



## Clinical trial results:

### A Phase 2b, Randomized, Multicenter, Double-Blind, Dose-Ranging Study to Assess the Efficacy, Safety and Pharmacokinetics of Intravenous TAK-954 in Critically Ill Patients With Enteral Feeding Intolerance

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2017-003206-41 |
| Trial protocol           | GB             |
| Global end of trial date | 29 August 2018 |

#### Results information

|                                |                   |
|--------------------------------|-------------------|
| Result version number          | v1 (current)      |
| This version publication date  | 30 September 2020 |
| First version publication date | 30 September 2020 |

#### Trial information

##### Trial identification

|                       |              |
|-----------------------|--------------|
| Sponsor protocol code | TAK-954-2002 |
|-----------------------|--------------|

##### Additional study identifiers

|                                    |                  |
|------------------------------------|------------------|
| ISRCTN number                      | -                |
| ClinicalTrials.gov id (NCT number) | NCT03477903      |
| WHO universal trial number (UTN)   | U1111-1208-1831  |
| Other trial identifiers            | 18/NE/0139: NRES |

Notes:

##### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Millennium Pharmaceuticals, Inc., a wholly owned subsidiary of Takeda Pharmaceutical Company, Ltd. |
| Sponsor organisation address | 35 Landsdowne St., Cambridge, United States, 02139   |
| Public contact               | Study Manager, Takeda Development Centre Europe Ltd., + 44 1256 894003,                            |
| Scientific contact           | Study Manager, Takeda Development Centre Europe Ltd., + 44 1256 894003,                            |

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                       | 29 August 2018 |
| Is this the analysis of the primary completion data? | Yes            |
| Primary completion date                              | 29 August 2018 |
| Global end of trial reached?                         | Yes            |
| Global end of trial date                             | 29 August 2018 |
| Was the trial ended prematurely?                     | No             |

Notes:

## General information about the trial

Main objective of the trial:

The purpose of this study is to assess the treatment effect of intravenous TAK-954 in improving the average daily protein adequacy received through enteral nutrition in critically-ill participants developing EFI.

Due to the constraints/requirements of the EudraCT database and concern for participant data privacy, zero subjects are being listed in the below fields.

Protection of trial subjects:

The informed consent form, subject authorization form and subject information sheet (if applicable) describe the planned and permitted uses, transfers, and disclosures of the subject's personal health information for purposes of conducting the study. The informed consent form and the subject information sheet (if applicable) further explain the nature of the study, its objectives, and potential risks and benefits, as well as the date informed consent is given.

Background therapy: -

Evidence for comparator: -

|   |                |
|---|----------------|
| Actual start date of recruitment                          | 25 August 2018 |
| 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 | United States: 99999 |
| Worldwide total number of subjects   | 99999                |
| EEA total number of subjects         | 0                    |

Notes:

### Subjects enrolled per age group

|   |   |
|---|---|
| In utero                                  | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days)                      | 0 |
| Infants and toddlers (28 days-23 months)  | 0 |
| Children (2-11 years)                     | 0 |
| Adolescents (12-17 years)                 | 0 |

|                      |       |
|----------------------|-------|
| Adults (18-64 years) | 99999 |
| From 65 to 84 years  | 0     |
| 85 years and over    | 0     |

## Subject disposition

### Recruitment

Recruitment details:

99999 is "Not applicable" value or 0 participants. Due to the constraints/requirements of the EudraCT database and concern for participant data privacy, zero subjects are being listed in the below fields.

### Pre-assignment

Screening details:

N/A

### Period 1

|                              |  |
|------------------------------|--|
| Period 1 title               | Overall Study (overall period)         |
| Is this the baseline period? | Yes                                    |
| Allocation method            | Randomised - controlled                |
| Blinding used                | Double blind                           |
| Roles blinded                | Subject, Investigator, Carer, Assessor |

### Arms

|  |                                       |
|--|---------------------------------------|
| <b>Arm title</b>                       | Overall                               |
| Arm description: -                     |                                       |
| Arm type                               | Experimental                          |
| Investigational medicinal product name | TAK-954                               |
| Investigational medicinal product code | TAK-954                               |
| Other name                             |                                       |
| Pharmaceutical forms                   | Concentrate for solution for infusion |
| Routes of administration               | Intravenous use                       |

Dosage and administration details:

0.1 milligram (mg), intravenously, administered as 60 minute-infusion, once daily along with 2 milliliter (mL) normal saline injection, intravenously, three times a day for a minimum of 5 days up to a maximum of 14 days.

| Number of subjects in period 1 | Overall |
|--------------------------------|---------|
| Started                        | 99999   |
| Completed                      | 99999   |

## Baseline characteristics

### Reporting groups

|                       |         |
|-----------------------|---------|
| Reporting group title | Overall |
|-----------------------|---------|

Reporting group description: -

| Reporting group values  | Overall | Total |  |
|---|---------|-------|--|
| Number of subjects  | 99999   | 99999 |  |
| Age Categorical   |         |       |  |
| Due to the low number of participants enrolled at only 1 site, 0 participants are reported due to the risk of identification of a person. |         |       |  |
| Units: Subjects   |         |       |  |
| In utero  | 0       | 0     |  |
| Preterm newborn infants (gestational age < 37 wks)  | 0       | 0     |  |
| Newborns (0-27 days)  | 0       | 0     |  |
| Infants and toddlers (28 days-23 months)  | 0       | 0     |  |
| Children (2-11 years)   | 0       | 0     |  |
| Adolescents (12-17 years)   | 0       | 0     |  |
| Adults (18-64 years)  | 99999   | 99999 |  |
| From 65-84 years  | 0       | 0     |  |
| 85 years and over   | 0       | 0     |  |
| Age Continuous  |         |       |  |
| Due to the low number of participants enrolled at only 1 site, 0 participants are reported due to the risk of identification of a person. |         |       |  |
| Units: years  |         |       |  |
| arithmetic mean   | 0       |       |  |
| standard deviation  | ± 0     | -     |  |
| Gender Categorical  |         |       |  |
| Due to the low number of participants enrolled at only 1 site, 0 participants are reported due to the risk of identification of a person. |         |       |  |
| Units: Subjects   |         |       |  |
| Female  | 99999   | 99999 |  |
| Male  | 0       | 0     |  |

## End points

### End points reporting groups

|                                |         |
|--------------------------------|---------|
| Reporting group title          | Overall |
| Reporting group description: - |         |

### Primary: Average Daily Protein Adequacy Over the First 5 Days of Treatment

|                 |  |
|-----------------|--|
| End point title | Average Daily Protein Adequacy Over the First 5 Days of Treatment <sup>[1]</sup> |
|-----------------|--|

End point description:

Average daily protein adequacy received through enteral nutrition is defined as the percentage of goal protein delivered per day, where percentage of goal protein delivered is calculated as the ratio of actual protein achievement to the total participant-specific target protein prescribed. The value for each of the 5 days was averaged. No data displayed because Endpoint has zero total participants analyzed.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Days 1 to 5

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Not applicable

| End point values            | Overall          |  |  |  |
|-----------------------------|------------------|--|--|--|
| Subject group type          | Reporting group  |  |  |  |
| Number of subjects analysed | 0 <sup>[2]</sup> |  |  |  |
| Units: number               |                  |  |  |  |

Notes:

[2] - Due to low number of participants enrolled at only 1 site, 0 reported due to risk of identification.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Average Daily Protein Adequacy Over the Study Treatment Period

|                 |  |
|-----------------|--|
| End point title | Average Daily Protein Adequacy Over the Study Treatment Period |
|-----------------|--|

End point description:

Average daily protein adequacy received through enteral nutrition is defined as percentage of goal protein delivered per day, where percentage of protein goal delivered is calculated as the ratio of actual protein achievement to the total participant-specific target protein prescribed. The value for each of the 14 days was averaged. No data displayed because Endpoint has zero total participants analyzed.

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

End point timeframe:

Days 1 to 14

| End point values            | Overall          |  |  |  |
|-----------------------------|------------------|--|--|--|
| Subject group type          | Reporting group  |  |  |  |
| Number of subjects analysed | 0 <sup>[3]</sup> |  |  |  |
| Units: number               |                  |  |  |  |

Notes:

[3] - Due to low number of participants enrolled at only 1 site, 0 reported due to risk of identification.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Average Daily Change in 24-hour Gastric Residual Volume (GRV) Over the First 5 Days of Study Treatment

|                 |  |
|-----------------|--|
| End point title | Average Daily Change in 24-hour Gastric Residual Volume (GRV) Over the First 5 Days of Study Treatment |
|-----------------|--|

End point description:

GRV is defined as the volume of fluid remaining in the stomach at a point in time during enteral nutrition feeding. The value for each of the 5 days was averaged. No data displayed because Endpoint has zero total participants analyzed.

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

End point timeframe:

Days 1 to 5

| End point values            | Overall          |  |  |  |
|-----------------------------|------------------|--|--|--|
| Subject group type          | Reporting group  |  |  |  |
| Number of subjects analysed | 0 <sup>[4]</sup> |  |  |  |
| Units: number               |                  |  |  |  |

Notes:

[4] - Due to low number of participants enrolled at only 1 site, 0 reported due to risk of identification.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Average Daily Caloric Adequacy

|                 |                                |
|-----------------|--------------------------------|
| End point title | Average Daily Caloric Adequacy |
|-----------------|--------------------------------|

End point description:

Average daily caloric adequacy received through enteral nutrition was defined by percentage of goal calories achieved per day (percentage calorie goal achieved=actual calorie achievement/total participant-specific target calories). The values in the 5-day period and the 14-day period were averaged. No data displayed because Endpoint has zero total participants analyzed.

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

End point timeframe:

Days 1 to 5 and Days 1 to 14

| End point values            | Overall          |  |  |  |
|-----------------------------|------------------|--|--|--|
| Subject group type          | Reporting group  |  |  |  |
| Number of subjects analysed | 0 <sup>[5]</sup> |  |  |  |
| Units: number               |                  |  |  |  |

Notes:

[5] - Due to low number of participants enrolled at only 1 site, 0 reported due to risk of identification.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Time to Resolution of Enteral Feeding Intolerance (EFI)

|                 |   |
|-----------------|---|
| End point title | Time to Resolution of Enteral Feeding Intolerance (EFI) |
|-----------------|---|

End point description:

Time to resolution of EFI is defined as the time needed to achieve GRV less than or equal to 250 ml in the absence of vomiting/retching. No data displayed because Endpoint has zero total participants analyzed.

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

End point timeframe:

Days 1 to 14 or until resolution of EFI, whichever occurs first

| End point values            | Overall          |  |  |  |
|-----------------------------|------------------|--|--|--|
| Subject group type          | Reporting group  |  |  |  |
| Number of subjects analysed | 0 <sup>[6]</sup> |  |  |  |
| Units: number               |                  |  |  |  |

Notes:

[6] - Due to low number of participants enrolled at only 1 site, 0 reported due to risk of identification.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Participants Achieving at Least 80% of Daily Goal Calories

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants Achieving at Least 80% of Daily Goal Calories |
|-----------------|--|

End point description:

No data displayed because Outcome Measure has zero total participants analyzed.

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

End point timeframe:

Days 1 to 14 or end of treatment



| End point values            | Overall          |  |  |  |
|-----------------------------|------------------|--|--|--|
| Subject group type          | Reporting group  |  |  |  |
| Number of subjects analysed | 0 <sup>[7]</sup> |  |  |  |
| Units: number               |                  |  |  |  |

Notes:

[7] - Due to low number of participants enrolled at only 1 site, 0 reported due to risk of identification.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Participants Achieving at Least 80% of Daily Goal Protein

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants Achieving at Least 80% of Daily Goal Protein |
|-----------------|---|

End point description:

No data displayed because Outcome Measure has zero total participants analyzed.

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

End point timeframe:

Days 1 to 14 or end of treatment

| End point values            | Overall          |  |  |  |
|-----------------------------|------------------|--|--|--|
| Subject group type          | Reporting group  |  |  |  |
| Number of subjects analysed | 0 <sup>[8]</sup> |  |  |  |
| Units: number               |                  |  |  |  |

Notes:

[8] - Due to low number of participants enrolled at only 1 site, 0 reported due to risk of identification.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Ctrough: Observed Concentration at the End of a Dosing Interval of TAK-954

|                 |  |
|-----------------|--|
| End point title | Ctrough: Observed Concentration at the End of a Dosing Interval of TAK-954 |
|-----------------|--|

End point description:

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

End point timeframe:

Day 5 pre-dose

|                             |                  |  |  |  |
|-----------------------------|------------------|--|--|--|
| <b>End point values</b>     | Overall          |  |  |  |
| Subject group type          | Reporting group  |  |  |  |
| Number of subjects analysed | 0 <sup>[9]</sup> |  |  |  |
| Units: number               |                  |  |  |  |

Notes:

[9] - Due to low number of participants enrolled at only 1 site, 0 reported due to risk of identification.

## Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information<sup>[1]</sup>

Timeframe for reporting adverse events:

Up to 4 days

Adverse event reporting additional description:

At each visit the investigator had to document any occurrence of AEs and abnormal laboratory findings. Any event spontaneously reported by the subject or observed by the investigator was recorded, irrespective of the relation to study treatment. Due to the low number of participants enrolled at only 1 site, 0 reported due to risk of identification.

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

### Dictionary used

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

|                    |   |
|--------------------|---|
| Dictionary version | 0 |
|--------------------|---|

### Reporting groups

|                       |                |
|-----------------------|----------------|
| Reporting group title | TAK-954 0,1 mg |
|-----------------------|----------------|

Reporting group description:

TTAK-954 0.1 milligrams (mg), intravenously, administered as 60 minute-infusion, once daily along with 2 milliliters (mL) normal saline injection, intravenously, three times a day for a minimum of 5 days up to a maximum of 14 days.

| Serious adverse events                            | TAK-954 0,1 mg    |  |  |
|---|-------------------|--|--|
| Total subjects affected by serious adverse events |                   |  |  |
| subjects affected / exposed                       | 0 / 99999 (0.00%) |  |  |
| number of deaths (all causes)                     | 0                 |  |  |
| number of deaths resulting from adverse events    | 0                 |  |  |

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

| Non-serious adverse events                            | TAK-954 0,1 mg    |  |  |
|---|-------------------|--|--|
| Total subjects affected by non-serious adverse events |                   |  |  |
| subjects affected / exposed                           | 0 / 99999 (0.00%) |  |  |

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: Not applicable

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported