



## Clinical trial results:

### A Phase 2, Long-Term Extension (LTE) Study With Elsubrutinib and Upadacitinib Given Alone or in Combination (ABBV-599) in Subjects With Moderately to Severely Active Systemic Lupus Erythematosus Who Have Completed the M19-130 Phase 2 Randomized Controlled Trial (RCT)

#### Summary

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2020-001690-72  |
| Trial protocol           | NL HU DE BG IT  |
| Global end of trial date | 03 January 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 | M20-186 |
|-----------------------|---------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT04451772 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | AbbVie Deutschland GmbH & Co. KG  |
| Sponsor organisation address | AbbVie House, Vanwall Business Park, Vanwall Road, Maidenhead, Berkshire, United Kingdom, SL6-4UB                                     |
| Public contact               | Global Medical Services, AbbVie, 001 8006339110, <a href="mailto:abbvieclinicaltrials@abbvie.com">abbvieclinicaltrials@abbvie.com</a> |
| Scientific contact           | Global Medical Services, AbbVie, 001 8006339110, <a href="mailto:abbvieclinicaltrials@abbvie.com">abbvieclinicaltrials@abbvie.com</a> |

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                       | 03 January 2024 |
| Is this the analysis of the primary completion data? | No              |

|                                  |                 |
|----------------------------------|-----------------|
| Global end of trial reached?     | Yes             |
| Global end of trial date         | 03 January 2024 |
| Was the trial ended prematurely? | No              |

Notes:

## General information about the trial

Main objective of the trial:

Systemic Lupus Erythematosus (SLE) is an immune-mediated disease associated with inflammation of multiple organ systems. This study will evaluate how well elsubrutinib and upadacitinib given alone or as the ABBV-599 combination (elsubrutinib/upadacitinib) works within the body, in participants who completed study M19-130. This study will assess the change in disease symptoms.

ABBV-599 is an investigational drug being developed for the treatment of Systemic Lupus Erythematosus (SLE). Adult participants with a diagnosis of SLE will be enrolled and will receive oral elsubrutinib capsules and/or oral upadacitinib tablets once daily for up to 56 weeks. Participants who were receiving elsubrutinib and/or upadacitinib in M19-130 will continue to receive the same treatment in this study. Participants who were receiving placebo in M19-130 will be re-randomized to one of the 2 combination treatment arms in this study.

Protection of trial subjects:

Subjects or their legally authorized representative (if required per local regulations) must have understood and personally, voluntarily signed and dated an informed consent, approved by an independent ethics committee (IEC)/institutional review board (IRB), prior to the initiation of any screening or study-specific procedures. In Japan, subjects under 20 years of age must have voluntarily signed and dated an informed consent, in addition to their parent or legal guardian. Legally authorized representation did not apply in the case of Germany and France, and protected persons such as minors, adults under guardianship, pregnant women, persons deprived of their liberty and persons incapable or unable to express their consent were not included in the study.

Background therapy: -

Evidence for comparator: -

|   |              |
|---|--------------|
| Actual start date of recruitment                          | 27 July 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 | Argentina: 19 |
| Country: Number of subjects enrolled | Australia: 3  |
| Country: Number of subjects enrolled | Bulgaria: 3   |
| Country: Number of subjects enrolled | China: 6      |
| Country: Number of subjects enrolled | Colombia: 15  |
| Country: Number of subjects enrolled | Germany: 3    |
| Country: Number of subjects enrolled | Hungary: 9    |
| Country: Number of subjects enrolled | Italy: 1      |

|                                      |                       |
|--------------------------------------|-----------------------|
| Country: Number of subjects enrolled | Japan: 13             |
| Country: Number of subjects enrolled | Korea, Republic of: 1 |
| Country: Number of subjects enrolled | Mexico: 15            |
| Country: Number of subjects enrolled | New Zealand: 3        |
| Country: Number of subjects enrolled | Poland: 9             |
| Country: Number of subjects enrolled | Puerto Rico: 10       |
| Country: Number of subjects enrolled | Spain: 9              |
| Country: Number of subjects enrolled | Taiwan: 16            |
| Country: Number of subjects enrolled | United Kingdom: 4     |
| Country: Number of subjects enrolled | United States: 46     |
| Worldwide total number of subjects   | 185                   |
| EEA total number of subjects         | 34                    |

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)                      | 180 |
| From 65 to 84 years                       | 5   |
| 85 years and over                         | 0   |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Subjects who completed Study M19-130 were eligible to enroll in this study. Only those subjects who met all of the specified eligibility criteria had the option to enter this long-term extension (LTE) study to receive continued therapy, provided the subject was willing and the investigator believed that continuing therapy was appropriate.

### Period 1

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

### Arms

|                              |  |
|------------------------------|--|
| Are arms mutually exclusive? | Yes                                      |
| <b>Arm title</b>             | ABBV-599 High Dose -> ABBV-599 High Dose |

Arm description:

Participants received elsubrutinib 60 mg capsules once a day by mouth and upadacitinib 30 mg film-coated tablets once a day by mouth for 48 weeks in Study M19-130. Participants continued on this regimen in the current study (M20-186) for up to 56 weeks.

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Elsubrutinib |
| Investigational medicinal product code |              |
| Other name                             | ABBV-105     |
| Pharmaceutical forms                   | Capsule      |
| Routes of administration               | Oral use     |

Dosage and administration details:

Capsule; Oral

|  |                    |
|--|--------------------|
| Investigational medicinal product name | Upadacitinib       |
| Investigational medicinal product code |                    |
| Other name                             | ABT-494, RINVOQ    |
| Pharmaceutical forms                   | Film-coated tablet |
| Routes of administration               | Oral use           |

Dosage and administration details:

Film-coated tablet; Oral

|                  |  |
|------------------|--|
| <b>Arm title</b> | Els Pbo/Upa 30 mg -> Els Pbo/Upa 30 mg |
|------------------|--|

Arm description:

Participants received placebo capsules for elsubrutinib once a day by mouth and upadacitinib 30 mg film-coated tablets once a day by mouth for 48 weeks in Study M19-130. Participants continued on this regimen in the current study (M20-186) for up to 56 weeks.

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

|  |                          |
|--|--------------------------|
| Investigational medicinal product name | Placebo for Elsubrutinib |
| Investigational medicinal product code |                          |
| Other name                             |                          |
| Pharmaceutical forms                   | Capsule                  |
| Routes of administration               | Oral use                 |

Dosage and administration details:

Capsule; Oral

|  |                    |
|--|--------------------|
| Investigational medicinal product name | Upadacitinib       |
| Investigational medicinal product code |                    |
| Other name                             | ABT-494, RINVOQ    |
| Pharmaceutical forms                   | Film-coated tablet |
| Routes of administration               | Oral use           |

Dosage and administration details:

Film-coated tablet; Oral

|                  |                                       |
|------------------|---------------------------------------|
| <b>Arm title</b> | Els Pbo/Upa Pbo -> ABBV-599 High Dose |
|------------------|---------------------------------------|

Arm description:

Participants received placebo capsules for elsubrutinib once a day by mouth and placebo film-coated tablets for upadacitinib once a day by mouth for 48 weeks in Study M19-130. Participants received elsubrutinib 60 mg capsules once a day by mouth and upadacitinib 30 mg film-coated tablets once a day in the current study (M20-186) for up to 56 weeks.

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Elsubrutinib |
| Investigational medicinal product code |              |
| Other name                             | ABBV-105     |
| Pharmaceutical forms                   | Capsule      |
| Routes of administration               | Oral use     |

Dosage and administration details:

Capsule; Oral

|  |                    |
|--|--------------------|
| Investigational medicinal product name | Upadacitinib       |
| Investigational medicinal product code |                    |
| Other name                             | ABT-494, RINVOQ    |
| Pharmaceutical forms                   | Film-coated tablet |
| Routes of administration               | Oral use           |

Dosage and administration details:

Film-coated tablet; Oral

|                  |                              |
|------------------|------------------------------|
| <b>Arm title</b> | ABBV-599 Low -> ABBV-599 Low |
|------------------|------------------------------|

Arm description:

Participants received elsubrutinib 60 mg capsules once a day by mouth and upadacitinib 15 mg film-coated tablets once a day by mouth for 48 weeks in Study M19-130. Participants continued on this regimen in the current study (M20-186) for up to 56 weeks.

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Elsubrutinib |
| Investigational medicinal product code |              |
| Other name                             | ABBV-105     |
| Pharmaceutical forms                   | Capsule      |
| Routes of administration               | Oral use     |

Dosage and administration details:

Capsule; Oral

|  |                    |
|--|--------------------|
| Investigational medicinal product name                         | Upadacitinib       |
| Investigational medicinal product code                         |                    |
| Other name   | ABT-494, RINVOQ    |
| Pharmaceutical forms   | Film-coated tablet |
| Routes of administration                                       | Oral use           |
| Dosage and administration details:<br>Film-coated tablet; Oral |                    |

|                  |  |
|------------------|--|
| <b>Arm title</b> | Els 60 mg/Upa Pbo -> Els 60 mg/Upa Pbo |
|------------------|--|

Arm description:

Participants received elsubrutinib 60 mg capsules once a day by mouth and placebo film-coated tablets for upadacitinib once a day by mouth for 48 weeks in Study M19-130. Participants continued on this regimen in the current study (M20-186) for up to 56 weeks.

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Elsubrutinib |
| Investigational medicinal product code |              |
| Other name                             | ABBV-105     |
| Pharmaceutical forms                   | Capsule      |
| Routes of administration               | Oral use     |

Dosage and administration details:

Capsule; Oral

|  |                          |
|--|--------------------------|
| Investigational medicinal product name | Placebo for Upadacitinib |
| Investigational medicinal product code |                          |
| Other name                             |                          |
| Pharmaceutical forms                   | Film-coated tablet       |
| Routes of administration               | Oral use                 |

Dosage and administration details:

Film-coated tablet; Oral

|                  |                               |
|------------------|-------------------------------|
| <b>Arm title</b> | Els + Upa Pbo -> ABBV-599 Low |
|------------------|-------------------------------|

Arm description:

Participants received placebo capsules for elsubrutinib once a day by mouth and placebo film-coated tablets for upadacitinib once a day by mouth for 48 weeks in Study M19-130. Participants received elsubrutinib 60 mg capsules once a day by mouth and upadacitinib 15 mg film-coated tablets once a day by mouth for 48 weeks in the current study (M20-186) for up to 56 weeks.

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Elsubrutinib |
| Investigational medicinal product code |              |
| Other name                             | ABBV-105     |
| Pharmaceutical forms                   | Capsule      |
| Routes of administration               | Oral use     |

Dosage and administration details:

Capsule; Oral

|  |                    |
|--|--------------------|
| Investigational medicinal product name | Upadacitinib       |
| Investigational medicinal product code |                    |
| Other name                             | ABT-494, RINVOQ    |
| Pharmaceutical forms                   | Film-coated tablet |
| Routes of administration               | Oral use           |

Dosage and administration details:

Film-coated tablet; Oral

| <b>Number of subjects in period 1</b>           | ABBV-599 High Dose -> ABBV-599 High Dose | Els Pbo/Upa 30 mg -> Els Pbo/Upa 30 mg | Els Pbo/Upa Pbo -> ABBV-599 High Dose |
|---|--|--|---------------------------------------|
| Started   | 45                                       | 47                                     | 35                                    |
| Completed                                       | 41                                       | 38                                     | 31                                    |
| Not completed                                   | 4  | 9                                      | 4                                     |
| Sponsor decision based on interim analysis data | -  | -                                      | -                                     |
| Adverse event, non-fatal                        | 1  | -                                      | 1                                     |
| Other, not specified                            | 1  | 2                                      | 1                                     |
| Withdrawal by subject                           | 2  | 7                                      | 2                                     |

| <b>Number of subjects in period 1</b>           | ABBV-599 Low -> ABBV-599 Low | Els 60 mg/Upa Pbo -> Els 60 mg/Upa Pbo | Els + Upa Pbo -> ABBV-599 Low |
|---|------------------------------|--|-------------------------------|
| Started   | 19                           | 25                                     | 14                            |
| Completed                                       | 6                            | 1                                      | 1                             |
| Not completed                                   | 13                           | 24                                     | 13                            |
| Sponsor decision based on interim analysis data | 11                           | 23                                     | 9                             |
| Adverse event, non-fatal                        | 1                            | -                                      | 3                             |
| Other, not specified                            | -                            | -                                      | 1                             |
| Withdrawal by subject                           | 1                            | 1                                      | -                             |

## Baseline characteristics

### Reporting groups

|  |  |
|--|--|
| Reporting group title  | ABBV-599 High Dose -> ABBV-599 High Dose |
| Reporting group description:<br>Participants received elsubrutinib 60 mg capsules once a day by mouth and upadacitinib 30 mg film-coated tablets once a day by mouth for 48 weeks in Study M19-130. Participants continued on this regimen in the current study (M20-186) for up to 56 weeks.  |  |
| Reporting group title  | Els Pbo/Upa 30 mg -> Els Pbo/Upa 30 mg   |
| Reporting group description:<br>Participants received placebo capsules for elsubrutinib once a day by mouth and upadacitinib 30 mg film-coated tablets once a day by mouth for 48 weeks in Study M19-130. Participants continued on this regimen in the current study (M20-186) for up to 56 weeks.  |  |
| Reporting group title  | Els Pbo/Upa Pbo -> ABBV-599 High Dose    |
| Reporting group description:<br>Participants received placebo capsules for elsubrutinib once a day by mouth and placebo film-coated tablets for upadacitinib once a day by mouth for 48 weeks in Study M19-130. Participants received elsubrutinib 60 mg capsules once a day by mouth and upadacitinib 30 mg film-coated tablets once a day in the current study (M20-186) for up to 56 weeks.                       |  |
| Reporting group title  | ABBV-599 Low -> ABBV-599 Low             |
| Reporting group description:<br>Participants received elsubrutinib 60 mg capsules once a day by mouth and upadacitinib 15 mg film-coated tablets once a day by mouth for 48 weeks in Study M19-130. Participants continued on this regimen in the current study (M20-186) for up to 56 weeks.  |  |
| Reporting group title  | Els 60 mg/Upa Pbo -> Els 60 mg/Upa Pbo   |
| Reporting group description:<br>Participants received elsubrutinib 60 mg capsules once a day by mouth and placebo film-coated tablets for upadacitinib once a day by mouth for 48 weeks in Study M19-130. Participants continued on this regimen in the current study (M20-186) for up to 56 weeks.  |  |
| Reporting group title  | Els + Upa Pbo -> ABBV-599 Low            |
| Reporting group description:<br>Participants received placebo capsules for elsubrutinib once a day by mouth and placebo film-coated tablets for upadacitinib once a day by mouth for 48 weeks in Study M19-130. Participants received elsubrutinib 60 mg capsules once a day by mouth and upadacitinib 15 mg film-coated tablets once a day by mouth for 48 weeks in the current study (M20-186) for up to 56 weeks. |  |

| Reporting group values  | ABBV-599 High Dose -> ABBV-599 High Dose | Els Pbo/Upa 30 mg -> Els Pbo/Upa 30 mg | Els Pbo/Upa Pbo -> ABBV-599 High Dose |
|---|--|--|---------------------------------------|
| Number of subjects  | 45                                       | 47                                     | 35                                    |
| Age categorical<br>Units: Subjects                                      |  |  |                                       |
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation | 42.8<br>± 11.39                          | 42.5<br>± 12.00                        | 40.6<br>± 11.75                       |
| Gender categorical<br>Units: Subjects                                   |  |  |                                       |
| Female  | 42                                       | 42                                     | 35                                    |
| Male  | 3  | 5                                      | 0                                     |



|   |    |    |    |
|---|----|----|----|
| Race                                      |    |    |    |
| Units: Subjects                           |    |    |    |
| American Indian or Alaska Native          | 3  | 0  | 2  |
| Asian                                     | 6  | 10 | 12 |
| Native Hawaiian or Other Pacific Islander | 0  | 0  | 0  |
| Black or African American                 | 2  | 6  | 0  |
| White                                     | 32 | 26 | 20 |
| More than one race                        | 2  | 5  | 1  |
| Unknown or Not Reported                   | 0  | 0  | 0  |

|                               |                                 |  |                                  |
|-------------------------------|---------------------------------|--|----------------------------------|
| <b>Reporting group values</b> | ABBV-599 Low -><br>ABBV-599 Low | Els 60 mg/Upa Pbo -<br>> Els 60 mg/Upa Pbo | Els + Upa Pbo -><br>ABBV-599 Low |
| Number of subjects            | 19                              | 25   | 14                               |
| Age categorical               |                                 |  |                                  |
| Units: Subjects               |                                 |  |                                  |

|   |         |         |         |
|---|---------|---------|---------|
| Age continuous                            |         |         |         |
| Units: years                              |         |         |         |
| arithmetic mean                           | 38.3    | 41.2    | 42.5    |
| standard deviation                        | ± 10.52 | ± 11.60 | ± 11.57 |
| Gender categorical                        |         |         |         |
| Units: Subjects                           |         |         |         |
| Female                                    | 18      | 24      | 14      |
| Male                                      | 1       | 1       | 0       |
| Race                                      |         |         |         |
| Units: Subjects                           |         |         |         |
| American Indian or Alaska Native          | 1       | 2       | 0       |
| Asian                                     | 6       | 3       | 2       |
| Native Hawaiian or Other Pacific Islander | 0       | 0       | 0       |
| Black or African American                 | 1       | 1       | 1       |
| White                                     | 10      | 16      | 10      |
| More than one race                        | 1       | 3       | 1       |
| Unknown or Not Reported                   | 0       | 0       | 0       |

|                               |       |  |  |
|-------------------------------|-------|--|--|
| <b>Reporting group values</b> | Total |  |  |
| Number of subjects            | 185   |  |  |
| Age categorical               |       |  |  |
| Units: Subjects               |       |  |  |

|                    |     |  |  |
|--------------------|-----|--|--|
| Age continuous     |     |  |  |
| Units: years       |     |  |  |
| arithmetic mean    |     |  |  |
| standard deviation | -   |  |  |
| Gender categorical |     |  |  |
| Units: Subjects    |     |  |  |
| Female             | 175 |  |  |
| Male               | 10  |  |  |

|   |     |  |  |
|---|-----|--|--|
| Race                                      |     |  |  |
| Units: Subjects                           |     |  |  |
| American Indian or Alaska Native          | 8   |  |  |
| Asian                                     | 39  |  |  |
| Native Hawaiian or Other Pacific Islander | 0   |  |  |
| Black or African American                 | 11  |  |  |
| White                                     | 114 |  |  |
| More than one race                        | 13  |  |  |
| Unknown or Not Reported                   | 0   |  |  |

## End points

### End points reporting groups

|  |  |
|--|--|
| Reporting group title  | ABBV-599 High Dose -> ABBV-599 High Dose |
| Reporting group description:<br>Participants received elsubrutinib 60 mg capsules once a day by mouth and upadacitinib 30 mg film-coated tablets once a day by mouth for 48 weeks in Study M19-130. Participants continued on this regimen in the current study (M20-186) for up to 56 weeks.  |  |
| Reporting group title  | Els Pbo/Upa 30 mg -> Els Pbo/Upa 30 mg   |
| Reporting group description:<br>Participants received placebo capsules for elsubrutinib once a day by mouth and upadacitinib 30 mg film-coated tablets once a day by mouth for 48 weeks in Study M19-130. Participants continued on this regimen in the current study (M20-186) for up to 56 weeks.  |  |
| Reporting group title  | Els Pbo/Upa Pbo -> ABBV-599 High Dose    |
| Reporting group description:<br>Participants received placebo capsules for elsubrutinib once a day by mouth and placebo film-coated tablets for upadacitinib once a day by mouth for 48 weeks in Study M19-130. Participants received elsubrutinib 60 mg capsules once a day by mouth and upadacitinib 30 mg film-coated tablets once a day in the current study (M20-186) for up to 56 weeks.                       |  |
| Reporting group title  | ABBV-599 Low -> ABBV-599 Low             |
| Reporting group description:<br>Participants received elsubrutinib 60 mg capsules once a day by mouth and upadacitinib 15 mg film-coated tablets once a day by mouth for 48 weeks in Study M19-130. Participants continued on this regimen in the current study (M20-186) for up to 56 weeks.  |  |
| Reporting group title  | Els 60 mg/Upa Pbo -> Els 60 mg/Upa Pbo   |
| Reporting group description:<br>Participants received elsubrutinib 60 mg capsules once a day by mouth and placebo film-coated tablets for upadacitinib once a day by mouth for 48 weeks in Study M19-130. Participants continued on this regimen in the current study (M20-186) for up to 56 weeks.  |  |
| Reporting group title  | Els + Upa Pbo -> ABBV-599 Low            |
| Reporting group description:<br>Participants received placebo capsules for elsubrutinib once a day by mouth and placebo film-coated tablets for upadacitinib once a day by mouth for 48 weeks in Study M19-130. Participants received elsubrutinib 60 mg capsules once a day by mouth and upadacitinib 15 mg film-coated tablets once a day by mouth for 48 weeks in the current study (M20-186) for up to 56 weeks. |  |

### Primary: Number of Participants With Treatment-Emergent Adverse Events

|  |  |
|--|--|
| End point title  | Number of Participants With Treatment-Emergent Adverse Events <sup>[1]</sup> |
| End point description:<br>Adverse event (AE): any untoward medical occurrence in a patient/clinical investigation subject administered a pharmaceutical product and which doesn't necessarily have a causal relationship with this Tx. Serious adverse event (SAE): an event that results in death, is life-threatening, requires or prolongs hospitalization, results in a congenital anomaly, persistent or significant disability/incapacity or is an important medical event that, based on medical judgment, may jeopardize the subject and may require medical or surgical intervention to prevent any of the outcomes listed above. Treatment-emergent events (TEAEs) are defined as an adverse event with an onset date that is on or after the first dose of study drug from Study M20-186, and no more than 30 days after the last dose of study drug from Study M20-186. For more details on adverse events please see the Adverse Event section. |  |
| Analysis population: subjects rcvd $\geq 1$ dose of study drug in Study M20-186, grouped by Tx rcvd  |  |
| End point type   | Primary  |

End point timeframe:

From the first dose of study drug in Study M20-186 up to 30 days after the last dose of study drug, up to 442 days

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: Descriptive data are summarized for this end point per protocol.

| End point values            | ABBV-599 High Dose -> ABBV-599 High Dose | Els Pbo/Upa 30 mg -> Els Pbo/Upa 30 mg | Els Pbo/Upa Pbo -> ABBV-599 High Dose | ABBV-599 Low -> ABBV-599 Low |
|-----------------------------|--|--|---------------------------------------|------------------------------|
| Subject group type          | Reporting group                          | Reporting group                        | Reporting group                       | Reporting group              |
| Number of subjects analysed | 45                                       | 47                                     | 35                                    | 19                           |
| Units: participants         |  |  |                                       |                              |
| Any TEAE                    | 34                                       | 31                                     | 30                                    | 11                           |
| TESAE                       | 5  | 5                                      | 1                                     | 2                            |

| End point values            | Els 60 mg/Upa Pbo -> Els 60 mg/Upa Pbo | Els + Upa Pbo -> ABBV-599 Low |  |  |
|-----------------------------|--|-------------------------------|--|--|
| Subject group type          | Reporting group                        | Reporting group               |  |  |
| Number of subjects analysed | 25                                     | 14                            |  |  |
| Units: participants         |  |                               |  |  |
| Any TEAE                    | 11                                     | 7                             |  |  |
| TESAE                       | 1                                      | 2                             |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants Achieving Systemic Lupus Erythematosus (SLE) Responder Index (SRI)-4

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants Achieving Systemic Lupus Erythematosus (SLE) Responder Index (SRI)-4 <sup>[2]</sup> |
|-----------------|--|

End point description:

SLE Responder Index (SRI)-4 is defined as follows with all criteria compared to Baseline in Study M19-130:

- ≥4-point reduction in Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) score
- No worsening of the overall condition (< 0.3 point increase in Physician's Global Assessment [PhGA])
- No new British Isles Lupus Assessment Group (BILAG) A or more than 1 new BILAG B disease activity scores (i.e., no organ system changes from baseline B/C/D/E to A and no more than 1 organ system changes from baseline C/D/E to B). A letter score is assigned to each organ system with following indications: A = severe, B = moderate, C = mild, D = inactive with prior history, and E = inactive with no history.

Analysis population: Full Analysis Set: all randomized subjects who received at least 1 dose of study drug in Study M20-186; as observed (AO) analysis.

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

End point timeframe:

Baseline of Study M19-130 (Week 0), Weeks 56, 64, 72, 80, 88, 96, 104

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: When 50% of planned participants in Study M19-130 had completed Week 24 or withdrawn from the study, the ABBV-599 Low Dose and elsubrutinib 60 mg treatment groups were terminated as these groups did not meet projected efficacy. Per protocol, terminated groups were removed from the efficacy analyses.

| End point values                  | ABBV-599 High Dose -> ABBV-599 High Dose | Els Pbo/Upa 30 mg -> Els Pbo/Upa 30 mg | Els Pbo/Upa Pbo -> ABBV-599 High Dose |  |
|-----------------------------------|--|--|---------------------------------------|--|
| Subject group type                | Reporting group                          | Reporting group                        | Reporting group                       |  |
| Number of subjects analysed       | 45                                       | 46                                     | 35                                    |  |
| Units: percentage of participants |  |  |                                       |  |
| number (confidence interval 95%)  |  |  |                                       |  |
| Week 56 (n=45, 46, 35)            | 71.1 (57.9 to 84.4)                      | 76.1 (63.8 to 88.4)                    | 54.3 (37.8 to 70.8)                   |  |
| Week 64 (n=44, 45, 34)            | 70.5 (57.0 to 83.9)                      | 75.6 (63.0 to 88.1)                    | 58.8 (42.3 to 75.4)                   |  |
| Week 72 (n=41, 45, 34)            | 80.5 (68.4 to 92.6)                      | 88.9 (79.7 to 98.1)                    | 64.7 (48.6 to 80.8)                   |  |
| Week 80 (n=40, 45, 33)            | 75.0 (61.6 to 88.4)                      | 82.2 (71.1 to 93.4)                    | 57.6 (40.7 to 74.4)                   |  |
| Week 88 (n=40, 42, 33)            | 82.5 (70.7 to 94.3)                      | 85.7 (75.1 to 96.3)                    | 48.5 (31.4 to 65.5)                   |  |
| Week 96 (n=41, 39, 32)            | 82.9 (71.4 to 94.4)                      | 76.9 (63.7 to 90.1)                    | 62.5 (45.7 to 79.3)                   |  |
| Week 104 (n=41, 39, 31)           | 85.4 (74.5 to 96.2)                      | 82.1 (70.0 to 94.1)                    | 61.3 (44.1 to 78.4)                   |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants Achieving British Isles Lupus Assessment Group (BILAG)-Based Combined Lupus Assessment (BICLA) Response

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants Achieving British Isles Lupus Assessment Group (BILAG)-Based Combined Lupus Assessment (BICLA) Response <sup>[3]</sup> |
|-----------------|---|

End point description:

BICLA is a composite responder index. Achievement of BICLA response is defined as improvement in all initial A and B BILAG scores, with no more than one new BILAG B score without worsening of the overall condition (no worsening in Physician's Global Assessment [PhGA], < 0.3 point increase) and no worsening of the Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) score.

Analysis population: Full Analysis Set: all randomized participants who received at least 1 dose of study drug in Study M20-186; as observed (AO) analysis.

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

End point timeframe:

Baseline of Study M19-130 (Week 0), Weeks 56, 64, 72, 80, 88, 96, 104

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: When 50% of planned participants in Study M19-130 had completed Week 24 or withdrawn from the study, the ABBV-599 Low Dose and elsubrutinib 60 mg treatment groups were terminated as these groups did not meet projected efficacy. Per protocol, terminated groups were removed from the efficacy analyses.

| <b>End point values</b>           | ABBV-599 High Dose -> ABBV-599 High Dose | Els Pbo/Upa 30 mg -> Els Pbo/Upa 30 mg | Els Pbo/Upa Pbo -> ABBV-599 High Dose |  |
|-----------------------------------|--|--|---------------------------------------|--|
| Subject group type                | Reporting group                          | Reporting group                        | Reporting group                       |  |
| Number of subjects analysed       | 45                                       | 46                                     | 35                                    |  |
| Units: percentage of participants |  |  |                                       |  |
| number (confidence interval 95%)  |  |  |                                       |  |
| Week 56 (n=45, 46, 35)            | 73.3 (60.4 to 86.3)                      | 67.4 (53.8 to 80.9)                    | 60.0 (43.8 to 76.2)                   |  |
| Week 64 (n=44, 45, 34)            | 75.0 (62.2 to 87.8)                      | 84.4 (73.9 to 95.0)                    | 55.9 (39.2 to 72.6)                   |  |
| Week 72 (n=41, 45, 34)            | 73.2 (59.6 to 86.7)                      | 88.9 (79.7 to 98.1)                    | 61.8 (45.4 to 78.1)                   |  |
| Week 80 (n=40, 45, 33)            | 70.0 (55.8 to 84.2)                      | 77.8 (65.6 to 89.9)                    | 57.6 (40.7 to 74.4)                   |  |
| Week 88 (n=40, 42, 33)            | 80.0 (67.6 to 92.4)                      | 85.7 (75.1 to 96.3)                    | 57.6 (40.7 to 74.4)                   |  |
| Week 96 (n=41, 39, 32)            | 78.0 (65.4 to 90.7)                      | 76.9 (63.7 to 90.1)                    | 59.4 (42.4 to 76.4)                   |  |
| Week 104 (n=41, 39, 31)           | 78.0 (65.4 to 90.7)                      | 69.2 (54.7 to 83.7)                    | 54.8 (37.3 to 72.4)                   |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Daily Prednisone Dose Over Time

|                 |  |
|-----------------|--|
| End point title | Change From Baseline in Daily Prednisone Dose Over Time <sup>[4]</sup> |
|-----------------|--|

End point description:

Participants' current use of steroid therapy was assessed at each study visit, and the amount of daily prednisone was documented.

Analysis population: Full Analysis Set: all randomized participants who received at least 1 dose of study drug in Study M20-186; as observed (AO) analysis.

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

End point timeframe:

Baseline of M19-130 (Week 0), Weeks 56, 64, 72, 80, 88, 96, 104

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: When 50% of planned participants in Study M19-130 had completed Week 24 or withdrawn from the study, the ABBV-599 Low Dose and elsubrutinib 60 mg treatment groups were terminated as these groups did not meet projected efficacy. Per protocol, terminated groups were removed from the efficacy analyses.

| End point values                     | ABBV-599 High Dose -> ABBV-599 High Dose | Els Pbo/Upa 30 mg -> Els Pbo/Upa 30 mg | Els Pbo/Upa Pbo -> ABBV-599 High Dose |  |
|--------------------------------------|--|--|---------------------------------------|--|
| Subject group type                   | Reporting group                          | Reporting group                        | Reporting group                       |  |
| Number of subjects analysed          | 45                                       | 47                                     | 35                                    |  |
| Units: mg                            |  |  |                                       |  |
| arithmetic mean (standard deviation) |  |  |                                       |  |
| Week 56 (n=45, 47, 35)               | -3.9 (± 5.96)                            | -3.5 (± 5.99)                          | -4.9 (± 6.99)                         |  |
| Week 64 (n=45, 46, 35)               | -4.2 (± 5.51)                            | -3.7 (± 5.97)                          | -5.0 (± 6.87)                         |  |
| Week 72 (n=42, 46, 34)               | -4.0 (± 6.59)                            | -4.9 (± 7.23)                          | -5.2 (± 6.88)                         |  |
| Week 80 (n=41, 45, 34)               | -5.1 (± 5.96)                            | -4.4 (± 8.05)                          | -5.2 (± 6.88)                         |  |
| Week 88 (n=41, 42, 33)               | -5.5 (± 5.83)                            | -5.2 (± 6.02)                          | -6.2 (± 7.04)                         |  |
| Week 96 (n=41, 40, 32)               | -5.5 (± 5.88)                            | -5.7 (± 5.78)                          | -7.3 (± 6.54)                         |  |
| Week 104 (n=41, 39, 31)              | -5.8 (± 6.02)                            | -5.5 (± 5.65)                          | -7.7 (± 6.64)                         |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Flares Per Patient-year by Safety of Estrogens in Lupus Erythematosus National Assessment (SELENA) SLE Disease Activity Index (SLEDAI) Flare Index Through Week 104

|                 |  |
|-----------------|--|
| End point title | Number of Flares Per Patient-year by Safety of Estrogens in Lupus Erythematosus National Assessment (SELENA) SLE Disease Activity Index (SLEDAI) Flare Index Through Week 104 <sup>[5]</sup> |
|-----------------|--|

End point description:

The SELENA SLEDAI flare index defines mild/moderate or severe SLE flares using the SLEDAI score, definitions of worsening signs and symptoms, treatment changes, and Physician's Global Assessment of Disease Activity.

Analysis population: Full Analysis Set: all randomized participants who received at least 1 dose of study drug in Study M20-186; as observed (AO) analysis.

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

End point timeframe:

From Week 56 through Week 104

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: When 50% of planned participants in Study M19-130 had completed Week 24 or withdrawn from the study, the ABBV-599 Low Dose and elsubrutinib 60 mg treatment groups were terminated as these groups did not meet projected efficacy. Per protocol, terminated groups were removed from the efficacy analyses.

| End point values                 | ABBV-599 High Dose -> ABBV-599 High Dose | Els Pbo/Upa 30 mg -> Els Pbo/Upa 30 mg | Els Pbo/Upa Pbo -> ABBV-599 High Dose |  |
|----------------------------------|--|--|---------------------------------------|--|
| Subject group type               | Reporting group                          | Reporting group                        | Reporting group                       |  |
| Number of subjects analysed      | 45                                       | 47                                     | 35                                    |  |
| Units: Events per patient-year   |  |  |                                       |  |
| number (confidence interval 95%) |  |  |                                       |  |
| Mild/Moderate                    | 0.62 (0.39 to 0.84)                      | 1.41 (1.06 to 1.75)                    | 1.39 (0.99 to 1.78)                   |  |

|         |                     |                      |                     |  |
|---------|---------------------|----------------------|---------------------|--|
| Severe  | 0.00 (0.00 to 0.00) | 0.04 (-0.02 to 0.10) | 0.17 (0.03 to 0.31) |  |
| Overall | 0.62 (0.39 to 0.84) | 1.45 (1.10 to 1.80)  | 1.56 (1.14 to 1.97) |  |

## Statistical analyses

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No statistical analyses for this end point



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

All-cause mortality and adverse events were collected from the time informed consent was signed through the end of the study.

Adverse event reporting additional description:

Median time on follow-up was for 422 days for the ABBV-599 High -> ABBV-599 High group; 423 days for the Upa -> Upa and Pbo -> ABBV-599 High groups; 245 days for the ABBV-599 Low -> ABBV-599 Low group; 163 days for the Els -> Els group; and 142.5 days for the Pbo -> ABBV-599 Low group.

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

### Dictionary used

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

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

### Reporting groups

|                       |  |
|-----------------------|--|
| Reporting group title | ABBV-599 High Dose -> ABBV-599 High Dose |
|-----------------------|--|

Reporting group description:

Participants received elsubrutinib 60 mg capsules once a day by mouth and upadacitinib 30 mg filmcoated tablets once a day by mouth for 48 weeks in Study M19-130. Participants continued on this regimen in the current study (M20-186) for up to 56 weeks.

|                       |  |
|-----------------------|--|
| Reporting group title | Els Pbo/Upa 30 mg -> Els Pbo/Upa 30 mg |
|-----------------------|--|

Reporting group description:

Participants received placebo capsules for elsubrutinib once a day by mouth and upadacitinib 30 mg film-coated tablets once a day by mouth for 48 weeks in Study M19-130. Participants continued on this regimen in the current study (M20-186) for up to 56 weeks.

|                       |                                       |
|-----------------------|---------------------------------------|
| Reporting group title | Els Pbo/Upa Pbo -> ABBV-599 High Dose |
|-----------------------|---------------------------------------|

Reporting group description:

Participants received placebo capsules for elsubrutinib once a day by mouth and placebo film-coated tablets for upadacitinib once a day by mouth for 48 weeks in Study M19-130. Participants received elsubrutinib 60 mg capsules once a day by mouth and upadacitinib 30 mg film-coated tablets once a day in the current study (M20-186) for up to 56 weeks.

|                       |                              |
|-----------------------|------------------------------|
| Reporting group title | ABBV-599 Low -> ABBV-599 Low |
|-----------------------|------------------------------|

Reporting group description:

Participants received elsubrutinib 60 mg capsules once a day by mouth and upadacitinib 15 mg filmcoated tablets once a day by mouth for 48 weeks in Study M19-130. Participants continued on this regimen in the current study (M20-186) for up to 56 weeks.

|                       |  |
|-----------------------|--|
| Reporting group title | Els 60 mg/Upa Pbo -> Els 60 mg/Upa Pbo |
|-----------------------|--|

Reporting group description:

Participants received elsubrutinib 60 mg capsules once a day by mouth and placebo film-coated tablets for upadacitinib once a day by mouth for 48 weeks in Study M19-130. Participants continued on this regimen in the current study (M20-186) for up to 56 weeks.

|                       |                               |
|-----------------------|-------------------------------|
| Reporting group title | Els + Upa Pbo -> ABBV-599 Low |
|-----------------------|-------------------------------|

Reporting group description:

Participants received placebo capsules for elsubrutinib once a day by mouth and placebo film-coated tablets for upadacitinib once a day by mouth for 48 weeks in Study M19-130. Participants received elsubrutinib 60 mg capsules once a day by mouth and upadacitinib 15 mg film-coated tablets once a day by mouth for 48 weeks in the current study (M20-186) for up to 56 weeks.

| Serious adverse events                            | ABBV-599 High Dose -> ABBV-599 High Dose | Els Pbo/Upa 30 mg -> Els Pbo/Upa 30 mg | Els Pbo/Upa Pbo -> ABBV-599 High Dose |
|---|--|--|---------------------------------------|
| Total subjects affected by serious adverse events |  |  |                                       |
| subjects affected / exposed                       | 5 / 45 (11.11%)                          | 5 / 47 (10.64%)                        | 1 / 35 (2.86%)                        |

|   |                |                |                |
|---|----------------|----------------|----------------|
| number of deaths (all causes)                                       | 0              | 0              | 0              |
| number of deaths resulting from adverse events                      | 0              | 0              | 0              |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                |                |                |
| UTERINE LEIOMYOMA   |                |                |                |
| subjects affected / exposed   | 0 / 45 (0.00%) | 0 / 47 (0.00%) | 0 / 35 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          | 0 / 0          |
| Injury, poisoning and procedural complications                      |                |                |                |
| FRACTURED SACRUM  |                |                |                |
| subjects affected / exposed   | 1 / 45 (2.22%) | 0 / 47 (0.00%) | 0 / 35 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          | 0 / 0          |
| JOINT DISLOCATION   |                |                |                |
| subjects affected / exposed   | 0 / 45 (0.00%) | 1 / 47 (2.13%) | 0 / 35 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          | 0 / 0          |
| LUMBAR VERTEBRAL FRACTURE   |                |                |                |
| subjects affected / exposed   | 1 / 45 (2.22%) | 0 / 47 (0.00%) | 0 / 35 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          | 0 / 0          |
| PELVIC FRACTURE   |                |                |                |
| subjects affected / exposed   | 1 / 45 (2.22%) | 0 / 47 (0.00%) | 0 / 35 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          | 0 / 0          |
| SUBDURAL HAEMATOMA  |                |                |                |
| subjects affected / exposed   | 0 / 45 (0.00%) | 0 / 47 (0.00%) | 0 / 35 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          | 0 / 0          |
| SKULL FRACTURED BASE  |                |                |                |
| subjects affected / exposed   | 0 / 45 (0.00%) | 0 / 47 (0.00%) | 0 / 35 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          | 0 / 0          |
| TRAUMATIC INTRACRANIAL HAEMORRHAGE                                  |                |                |                |

|  |                |                |                |
|--|----------------|----------------|----------------|
| subjects affected / exposed                          | 0 / 45 (0.00%) | 0 / 47 (0.00%) | 0 / 35 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Surgical and medical procedures                      |                |                |                |
| ABORTION INDUCED                                     |                |                |                |
| subjects affected / exposed                          | 1 / 45 (2.22%) | 0 / 47 (0.00%) | 0 / 35 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Nervous system disorders                             |                |                |                |
| CEREBRAL HAEMATOMA                                   |                |                |                |
| subjects affected / exposed                          | 0 / 45 (0.00%) | 0 / 47 (0.00%) | 0 / 35 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| NERVOUS SYSTEM DISORDER                              |                |                |                |
| subjects affected / exposed                          | 0 / 45 (0.00%) | 0 / 47 (0.00%) | 0 / 35 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| LUMBAR RADICULOPATHY                                 |                |                |                |
| subjects affected / exposed                          | 0 / 45 (0.00%) | 0 / 47 (0.00%) | 1 / 35 (2.86%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| MIGRAINE   |                |                |                |
| subjects affected / exposed                          | 1 / 45 (2.22%) | 0 / 47 (0.00%) | 0 / 35 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| General disorders and administration site conditions |                |                |                |
| SEROITIS   |                |                |                |
| subjects affected / exposed                          | 0 / 45 (0.00%) | 1 / 47 (2.13%) | 0 / 35 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| OEDEMA PERIPHERAL                                    |                |                |                |
| subjects affected / exposed                          | 1 / 45 (2.22%) | 0 / 47 (0.00%) | 0 / 35 (0.00%) |
| occurrences causally related to treatment / all      | 1 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |

|  |                |                |                |
|--|----------------|----------------|----------------|
| Gastrointestinal disorders                         |                |                |                |
| UPPER GASTROINTESTINAL<br>HAEMORRHAGE              |                |                |                |
| subjects affected / exposed                        | 1 / 45 (2.22%) | 0 / 47 (0.00%) | 0 / 35 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Reproductive system and breast<br>disorders        |                |                |                |
| CERVICAL DYSPLASIA                                 |                |                |                |
| subjects affected / exposed                        | 0 / 45 (0.00%) | 1 / 47 (2.13%) | 0 / 35 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 0          | 1 / 1          | 0 / 0          |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Musculoskeletal and connective tissue<br>disorders |                |                |                |
| SYSTEMIC LUPUS ERYTHEMATOSUS                       |                |                |                |
| subjects affected / exposed                        | 0 / 45 (0.00%) | 0 / 47 (0.00%) | 0 / 35 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Infections and infestations                        |                |                |                |
| ABSCESS LIMB                                       |                |                |                |
| subjects affected / exposed                        | 0 / 45 (0.00%) | 1 / 47 (2.13%) | 0 / 35 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 0          | 1 / 1          | 0 / 0          |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| COVID-19   |                |                |                |
| subjects affected / exposed                        | 1 / 45 (2.22%) | 1 / 47 (2.13%) | 0 / 35 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 1          | 0 / 1          | 0 / 0          |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| ESCHERICHIA SEPSIS                                 |                |                |                |
| subjects affected / exposed                        | 0 / 45 (0.00%) | 1 / 47 (2.13%) | 0 / 35 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| GASTROENTERITIS                                    |                |                |                |
| subjects affected / exposed                        | 0 / 45 (0.00%) | 0 / 47 (0.00%) | 0 / 35 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| TONSILLITIS  |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 45 (0.00%) | 1 / 47 (2.13%) | 0 / 35 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Metabolism and nutrition disorders              |                |                |                |
| HYPOGLYCAEMIA                                   |                |                |                |
| subjects affected / exposed                     | 0 / 45 (0.00%) | 0 / 47 (0.00%) | 0 / 35 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

| <b>Serious adverse events</b>                                       | ABBV-599 Low -><br>ABBV-599 Low | Els 60 mg/Upa Pbo -<br>> Els 60 mg/Upa<br>Pbo | Els + Upa Pbo -><br>ABBV-599 Low |
|---|---------------------------------|---|----------------------------------|
| Total subjects affected by serious adverse events                   |                                 |   |                                  |
| subjects affected / exposed   | 2 / 19 (10.53%)                 | 1 / 25 (4.00%)                                | 2 / 14 (14.29%)                  |
| number of deaths (all causes)                                       | 0                               | 0   | 0                                |
| number of deaths resulting from adverse events                      | 0                               | 0   | 0                                |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                 |   |                                  |
| UTERINE LEIOMYOMA   |                                 |   |                                  |
| subjects affected / exposed   | 0 / 19 (0.00%)                  | 0 / 25 (0.00%)                                | 1 / 14 (7.14%)                   |
| occurrences causally related to treatment / all                     | 0 / 0                           | 0 / 0   | 0 / 1                            |
| deaths causally related to treatment / all                          | 0 / 0                           | 0 / 0   | 0 / 0                            |
| Injury, poisoning and procedural complications                      |                                 |   |                                  |
| FRACTURED SACRUM  |                                 |   |                                  |
| subjects affected / exposed   | 0 / 19 (0.00%)                  | 0 / 25 (0.00%)                                | 0 / 14 (0.00%)                   |
| occurrences causally related to treatment / all                     | 0 / 0                           | 0 / 0   | 0 / 0                            |
| deaths causally related to treatment / all                          | 0 / 0                           | 0 / 0   | 0 / 0                            |
| JOINT DISLOCATION   |                                 |   |                                  |
| subjects affected / exposed   | 0 / 19 (0.00%)                  | 0 / 25 (0.00%)                                | 0 / 14 (0.00%)                   |
| occurrences causally related to treatment / all                     | 0 / 0                           | 0 / 0   | 0 / 0                            |
| deaths causally related to treatment / all                          | 0 / 0                           | 0 / 0   | 0 / 0                            |
| LUMBAR VERTEBRAL FRACTURE   |                                 |   |                                  |
| subjects affected / exposed   | 0 / 19 (0.00%)                  | 0 / 25 (0.00%)                                | 0 / 14 (0.00%)                   |
| occurrences causally related to treatment / all                     | 0 / 0                           | 0 / 0   | 0 / 0                            |
| deaths causally related to treatment / all                          | 0 / 0                           | 0 / 0   | 0 / 0                            |
| PELVIC FRACTURE   |                                 |   |                                  |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 19 (0.00%) | 0 / 25 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| SUBDURAL HAEMATOMA                              |                |                |                |
| subjects affected / exposed                     | 1 / 19 (5.26%) | 0 / 25 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| SKULL FRACTURED BASE                            |                |                |                |
| subjects affected / exposed                     | 1 / 19 (5.26%) | 0 / 25 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| TRAUMATIC INTRACRANIAL HAEMORRHAGE              |                |                |                |
| subjects affected / exposed                     | 1 / 19 (5.26%) | 0 / 25 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Surgical and medical procedures                 |                |                |                |
| ABORTION INDUCED                                |                |                |                |
| subjects affected / exposed                     | 0 / 19 (0.00%) | 0 / 25 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Nervous system disorders                        |                |                |                |
| CEREBRAL HAEMATOMA                              |                |                |                |
| subjects affected / exposed                     | 1 / 19 (5.26%) | 0 / 25 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| NERVOUS SYSTEM DISORDER                         |                |                |                |
| subjects affected / exposed                     | 1 / 19 (5.26%) | 0 / 25 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| LUMBAR RADICULOPATHY                            |                |                |                |
| subjects affected / exposed                     | 0 / 19 (0.00%) | 0 / 25 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

|  |                |                |                |
|--|----------------|----------------|----------------|
| MIGRAINE   |                |                |                |
| subjects affected / exposed                          | 0 / 19 (0.00%) | 0 / 25 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| General disorders and administration site conditions |                |                |                |
| SEROSITIS  |                |                |                |
| subjects affected / exposed                          | 0 / 19 (0.00%) | 0 / 25 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| OEDEMA PERIPHERAL                                    |                |                |                |
| subjects affected / exposed                          | 0 / 19 (0.00%) | 0 / 25 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastrointestinal disorders                           |                |                |                |
| UPPER GASTROINTESTINAL HAEMORRHAGE                   |                |                |                |
| subjects affected / exposed                          | 0 / 19 (0.00%) | 0 / 25 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Reproductive system and breast disorders             |                |                |                |
| CERVICAL DYSPLASIA                                   |                |                |                |
| subjects affected / exposed                          | 0 / 19 (0.00%) | 0 / 25 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Musculoskeletal and connective tissue disorders      |                |                |                |
| SYSTEMIC LUPUS ERYTHEMATOSUS                         |                |                |                |
| subjects affected / exposed                          | 0 / 19 (0.00%) | 0 / 25 (0.00%) | 1 / 14 (7.14%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Infections and infestations                          |                |                |                |
| ABSCESS LIMB   |                |                |                |
| subjects affected / exposed                          | 0 / 19 (0.00%) | 0 / 25 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| COVID-19   |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 19 (0.00%) | 0 / 25 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>ESCHERICHIA SEPSIS</b>                       |                |                |                |
| subjects affected / exposed                     | 0 / 19 (0.00%) | 0 / 25 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>GASTROENTERITIS</b>                          |                |                |                |
| subjects affected / exposed                     | 0 / 19 (0.00%) | 1 / 25 (4.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>TONSILLITIS</b>                              |                |                |                |
| subjects affected / exposed                     | 0 / 19 (0.00%) | 0 / 25 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Metabolism and nutrition disorders</b>       |                |                |                |
| <b>HYPOGLYCAEMIA</b>                            |                |                |                |
| subjects affected / exposed                     | 1 / 19 (5.26%) | 0 / 25 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

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

| <b>Non-serious adverse events</b>                     | ABBV-599 High Dose -> ABBV-599 High Dose | Els Pbo/Upa 30 mg -> Els Pbo/Upa 30 mg | Els Pbo/Upa Pbo -> ABBV-599 High Dose |
|---|--|--|---------------------------------------|
| Total subjects affected by non-serious adverse events |  |  |                                       |
| subjects affected / exposed                           | 24 / 45 (53.33%)                         | 18 / 47 (38.30%)                       | 30 / 35 (85.71%)                      |
| <b>Vascular disorders</b>                             |  |  |                                       |
| <b>HAEMATOMA</b>                                      |  |  |                                       |
| subjects affected / exposed                           | 0 / 45 (0.00%)                           | 1 / 47 (2.13%)                         | 0 / 35 (0.00%)                        |
| occurrences (all)                                     | 0  | 4                                      | 0                                     |
| <b>HYPERTENSION</b>                                   |  |  |                                       |
| subjects affected / exposed                           | 1 / 45 (2.22%)                           | 1 / 47 (2.13%)                         | 0 / 35 (0.00%)                        |
| occurrences (all)                                     | 1  | 1                                      | 0                                     |
| <b>HYPOTENSION</b>                                    |  |  |                                       |



|   |                     |                     |                     |
|---|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)        | 0 / 45 (0.00%)<br>0 | 0 / 47 (0.00%)<br>0 | 0 / 35 (0.00%)<br>0 |
| General disorders and administration<br>site conditions |                     |                     |                     |
| ASTHENIA  |                     |                     |                     |
| subjects affected / exposed<br>occurrences (all)        | 0 / 45 (0.00%)<br>0 | 0 / 47 (0.00%)<br>0 | 0 / 35 (0.00%)<br>0 |
| GRANULOMA   |                     |                     |                     |
| subjects affected / exposed<br>occurrences (all)        | 0 / 45 (0.00%)<br>0 | 0 / 47 (0.00%)<br>0 | 0 / 35 (0.00%)<br>0 |
| OEDEMA  |                     |                     |                     |
| subjects affected / exposed<br>occurrences (all)        | 0 / 45 (0.00%)<br>0 | 0 / 47 (0.00%)<br>0 | 0 / 35 (0.00%)<br>0 |
| INFLUENZA LIKE ILLNESS                                  |                     |                     |                     |
| subjects affected / exposed<br>occurrences (all)        | 0 / 45 (0.00%)<br>0 | 0 / 47 (0.00%)<br>0 | 0 / 35 (0.00%)<br>0 |
| PYREXIA   |                     |                     |                     |
| subjects affected / exposed<br>occurrences (all)        | 1 / 45 (2.22%)<br>2 | 1 / 47 (2.13%)<br>1 | 1 / 35 (2.86%)<br>1 |
| OEDEMA PERIPHERAL                                       |                     |                     |                     |
| subjects affected / exposed<br>occurrences (all)        | 0 / 45 (0.00%)<br>0 | 0 / 47 (0.00%)<br>0 | 0 / 35 (0.00%)<br>0 |
| Reproductive system and breast<br>disorders             |                     |                     |                     |
| HEAVY MENSTRUAL BLEEDING                                |                     |                     |                     |
| subjects affected / exposed<br>occurrences (all)        | 0 / 45 (0.00%)<br>0 | 0 / 47 (0.00%)<br>0 | 0 / 35 (0.00%)<br>0 |
| Respiratory, thoracic and mediastinal<br>disorders      |                     |                     |                     |
| DYSPNOEA  |                     |                     |                     |
| subjects affected / exposed<br>occurrences (all)        | 0 / 45 (0.00%)<br>0 | 1 / 47 (2.13%)<br>1 | 2 / 35 (5.71%)<br>2 |
| NASAL CONGESTION  |                     |                     |                     |
| subjects affected / exposed<br>occurrences (all)        | 0 / 45 (0.00%)<br>0 | 0 / 47 (0.00%)<br>0 | 0 / 35 (0.00%)<br>0 |
| HYPERSENSITIVITY PNEUMONITIS                            |                     |                     |                     |
| subjects affected / exposed<br>occurrences (all)        | 0 / 45 (0.00%)<br>0 | 0 / 47 (0.00%)<br>0 | 0 / 35 (0.00%)<br>0 |

|  |   |  |   |
|--|---|--|---|
| SINUS PAIN<br>subjects affected / exposed<br>occurrences (all)   | 0 / 45 (0.00%)<br>0   | 0 / 47 (0.00%)<br>0  | 0 / 35 (0.00%)<br>0   |
| Psychiatric disorders<br>INSOMNIA<br>subjects affected / exposed<br>occurrences (all)  | 0 / 45 (0.00%)<br>0   | 0 / 47 (0.00%)<br>0  | 1 / 35 (2.86%)<br>1   |
| Investigations<br>NEUTROPHIL COUNT DECREASED<br>subjects affected / exposed<br>occurrences (all)   | 1 / 45 (2.22%)<br>2   | 0 / 47 (0.00%)<br>0  | 1 / 35 (2.86%)<br>1   |
| Injury, poisoning and procedural complications<br>ANIMAL BITE<br>subjects affected / exposed<br>occurrences (all)<br><br>FALL<br>subjects affected / exposed<br>occurrences (all)<br><br>IMMUNISATION REACTION<br>subjects affected / exposed<br>occurrences (all)<br><br>LOWER LIMB FRACTURE<br>subjects affected / exposed<br>occurrences (all)<br><br>SKIN LACERATION<br>subjects affected / exposed<br>occurrences (all) | 0 / 45 (0.00%)<br>0<br><br>0 / 45 (0.00%)<br>0<br><br>0 / 45 (0.00%)<br>0<br><br>0 / 45 (0.00%)<br>0<br><br>0 / 45 (0.00%)<br>0 | 0 / 47 (0.00%)<br>0<br><br>0 / 47 (0.00%)<br>0<br><br>0 / 47 (0.00%)<br>0<br><br>0 / 47 (0.00%)<br>1 / 47 (2.13%)<br>2 | 2 / 35 (5.71%)<br>2<br><br>0 / 35 (0.00%)<br>0<br><br>0 / 35 (0.00%)<br>0<br><br>0 / 35 (0.00%)<br>0<br><br>0 / 35 (0.00%)<br>0 |
| Congenital, familial and genetic disorders<br>TYPE V HYPERLIPIDAEMIA<br>subjects affected / exposed<br>occurrences (all)<br><br>PYLORIC STENOSIS<br>subjects affected / exposed<br>occurrences (all)   | 0 / 45 (0.00%)<br>0<br><br>0 / 45 (0.00%)<br>0  | 0 / 47 (0.00%)<br>0<br><br>0 / 47 (0.00%)<br>0   | 0 / 35 (0.00%)<br>0<br><br>0 / 35 (0.00%)<br>0  |
| Cardiac disorders  |   |  |   |

|   |                     |                     |                     |
|---|---------------------|---------------------|---------------------|
| MITRAL VALVE INCOMPETENCE<br>subjects affected / exposed<br>occurrences (all) | 0 / 45 (0.00%)<br>0 | 0 / 47 (0.00%)<br>0 | 0 / 35 (0.00%)<br>0 |
| Nervous system disorders  |                     |                     |                     |
| MIGRAINE<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 45 (0.00%)<br>0 | 0 / 47 (0.00%)<br>0 | 3 / 35 (8.57%)<br>3 |
| HEADACHE<br>subjects affected / exposed<br>occurrences (all)                  | 2 / 45 (4.44%)<br>3 | 1 / 47 (2.13%)<br>1 | 2 / 35 (5.71%)<br>2 |
| DIZZINESS<br>subjects affected / exposed<br>occurrences (all)                 | 1 / 45 (2.22%)<br>1 | 0 / 47 (0.00%)<br>0 | 0 / 35 (0.00%)<br>0 |
| BRAIN OEDEMA<br>subjects affected / exposed<br>occurrences (all)              | 0 / 45 (0.00%)<br>0 | 0 / 47 (0.00%)<br>0 | 0 / 35 (0.00%)<br>0 |
| POST HERPETIC NEURALGIA<br>subjects affected / exposed<br>occurrences (all)   | 0 / 45 (0.00%)<br>0 | 0 / 47 (0.00%)<br>0 | 1 / 35 (2.86%)<br>1 |
| SYNCOPE<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 45 (0.00%)<br>0 | 0 / 47 (0.00%)<br>0 | 0 / 35 (0.00%)<br>0 |
| Blood and lymphatic system disorders  |                     |                     |                     |
| LEUKOCYTOSIS<br>subjects affected / exposed<br>occurrences (all)              | 0 / 45 (0.00%)<br>0 | 0 / 47 (0.00%)<br>0 | 0 / 35 (0.00%)<br>0 |
| ANAEMIA<br>subjects affected / exposed<br>occurrences (all)                   | 1 / 45 (2.22%)<br>1 | 0 / 47 (0.00%)<br>0 | 0 / 35 (0.00%)<br>0 |
| IRON DEFICIENCY ANAEMIA<br>subjects affected / exposed<br>occurrences (all)   | 0 / 45 (0.00%)<br>0 | 0 / 47 (0.00%)<br>0 | 0 / 35 (0.00%)<br>0 |
| THROMBOCYTOSIS<br>subjects affected / exposed<br>occurrences (all)            | 0 / 45 (0.00%)<br>0 | 0 / 47 (0.00%)<br>0 | 0 / 35 (0.00%)<br>0 |
| Eye disorders   |                     |                     |                     |

|  |                |                |                |
|--|----------------|----------------|----------------|
| CATARACT                               |                |                |                |
| subjects affected / exposed            | 0 / 45 (0.00%) | 0 / 47 (0.00%) | 1 / 35 (2.86%) |
| occurrences (all)                      | 0              | 0              | 1              |
| DRY EYE                                |                |                |                |
| subjects affected / exposed            | 0 / 45 (0.00%) | 0 / 47 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Gastrointestinal disorders             |                |                |                |
| ABDOMINAL PAIN                         |                |                |                |
| subjects affected / exposed            | 0 / 45 (0.00%) | 0 / 47 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| CONSTIPATION                           |                |                |                |
| subjects affected / exposed            | 0 / 45 (0.00%) | 0 / 47 (0.00%) | 2 / 35 (5.71%) |
| occurrences (all)                      | 0              | 0              | 2              |
| DUODENAL ULCER                         |                |                |                |
| subjects affected / exposed            | 0 / 45 (0.00%) | 0 / 47 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| GASTRITIS                              |                |                |                |
| subjects affected / exposed            | 1 / 45 (2.22%) | 0 / 47 (0.00%) | 1 / 35 (2.86%) |
| occurrences (all)                      | 1              | 0              | 1              |
| GASTROOESOPHAGEAL REFLUX DISEASE       |                |                |                |
| subjects affected / exposed            | 1 / 45 (2.22%) | 0 / 47 (0.00%) | 1 / 35 (2.86%) |
| occurrences (all)                      | 1              | 0              | 1              |
| IMPAIRED GASTRIC EMPTYING              |                |                |                |
| subjects affected / exposed            | 0 / 45 (0.00%) | 0 / 47 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| LARGE INTESTINAL ULCER                 |                |                |                |
| subjects affected / exposed            | 0 / 45 (0.00%) | 0 / 47 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| VOMITING                               |                |                |                |
| subjects affected / exposed            | 0 / 45 (0.00%) | 0 / 47 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| NAUSEA                                 |                |                |                |
| subjects affected / exposed            | 1 / 45 (2.22%) | 1 / 47 (2.13%) | 0 / 35 (0.00%) |
| occurrences (all)                      | 2              | 1              | 0              |
| Skin and subcutaneous tissue disorders |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| RASH  |                |                |                |
| subjects affected / exposed                     | 1 / 45 (2.22%) | 0 / 47 (0.00%) | 2 / 35 (5.71%) |
| occurrences (all)                               | 1              | 0              | 2              |
| PRURITUS  |                |                |                |
| subjects affected / exposed                     | 4 / 45 (8.89%) | 0 / 47 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all)                               | 5              | 0              | 0              |
| CUTANEOUS VASCULITIS                            |                |                |                |
| subjects affected / exposed                     | 0 / 45 (0.00%) | 0 / 47 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| ACNE  |                |                |                |
| subjects affected / exposed                     | 1 / 45 (2.22%) | 0 / 47 (0.00%) | 2 / 35 (5.71%) |
| occurrences (all)                               | 1              | 0              | 2              |
| SKIN ULCER                                      |                |                |                |
| subjects affected / exposed                     | 0 / 45 (0.00%) | 0 / 47 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Renal and urinary disorders                     |                |                |                |
| LUPUS NEPHRITIS                                 |                |                |                |
| subjects affected / exposed                     | 0 / 45 (0.00%) | 0 / 47 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| PROTEINURIA                                     |                |                |                |
| subjects affected / exposed                     | 1 / 45 (2.22%) | 0 / 47 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all)                               | 1              | 0              | 0              |
| Musculoskeletal and connective tissue disorders |                |                |                |
| BACK PAIN                                       |                |                |                |
| subjects affected / exposed                     | 0 / 45 (0.00%) | 1 / 47 (2.13%) | 0 / 35 (0.00%) |
| occurrences (all)                               | 0              | 1              | 0              |
| ARTHRALGIA                                      |                |                |                |
| subjects affected / exposed                     | 1 / 45 (2.22%) | 0 / 47 (0.00%) | 2 / 35 (5.71%) |
| occurrences (all)                               | 1              | 0              | 2              |
| CONNECTIVE TISSUE DISORDER                      |                |                |                |
| subjects affected / exposed                     | 0 / 45 (0.00%) | 0 / 47 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| MUSCLE SPASMS                                   |                |                |                |
| subjects affected / exposed                     | 0 / 45 (0.00%) | 0 / 47 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Infections and infestations                     |                |                |                |

|                              |                 |                  |                 |
|------------------------------|-----------------|------------------|-----------------|
| CELLULITIS                   |                 |                  |                 |
| subjects affected / exposed  | 0 / 45 (0.00%)  | 3 / 47 (6.38%)   | 0 / 35 (0.00%)  |
| occurrences (all)            | 0               | 6                | 0               |
| COVID-19                     |                 |                  |                 |
| subjects affected / exposed  | 8 / 45 (17.78%) | 11 / 47 (23.40%) | 7 / 35 (20.00%) |
| occurrences (all)            | 8               | 11               | 7               |
| DIVERTICULITIS               |                 |                  |                 |
| subjects affected / exposed  | 0 / 45 (0.00%)  | 0 / 47 (0.00%)   | 0 / 35 (0.00%)  |
| occurrences (all)            | 0               | 0                | 0               |
| EAR INFECTION                |                 |                  |                 |
| subjects affected / exposed  | 0 / 45 (0.00%)  | 0 / 47 (0.00%)   | 0 / 35 (0.00%)  |
| occurrences (all)            | 0               | 0                | 0               |
| GASTROENTERITIS              |                 |                  |                 |
| subjects affected / exposed  | 1 / 45 (2.22%)  | 0 / 47 (0.00%)   | 2 / 35 (5.71%)  |
| occurrences (all)            | 1               | 0                | 2               |
| EPSTEIN-BARR VIRUS INFECTION |                 |                  |                 |
| subjects affected / exposed  | 0 / 45 (0.00%)  | 0 / 47 (0.00%)   | 0 / 35 (0.00%)  |
| occurrences (all)            | 0               | 0                | 0               |
| HERPES ZOSTER                |                 |                  |                 |
| subjects affected / exposed  | 2 / 45 (4.44%)  | 1 / 47 (2.13%)   | 1 / 35 (2.86%)  |
| occurrences (all)            | 2               | 1                | 1               |
| ORAL HERPES                  |                 |                  |                 |
| subjects affected / exposed  | 2 / 45 (4.44%)  | 2 / 47 (4.26%)   | 2 / 35 (5.71%)  |
| occurrences (all)            | 2               | 2                | 2               |
| NASOPHARYNGITIS              |                 |                  |                 |
| subjects affected / exposed  | 3 / 45 (6.67%)  | 2 / 47 (4.26%)   | 2 / 35 (5.71%)  |
| occurrences (all)            | 4               | 2                | 2               |
| MYCOPLASMA INFECTION         |                 |                  |                 |
| subjects affected / exposed  | 1 / 45 (2.22%)  | 0 / 47 (0.00%)   | 0 / 35 (0.00%)  |
| occurrences (all)            | 1               | 0                | 0               |
| OTITIS MEDIA                 |                 |                  |                 |
| subjects affected / exposed  | 0 / 45 (0.00%)  | 1 / 47 (2.13%)   | 1 / 35 (2.86%)  |
| occurrences (all)            | 0               | 2                | 1               |
| TINEA PEDIS                  |                 |                  |                 |
| subjects affected / exposed  | 0 / 45 (0.00%)  | 0 / 47 (0.00%)   | 2 / 35 (5.71%)  |
| occurrences (all)            | 0               | 0                | 3               |

|                                    |                 |                |                 |
|------------------------------------|-----------------|----------------|-----------------|
| TINEA VERSICOLOUR                  |                 |                |                 |
| subjects affected / exposed        | 0 / 45 (0.00%)  | 0 / 47 (0.00%) | 0 / 35 (0.00%)  |
| occurrences (all)                  | 0               | 0              | 0               |
| SINUSITIS                          |                 |                |                 |
| subjects affected / exposed        | 0 / 45 (0.00%)  | 0 / 47 (0.00%) | 0 / 35 (0.00%)  |
| occurrences (all)                  | 0               | 0              | 0               |
| TONSILLITIS                        |                 |                |                 |
| subjects affected / exposed        | 0 / 45 (0.00%)  | 0 / 47 (0.00%) | 0 / 35 (0.00%)  |
| occurrences (all)                  | 0               | 0              | 0               |
| UPPER RESPIRATORY TRACT INFECTION  |                 |                |                 |
| subjects affected / exposed        | 4 / 45 (8.89%)  | 3 / 47 (6.38%) | 6 / 35 (17.14%) |
| occurrences (all)                  | 5               | 4              | 7               |
| URINARY TRACT INFECTION            |                 |                |                 |
| subjects affected / exposed        | 7 / 45 (15.56%) | 3 / 47 (6.38%) | 6 / 35 (17.14%) |
| occurrences (all)                  | 9               | 7              | 8               |
| VAGINAL INFECTION                  |                 |                |                 |
| subjects affected / exposed        | 0 / 45 (0.00%)  | 0 / 47 (0.00%) | 0 / 35 (0.00%)  |
| occurrences (all)                  | 0               | 0              | 0               |
| Metabolism and nutrition disorders |                 |                |                 |
| HYPOCALCAEMIA                      |                 |                |                 |
| subjects affected / exposed        | 0 / 45 (0.00%)  | 0 / 47 (0.00%) | 0 / 35 (0.00%)  |
| occurrences (all)                  | 0               | 0              | 0               |
| TYPE 2 DIABETES MELLITUS           |                 |                |                 |
| subjects affected / exposed        | 0 / 45 (0.00%)  | 0 / 47 (0.00%) | 0 / 35 (0.00%)  |
| occurrences (all)                  | 0               | 0              | 0               |
| HYPONATRAEMIA                      |                 |                |                 |
| subjects affected / exposed        | 0 / 45 (0.00%)  | 0 / 47 (0.00%) | 0 / 35 (0.00%)  |
| occurrences (all)                  | 0               | 0              | 0               |
| HYPOMAGNESAEMIA                    |                 |                |                 |
| subjects affected / exposed        | 0 / 45 (0.00%)  | 0 / 47 (0.00%) | 0 / 35 (0.00%)  |
| occurrences (all)                  | 0               | 0              | 0               |
| HYPOKALAEMIA                       |                 |                |                 |
| subjects affected / exposed        | 0 / 45 (0.00%)  | 0 / 47 (0.00%) | 0 / 35 (0.00%)  |
| occurrences (all)                  | 0               | 0              | 0               |

|                                   |                              |                                    |                               |
|-----------------------------------|------------------------------|------------------------------------|-------------------------------|
| <b>Non-serious adverse events</b> | ABBV-599 Low -> ABBV-599 Low | Els 60 mg/Upa Pbo -> Els 60 mg/Upa | Els + Upa Pbo -> ABBV-599 Low |
|-----------------------------------|------------------------------|------------------------------------|-------------------------------|

|   |                  | Pbo             |                 |
|---|------------------|-----------------|-----------------|
| Total subjects affected by non-serious adverse events |                  |                 |                 |
| subjects affected / exposed                           | 11 / 19 (57.89%) | 4 / 25 (16.00%) | 6 / 14 (42.86%) |
| Vascular disorders                                    |                  |                 |                 |
| HAEMATOMA   |                  |                 |                 |
| subjects affected / exposed                           | 1 / 19 (5.26%)   | 0 / 25 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)                                     | 1                | 0               | 0               |
| HYPERTENSION  |                  |                 |                 |
| subjects affected / exposed                           | 2 / 19 (10.53%)  | 0 / 25 (0.00%)  | 1 / 14 (7.14%)  |
| occurrences (all)                                     | 2                | 0               | 1               |
| HYPOTENSION   |                  |                 |                 |
| subjects affected / exposed                           | 1 / 19 (5.26%)   | 0 / 25 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)                                     | 1                | 0               | 0               |
| General disorders and administration site conditions  |                  |                 |                 |
| ASTHENIA  |                  |                 |                 |
| subjects affected / exposed                           | 1 / 19 (5.26%)   | 0 / 25 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)                                     | 1                | 0               | 0               |
| GRANULOMA   |                  |                 |                 |
| subjects affected / exposed                           | 1 / 19 (5.26%)   | 0 / 25 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)                                     | 1                | 0               | 0               |
| OEDEMA  |                  |                 |                 |
| subjects affected / exposed                           | 0 / 19 (0.00%)   | 0 / 25 (0.00%)  | 1 / 14 (7.14%)  |
| occurrences (all)                                     | 0                | 0               | 1               |
| INFLUENZA LIKE ILLNESS                                |                  |                 |                 |
| subjects affected / exposed                           | 1 / 19 (5.26%)   | 0 / 25 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)                                     | 1                | 0               | 0               |
| PYREXIA   |                  |                 |                 |
| subjects affected / exposed                           | 1 / 19 (5.26%)   | 0 / 25 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)                                     | 1                | 0               | 0               |
| OEDEMA PERIPHERAL                                     |                  |                 |                 |
| subjects affected / exposed                           | 1 / 19 (5.26%)   | 1 / 25 (4.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)                                     | 1                | 1               | 0               |
| Reproductive system and breast disorders              |                  |                 |                 |
| HEAVY MENSTRUAL BLEEDING                              |                  |                 |                 |
| subjects affected / exposed                           | 0 / 19 (0.00%)   | 0 / 25 (0.00%)  | 1 / 14 (7.14%)  |
| occurrences (all)                                     | 0                | 0               | 1               |



|   |                |                |                |
|---|----------------|----------------|----------------|
| Respiratory, thoracic and mediastinal disorders |                |                |                |
| DYSпноEA  |                |                |                |
| subjects affected / exposed                     | 0 / 19 (0.00%) | 0 / 25 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| NASAL CONGESTION                                |                |                |                |
| subjects affected / exposed                     | 1 / 19 (5.26%) | 0 / 25 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all)                               | 1              | 0              | 0              |
| HYPERSENSITIVITY PNEUMONITIS                    |                |                |                |
| subjects affected / exposed                     | 0 / 19 (0.00%) | 0 / 25 (0.00%) | 1 / 14 (7.14%) |
| occurrences (all)                               | 0              | 0              | 1              |
| SINUS PAIN                                      |                |                |                |
| subjects affected / exposed                     | 1 / 19 (5.26%) | 0 / 25 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all)                               | 1              | 0              | 0              |
| Psychiatric disorders                           |                |                |                |
| INSOMNIA  |                |                |                |
| subjects affected / exposed                     | 1 / 19 (5.26%) | 0 / 25 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all)                               | 1              | 0              | 0              |
| Investigations                                  |                |                |                |
| NEUTROPHIL COUNT DECREASED                      |                |                |                |
| subjects affected / exposed                     | 1 / 19 (5.26%) | 0 / 25 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all)                               | 1              | 0              | 0              |
| Injury, poisoning and procedural complications  |                |                |                |
| ANIMAL BITE                                     |                |                |                |
| subjects affected / exposed                     | 0 / 19 (0.00%) | 0 / 25 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| FALL  |                |                |                |
| subjects affected / exposed                     | 1 / 19 (5.26%) | 0 / 25 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all)                               | 2              | 0              | 0              |
| IMMUNISATION REACTION                           |                |                |                |
| subjects affected / exposed                     | 0 / 19 (0.00%) | 0 / 25 (0.00%) | 1 / 14 (7.14%) |
| occurrences (all)                               | 0              | 0              | 1              |
| LOWER LIMB FRACTURE                             |                |                |                |
| subjects affected / exposed                     | 1 / 19 (5.26%) | 0 / 25 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all)                               | 1              | 0              | 0              |
| SKIN LACERATION                                 |                |                |                |

|  |                     |                     |                     |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)   | 1 / 19 (5.26%)<br>2 | 0 / 25 (0.00%)<br>0 | 0 / 14 (0.00%)<br>0 |
| Congenital, familial and genetic disorders<br>TYPE V HYPERLIPIDAEMIA<br>subjects affected / exposed<br>occurrences (all) | 1 / 19 (5.26%)<br>1 | 0 / 25 (0.00%)<br>0 | 0 / 14 (0.00%)<br>0 |
| PYLORIC STENOSIS<br>subjects affected / exposed<br>occurrences (all)   | 1 / 19 (5.26%)<br>1 | 0 / 25 (0.00%)<br>0 | 0 / 14 (0.00%)<br>0 |
| Cardiac disorders<br>MITRAL VALVE INCOMPETENCE<br>subjects affected / exposed<br>occurrences (all)                       | 1 / 19 (5.26%)<br>1 | 0 / 25 (0.00%)<br>0 | 0 / 14 (0.00%)<br>0 |
| Nervous system disorders<br>MIGRAINE<br>subjects affected / exposed<br>occurrences (all)                                 | 0 / 19 (0.00%)<br>0 | 0 / 25 (0.00%)<br>0 | 0 / 14 (0.00%)<br>0 |
| HEADACHE<br>subjects affected / exposed<br>occurrences (all)   | 1 / 19 (5.26%)<br>1 | 0 / 25 (0.00%)<br>0 | 0 / 14 (0.00%)<br>0 |
| DIZZINESS<br>subjects affected / exposed<br>occurrences (all)  | 1 / 19 (5.26%)<br>1 | 0 / 25 (0.00%)<br>0 | 0 / 14 (0.00%)<br>0 |
| BRAIN OEDEMA<br>subjects affected / exposed<br>occurrences (all)   | 1 / 19 (5.26%)<br>1 | 0 / 25 (0.00%)<br>0 | 0 / 14 (0.00%)<br>0 |
| POST HERPETIC NEURALGIA<br>subjects affected / exposed<br>occurrences (all)  | 0 / 19 (0.00%)<br>0 | 0 / 25 (0.00%)<br>0 | 1 / 14 (7.14%)<br>1 |
| SYNCOPE<br>subjects affected / exposed<br>occurrences (all)  | 1 / 19 (5.26%)<br>1 | 0 / 25 (0.00%)<br>0 | 0 / 14 (0.00%)<br>0 |
| Blood and lymphatic system disorders<br>LEUKOCYTOSIS<br>subjects affected / exposed<br>occurrences (all)                 | 1 / 19 (5.26%)<br>1 | 0 / 25 (0.00%)<br>0 | 0 / 14 (0.00%)<br>0 |

|                                  |                |                |                |
|----------------------------------|----------------|----------------|----------------|
| ANAEMIA                          |                |                |                |
| subjects affected / exposed      | 0 / 19 (0.00%) | 0 / 25 (0.00%) | 1 / 14 (7.14%) |
| occurrences (all)                | 0              | 0              | 1              |
| IRON DEFICIENCY ANAEMIA          |                |                |                |
| subjects affected / exposed      | 1 / 19 (5.26%) | 0 / 25 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all)                | 1              | 0              | 0              |
| THROMBOCYTOSIS                   |                |                |                |
| subjects affected / exposed      | 1 / 19 (5.26%) | 0 / 25 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all)                | 1              | 0              | 0              |
| Eye disorders                    |                |                |                |
| CATARACT                         |                |                |                |
| subjects affected / exposed      | 1 / 19 (5.26%) | 0 / 25 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all)                | 1              | 0              | 0              |
| DRY EYE                          |                |                |                |
| subjects affected / exposed      | 0 / 19 (0.00%) | 0 / 25 (0.00%) | 1 / 14 (7.14%) |
| occurrences (all)                | 0              | 0              | 1              |
| Gastrointestinal disorders       |                |                |                |
| ABDOMINAL PAIN                   |                |                |                |
| subjects affected / exposed      | 1 / 19 (5.26%) | 0 / 25 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all)                | 1              | 0              | 0              |
| CONSTIPATION                     |                |                |                |
| subjects affected / exposed      | 0 / 19 (0.00%) | 0 / 25 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all)                | 0              | 0              | 0              |
| DUODENAL ULCER                   |                |                |                |
| subjects affected / exposed      | 1 / 19 (5.26%) | 0 / 25 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all)                | 1              | 0              | 0              |
| GASTRITIS                        |                |                |                |
| subjects affected / exposed      | 0 / 19 (0.00%) | 0 / 25 (0.00%) | 1 / 14 (7.14%) |
| occurrences (all)                | 0              | 0              | 1              |
| GASTROOESOPHAGEAL REFLUX DISEASE |                |                |                |
| subjects affected / exposed      | 0 / 19 (0.00%) | 0 / 25 (0.00%) | 1 / 14 (7.14%) |
| occurrences (all)                | 0              | 0              | 1              |
| IMPAIRED GASTRIC EMPTYING        |                |                |                |
| subjects affected / exposed      | 1 / 19 (5.26%) | 0 / 25 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all)                | 1              | 0              | 0              |
| LARGE INTESTINAL ULCER           |                |                |                |

|  |                     |                     |                     |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)   | 0 / 19 (0.00%)<br>0 | 0 / 25 (0.00%)<br>0 | 1 / 14 (7.14%)<br>1 |
| VOMITING<br>subjects affected / exposed<br>occurrences (all)   | 1 / 19 (5.26%)<br>1 | 0 / 25 (0.00%)<br>0 | 0 / 14 (0.00%)<br>0 |
| NAUSEA<br>subjects affected / exposed<br>occurrences (all)   | 1 / 19 (5.26%)<br>1 | 0 / 25 (0.00%)<br>0 | 1 / 14 (7.14%)<br>1 |
| Skin and subcutaneous tissue disorders<br>RASH<br>subjects affected / exposed<br>occurrences (all)               | 1 / 19 (5.26%)<br>1 | 0 / 25 (0.00%)<br>0 | 0 / 14 (0.00%)<br>0 |
| PRURITUS<br>subjects affected / exposed<br>occurrences (all)   | 0 / 19 (0.00%)<br>0 | 0 / 25 (0.00%)<br>0 | 0 / 14 (0.00%)<br>0 |
| CUTANEOUS VASCULITIS<br>subjects affected / exposed<br>occurrences (all)   | 1 / 19 (5.26%)<br>1 | 0 / 25 (0.00%)<br>0 | 0 / 14 (0.00%)<br>0 |
| ACNE<br>subjects affected / exposed<br>occurrences (all)   | 0 / 19 (0.00%)<br>0 | 0 / 25 (0.00%)<br>0 | 0 / 14 (0.00%)<br>0 |
| SKIN ULCER<br>subjects affected / exposed<br>occurrences (all)   | 1 / 19 (5.26%)<br>1 | 0 / 25 (0.00%)<br>0 | 0 / 14 (0.00%)<br>0 |
| Renal and urinary disorders<br>LUPUS NEPHRITIS<br>subjects affected / exposed<br>occurrences (all)               | 1 / 19 (5.26%)<br>1 | 0 / 25 (0.00%)<br>0 | 0 / 14 (0.00%)<br>0 |
| PROTEINURIA<br>subjects affected / exposed<br>occurrences (all)  | 1 / 19 (5.26%)<br>1 | 0 / 25 (0.00%)<br>0 | 0 / 14 (0.00%)<br>0 |
| Musculoskeletal and connective tissue disorders<br>BACK PAIN<br>subjects affected / exposed<br>occurrences (all) | 1 / 19 (5.26%)<br>1 | 0 / 25 (0.00%)<br>0 | 1 / 14 (7.14%)<br>1 |
| ARTHRALGIA   |                     |                     |                     |

|                              |                |                |                |
|------------------------------|----------------|----------------|----------------|
| subjects affected / exposed  | 0 / 19 (0.00%) | 0 / 25 (0.00%) | 1 / 14 (7.14%) |
| occurrences (all)            | 0              | 0              | 1              |
| CONNECTIVE TISSUE DISORDER   |                |                |                |
| subjects affected / exposed  | 0 / 19 (0.00%) | 0 / 25 (0.00%) | 1 / 14 (7.14%) |
| occurrences (all)            | 0              | 0              | 1              |
| MUSCLE SPASMS                |                |                |                |
| subjects affected / exposed  | 1 / 19 (5.26%) | 0 / 25 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all)            | 1              | 0              | 0              |
| Infections and infestations  |                |                |                |
| CELLULITIS                   |                |                |                |
| subjects affected / exposed  | 0 / 19 (0.00%) | 1 / 25 (4.00%) | 0 / 14 (0.00%) |
| occurrences (all)            | 0              | 1              | 0              |
| COVID-19                     |                |                |                |
| subjects affected / exposed  | 0 / 19 (0.00%) | 1 / 25 (4.00%) | 0 / 14 (0.00%) |
| occurrences (all)            | 0              | 1              | 0              |
| DIVERTICULITIS               |                |                |                |
| subjects affected / exposed  | 1 / 19 (5.26%) | 0 / 25 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all)            | 1              | 0              | 0              |
| EAR INFECTION                |                |                |                |
| subjects affected / exposed  | 0 / 19 (0.00%) | 1 / 25 (4.00%) | 1 / 14 (7.14%) |
| occurrences (all)            | 0              | 1              | 1              |
| GASTROENTERITIS              |                |                |                |
| subjects affected / exposed  | 0 / 19 (0.00%) | 0 / 25 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all)            | 0              | 0              | 0              |
| EPSTEIN-BARR VIRUS INFECTION |                |                |                |
| subjects affected / exposed  | 1 / 19 (5.26%) | 0 / 25 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all)            | 1              | 0              | 0              |
| HERPES ZOSTER                |                |                |                |
| subjects affected / exposed  | 0 / 19 (0.00%) | 0 / 25 (0.00%) | 1 / 14 (7.14%) |
| occurrences (all)            | 0              | 0              | 1              |
| ORAL HERPES                  |                |                |                |
| subjects affected / exposed  | 0 / 19 (0.00%) | 0 / 25 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all)            | 0              | 0              | 0              |
| NASOPHARYNGITIS              |                |                |                |
| subjects affected / exposed  | 0 / 19 (0.00%) | 0 / 25 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all)            | 0              | 0              | 0              |

|                                    |                 |                |                |
|------------------------------------|-----------------|----------------|----------------|
| MYCOPLASMA INFECTION               |                 |                |                |
| subjects affected / exposed        | 0 / 19 (0.00%)  | 0 / 25 (0.00%) | 1 / 14 (7.14%) |
| occurrences (all)                  | 0               | 0              | 1              |
| OTITIS MEDIA                       |                 |                |                |
| subjects affected / exposed        | 1 / 19 (5.26%)  | 0 / 25 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all)                  | 1               | 0              | 0              |
| TINEA PEDIS                        |                 |                |                |
| subjects affected / exposed        | 0 / 19 (0.00%)  | 0 / 25 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all)                  | 0               | 0              | 0              |
| TINEA VERSICOLOUR                  |                 |                |                |
| subjects affected / exposed        | 0 / 19 (0.00%)  | 0 / 25 (0.00%) | 1 / 14 (7.14%) |
| occurrences (all)                  | 0               | 0              | 1              |
| SINUSITIS                          |                 |                |                |
| subjects affected / exposed        | 1 / 19 (5.26%)  | 0 / 25 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all)                  | 1               | 0              | 0              |
| TONSILLITIS                        |                 |                |                |
| subjects affected / exposed        | 0 / 19 (0.00%)  | 0 / 25 (0.00%) | 1 / 14 (7.14%) |
| occurrences (all)                  | 0               | 0              | 1              |
| UPPER RESPIRATORY TRACT INFECTION  |                 |                |                |
| subjects affected / exposed        | 0 / 19 (0.00%)  | 1 / 25 (4.00%) | 0 / 14 (0.00%) |
| occurrences (all)                  | 0               | 1              | 0              |
| URINARY TRACT INFECTION            |                 |                |                |
| subjects affected / exposed        | 3 / 19 (15.79%) | 1 / 25 (4.00%) | 1 / 14 (7.14%) |
| occurrences (all)                  | 4               | 1              | 1              |
| VAGINAL INFECTION                  |                 |                |                |
| subjects affected / exposed        | 0 / 19 (0.00%)  | 0 / 25 (0.00%) | 1 / 14 (7.14%) |
| occurrences (all)                  | 0               | 0              | 1              |
| Metabolism and nutrition disorders |                 |                |                |
| HYPOCALCAEMIA                      |                 |                |                |
| subjects affected / exposed        | 1 / 19 (5.26%)  | 0 / 25 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all)                  | 1               | 0              | 0              |
| TYPE 2 DIABETES MELLITUS           |                 |                |                |
| subjects affected / exposed        | 1 / 19 (5.26%)  | 0 / 25 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all)                  | 1               | 0              | 0              |
| HYPONATRAEMIA                      |                 |                |                |

|                             |                 |                |                |
|-----------------------------|-----------------|----------------|----------------|
| subjects affected / exposed | 1 / 19 (5.26%)  | 0 / 25 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all)           | 1               | 0              | 0              |
| HYPOMAGNESAEMIA             |                 |                |                |
| subjects affected / exposed | 1 / 19 (5.26%)  | 0 / 25 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all)           | 1               | 0              | 0              |
| HYPOKALAEMIA                |                 |                |                |
| subjects affected / exposed | 2 / 19 (10.53%) | 0 / 25 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all)           | 2               | 0              | 0              |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date            | Amendment   |
|-----------------|---|
| 21 July 2020    | <p>Version 2.0/Amendment 1</p> <ul style="list-style-type: none"><li>• Revised the objectives to assess longer term safety, tolerability, and efficacy data</li><li>• Added a reassessment of treatment assignments based on Study M19-130 interim analysis</li><li>• Clarified eligibility criteria referring to active, chronic, or recurrent viral or bacterial infections</li><li>• Added leflunomide, cyclosporine and tacrolimus to list of permitted concomitant medications</li><li>• Added discontinuation criteria for subjects with serious infections and/or TB</li></ul>   |
| 28 October 2020 | <p>Version 3.0/Amendment 2</p> <ul style="list-style-type: none"><li>• Incorporated necessary protocol modifications to account for COVID-19 infections</li><li>• Added 2 additional efficacy endpoints: change in PhGA from M19-130 Baseline and change in PtGA from M19-130 Baseline</li><li>• Added the following as areas of safety interest: active TB; adjudicated GI perforations; and adjudicated embolic and thrombotic events (non- cardiac, non-CNS) including venous thromboembolic events defined as pulmonary embolism and deep vein thrombosis</li><li>• Removed the following from the list of areas of safety interest: increased serum creatinine and CPK elevation</li><li>• Added further clarification that Study M20-186 is primarily a study of longer-term safety and that efficacy outcomes are considered secondary</li></ul>   |
| 26 October 2021 | <p>Version 4.0/Amendment 3</p> <ul style="list-style-type: none"><li>• Treatment groups were clarified based on the completed Study M19-130 Interim Analysis</li><li>• Clarified that subjects will need to successfully complete 48 weeks of Study M19-130 on placebo or a group that is currently active after the planned Study M19-130 Interim Analysis and meet all eligibility criteria to be considered eligible to enroll into LTE Study M20-186</li><li>• Added the statement, "At the Sponsor's discretion, doses of study drug(s) selected for continuation in LTE Study M20-186 may be reassigned or discontinued at any time based on the outcome assessment of the Study M19-130 Interim Analysis."</li><li>• Added the statement, "If the study is partially terminated, a subject in a terminated group will be asked to return for a PD visit and to perform a 30-day follow-up phone call after the last dose of study drug."</li></ul> |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats



None reported