



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:

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.

| | |
|----------------------------|-----|
| 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

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 trial 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 | | | |
| Thrombotic 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 | | | |
| Asthenia | | | |
| 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 | | |

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

| | | | |
|------------------------------------|----------------|--|--|
| 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