



## Clinical trial results:

### A Phase 3, Randomized, Double-Blind Clinical Trial to Evaluate the Efficacy and Safety of Abatacept SC with Standard Treatment Compared to Standard Treatment Alone in Improving Disease Activity in Adults with Active Idiopathic Inflammatory Myopathy (IIM)

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2016-002269-77 |
| Trial protocol           | DE CZ SE FR IT |
| Global end of trial date | 02 August 2022 |

#### Results information

|                                |                |
|--------------------------------|----------------|
| Result version number          | v1             |
| This version publication date  | 17 August 2023 |
| First version publication date | 17 August 2023 |

#### Trial information

##### Trial identification

|                       |           |
|-----------------------|-----------|
| Sponsor protocol code | IM101-611 |
|-----------------------|-----------|

##### Additional study identifiers

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

Notes:

#### Sponsors

|                              |                                                                                                 |
|------------------------------|-------------------------------------------------------------------------------------------------|
| Sponsor organisation name    | Bristol-Myers Squibb                                                                            |
| Sponsor organisation address | Chaussée de la Hulpe 185, Brussels, Belgium, 1170                                               |
| Public contact               | EU Study Start-Up Unit, Bristol-Myers Squibb International Corporation, Clinical.Trials@bms.com |
| Scientific contact           | Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, Clinical.Trials@bms.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                       | 22 December 2022 |
| Is this the analysis of the primary completion data? | No               |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 02 August 2022   |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective for this study is to compare the clinical efficacy of weekly abatacept in combination with standard treatment to standard treatment alone by assessing the percentage of subjects who achieve the IMACS DOI by Week 24 compared to baseline, defined as:

- An improvement of  $\geq 20\%$  in 3 IMACS core measures, AND
- No more than 2 IMACS core measure scores worsen by  $\geq 25\%$ , AND
- Manual Muscle Test (MMT-8) may not decrease by  $\geq 25\%$

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial participants were followed.

Background therapy: -

Evidence for comparator: -

|                                                           |             |
|-----------------------------------------------------------|-------------|
| Actual start date of recruitment                          | 04 May 2017 |
| Long term follow-up planned                               | No          |
| Independent data monitoring committee (IDMC) involvement? | Yes         |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                        |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Brazil: 24             |
| Country: Number of subjects enrolled | Czechia: 7             |
| Country: Number of subjects enrolled | France: 4              |
| Country: Number of subjects enrolled | Germany: 1             |
| Country: Number of subjects enrolled | Italy: 4               |
| Country: Number of subjects enrolled | Japan: 21              |
| Country: Number of subjects enrolled | Korea, Republic of: 15 |
| Country: Number of subjects enrolled | Mexico: 20             |
| Country: Number of subjects enrolled | Sweden: 4              |
| Country: Number of subjects enrolled | United States: 48      |
| Worldwide total number of subjects   | 148                    |
| EEA total number of subjects         | 20                     |

Notes:

| <b>Subjects enrolled per age group</b>    |     |
|-------------------------------------------|-----|
| 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)                      | 133 |
| From 65 to 84 years                       | 15  |
| 85 years and over                         | 0   |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

148 were randomized and treated

### Period 1

|                              |                                |
|------------------------------|--------------------------------|
| Period 1 title               | Double-Blind Period (24 weeks) |
| Is this the baseline period? | Yes                            |
| Allocation method            | Randomised - controlled        |
| Blinding used                | Double blind                   |
| Roles blinded                | Subject, Investigator          |

### Arms

|                              |     |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

|                  |                                |
|------------------|--------------------------------|
| <b>Arm title</b> | Abatacept + Standard Treatment |
|------------------|--------------------------------|

Arm description:

Participants receive subcutaneous abatacept (125 mg weekly) in combination with standard treatment for the first 24 weeks (6 months) during the double-blind period. Participants continue to receive abatacept in the Open-Label and Long-Term Open Label Periods.

|                                        |                                              |
|----------------------------------------|----------------------------------------------|
| Arm type                               | Experimental                                 |
| Investigational medicinal product name | Abatacept                                    |
| Investigational medicinal product code |                                              |
| Other name                             |                                              |
| Pharmaceutical forms                   | Solution for injection in pre-filled syringe |
| Routes of administration               | Subcutaneous use                             |

Dosage and administration details:

Abatacept SC 125 mg in 1 ml pre-filled syringes

|                  |                              |
|------------------|------------------------------|
| <b>Arm title</b> | Placebo + Standard Treatment |
|------------------|------------------------------|

Arm description:

Participants receive placebo (to match subcutaneous abatacept) in combination with standard treatment for the first 24 weeks (6 months) during the double-blind period. Participants then switch from placebo to abatacept in the Open-Label and Long-Term Open Label Periods.

|                                        |                                              |
|----------------------------------------|----------------------------------------------|
| Arm type                               | Placebo                                      |
| Investigational medicinal product name | Placebo                                      |
| Investigational medicinal product code |                                              |
| Other name                             |                                              |
| Pharmaceutical forms                   | Solution for injection in pre-filled syringe |
| Routes of administration               | Subcutaneous use                             |

Dosage and administration details:

Placebo to match abatacept SC in 1 ml pre-filled syringes

| Number of subjects in period 1                     | Abatacept + Standard Treatment | Placebo + Standard Treatment |
|----------------------------------------------------|--------------------------------|------------------------------|
| Started                                            | 75                             | 73                           |
| Completed                                          | 69                             | 65                           |
| Not completed                                      | 6                              | 8                            |
| Poor/Non-Compliance                                | -                              | 1                            |
| Participant withdrew consent                       | 1                              | 1                            |
| Adverse event, non-fatal                           | -                              | 2                            |
| Participant no longer meets study criteria         | 1                              | -                            |
| Other reasons                                      | -                              | 1                            |
| Lost to follow-up                                  | 1                              | -                            |
| Lack of efficacy                                   | 2                              | 2                            |
| Participant request to discontinue study treatment | 1                              | 1                            |

## Period 2

|                              |                             |
|------------------------------|-----------------------------|
| Period 2 title               | Open-Label (OL) Period      |
| Is this the baseline period? | No                          |
| Allocation method            | Non-randomised - controlled |
| Blinding used                | Not blinded                 |

## Arms

|                              |                                |
|------------------------------|--------------------------------|
| Are arms mutually exclusive? | Yes                            |
| <b>Arm title</b>             | Abatacept + Standard Treatment |

### Arm description:

Participants receive subcutaneous abatacept (125 mg weekly) in combination with standard treatment for the first 24 weeks (6 months) during the double-blind period. Participants continue to receive abatacept in the Open-Label and Long-Term Open Label Periods.

|                                        |                                              |
|----------------------------------------|----------------------------------------------|
| Arm type                               | Experimental                                 |
| Investigational medicinal product name | Abatacept                                    |
| Investigational medicinal product code |                                              |
| Other name                             |                                              |
| Pharmaceutical forms                   | Solution for injection in pre-filled syringe |
| Routes of administration               | Subcutaneous use                             |

### Dosage and administration details:

Abatacept SC 125 mg in 1 ml pre-filled syringes

|                  |                              |
|------------------|------------------------------|
| <b>Arm title</b> | Placebo + Standard Treatment |
|------------------|------------------------------|

### Arm description:

Participants receive placebo (to match subcutaneous abatacept) in combination with standard treatment for the first 24 weeks (6 months) during the double-blind period. Participants then switch from placebo to abatacept in the Open-Label and Long-Term Open Label Periods.

|          |              |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

|                                                 |                                              |
|-------------------------------------------------|----------------------------------------------|
| Investigational medicinal product name          | Abatacept                                    |
| Investigational medicinal product code          |                                              |
| Other name                                      |                                              |
| Pharmaceutical forms                            | Solution for injection in pre-filled syringe |
| Routes of administration                        | Subcutaneous use                             |
| Dosage and administration details:              |                                              |
| Abatacept SC 125 mg in 1 ml pre-filled syringes |                                              |

| Number of subjects in period 2 <sup>[1]</sup>      | Abatacept + Standard Treatment | Placebo + Standard Treatment |
|----------------------------------------------------|--------------------------------|------------------------------|
| Started                                            | 69                             | 63                           |
| Completed                                          | 65                             | 61                           |
| Not completed                                      | 4                              | 2                            |
| Lost to follow-up                                  | 1                              | -                            |
| Participants withdrew consent                      | -                              | 2                            |
| Lack of efficacy                                   | 2                              | -                            |
| Participant request to discontinue study treatment | 1                              | -                            |

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Not all participants who completed the preceding period moved onto the next period.

### Period 3

|                              |                             |
|------------------------------|-----------------------------|
| Period 3 title               | Long-Term Open Label        |
| Is this the baseline period? | No                          |
| Allocation method            | Non-randomised - controlled |
| Blinding used                | Not blinded                 |

### Arms

|                              |                                |
|------------------------------|--------------------------------|
| Are arms mutually exclusive? | Yes                            |
| <b>Arm title</b>             | Abatacept + Standard Treatment |

Arm description:

Participants receive subcutaneous abatacept (125 mg weekly) in combination with standard treatment for the first 24 weeks (6 months) during the double-blind period. Participants continue to receive abatacept in the Open-Label and Long-Term Open Label Periods.

|                                        |                                              |
|----------------------------------------|----------------------------------------------|
| Arm type                               | Experimental                                 |
| Investigational medicinal product name | Abatacept                                    |
| Investigational medicinal product code |                                              |
| Other name                             |                                              |
| Pharmaceutical forms                   | Solution for injection in pre-filled syringe |
| Routes of administration               | Subcutaneous use                             |

Dosage and administration details:

Abatacept SC 125 mg in 1 ml pre-filled syringes

|                  |                              |
|------------------|------------------------------|
| <b>Arm title</b> | Placebo + Standard Treatment |
|------------------|------------------------------|

Arm description:

Participants receive placebo (to match subcutaneous abatacept) in combination with standard treatment for the first 24 weeks (6 months) during the double-blind period. Participants then switch from placebo

to abatacept in the Open-Label and Long-Term Open Label Periods.

|                                        |                                              |
|----------------------------------------|----------------------------------------------|
| Arm type                               | Experimental                                 |
| Investigational medicinal product name | Abatacept                                    |
| Investigational medicinal product code |                                              |
| Other name                             |                                              |
| Pharmaceutical forms                   | Solution for injection in pre-filled syringe |
| Routes of administration               | Subcutaneous use                             |

Dosage and administration details:

Abatacept SC 125 mg in 1 ml pre-filled syringes

| <b>Number of subjects in period 3<sup>[2]</sup></b> | <b>Abatacept + Standard Treatment</b> | <b>Placebo + Standard Treatment</b> |
|-----------------------------------------------------|---------------------------------------|-------------------------------------|
| Started                                             | 25                                    | 21                                  |
| Completed                                           | 1                                     | 0                                   |
| Not completed                                       | 24                                    | 21                                  |
| Participant withdrew consent                        | 1                                     | -                                   |
| Adverse event, non-fatal                            | 1                                     | 2                                   |
| Lack of efficacy                                    | 1                                     | 1                                   |
| Administrative reason by sponsor                    | 20                                    | 17                                  |
| Participant request to discontinue study treatment  | 1                                     | 1                                   |

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Not all participants who completed the preceding period moved onto the next period.

## Baseline characteristics

### Reporting groups

|                       |                                |
|-----------------------|--------------------------------|
| Reporting group title | Abatacept + Standard Treatment |
|-----------------------|--------------------------------|

Reporting group description:

Participants receive subcutaneous abatacept (125 mg weekly) in combination with standard treatment for the first 24 weeks (6 months) during the double-blind period. Participants continue to receive abatacept in the Open-Label and Long-Term Open Label Periods.

|                       |                              |
|-----------------------|------------------------------|
| Reporting group title | Placebo + Standard Treatment |
|-----------------------|------------------------------|

Reporting group description:

Participants receive placebo (to match subcutaneous abatacept) in combination with standard treatment for the first 24 weeks (6 months) during the double-blind period. Participants then switch from placebo to abatacept in the Open-Label and Long-Term Open Label Periods.

| Reporting group values           | Abatacept + Standard Treatment | Placebo + Standard Treatment | Total |
|----------------------------------|--------------------------------|------------------------------|-------|
| Number of subjects               | 75                             | 73                           | 148   |
| Age Categorical                  |                                |                              |       |
| Units: Participants              |                                |                              |       |
| 16-29 years old                  | 9                              | 9                            | 18    |
| 30-39 years old                  | 8                              | 14                           | 22    |
| 40-49 years old                  | 14                             | 14                           | 28    |
| 50-59 years old                  | 31                             | 19                           | 50    |
| >/= 60 years old                 | 13                             | 17                           | 30    |
| Age Continuous                   |                                |                              |       |
| Units: Years                     |                                |                              |       |
| arithmetic mean                  | 49.3                           | 48.1                         |       |
| standard deviation               | ± 14.41                        | ± 14.09                      | -     |
| Sex: Female, Male                |                                |                              |       |
| Units: Participants              |                                |                              |       |
| Female                           | 52                             | 54                           | 106   |
| Male                             | 23                             | 19                           | 42    |
| Ethnicity (NIH/OMB)              |                                |                              |       |
| Units: Subjects                  |                                |                              |       |
| Hispanic or Latino               | 7                              | 3                            | 10    |
| Not Hispanic or Latino           | 19                             | 19                           | 38    |
| Unknown or Not Reported          | 49                             | 51                           | 100   |
| Race/Ethnicity, Customized       |                                |                              |       |
| Units: Subjects                  |                                |                              |       |
| American Indian or Alaska Native | 3                              | 3                            | 6     |
| Asian                            | 10                             | 6                            | 16    |
| Black or African American        | 9                              | 8                            | 17    |
| White                            | 42                             | 42                           | 84    |
| Japanese                         | 11                             | 10                           | 21    |
| Other                            | 0                              | 3                            | 3     |
| Unknown                          | 0                              | 1                            | 1     |



## End points

### End points reporting groups

|                                                                                                                                                                                                                                                                                                                |                                |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------|
| Reporting group title                                                                                                                                                                                                                                                                                          | Abatacept + Standard Treatment |
| Reporting group description:<br>Participants receive subcutaneous abatacept (125 mg weekly) in combination with standard treatment for the first 24 weeks (6 months) during the double-blind period. Participants continue to receive abatacept in the Open-Label and Long-Term Open Label Periods.            |                                |
| Reporting group title                                                                                                                                                                                                                                                                                          | Placebo + Standard Treatment   |
| Reporting group description:<br>Participants receive placebo (to match subcutaneous abatacept) in combination with standard treatment for the first 24 weeks (6 months) during the double-blind period. Participants then switch from placebo to abatacept in the Open-Label and Long-Term Open Label Periods. |                                |
| Reporting group title                                                                                                                                                                                                                                                                                          | Abatacept + Standard Treatment |
| Reporting group description:<br>Participants receive subcutaneous abatacept (125 mg weekly) in combination with standard treatment for the first 24 weeks (6 months) during the double-blind period. Participants continue to receive abatacept in the Open-Label and Long-Term Open Label Periods.            |                                |
| Reporting group title                                                                                                                                                                                                                                                                                          | Placebo + Standard Treatment   |
| Reporting group description:<br>Participants receive placebo (to match subcutaneous abatacept) in combination with standard treatment for the first 24 weeks (6 months) during the double-blind period. Participants then switch from placebo to abatacept in the Open-Label and Long-Term Open Label Periods. |                                |
| Reporting group title                                                                                                                                                                                                                                                                                          | Abatacept + Standard Treatment |
| Reporting group description:<br>Participants receive subcutaneous abatacept (125 mg weekly) in combination with standard treatment for the first 24 weeks (6 months) during the double-blind period. Participants continue to receive abatacept in the Open-Label and Long-Term Open Label Periods.            |                                |
| Reporting group title                                                                                                                                                                                                                                                                                          | Placebo + Standard Treatment   |
| Reporting group description:<br>Participants receive placebo (to match subcutaneous abatacept) in combination with standard treatment for the first 24 weeks (6 months) during the double-blind period. Participants then switch from placebo to abatacept in the Open-Label and Long-Term Open Label Periods. |                                |

### Primary: Number of Participants Achieving International Myositis Assessment and Clinical Studies Definition of Improvement (IMACS DOI) at Week 24 Without Rescue

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                         |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | Number of Participants Achieving International Myositis Assessment and Clinical Studies Definition of Improvement (IMACS DOI) at Week 24 Without Rescue |
| End point description:<br>The number of participants who achieve IMACS DOI (International Myositis Assessment and Clinical Studies definition of improvement) without rescue medication at week 24.<br><br>The IMACS DOI is: An improvement of $\geq 20\%$ from baseline in 3 IMACS core measures, no more than 2 IMACS core measure scores worsen by $\geq 25\%$ from baseline, and no more than 2 IMACS core measure scores worsen by $\geq 25\%$ from baseline.<br><br>IMACS core measures are: Physician Global Assessment of Disease Activity (PGA), Patient (Subject) Global Assessment of Disease Activity (SGA), Manual Muscle Test (MMT-8), Health Assessment Questionnaire-Disability Index (HAQ-DI), Muscle Enzyme levels, Myositis Disease Activity Assessment Tool (MDAAT) Extramuscular Global Activity. |                                                                                                                                                         |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | Primary                                                                                                                                                 |
| End point timeframe:<br>From first dose to 24 weeks after first dose. (Approximately 169 days)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                                                         |

| <b>End point values</b>     | Abatacept +<br>Standard<br>Treatment | Placebo +<br>Standard<br>Treatment |  |  |
|-----------------------------|--------------------------------------|------------------------------------|--|--|
| Subject group type          | Reporting group                      | Reporting group                    |  |  |
| Number of subjects analysed | 75                                   | 73                                 |  |  |
| Units: Participants         | 42                                   | 31                                 |  |  |

## Statistical analyses

|                                         |                                                               |
|-----------------------------------------|---------------------------------------------------------------|
| <b>Statistical analysis title</b>       | IMACs DOI at week 24                                          |
| Comparison groups                       | Placebo + Standard Treatment v Abatacept + Standard Treatment |
| Number of subjects included in analysis | 148                                                           |
| Analysis specification                  | Pre-specified                                                 |
| Analysis type                           |                                                               |
| P-value                                 | = 0.083                                                       |
| Method                                  | Regression, Logistic                                          |
| Parameter estimate                      | Odds ratio (OR)                                               |
| Point estimate                          | 1.8                                                           |
| Confidence interval                     |                                                               |
| level                                   | 95 %                                                          |
| sides                                   | 2-sided                                                       |
| lower limit                             | 0.9                                                           |
| upper limit                             | 3.5                                                           |

## Secondary: Mean change in Health Assessment Questionnaire-Disability Index (HAQ-DI) from baseline to Week 24

|                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
|------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title        | Mean change in Health Assessment Questionnaire-Disability Index (HAQ-DI) from baseline to Week 24                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| End point description: | The adjusted mean change from baseline in the Health Assessment Questionnaire-Disability Index (HAQ-DI). HAQ-DI is a patient-reported outcome measuring disability by asking a total of 20 questions in eight categories of function: dressing, arising, eating, walking, hygiene, reach, grip, and activities. If an aid or device is used or if help is required from another individual, then the minimum score for that section is 2. The highest component score in each category determines the score for the category and scores are averaged to give the disability index. The HAQ scale ranges from 0 (no difficulties) to 3 (unable to do). |
| End point type         | Secondary                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| End point timeframe:   | From first dose to 24 weeks after first dose. (Approximately 169 days)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |

| End point values                 | Abatacept + Standard Treatment | Placebo + Standard Treatment |  |  |
|----------------------------------|--------------------------------|------------------------------|--|--|
| Subject group type               | Reporting group                | Reporting group              |  |  |
| Number of subjects analysed      | 66                             | 62                           |  |  |
| Units: Score on a scale          |                                |                              |  |  |
| arithmetic mean (standard error) | -0.31 (± 0.067)                | -0.20 (± 0.069)              |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Mean Change in Muscle Endurance Using the Myositis Function Index (FI-2) from Baseline to Week 24

|                 |                                                                                                   |
|-----------------|---------------------------------------------------------------------------------------------------|
| End point title | Mean Change in Muscle Endurance Using the Myositis Function Index (FI-2) from Baseline to Week 24 |
|-----------------|---------------------------------------------------------------------------------------------------|

End point description:

The adjusted mean change from baseline in Myositis FI-2 scores is assessing muscle endurance impairment by testing specific muscle groups. The 3 Score average includes shoulder flexion, hip flexion, and head lift. Each muscle group is scored as the number of correctly performed repetitions with 60 maximal number of repetitions.

The total score is based on hip flexion, shoulder flexion (R/L) and neck divided by 3 (range 0-60 repetitions).

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From first dose to 24 weeks after first dose. (Approximately 169 days)

| End point values                 | Abatacept + Standard Treatment | Placebo + Standard Treatment |  |  |
|----------------------------------|--------------------------------|------------------------------|--|--|
| Subject group type               | Reporting group                | Reporting group              |  |  |
| Number of subjects analysed      | 59                             | 58                           |  |  |
| Units: Number of repetitions     |                                |                              |  |  |
| arithmetic mean (standard error) | 4.1 (± 1.33)                   | 1.2 (± 1.38)                 |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Mean change in Myositis Disease Activity Assessment Tool (MDAAT) assessment of extra-muscular from baseline to Week 24

|                 |                                                                                                                        |
|-----------------|------------------------------------------------------------------------------------------------------------------------|
| End point title | Mean change in Myositis Disease Activity Assessment Tool (MDAAT) assessment of extra-muscular from baseline to Week 24 |
|-----------------|------------------------------------------------------------------------------------------------------------------------|

End point description:

The adjusted mean change from baseline in the Myositis Disease Activity Assessment Tool (MDAAT) assessment of extra-muscular uses a 100 mm Visual Analog Scale (VAS) scale. This VAS assesses the

overall extra-muscular clinical features based upon: 1) The presence of clinical features or symptoms within the previous 4 weeks that are due to active disease. 2) The judgment that the feature is due to the myositis disease process. 3) The concept that disease activity is defined as a potentially reversible finding. 4) A clinical, functional, and laboratory assessments.

The scoring is performed by the investigator and ranges from 0 (absent extra-muscular disease activity) to 100 (maximum extra-muscular disease activity).

|                                                                        |           |
|------------------------------------------------------------------------|-----------|
| End point type                                                         | Secondary |
| End point timeframe:                                                   |           |
| From first dose to 24 weeks after first dose. (Approximately 169 days) |           |

| End point values                 | Abatacept + Standard Treatment | Placebo + Standard Treatment |  |  |
|----------------------------------|--------------------------------|------------------------------|--|--|
| Subject group type               | Reporting group                | Reporting group              |  |  |
| Number of subjects analysed      | 63                             | 60                           |  |  |
| Units: Score on a scale          |                                |                              |  |  |
| arithmetic mean (standard error) | -1.56 ( $\pm$ 0.202)           | -1.40 ( $\pm$ 0.208)         |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants Experiencing Adverse Events (AE) in the Double-Blind Period

|                 |                                                                                    |
|-----------------|------------------------------------------------------------------------------------|
| End point title | Number of Participants Experiencing Adverse Events (AE) in the Double-Blind Period |
|-----------------|------------------------------------------------------------------------------------|

End point description:

The number of treated participants experiencing an adverse event. An Adverse Event (AE) is defined as any new untoward medical occurrence or worsening of a preexisting medical condition in participants administered a study drug and that does not necessarily have a causal relationship with the treatment.

|                                                                                                                                                           |           |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------|-----------|
| End point type                                                                                                                                            | Secondary |
| End point timeframe:                                                                                                                                      |           |
| From first dose up to approximately 56 days post last dose date in double-blind period or first dose in open-label period. (Up to approximately 274 days) |           |

| End point values            | Abatacept + Standard Treatment | Placebo + Standard Treatment |  |  |
|-----------------------------|--------------------------------|------------------------------|--|--|
| Subject group type          | Reporting group                | Reporting group              |  |  |
| Number of subjects analysed | 75                             | 73                           |  |  |
| Units: Participants         | 52                             | 55                           |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Myositis Response Criteria (MRC) Total Improvement Score From Baseline to Week 24

|                 |                                                                                   |
|-----------------|-----------------------------------------------------------------------------------|
| End point title | Myositis Response Criteria (MRC) Total Improvement Score From Baseline to Week 24 |
|-----------------|-----------------------------------------------------------------------------------|

End point description:

The Myositis Response Criteria (MRC) is a continuous total improvement score from baseline (range 0-100) based on the sum of the absolute percent change in the 6 core domains (weighted) used in the IMACS DOI (International Myositis Assessment and Clinical Studies definition of improvement)

IMACS core measures are: Physician Global Assessment of Disease Activity (PGA), Patient (Subject) Global Assessment of Disease Activity (SGA), Manual Muscle Test (MMT-8), Health Assessment Questionnaire-Disability Index (HAQ-DI), Muscle Enzyme levels, Myositis Disease Activity Assessment Tool (MDAAT) Extramuscular Global Activity.

The total improvement score ranges between 0 and 100 percent corresponds to the degree of improvement, with higher scores corresponding to a greater degree of improvement (  $\geq 20$  represents minimal improvement, a score of  $\geq 40$  represents moderate improvement, and a score of  $\geq 60$  represents major improvement).

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From first dose to 24 weeks after first dose. (Approximately 169 days)

| End point values                 | Abatacept + Standard Treatment | Placebo + Standard Treatment |  |  |
|----------------------------------|--------------------------------|------------------------------|--|--|
| Subject group type               | Reporting group                | Reporting group              |  |  |
| Number of subjects analysed      | 62                             | 58                           |  |  |
| Units: Score on a scale          |                                |                              |  |  |
| arithmetic mean (standard error) | 40.83 ( $\pm$ 2.873)           | 37.22 ( $\pm$ 2.963)         |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants Experiencing Serious Adverse Events (SAE) in the Double-Blind Period

|                 |                                                                                             |
|-----------------|---------------------------------------------------------------------------------------------|
| End point title | Number of Participants Experiencing Serious Adverse Events (SAE) in the Double-Blind Period |
|-----------------|---------------------------------------------------------------------------------------------|

End point description:

The number of treated participants experiencing a Serious Adverse Event (SAE). A Serious Adverse Event (SAE) is any untoward medical occurrence that at any dose: results in death, is life-threatening, requires inpatient hospitalization or causes prolongation of existing hospitalization, results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect, or is an important medical event.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From first dose up to approximately 56 days post last dose date in double-blind period or first dose in open-label period. (Up to approximately 274 days)

| End point values            | Abatacept + Standard Treatment | Placebo + Standard Treatment |  |  |
|-----------------------------|--------------------------------|------------------------------|--|--|
| Subject group type          | Reporting group                | Reporting group              |  |  |
| Number of subjects analysed | 75                             | 73                           |  |  |
| Units: Participants         | 4                              | 4                            |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants Experiencing Adverse Events (AE) of Special Interest in the Double-Blind Period

|                 |                                                                                                        |
|-----------------|--------------------------------------------------------------------------------------------------------|
| End point title | Number of Participants Experiencing Adverse Events (AE) of Special Interest in the Double-Blind Period |
|-----------------|--------------------------------------------------------------------------------------------------------|

End point description:

The number of treated participants experiencing adverse events of special interest: infections, malignancies, autoimmune events, local injection site reactions, and systemic injection reactions.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From first dose up to approximately 56 days post last dose date in double-blind period or first dose in open-label period. (Up to approximately 274 days)

| End point values               | Abatacept + Standard Treatment | Placebo + Standard Treatment |  |  |
|--------------------------------|--------------------------------|------------------------------|--|--|
| Subject group type             | Reporting group                | Reporting group              |  |  |
| Number of subjects analysed    | 75                             | 73                           |  |  |
| Units: Participants            |                                |                              |  |  |
| Infections                     | 19                             | 31                           |  |  |
| Malignancies                   | 0                              | 0                            |  |  |
| Autoimmune Disorders           | 2                              | 3                            |  |  |
| Systemic Injection Reactions   | 4                              | 5                            |  |  |
| Local Injection Site Reactions | 1                              | 0                            |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants Experiencing Laboratory Test Abnormalities in the Double-Blind Period

|                 |                                                                                              |
|-----------------|----------------------------------------------------------------------------------------------|
| End point title | Number of Participants Experiencing Laboratory Test Abnormalities in the Double-Blind Period |
|-----------------|----------------------------------------------------------------------------------------------|

**End point description:**

The number of participants experiencing laboratory test abnormalities. Laboratory analysis was performed on the following: hematology, liver and kidney function, electrolytes, other chemistry testing (glucose, protein, cardiac), and urine chemistry. Only tests with participants experiencing abnormalities were reported.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

**End point timeframe:**

From first dose up to approximately 56 days post last dose date in double-blind period or first dose in open-label period. (Up to approximately 274 days)

| <b>End point values</b>                  | Abatacept +<br>Standard<br>Treatment | Placebo +<br>Standard<br>Treatment |  |  |
|------------------------------------------|--------------------------------------|------------------------------------|--|--|
| Subject group type                       | Reporting group                      | Reporting group                    |  |  |
| Number of subjects analysed              | 75                                   | 73                                 |  |  |
| Units: Participants                      |                                      |                                    |  |  |
| LOW LEUKOCYTES                           | 1                                    | 0                                  |  |  |
| HIGH LEUKOCYTES                          | 2                                    | 4                                  |  |  |
| HIGH EOSINOPHILS (ABSOLUTE)              | 3                                    | 2                                  |  |  |
| LOW LYMPHOCYTES (ABSOLUTE)               | 17                                   | 14                                 |  |  |
| LOW NEUTROPHILS + BANDS<br>(ABSOLUTE)    | 1                                    | 0                                  |  |  |
| HIGH ALANINE AMINOTRANSFERASE<br>(ALT)   | 1                                    | 1                                  |  |  |
| HIGH ASPARTATE AMINOTRANSFERASE<br>(AST) | 0                                    | 1                                  |  |  |
| HIGH G-GLUTAMYL TRANSFERASE<br>(GGT)     | 4                                    | 1                                  |  |  |
| HIGH BLOOD UREA NITROGEN                 | 0                                    | 1                                  |  |  |
| HIGH CREATININE                          | 3                                    | 3                                  |  |  |
| HIGH CALCIUM, TOTAL                      | 1                                    | 0                                  |  |  |
| LOW PHOSPHORUS, INORGANIC                | 0                                    | 1                                  |  |  |
| HIGH PHOSPHORUS, INORGANIC               | 1                                    | 0                                  |  |  |
| HIGH SODIUM, SERUM                       | 0                                    | 1                                  |  |  |
| LOW GLUCOSE, SERUM                       | 4                                    | 3                                  |  |  |
| HIGH GLUCOSE, SERUM                      | 8                                    | 8                                  |  |  |
| HIGH PROTEIN, TOTAL                      | 0                                    | 1                                  |  |  |
| HIGH CREATINE KINASE (CK)                | 0                                    | 4                                  |  |  |
| HIGH LACTATE DEHYDROGENASE (LD)          | 0                                    | 1                                  |  |  |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Number of Participants Experiencing Adverse Events (AE) in the Cumulative Abatacept Period**

|                 |                                                                                            |
|-----------------|--------------------------------------------------------------------------------------------|
| End point title | Number of Participants Experiencing Adverse Events (AE) in the Cumulative Abatacept Period |
|-----------------|--------------------------------------------------------------------------------------------|

**End point description:**

The number of treated participants experiencing an adverse event. An Adverse Event (AE) is defined as

any new untoward medical occurrence or worsening of a preexisting medical condition in participants administered a study drug and that does not necessarily have a causal relationship with the treatment.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From first dose up to approximately 56 days post last dose (up to approximately 54 months)

| End point values            | Abatacept + Standard Treatment | Placebo + Standard Treatment |  |  |
|-----------------------------|--------------------------------|------------------------------|--|--|
| Subject group type          | Reporting group                | Reporting group              |  |  |
| Number of subjects analysed | 75                             | 63                           |  |  |
| Units: Participants         | 64                             | 39                           |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants Experiencing Serious Adverse Events (SAE) in the Cumulative Abatacept Period

|                 |                                                                                                     |
|-----------------|-----------------------------------------------------------------------------------------------------|
| End point title | Number of Participants Experiencing Serious Adverse Events (SAE) in the Cumulative Abatacept Period |
|-----------------|-----------------------------------------------------------------------------------------------------|

End point description:

The number of treated participants experiencing a Serious Adverse Event (SAE). A Serious Adverse Event (SAE) is any untoward medical occurrence that at any dose: results in death, is life-threatening, requires inpatient hospitalization or causes prolongation of existing hospitalization, results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect, or is an important medical event.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From first dose up to approximately 56 days post last dose (up to approximately 54 months)

| End point values            | Abatacept + Standard Treatment | Placebo + Standard Treatment |  |  |
|-----------------------------|--------------------------------|------------------------------|--|--|
| Subject group type          | Reporting group                | Reporting group              |  |  |
| Number of subjects analysed | 75                             | 63                           |  |  |
| Units: Participants         | 14                             | 8                            |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants Experiencing Adverse Events (AE) of Special Interest in the Cumulative Abatacept Period



|                                                                                                                                                                                                                              |                                                                                                                |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                              | Number of Participants Experiencing Adverse Events (AE) of Special Interest in the Cumulative Abatacept Period |
| End point description:<br>The number of treated participants experiencing adverse events of special interest: infections, malignancies, autoimmune events, local injection site reactions, and systemic injection reactions. |                                                                                                                |
| End point type                                                                                                                                                                                                               | Secondary                                                                                                      |
| End point timeframe:<br>From first dose up to approximately 56 days post last dose (up to approximately 54 months)                                                                                                           |                                                                                                                |

| End point values               | Abatacept + Standard Treatment | Placebo + Standard Treatment |  |  |
|--------------------------------|--------------------------------|------------------------------|--|--|
| Subject group type             | Reporting group                | Reporting group              |  |  |
| Number of subjects analysed    | 75                             | 63                           |  |  |
| Units: Participants            |                                |                              |  |  |
| Infections and infestations    | 34                             | 19                           |  |  |
| Malignancies                   | 0                              | 0                            |  |  |
| Autoimmune Disorders           | 5                              | 4                            |  |  |
| Systemic Injection Reactions   | 5                              | 3                            |  |  |
| Local Injection Site Reactions | 2                              | 2                            |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants Experiencing Laboratory Test Abnormalities in the Open-Label Period

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                            |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | Number of Participants Experiencing Laboratory Test Abnormalities in the Open-Label Period |
| End point description:<br>The number of participants experiencing laboratory test abnormalities. Laboratory analysis was performed on the following: hematology, liver and kidney function, electrolytes, other chemistry testing (glucose, protein, cardiac), and urine chemistry. Only tests with participants experiencing abnormalities were reported. For participants who enter the Japan open-label extension period or long-term extension period, assessments after the first dose in the open-label period and before the first dose date in the subsequent period are included. For participants who prematurely discontinue the open-label period or complete the open-label period but do not enter the Japan open-label extension period or long-term extension period, assessments after the first dose in the open-label period and up to 56 days post last dose are included. 99999 = N/A - no participants had laboratory reports for this analyte. |                                                                                            |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | Secondary                                                                                  |
| End point timeframe:<br>From first dose in open label period to first dose date in the subsequent period or up to 56 days post last dose (up to approximately 666 days)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                            |

| End point values                      | Abatacept + Standard Treatment | Placebo + Standard Treatment |  |  |
|---------------------------------------|--------------------------------|------------------------------|--|--|
| Subject group type                    | Reporting group                | Reporting group              |  |  |
| Number of subjects analysed           | 69                             | 64                           |  |  |
| Units: Participants                   |                                |                              |  |  |
| LOW HEMOGLOBIN                        | 0                              | 1                            |  |  |
| LOW LEUKOCYTES                        | 2                              | 1                            |  |  |
| HIGH LEUKOCYTES                       | 2                              | 0                            |  |  |
| HIGH EOSINOPHILS (ABSOLUTE)           | 2                              | 0                            |  |  |
| LOW LYMPHOCYTES (ABSOLUTE)            | 15                             | 9                            |  |  |
| HIGH LYMPHOCYTES (ABSOLUTE)           | 1                              | 0                            |  |  |
| LOW NEUTROPHILS + BANDS (ABSOLUTE)    | 2                              | 0                            |  |  |
| HIGH ALANINE AMINOTRANSFERASE (ALT)   | 1                              | 0                            |  |  |
| HIGH ALKALINE PHOSPHATASE (ALP)       | 0                              | 2                            |  |  |
| HIGH ASPARTATE AMINOTRANSFERASE (AST) | 0                              | 1                            |  |  |
| HIGH G-GLUTAMYL TRANSFERASE (GGT)     | 2                              | 1                            |  |  |
| HIGH BLOOD UREA NITROGEN              | 2                              | 1                            |  |  |
| HIGH CREATININE                       | 6                              | 1                            |  |  |
| HIGH POTASSIUM, SERUM                 | 1                              | 0                            |  |  |
| LOW GLUCOSE, SERUM                    | 1                              | 1                            |  |  |
| HIGH GLUCOSE, SERUM                   | 3                              | 4                            |  |  |
| LOW ALBUMIN                           | 0                              | 1                            |  |  |
| HIGH CREATINE KINASE (CK)             | 3                              | 5                            |  |  |
| HIGH LACTATE DEHYDROGENASE (LD)       | 0                              | 1                            |  |  |
| HIGH BLOOD, URINE                     | 2                              | 99999                        |  |  |
| HIGH WBC, URINE                       | 1                              | 99999                        |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants Experiencing Laboratory Test Abnormalities in the Long-Term Open Label Period

|                 |                                                                                                      |
|-----------------|------------------------------------------------------------------------------------------------------|
| End point title | Number of Participants Experiencing Laboratory Test Abnormalities in the Long-Term Open Label Period |
|-----------------|------------------------------------------------------------------------------------------------------|

End point description:

The number of participants experiencing laboratory test abnormalities. Laboratory analysis was performed on the following: hematology, liver and kidney function, electrolytes, other chemistry testing (glucose, protein, cardiac), and urine chemistry. Only tests with participants experiencing abnormalities were reported. For participants who completed/discontinued the Long-Term Extension Period, assessments after the first dose in the Long-Term Extension Period and up to 56 days post last dose in the Long-Term Extension Period are included.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From first dose in the Long-Term Open Label Period up to 56 days post last dose in the Long-Term Open Label Period (up to approximately 958 days)

| <b>End point values</b>     | Abatacept +<br>Standard<br>Treatment | Placebo +<br>Standard<br>Treatment |  |  |
|-----------------------------|--------------------------------------|------------------------------------|--|--|
| Subject group type          | Reporting group                      | Reporting group                    |  |  |
| Number of subjects analysed | 22                                   | 21                                 |  |  |
| Units: Participants         |                                      |                                    |  |  |
| LOW HEMOGLOBIN              | 1                                    | 0                                  |  |  |
| LOW LYMPHOCYTES (ABSOLUTE)  | 1                                    | 4                                  |  |  |
| HIGH BLOOD UREA NITROGEN    | 2                                    | 0                                  |  |  |
| HIGH CREATININE             | 2                                    | 1                                  |  |  |
| HIGH GLUCOSE, SERUM         | 1                                    | 0                                  |  |  |
| HIGH CREATINE KINASE (CK)   | 1                                    | 0                                  |  |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

All-cause mortality was assessed from participants first dose to their study completion (up to approximately 55 months) SAEs and Other AEs were assessed from first dose to 100 days following last dose (up to approximately 55 months)

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 25.1 |
|--------------------|------|

### Reporting groups

|                       |                              |
|-----------------------|------------------------------|
| Reporting group title | Placebo + Standard Treatment |
|-----------------------|------------------------------|

Reporting group description:

Participants receive placebo (to match subcutaneous abatacept) in combination with standard treatment.

|                       |                                |
|-----------------------|--------------------------------|
| Reporting group title | Abatacept + Standard Treatment |
|-----------------------|--------------------------------|

Reporting group description:

Participants receive subcutaneous abatacept (125 mg weekly) in combination with standard treatment.

| Serious adverse events                                              | Placebo + Standard Treatment | Abatacept + Standard Treatment |  |
|---------------------------------------------------------------------|------------------------------|--------------------------------|--|
| Total subjects affected by serious adverse events                   |                              |                                |  |
| subjects affected / exposed                                         | 5 / 73 (6.85%)               | 22 / 138 (15.94%)              |  |
| number of deaths (all causes)                                       | 1                            | 0                              |  |
| number of deaths resulting from adverse events                      |                              |                                |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                              |                                |  |
| Lymphoproliferative disorder                                        |                              |                                |  |
| subjects affected / exposed                                         | 0 / 73 (0.00%)               | 1 / 138 (0.72%)                |  |
| occurrences causally related to treatment / all                     | 0 / 0                        | 0 / 1                          |  |
| deaths causally related to treatment / all                          | 0 / 0                        | 0 / 0                          |  |
| Vascular disorders                                                  |                              |                                |  |
| Peripheral arterial occlusive disease                               |                              |                                |  |
| subjects affected / exposed                                         | 0 / 73 (0.00%)               | 1 / 138 (0.72%)                |  |
| occurrences causally related to treatment / all                     | 0 / 0                        | 0 / 1                          |  |
| deaths causally related to treatment / all                          | 0 / 0                        | 0 / 0                          |  |
| General disorders and administration site conditions                |                              |                                |  |
| Influenza like illness                                              |                              |                                |  |

|                                                 |                |                 |  |
|-------------------------------------------------|----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 73 (0.00%) | 1 / 138 (0.72%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Respiratory, thoracic and mediastinal disorders |                |                 |  |
| Pulmonary fibrosis                              |                |                 |  |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 1 / 138 (0.72%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Hypoxia                                         |                |                 |  |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 1 / 138 (0.72%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Acute respiratory failure                       |                |                 |  |
| subjects affected / exposed                     | 1 / 73 (1.37%) | 0 / 138 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 1          | 0 / 0           |  |
| Psychiatric disorders                           |                |                 |  |
| Obsessive-compulsive disorder                   |                |                 |  |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 1 / 138 (0.72%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Injury, poisoning and procedural complications  |                |                 |  |
| Comminuted fracture                             |                |                 |  |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 1 / 138 (0.72%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Femur fracture                                  |                |                 |  |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 1 / 138 (0.72%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Spinal compression fracture                     |                |                 |  |

|                                                 |                |                 |  |
|-------------------------------------------------|----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 73 (0.00%) | 2 / 138 (1.45%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 3           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Cardiac disorders                               |                |                 |  |
| Coronary artery disease                         |                |                 |  |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 1 / 138 (0.72%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Eye disorders                                   |                |                 |  |
| Glaucoma                                        |                |                 |  |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 1 / 138 (0.72%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Gastrointestinal disorders                      |                |                 |  |
| Large intestine polyp                           |                |                 |  |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 2 / 138 (1.45%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Upper gastrointestinal haemorrhage              |                |                 |  |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 1 / 138 (0.72%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Vomiting                                        |                |                 |  |
| subjects affected / exposed                     | 1 / 73 (1.37%) | 0 / 138 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Skin and subcutaneous tissue disorders          |                |                 |  |
| Dermatomyositis                                 |                |                 |  |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 1 / 138 (0.72%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Renal and urinary disorders                     |                |                 |  |
| Haematuria                                      |                |                 |  |

|                                                 |                |                 |  |
|-------------------------------------------------|----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 73 (0.00%) | 1 / 138 (0.72%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Renal failure                                   |                |                 |  |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 1 / 138 (0.72%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Nephrolithiasis                                 |                |                 |  |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 1 / 138 (0.72%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Musculoskeletal and connective tissue disorders |                |                 |  |
| Polymyositis                                    |                |                 |  |
| subjects affected / exposed                     | 1 / 73 (1.37%) | 2 / 138 (1.45%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Myositis                                        |                |                 |  |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 1 / 138 (0.72%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Muscular weakness                               |                |                 |  |
| subjects affected / exposed                     | 1 / 73 (1.37%) | 1 / 138 (0.72%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Infections and infestations                     |                |                 |  |
| Appendicitis                                    |                |                 |  |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 1 / 138 (0.72%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| COVID-19                                        |                |                 |  |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 1 / 138 (0.72%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |

|                                                 |                |                 |  |
|-------------------------------------------------|----------------|-----------------|--|
| Cellulitis                                      |                |                 |  |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 2 / 138 (1.45%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 2 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Gastroenteritis                                 |                |                 |  |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 1 / 138 (0.72%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Herpes zoster                                   |                |                 |  |
| subjects affected / exposed                     | 1 / 73 (1.37%) | 1 / 138 (0.72%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 1 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Sepsis                                          |                |                 |  |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 1 / 138 (0.72%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Urinary tract infection                         |                |                 |  |
| subjects affected / exposed                     | 0 / 73 (0.00%) | 3 / 138 (2.17%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 3 / 4           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |

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

| <b>Non-serious adverse events</b>                     | Placebo + Standard Treatment | Abatacept + Standard Treatment |  |
|-------------------------------------------------------|------------------------------|--------------------------------|--|
| Total subjects affected by non-serious adverse events |                              |                                |  |
| subjects affected / exposed                           | 23 / 73 (31.51%)             | 31 / 138 (22.46%)              |  |
| Injury, poisoning and procedural complications        |                              |                                |  |
| Fall                                                  |                              |                                |  |
| subjects affected / exposed                           | 4 / 73 (5.48%)               | 4 / 138 (2.90%)                |  |
| occurrences (all)                                     | 5                            | 5                              |  |
| Vascular disorders                                    |                              |                                |  |
| Hypertension                                          |                              |                                |  |
| subjects affected / exposed                           | 1 / 73 (1.37%)               | 7 / 138 (5.07%)                |  |
| occurrences (all)                                     | 1                            | 7                              |  |



|                                                                                                                                                                         |                                                 |                                                   |  |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------|---------------------------------------------------|--|
| Nervous system disorders<br>Headache<br>subjects affected / exposed<br>occurrences (all)                                                                                | 7 / 73 (9.59%)<br>7                             | 8 / 138 (5.80%)<br>12                             |  |
| Musculoskeletal and connective tissue disorders<br>Back pain<br>subjects affected / exposed<br>occurrences (all)                                                        | 2 / 73 (2.74%)<br>2                             | 7 / 138 (5.07%)<br>7                              |  |
| Infections and infestations<br>Influenza<br>subjects affected / exposed<br>occurrences (all)<br><br>Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all) | 6 / 73 (8.22%)<br>6<br><br>8 / 73 (10.96%)<br>8 | 3 / 138 (2.17%)<br>3<br><br>9 / 138 (6.52%)<br>14 |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date          | Amendment                                                                                                                                                                                                                                                                                                                              |
|---------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 10 March 2017 | Clarifies the target population (Inclusion/Exclusion criteria), randomization stratification criteria, exploratory endpoints, study procedures and sub-studies, training requirements for site staff, the process for adjudication, the duration of samples retention for additional research and the duration of post drug follow-up. |
| 09 May 2018   | Clarifies language and allowable concomitant medication and adjusts criteria to improve subject selection.                                                                                                                                                                                                                             |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Secondary Endpoint (Number of Participants Experiencing Laboratory Test Abnormalities in the Open-Label Period) is pending re-analysis. Updates expected September 2023.

Notes: