Yes
Global end of trial date	27 November 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of antiPD-L1 Ab Durvalumab in patients with MPM relapsing after first line treatment with pemetrexed plus platinum-based drugs.

Protection of trial subjects:

NA

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 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	Italy: 69
Worldwide total number of subjects	69
EEA total number of subjects	69

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)	16
From 65 to 84 years	53
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients who experience prog after one line of platinum-derivative+pemetrexed regimen will be considered for the study. The first day of the first treatment cycle will be considered as day one of the trial for all subsequent activity and safety evaluations. Patients will receive Durvalumab at the dose and regimens described above every 4 weeks.

Pre-assignment

Screening details:

NA

Period 1

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

Arms

Arm title	Single arm

Arm description:

Patients will receive Durvalumab at the dose and regimens described above every 4 weeks until evidence of disease progression or occurrence of unacceptable toxicity.
Patients who show evidence of disease progression but appear to tolerate Durvalumab well, for whom no other treatment options exist and who, at the judgement of the investigator, may still enjoy clinical benefit, will be classified as failures and offered the possibility to continue treatment with extended follow up.

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

Dosage and administration details:

Durvalumab at a standard dose of 1500 mg IV Q4W. Durvalumab will be delivered in infusion bags with IV infusion lines with product contacting surfaces of polyvinylchloride (PVC) and Polyolefin and 0.2 µm in-line filters (filter membrane of PES). The initial dose of durvalumab will be delivered over 60 (± 15) minutes. If the first infusion is tolerated without infusion associated AEs, the second infusion may be delivered over 30 (± 10) minutes. If the 30-minute infusion is well tolerated, all subsequent infusions may be delivered over 30 (± 10) minutes.

Number of subjects in period 1	Single arm
Started	69
Completed	69

Baseline characteristics

Reporting groups

Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	69	69	
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)	16	16	
From 65-84 years	53	53	
85 years and over	0	0	
Age continuous Units: years			
median	69.9		
inter-quartile range (Q1-Q3)	65.0 to 76.3	-	
Gender categorical Units: Subjects			
Female	25	25	
Male	44	44	

Subject analysis sets

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

Subject analysis set description:

The ITT analysis set is defined as all patients included in the study, without major violations of eligibility criteria.

Subject analysis set title	Safety
Subject analysis set type	Safety analysis

Subject analysis set description:

The Safety analysis set includes all subjects who provided informed consent and were included in the study, who had no major violations of eligibility criteria, and who received at least one dose of treatment

Subject analysis set title	PP primary
Subject analysis set type	Per protocol

Subject analysis set description:

The PP analysis set includes all enrolled patients, without major eligibility criteria who have received at least 2 cycles of treatment

Reporting group values	ITT	Safety	PP primary
Number of subjects	69	69	47
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	16	16	13
From 65-84 years	53	53	34
85 years and over	0	0	0
Age continuous Units: years			
median	69.9	69.9	69.6
inter-quartile range (Q1-Q3)	65.0 to 76.3	65.0 to 76.3	63.6 to 74.8
Gender categorical Units: Subjects			
Female	25	25	18
Male	44	44	29

End points

End points reporting groups

Reporting group title	Single arm

Reporting group description:

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Subject analysis set title	PP primary
Subject analysis set type	Per protocol

Subject analysis set description:

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Primary: PFS 16 weeks

End point title	PFS 16 weeks

End point description:

End point type	Primary

End point timeframe:

16 weeks

End point values	Single arm	PP primary		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	47	47		
Units: patients	11	11		

Statistical analyses

Statistical analysis title	Progression Free Survival rate at 16weeks
Comparison groups	Single arm v PP primary

Number of subjects included in analysis	94
Analysis specification	Pre-specified
Analysis type	other[1]
Parameter estimate	Proportion of patients alive without PD
Point estimate	23.4
Confidence interval	
level	90 %
sides	2-sided
lower limit	13.7
upper limit	35.8
Variability estimate	Standard deviation

Notes:

[1] - The trail was a single arm study, no statistical comparison was planned

Adverse events

Adverse events information	
Timeframe for reporting adverse events: During treatment	
Assessment type	Systematic
Dictionary used	
Dictionary name	NCI-CTCAE
Dictionary version	4.0
Reporting groups	
Reporting group title	Overall

Reporting group description: -

Serious adverse events	Overall		
Total subjects affected by serious adverse events			
subjects affected / exposed	29 / 69 (42.03%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Investigations			
Amilasi increased			
subjects affected / exposed	1 / 69 (1.45%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Lipasi increased			
subjects affected / exposed	1 / 69 (1.45%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	1 / 69 (1.45%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Thrombolic event			
subjects affected / exposed	1 / 69 (1.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Cardiac disorders			
Acute cardiac event			
subjects affected / exposed	1 / 69 (1.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Pericardial effusion			
subjects affected / exposed	4 / 69 (5.80%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Atrial fibrillation			
subjects affected / exposed	2 / 69 (2.90%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Astenia			
subjects affected / exposed	1 / 69 (1.45%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Sudden death			
subjects affected / exposed	1 / 69 (1.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	1 / 1		
Pyrexia			
subjects affected / exposed	1 / 69 (1.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Ischemic colitis			
subjects affected / exposed	1 / 69 (1.45%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Nausea			

subjects affected / exposed	1 / 69 (1.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intestinal obstruction			
subjects affected / exposed	2 / 69 (2.90%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ascites			
subjects affected / exposed	1 / 69 (1.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Dyspnea			
subjects affected / exposed	5 / 69 (7.25%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 2		
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 69 (1.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Respiratory acidosis			
subjects affected / exposed	1 / 69 (1.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Soft tissue infection			
subjects affected / exposed	1 / 69 (1.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	1 / 69 (1.45%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Decreased appetite			
subjects affected / exposed	1 / 69 (1.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cachexia			
subjects affected / exposed	1 / 69 (1.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		

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

Non-serious adverse events	Overall		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	58 / 69 (84.06%)		
Investigations			
Blood creatinine increased			
subjects affected / exposed	3 / 69 (4.35%)		
occurrences (all)	3		
Vascular disorders			
Embolism			
subjects affected / exposed	3 / 69 (4.35%)		
occurrences (all)	3		
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	3 / 69 (4.35%)		
occurrences (all)	3		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	14 / 69 (20.29%)		
occurrences (all)	17		
Pyrexia			
subjects affected / exposed	9 / 69 (13.04%)		
occurrences (all)	9		
Non-cardiac chest pain			
subjects affected / exposed	4 / 69 (5.80%)		
occurrences (all)	5		

Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	 5 / 69 (7.25%) 6		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	 7 / 69 (10.14%) 10 4 / 69 (5.80%) 4 4 / 69 (5.80%) 4		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Dyspnoea subjects affected / exposed occurrences (all) Dyspnea subjects affected / exposed occurrences (all)	 14 / 69 (20.29%) 15 14 / 69 (20.29%) 19 4 / 69 (5.80%) 4		
Skin and subcutaneous tissue disorders Dry skin subjects affected / exposed occurrences (all) Pruritus subjects affected / exposed occurrences (all)	 3 / 69 (4.35%) 3 3 / 69 (4.35%) 4		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all) Muscular weakness	 6 / 69 (8.70%) 7 		

subjects affected / exposed	5 / 69 (7.25%)		
occurrences (all)	6		
Musculoskeletal chest pain			
subjects affected / exposed	5 / 69 (7.25%)		
occurrences (all)	8		
Arthralgia			
subjects affected / exposed	4 / 69 (5.80%)		
occurrences (all)	5		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	5 / 69 (7.25%)		
occurrences (all)	5		

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