



## Clinical trial results:

### An Open-Label, Multicenter, Follow-up Trial of ARGX-113-1904 to Evaluate the Safety, Tolerability, and Efficacy of Efgartigimod PH20 SC in Patients with Pemphigus (ADDRESS+)

#### Summary

|                          |                      |
|--------------------------|----------------------|
| EudraCT number           | 2020-002917-16       |
| Trial protocol           | DE HU ES GR BG FR IT |
| Global end of trial date | 25 March 2024        |

#### Results information

|                                |                 |
|--------------------------------|-----------------|
| Result version number          | v1 (current)    |
| This version publication date  | 04 January 2025 |
| First version publication date | 04 January 2025 |

#### Trial information

##### Trial identification

|                       |               |
|-----------------------|---------------|
| Sponsor protocol code | ARGX-113-1905 |
|-----------------------|---------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT04598477 |
| WHO universal trial number (UTN)   | -           |

Notes:

##### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | argenx BV   |
| Sponsor organisation address | Industriepark Zwijnaarde 7, Zwijnaarde (Ghent), Belgium, 9052 |
| Public contact               | Regulatory, argenx BV, 0032 93103400, regulatory@argenx.com   |
| Scientific contact           | Regulatory, argenx BV, 0032 93103400, regulatory@argenx.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                       | 31 October 2024 |
| Is this the analysis of the primary completion data? | No              |

|                                  |               |
|----------------------------------|---------------|
| Global end of trial reached?     | Yes           |
| Global end of trial date         | 25 March 2024 |
| Was the trial ended prematurely? | Yes           |

Notes:

## General information about the trial

Main objective of the trial:

To assess the long-term safety of treatment, tolerability, and efficacy of efgartigimod PH20 SC in participants with pemphigus vulgaris (PV) or pemphigus foliaceus (PF) who participated in ARGX-113-1904

Protection of trial subjects:

The protocol, protocol amendments, ICFs, Investigator Brochure, and participant recruitment information were approved by the IEC/IRB and regulatory agency before participants were enrolled. This study was conducted in accordance with the protocol and consensus ethical principles derived from international guidelines, including the Declaration of Helsinki, applicable ICH GCP guidelines, and applicable laws and regulations. Participants were required to sign a statement of informed consent that met the requirements of the local regulations, ICH guidelines, Health Insurance Portability and Accountability Act requirements, where applicable, and the IRB/IEC or study center.

Background therapy:

Similar to the antecedent study ARGX-113-1904, participants could also receive concomitant prednisone. Investigators could increase or decrease the dose based on protocol-specified criteria.

Evidence for comparator:

Not applicable

|   |                 |
|---|-----------------|
| Actual start date of recruitment                          | 25 October 2020 |
| 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 | Australia: 4           |
| Country: Number of subjects enrolled | China: 25              |
| Country: Number of subjects enrolled | Georgia: 6             |
| Country: Number of subjects enrolled | India: 11              |
| Country: Number of subjects enrolled | Japan: 8               |
| Country: Number of subjects enrolled | Serbia: 1              |
| Country: Number of subjects enrolled | Türkiye: 3             |
| Country: Number of subjects enrolled | United Kingdom: 2      |
| Country: Number of subjects enrolled | Ukraine: 12            |
| Country: Number of subjects enrolled | United States: 13      |
| Country: Number of subjects enrolled | Russian Federation: 15 |
| Country: Number of subjects enrolled | Poland: 17             |
| Country: Number of subjects enrolled | Romania: 2             |
| Country: Number of subjects enrolled | Spain: 4               |

|                                      |              |
|--------------------------------------|--------------|
| Country: Number of subjects enrolled | Bulgaria: 13 |
| Country: Number of subjects enrolled | France: 8    |
| Country: Number of subjects enrolled | Germany: 13  |
| Country: Number of subjects enrolled | Greece: 9    |
| Country: Number of subjects enrolled | Hungary: 6   |
| Country: Number of subjects enrolled | Italy: 11    |
| Worldwide total number of subjects   | 183          |
| EEA total number of subjects         | 83           |

Notes:

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### 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)                      | 159 |
| From 65 to 84 years                       | 24  |
| 85 years and over                         | 0   |

## Subject disposition

### Recruitment

Recruitment details:

This study was conducted at 76 sites that enrolled participants in 20 countries.

### Pre-assignment

Screening details:

A total of 183 participants rolled over from ARGX-113-1904. Of these, 57 participants had a CRmin status (complete remission on minimal prednisone therapy) at rollover of which 34 participants did not receive efgartigimod PH20 SC in this ARGX-113-1905 study.

### Period 1

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

Blinding implementation details:

This is an open label study.

### Arms

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

|                  |                                   |
|------------------|-----------------------------------|
| <b>Arm title</b> | Efgartigimod-efgartigimod PH20 SC |
|------------------|-----------------------------------|

Arm description:

Participants who received efgartigimod PH20 SC in antecedent study ARGX-113-1904.

|  |                        |
|--|------------------------|
| Arm type                               | Experimental           |
| Investigational medicinal product name | Efgartigimod PH20 SC   |
| Investigational medicinal product code | ARGX-113 PH20 SC       |
| Other name                             |                        |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Subcutaneous use       |

Dosage and administration details:

At baseline, eligible participants received efgartigimod PH20 SC according to their clinical status at the rollover visit and was administered until participants achieved CRmin. Participants could continue to receive a prednisone (or equivalent) dose according to their clinical status at the rollover visit, and the dose was tapered or escalated based on clinical status at the investigator's discretion following protocol-specified instructions.

|                  |                              |
|------------------|------------------------------|
| <b>Arm title</b> | Placebo-efgartigimod PH20 SC |
|------------------|------------------------------|

Arm description:

Participants who received placebo PH20 SC in antecedent study ARGX-113-1904.

|  |                        |
|--|------------------------|
| Arm type                               | Experimental           |
| Investigational medicinal product name | Efgartigimod PH20 SC   |
| Investigational medicinal product code | ARGX-113 PH20 SC       |
| Other name                             |                        |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Subcutaneous use       |

Dosage and administration details:

At baseline, eligible participants received efgartigimod PH20 SC according to their clinical status at the rollover visit and was administered until participants achieved CRmin. Participants could continue to receive a prednisone (or equivalent) dose according to their clinical status at the rollover visit, and the dose was tapered or escalated based on clinical status at the investigator's discretion following protocol-specified instructions.

| Number of subjects in period 1 | Efgartigimod-<br>efgartigimod PH20<br>SC | Placebo-efgartigimod<br>PH20 SC |
|--------------------------------|--|---------------------------------|
|                                |  |                                 |
| Started                        | 123                                      | 60                              |
| Completed                      | 64                                       | 23                              |
| Not completed                  | 59                                       | 37                              |
| Adverse event, serious fatal   | -  | 1                               |
| Required prohibited medication | -  | 1                               |
| Consent withdrawn by subject   | 16                                       | 12                              |
| Physician decision             | 7  | 2                               |
| Adverse event, non-fatal       | 2  | -                               |
| Not specified                  | 15                                       | 8                               |
| Pregnancy                      | -  | 1                               |
| Study terminated by sponsor    | 18                                       | 12                              |
| Lost to follow-up              | 1  | -                               |

## Baseline characteristics

### Reporting groups

|   |                                   |
|---|-----------------------------------|
| Reporting group title   | Efgartigimod-efgartigimod PH20 SC |
| Reporting group description:<br>Participants who received efgartigimod PH20 SC in antecedent study ARGX-113-1904. |                                   |
| Reporting group title   | Placebo-efgartigimod PH20 SC      |
| Reporting group description:<br>Participants who received placebo PH20 SC in antecedent study ARGX-113-1904.      |                                   |

| Reporting group values                | Efgartigimod-efgartigimod PH20 SC | Placebo-efgartigimod PH20 SC | Total |
|---------------------------------------|-----------------------------------|------------------------------|-------|
| Number of subjects                    | 123                               | 60                           | 183   |
| Age categorical<br>Units: Subjects    |                                   |                              |       |
| Adults (18-64 years)                  | 108                               | 51                           | 159   |
| From 65-84 years                      | 15                                | 9                            | 24    |
| Age continuous<br>Units: years        |                                   |                              |       |
| arithmetic mean                       | 50.1                              | 52.4                         |       |
| standard deviation                    | ± 11.40                           | ± 13.02                      | -     |
| Gender categorical<br>Units: Subjects |                                   |                              |       |
| Female                                | 61                                | 32                           | 93    |
| Male                                  | 62                                | 28                           | 90    |

## End points

### End points reporting groups

|   |                                   |
|---|-----------------------------------|
| Reporting group title   | Efgartigimod-efgartigimod PH20 SC |
| Reporting group description:<br>Participants who received efgartigimod PH20 SC in antecedent study ARGX-113-1904.   |                                   |
| Reporting group title   | Placebo-efgartigimod PH20 SC      |
| Reporting group description:<br>Participants who received placebo PH20 SC in antecedent study ARGX-113-1904.  |                                   |
| Subject analysis set title  | Rollover Analysis Set             |
| Subject analysis set type   | Full analysis                     |
| Subject analysis set description:<br>The rollover analysis set included all participants who rolled over from study ARGX-113-1904, regardless of whether or not they received efgartigimod PH20 SC treatment as part of this study. Additional restrictions to the analysis set might apply in the different outcome measures. These are described as notes to the number of subjects analyzed. |                                   |
| Subject analysis set title  | Safety Analysis Set               |
| Subject analysis set type   | Safety analysis                   |
| Subject analysis set description:<br>The safety analysis set included participants who received at least 1 dose of efgartigimod PH20 SC during this study. Additional restrictions to the analysis set might apply in the different outcome measures. These are described in the number of subjects analyzed.   |                                   |

### Primary: Incidence of Treatment-Emergent Adverse Events (TEAE), Adverse Events of Special Interest (AESI), and Serious Adverse Events (SAE)

|   |   |
|---|---|
| End point title   | Incidence of Treatment-Emergent Adverse Events (TEAE), Adverse Events of Special Interest (AESI), and Serious Adverse Events (SAE) <sup>[1]</sup> |
| End point description:<br>Incidence rates were calculated as $100 \times n / \text{PYFU}$ . PYFU=participant-years of follow-up. The safety data sets includes participants with pemphigus vulgaris (PV) and pemphigus foliaceus (PF).                |   |
| End point type  | Primary   |
| End point timeframe:<br>Up to Week 60   |   |
| Notes:<br>[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.<br>Justification: No statistical analysis was applied to this end point |   |

| End point values            | Efgartigimod-efgartigimod PH20 SC | Placebo-efgartigimod PH20 SC |  |  |
|-----------------------------|-----------------------------------|------------------------------|--|--|
| Subject group type          | Reporting group                   | Reporting group              |  |  |
| Number of subjects analysed | 101 <sup>[2]</sup>                | 48 <sup>[3]</sup>            |  |  |
| Units: number               |                                   |                              |  |  |
| number (not applicable)     |                                   |                              |  |  |
| TEAE                        | 116.4                             | 113.0                        |  |  |
| AESI                        | 72.0                              | 69.3                         |  |  |
| SAE                         | 24.5                              | 14.6                         |  |  |

Notes:

[2] - Safety set

[3] - Safety set

## Statistical analyses

No statistical analyses for this end point

### Secondary: Proportion of participants with pemphigus vulgaris (PV) and pemphigus foliaceus (PF) who achieve CRmin

|                 |  |
|-----------------|--|
| End point title | Proportion of participants with pemphigus vulgaris (PV) and pemphigus foliaceus (PF) who achieve CRmin |
|-----------------|--|

End point description:

CRmin defined as the absence of new lesions and complete healing of established lesions while the participant was receiving prednisone at  $\leq 10$  mg/day for at least 8 weeks.

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

End point timeframe:

Up to 60 weeks

| End point values            | Efgartigimod-<br>efgartigimod<br>PH20 SC | Placebo-<br>efgartigimod<br>PH20 SC |  |  |
|-----------------------------|--|-------------------------------------|--|--|
| Subject group type          | Reporting group                          | Reporting group                     |  |  |
| Number of subjects analysed | 101 <sup>[4]</sup>                       | 48 <sup>[5]</sup>                   |  |  |
| Units: participants, n      | 55                                       | 26                                  |  |  |

Notes:

[4] - Safety set

[5] - Safety set

## Statistical analyses

No statistical analyses for this end point

### Secondary: Proportion of participants with pemphigus vulgaris (PV) participants who achieve CRmin

|                 |  |
|-----------------|--|
| End point title | Proportion of participants with pemphigus vulgaris (PV) participants who achieve CRmin |
|-----------------|--|

End point description:

CRmin (complete clinical remission on minimal prednisone therapy) defined as the absence of new lesions and complete healing of established lesions while the participant was receiving prednisone at  $\leq 10$  mg/day for at least 8 weeks.

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

End point timeframe:

Up to 60 weeks

| End point values            | Efgartigimod-<br>efgartigimod<br>PH20 SC | Placebo-<br>efgartigimod<br>PH20 SC |  |  |
|-----------------------------|--|-------------------------------------|--|--|
| Subject group type          | Reporting group                          | Reporting group                     |  |  |
| Number of subjects analysed | 86 <sup>[6]</sup>                        | 41 <sup>[7]</sup>                   |  |  |
| Units: participants, n      | 47                                       | 22                                  |  |  |



Notes:

[6] - Safety set - Participants with PV only

[7] - Safety set - Participants with PV only

## Statistical analyses

No statistical analyses for this end point

### Secondary: Time to Disease Control (DC) in participants with pemphigus vulgaris (PV) and pemphigus foliaceus (PF)

|                 |  |
|-----------------|--|
| End point title | Time to Disease Control (DC) in participants with pemphigus vulgaris (PV) and pemphigus foliaceus (PF) |
|-----------------|--|

End point description:

Disease Control (DC) defined as absence of new lesions and the start of healing of established lesions.

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

End point timeframe:

Up to 52 weeks

| End point values                 | Efgartigimod-<br>efgartigimod<br>PH20 SC | Placebo-<br>efgartigimod<br>PH20 SC |  |  |
|----------------------------------|--|-------------------------------------|--|--|
| Subject group type               | Reporting group                          | Reporting group                     |  |  |
| Number of subjects analysed      | 26 <sup>[8]</sup>                        | 17 <sup>[9]</sup>                   |  |  |
| Units: days                      |  |                                     |  |  |
| median (confidence interval 95%) | 8.5 (8.0 to 15.0)                        | 15.0 (8.0 to 22.0)                  |  |  |

Notes:

[8] - Safety set – Participants with status DC at the roll-over visit were not included in the analysis

[9] - Safety set – Participants with status DC at the roll-over visit were not included in the analysis

## Statistical analyses

No statistical analyses for this end point

### Secondary: Time to Complete clinical remission (CR) in participants with pemphigus vulgaris (PV) and pemphigus foliaceus (PF)

|                 |  |
|-----------------|--|
| End point title | Time to Complete clinical remission (CR) in participants with pemphigus vulgaris (PV) and pemphigus foliaceus (PF) |
|-----------------|--|

End point description:

Measure Description CR (Complete clinical remission) defined as the absence of new lesions and complete healing of established lesions.

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

End point timeframe:

Up to 52 weeks

| End point values                 | Efgartigimod-<br>efgartigimod<br>PH20 SC | Placebo-<br>efgartigimod<br>PH20 SC |  |  |
|----------------------------------|--|-------------------------------------|--|--|
| Subject group type               | Reporting group                          | Reporting group                     |  |  |
| Number of subjects analysed      | 61 <sup>[10]</sup>                       | 34 <sup>[11]</sup>                  |  |  |
| Units: days                      |  |                                     |  |  |
| median (confidence interval 95%) | 66.0 (43.0 to 182.0)                     | 71.0 (41.0 to 100.0)                |  |  |

Notes:

[10] - Safety set – Participants with status CR at the roll-over visit were not included in this analysis

[11] - Safety set – Participants with status CR at the roll-over visit were not included in this analysis

## Statistical analyses

No statistical analyses for this end point

### Secondary: Time to Complete remission on minimal prednisone therapy (CRmin) in participants with pemphigus vulgaris (PV) and pemphigus foliaceus (PF)

|                 |  |
|-----------------|--|
| End point title | Time to Complete remission on minimal prednisone therapy (CRmin) in participants with pemphigus vulgaris (PV) and pemphigus foliaceus (PF) |
|-----------------|--|

End point description:

CRmin defined as the absence of new lesions and complete healing of established lesions while the participant was receiving prednisone at  $\leq 10$  mg/day for at least 8 weeks.

\* The value '9999' is a dummy number to indicate the number was not calculable.

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

End point timeframe:

Up to 52 weeks

| End point values                 | Efgartigimod-<br>efgartigimod<br>PH20 SC | Placebo-<br>efgartigimod<br>PH20 SC |  |  |
|----------------------------------|--|-------------------------------------|--|--|
| Subject group type               | Reporting group                          | Reporting group                     |  |  |
| Number of subjects analysed      | 83 <sup>[12]</sup>                       | 43 <sup>[13]</sup>                  |  |  |
| Units: days                      |  |                                     |  |  |
| median (confidence interval 95%) | 229.0 (161.0 to 9999)                    | 169.0 (141.0 to 322.0)              |  |  |

Notes:

[12] - Safety set – Participants with status CRmin at the rollover visit were not included in this analysis

[13] - Safety set – Participants with status CRmin at the rollover visit were not included in this analysis

## Statistical analyses

No statistical analyses for this end point

### Secondary: Time to Complete remission off therapy (CROff) in participants with pemphigus vulgaris (PV) and pemphigus foliaceus (PF)

|                 |  |
|-----------------|--|
| End point title | Time to Complete remission off therapy (CROff) in participants with pemphigus vulgaris (PV) and pemphigus foliaceus (PF) |
|-----------------|--|

End point description:

Complete remission off therapy (CROff) is defined as the absence of new and established lesions completely healed while the patient is receiving no prednisone therapy for at least 8 weeks.

\* The value '9999' is a dummy number to indicate the number was not calculable.

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

End point timeframe:  
up to 52 weeks

| End point values                 | Efgartigimod-<br>efgartigimod<br>PH20 SC | Placebo-<br>efgartigimod<br>PH20 SC |  |  |
|----------------------------------|--|-------------------------------------|--|--|
| Subject group type               | Reporting group                          | Reporting group                     |  |  |
| Number of subjects analysed      | 83 <sup>[14]</sup>                       | 43 <sup>[15]</sup>                  |  |  |
| Units: days                      |  |                                     |  |  |
| median (confidence interval 95%) | 9999 (9999 to 9999)                      | 9999 (9999 to 9999)                 |  |  |

Notes:

[14] - Safety set – Participants with status CROff at the rollover visit were not included in this analysis

[15] - Safety set – Participants with status CROff at the rollover visit were not included in this analysis

### Statistical analyses

No statistical analyses for this end point

### Secondary: Time to flare after CRmin in participants with pemphigus vulgaris (PV) and pemphigus foliaceus (PF)

|                 |   |
|-----------------|---|
| End point title | Time to flare after CRmin in participants with pemphigus vulgaris (PV) and pemphigus foliaceus (PF) |
|-----------------|---|

End point description:

CRmin defined as defined as the absence of new lesions and complete healing of established lesions while the participant was receiving prednisone at  $\leq 10$  mg/day for at least 8 weeks.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Up to 52 weeks       |           |

| End point values                 | Efgartigimod-<br>efgartigimod<br>PH20 SC | Placebo-<br>efgartigimod<br>PH20 SC |  |  |
|----------------------------------|--|-------------------------------------|--|--|
| Subject group type               | Reporting group                          | Reporting group                     |  |  |
| Number of subjects analysed      | 42 <sup>[16]</sup>                       | 23 <sup>[17]</sup>                  |  |  |
| Units: days                      |  |                                     |  |  |
| median (confidence interval 95%) | 339.0 (223.0 to 9999)                    | 168.0 (64.0 to 9999)                |  |  |

Notes:

[16] - Safety set - Only participants who achieved CRmin were considered for the analysis

[17] - Safety set - Only participants who achieved CRmin were considered for the analysis

### Statistical analyses

No statistical analyses for this end point

### Secondary: Rate of treatment failure in participants with pemphigus vulgaris (PV) and pemphigus foliaceus (PF)

|  |   |
|--|---|
| End point title  | Rate of treatment failure in participants with pemphigus vulgaris (PV) and pemphigus foliaceus (PF) |
| End point description:<br>The absence of DC with oral prednisone 1.5 mg/kg/day for a minimum of 3 weeks, or absence of DC due to prednisone-related SAE, or flare before CRmin resulting in withdrawal of the participant. |   |
| End point type   | Secondary   |
| End point timeframe:<br>Up to 52 weeks   |   |

| End point values            | Efgartigimod-<br>efgartigimod<br>PH20 SC | Placebo-<br>efgartigimod<br>PH20 SC |  |  |
|-----------------------------|--|-------------------------------------|--|--|
| Subject group type          | Reporting group                          | Reporting group                     |  |  |
| Number of subjects analysed | 101 <sup>[18]</sup>                      | 48 <sup>[19]</sup>                  |  |  |
| Units: number               | 3  | 1                                   |  |  |

Notes:

[18] - Safety set

[19] - Safety set

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Flares in participants with PV and PF

|  |   |
|--|---|
| End point title  | Number of Flares in participants with PV and PF |
| End point description:<br>A flare is defined as the appearance of 3 or more new lesions in a 4-week period that do not heal spontaneously within 1 week or the extension, of established lesions in a participant who had achieved DC. |   |
| End point type   | Secondary                                       |
| End point timeframe:<br>Up to 60 weeks   |   |

| End point values                     | Efgartigimod-<br>efgartigimod<br>PH20 SC | Placebo-<br>efgartigimod<br>PH20 SC |  |  |
|--------------------------------------|--|-------------------------------------|--|--|
| Subject group type                   | Reporting group                          | Reporting group                     |  |  |
| Number of subjects analysed          | 122 <sup>[20]</sup>                      | 59 <sup>[21]</sup>                  |  |  |
| Units: number                        |  |                                     |  |  |
| arithmetic mean (standard deviation) | 0.8 (± 1.03)                             | 0.7 (± 0.79)                        |  |  |

Notes:

[20] - Roll-over set - Only participants who achieved DC were considered for the analysis

[21] - Roll-over set - Only participants who achieved DC were considered for the analysis

### Statistical analyses

No statistical analyses for this end point

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**Secondary: Normalized Cumulative Prednisone Dose in participants with PV and PF**

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|                 |  |
|-----------------|--|
| End point title | Normalized Cumulative Prednisone Dose in participants with PV and PF |
|-----------------|--|

End point description:

Normalized Cumulative prednisone dose (NCPD, mg/kg/day) is the average daily intake of all weight-adjusted prednisone doses received during the study, taking into account the number of days in study

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

End point timeframe:

up to 60 weeks

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| End point values                 | Efgartigimod-<br>efgartigimod<br>PH20 SC | Placebo-<br>efgartigimod<br>PH20 SC |  |  |
|----------------------------------|--|-------------------------------------|--|--|
| Subject group type               | Reporting group                          | Reporting group                     |  |  |
| Number of subjects analysed      | 123 <sup>[22]</sup>                      | 60 <sup>[23]</sup>                  |  |  |
| Units: mg/kg/day                 |  |                                     |  |  |
| arithmetic mean (standard error) | 0.212 (±<br>0.2018)                      | 0.241 (±<br>0.2401)                 |  |  |

Notes:

[22] - For participants that do not achieve CRmin/CROff, NCPD until CRmin/CROff is not calculated

[23] - For participants that do not achieve CRmin/CROff, NCPD until CRmin/CROff is not calculated

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**Statistical analyses**

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Up to 60 weeks

Adverse event reporting additional description:

Participants who rolled over from the antecedent study ARGX-113-1904, and received at least 1 dose of efgartigimod PH20 SC during this ARGX-113-1905 study (Safety set). Laboratory abnormalities were reported as AEs.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 26.0 |
|--------------------|------|

### Reporting groups

|                       |                                  |
|-----------------------|----------------------------------|
| Reporting group title | Efgartigimodefgartigimod PH20 SC |
|-----------------------|----------------------------------|

Reporting group description:

Participants who received efgartigimod PH20 SC in antecedent study ARGX-113-1904.

|                       |                              |
|-----------------------|------------------------------|
| Reporting group title | Placebo-efgartigimod PH20 SC |
|-----------------------|------------------------------|

Reporting group description:

Participants who received placebo PH20 SC in antecedent study ARGX-113-1904.

| Serious adverse events                            | Efgartigimodefgartigimod PH20 SC | Placebo-efgartigimod PH20 SC |  |
|---|----------------------------------|------------------------------|--|
| Total subjects affected by serious adverse events |                                  |                              |  |
| subjects affected / exposed                       | 16 / 101 (15.84%)                | 4 / 48 (8.33%)               |  |
| number of deaths (all causes)                     | 0                                | 1                            |  |
| number of deaths resulting from adverse events    | 0                                | 1                            |  |
| Investigations                                    |                                  |                              |  |
| Blood immunoglobulin G decreased                  |                                  |                              |  |
| subjects affected / exposed                       | 1 / 101 (0.99%)                  | 0 / 48 (0.00%)               |  |
| occurrences causally related to treatment / all   | 1 / 1                            | 0 / 0                        |  |
| deaths causally related to treatment / all        | 0 / 0                            | 0 / 0                        |  |
| Blood pressure increased                          |                                  |                              |  |
| subjects affected / exposed                       | 1 / 101 (0.99%)                  | 0 / 48 (0.00%)               |  |
| occurrences causally related to treatment / all   | 0 / 1                            | 0 / 0                        |  |
| deaths causally related to treatment / all        | 0 / 0                            | 0 / 0                        |  |
| Injury, poisoning and procedural complications    |                                  |                              |  |
| Patella fracture                                  |                                  |                              |  |

|  |                 |                |  |
|--|-----------------|----------------|--|
| subjects affected / exposed                          | 0 / 101 (0.00%) | 1 / 48 (2.08%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1          |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          |  |
| Tibia fracture                                       |                 |                |  |
| subjects affected / exposed                          | 1 / 101 (0.99%) | 0 / 48 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          |  |
| Wound  |                 |                |  |
| subjects affected / exposed                          | 1 / 101 (0.99%) | 0 / 48 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          |  |
| Vascular disorders                                   |                 |                |  |
| Deep vein thrombosis                                 |                 |                |  |
| subjects affected / exposed                          | 1 / 101 (0.99%) | 0 / 48 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          |  |
| Hypertension   |                 |                |  |
| subjects affected / exposed                          | 1 / 101 (0.99%) | 0 / 48 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          |  |
| Shock haemorrhagic                                   |                 |                |  |
| subjects affected / exposed                          | 0 / 101 (0.00%) | 1 / 48 (2.08%) |  |
| 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 |                 |                |  |
| Disease progression                                  |                 |                |  |
| subjects affected / exposed                          | 2 / 101 (1.98%) | 0 / 48 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 2           | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          |  |
| Gastrointestinal disorders                           |                 |                |  |
| Anal fistula   |                 |                |  |
| subjects affected / exposed                          | 1 / 101 (0.99%) | 0 / 48 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          |  |

|   |                 |                |  |
|---|-----------------|----------------|--|
| Gastritis erosive                               |                 |                |  |
| subjects affected / exposed                     | 2 / 101 (1.98%) | 0 / 48 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Intestinal obstruction                          |                 |                |  |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 48 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Reflux gastritis                                |                 |                |  |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 48 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Respiratory, thoracic and mediastinal disorders |                 |                |  |
| Respiratory failure                             |                 |                |  |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 48 (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          |                 |                |  |
| Pemphigus                                       |                 |                |  |
| subjects affected / exposed                     | 3 / 101 (2.97%) | 1 / 48 (2.08%) |  |
| occurrences causally related to treatment / all | 1 / 3           | 1 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Musculoskeletal and connective tissue disorders |                 |                |  |
| Musculoskeletal pain                            |                 |                |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 1 / 48 (2.08%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Osteonecrosis                                   |                 |                |  |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 48 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Infections and infestations                     |                 |                |  |
| Anal abscess                                    |                 |                |  |



|   |                 |                |  |
|---|-----------------|----------------|--|
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 48 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| COVID-19  |                 |                |  |
| subjects affected / exposed                     | 2 / 101 (1.98%) | 0 / 48 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Epiglottitis                                    |                 |                |  |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 48 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Lung abscess                                    |                 |                |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 1 / 48 (2.08%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Pneumonia                                       |                 |                |  |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 48 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Sepsis  |                 |                |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 1 / 48 (2.08%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 1          |  |
| Septic shock                                    |                 |                |  |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 48 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Skin infection                                  |                 |                |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 1 / 48 (2.08%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          |  |
| 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>                     | Efgartigimod<br>efgartigimod PH20 SC | Placebo-efgartigimod<br>PH20 SC |  |
|---|--------------------------------------|---------------------------------|--|
| Total subjects affected by non-serious adverse events |                                      |                                 |  |
| subjects affected / exposed                           | 46 / 101 (45.54%)                    | 19 / 48 (39.58%)                |  |
| Investigations  |                                      |                                 |  |
| Blood lactate dehydrogenase increased                 |                                      |                                 |  |
| subjects affected / exposed                           | 7 / 101 (6.93%)                      | 1 / 48 (2.08%)                  |  |
| occurrences (all)                                     | 8                                    | 1                               |  |
| Blood uric acid increased                             |                                      |                                 |  |
| subjects affected / exposed                           | 5 / 101 (4.95%)                      | 0 / 48 (0.00%)                  |  |
| occurrences (all)                                     | 5                                    | 0                               |  |
| Glycosylated haemoglobin increased                    |                                      |                                 |  |
| subjects affected / exposed                           | 6 / 101 (5.94%)                      | 0 / 48 (0.00%)                  |  |
| occurrences (all)                                     | 6                                    | 0                               |  |
| Low density lipoprotein increased                     |                                      |                                 |  |
| subjects affected / exposed                           | 5 / 101 (4.95%)                      | 0 / 48 (0.00%)                  |  |
| occurrences (all)                                     | 8                                    | 0                               |  |
| Cardiac disorders                                     |                                      |                                 |  |
| Tachycardia   |                                      |                                 |  |
| subjects affected / exposed                           | 1 / 101 (0.99%)                      | 3 / 48 (6.25%)                  |  |
| occurrences (all)                                     | 1                                    | 3                               |  |
| Nervous system disorders                              |                                      |                                 |  |
| Headache  |                                      |                                 |  |
| subjects affected / exposed                           | 3 / 101 (2.97%)                      | 4 / 48 (8.33%)                  |  |
| occurrences (all)                                     | 11                                   | 4                               |  |
| General disorders and administration site conditions  |                                      |                                 |  |
| Injection site erythema                               |                                      |                                 |  |
| subjects affected / exposed                           | 4 / 101 (3.96%)                      | 3 / 48 (6.25%)                  |  |
| occurrences (all)                                     | 30                                   | 5                               |  |
| Blood and lymphatic system disorders                  |                                      |                                 |  |
| Increased tendency to bruise                          |                                      |                                 |  |
| subjects affected / exposed                           | 0 / 101 (0.00%)                      | 3 / 48 (6.25%)                  |  |
| occurrences (all)                                     | 0                                    | 3                               |  |
| Skin and subcutaneous tissue disorders                |                                      |                                 |  |

|   |   |  |  |
|---|---|--|--|
| Pruritus<br>subjects affected / exposed<br>occurrences (all)  | 2 / 101 (1.98%)<br>2  | 3 / 48 (6.25%)<br>5  |  |
| Renal and urinary disorders<br>Haematuria<br>subjects affected / exposed<br>occurrences (all)   | 2 / 101 (1.98%)<br>2  | 3 / 48 (6.25%)<br>4  |  |
| Musculoskeletal and connective tissue disorders<br>Myopathy<br>subjects affected / exposed<br>occurrences (all)   | 2 / 101 (1.98%)<br>2  | 3 / 48 (6.25%)<br>3  |  |
| Infections and infestations<br>COVID-19<br>subjects affected / exposed<br>occurrences (all)<br><br>Folliculitis<br>subjects affected / exposed<br>occurrences (all)<br><br>Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)<br><br>Oral candidiasis<br>subjects affected / exposed<br>occurrences (all)<br><br>Urinary tract infection<br>subjects affected / exposed<br>occurrences (all) | 12 / 101 (11.88%)<br>12<br><br>5 / 101 (4.95%)<br>6<br><br>5 / 101 (4.95%)<br>7<br><br>6 / 101 (5.94%)<br>8<br><br>5 / 101 (4.95%)<br>5 | 5 / 48 (10.42%)<br>5<br><br>1 / 48 (2.08%)<br>1<br><br>1 / 48 (2.08%)<br>4<br><br>0 / 48 (0.00%)<br>0<br><br>2 / 48 (4.17%)<br>2 |  |
| Metabolism and nutrition disorders<br>Hypercholesterolaemia<br>subjects affected / exposed<br>occurrences (all)   | 5 / 101 (4.95%)<br>5  | 0 / 48 (0.00%)<br>0  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date              | Amendment  |
|-------------------|--|
| 05 February 2021  | <p>Protocol, Version 2.0</p> <ul style="list-style-type: none"><li>• A secondary objective and endpoints were added to explore the feasibility of efgartigimod PH20 SC self-administration or caregiver-supported administration. Instructions were added and the schedule of activities updated to include self-administration or caregiver-supported administration and training.</li><li>• A secondary objective and endpoint were added to measure the health impact of glucocorticoid use in participants with pemphigus.</li><li>• Evaluating antibodies against rHuPH20 was changed from a secondary objective and endpoint to an exploratory objective and endpoint due to safety concerns.</li><li>• Lymphocyte dynamic changes was added as an endpoint to the exploratory objective to evaluate the disease-specific genetic background and effects of efgartigimod PH20 SC on the serological and immunological profiles.</li><li>• Assessments of vaccine-induced immunity in the context of efgartigimod PH20 SC administration were added.</li><li>• Changes to the contraceptive requirements based on new data about efgartigimod PH20 SC were implemented.</li><li>• A transition in efgartigimod concentration from 165 mg/mL to 180 mg/mL was implemented to reduce the volume for each 1000-mg SC injection.</li><li>• A new criterion was added allowing the withdrawal from the study of a participant for whom a severe AE, SAE, or clinically significant change in a laboratory test parameter was reported.</li></ul> |
| 05 September 2022 | <p>Protocol, Version 3.0</p> <ul style="list-style-type: none"><li>• The upper limit of the number of participants who could enter the study (originally up to 150) was removed after the sample size for ARGX-113-1904 was increased.</li><li>• The timing of samples collected for lymphocyte populations was updated to allow for long-term immunological profiling.</li><li>• Based on nonclinical teratogenicity and reproductive toxicity data, the inclusion and exclusion criteria were updated: (1) Female participants could stop their contraception method after the last IMP dose, (2) female participants and the female partners of male participants could become pregnant immediately after the study, and (3) male participants could donate sperm.</li><li>• Information on injection-site reactions and instructions on monitoring and reporting injection-site reactions were added.</li></ul>  |

Notes:

### 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.

Study was terminated prematurely by the Sponsor.

Notes: