



## Clinical trial results:

### A Phase IIa, Randomised, Double Blind, Placebo Controlled, Parallel Group, Multicentre Study of an Anti OX40L Monoclonal Antibody (KY1005) in Moderate to Severe Atopic Dermatitis

#### Summary

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2018-002299-41  |
| Trial protocol           | GB DE ES        |
| Global end of trial date | 08 October 2020 |

#### Results information

|                                |                 |
|--------------------------------|-----------------|
| Result version number          | v1 (current)    |
| This version publication date  | 08 October 2021 |
| First version publication date | 08 October 2021 |

#### Trial information

##### Trial identification

|                       |             |
|-----------------------|-------------|
| Sponsor protocol code | KY1005-CT02 |
|-----------------------|-------------|

##### Additional study identifiers

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

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Kymab Limited   |
| Sponsor organisation address | The Bennet Building (B930), Babraham Research Campus, Cambridge, United Kingdom, CB22 3AT |
| Public contact               | Development Clinical Trial Desk, Kymab Limited, Clinicaltrial@kymab.com                   |
| Scientific contact           | Development Clinical Trial Desk, Kymab Limited, Clinicaltrial@kymab.com                   |

Notes:

#### Paediatric regulatory details

|  |    |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP)       | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

## Results analysis stage

|  |                  |
|--|------------------|
| Analysis stage                                       | Final            |
| Date of interim/final analysis                       | 15 December 2020 |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 08 October 2020  |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 08 October 2020  |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

To explore the efficacy and safety of KY1005 on the signs of atopic dermatitis (AD) using the Eczema Area and Severity Index (EASI) and the incidence of treatment-emergent adverse events (TEAEs).

Protection of trial subjects:

This study was conducted in accordance with the protocol, all applicable regulatory requirements, the International Council for Harmonisation (ICH) E6 guideline for Good Clinical Practice (GCP) and the general principles of the Declaration of Helsinki.

Written informed consent for the study was obtained from each patient by the Investigator or suitably qualified designee before any protocol-specific procedures were carried out. Written information (including patient information sheets, ICFs, adverts, general practitioner letters) was only discussed with or given to patients once the IEC approved the document in writing.

Patients provided written informed consent on an IEC-approved ICF. Patients were re-consented and ICFs were re-signed before implementation of each protocol amendment, where applicable. Each patient's ICF was also signed and dated by the person who conducted the informed consent discussion. Informed consent was documented in the patient's medical records. The patient was given a copy of the information sheet and their signed and dated consent form, and the original ICF was filed in the Investigator site file (ISF).

Background therapy: -

Evidence for comparator: -

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 13 December 2018 |
| Long term follow-up planned                               | No               |
| Independent data monitoring committee (IDMC) involvement? | Yes              |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                   |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Poland: 72        |
| Country: Number of subjects enrolled | Spain: 9          |
| Country: Number of subjects enrolled | United Kingdom: 3 |
| Country: Number of subjects enrolled | Germany: 5        |
| Worldwide total number of subjects   | 89                |
| EEA total number of subjects         | 86                |

Notes:

### Subjects enrolled per age group

|  |   |
|--|---|
| In utero                               | 0 |
| Preterm newborn - gestational age < 37 | 0 |

|  |    |
|--|----|
| wk                                       |    |
| 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)                     | 88 |
| From 65 to 84 years                      | 1  |
| 85 years and over                        | 0  |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Subjects were screened within 29 to 8 days prior to baseline.

### Period 1

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

### Arms

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

|                  |                 |
|------------------|-----------------|
| <b>Arm title</b> | Low dose KY1005 |
|------------------|-----------------|

Arm description: -

|  |                       |
|--|-----------------------|
| Arm type                               | Experimental          |
| Investigational medicinal product name | KY1005                |
| Investigational medicinal product code |                       |
| Other name                             |                       |
| Pharmaceutical forms                   | Solution for infusion |
| Routes of administration               | Infusion              |

Dosage and administration details:

Patients received a low loading dose of KY1005 on Day 1, followed by three maintenance doses at 50% of the loading dose at 28-day intervals on Days 29, 57 and 85.

|                  |                  |
|------------------|------------------|
| <b>Arm title</b> | High dose KY1005 |
|------------------|------------------|

Arm description: -

|  |                       |
|--|-----------------------|
| Arm type                               | Experimental          |
| Investigational medicinal product name | KY1005                |
| Investigational medicinal product code |                       |
| Other name                             |                       |
| Pharmaceutical forms                   | Solution for infusion |
| Routes of administration               | Infusion              |

Dosage and administration details:

Patients received a high loading dose of KY1005 on Day 1, followed by three maintenance doses at 50% of the loading dose at 28-day intervals on Days 29, 57 and 85.

|                  |         |
|------------------|---------|
| <b>Arm title</b> | Placebo |
|------------------|---------|

Arm description: -

|  |                       |
|--|-----------------------|
| Arm type                               | Placebo               |
| Investigational medicinal product name | Placebo               |
| Investigational medicinal product code |                       |
| Other name                             |                       |
| Pharmaceutical forms                   | Solution for infusion |
| Routes of administration               | Infusion              |

Dosage and administration details:

Patients received placebo on Day 1, followed by three further doses at 28-day intervals on Days 29, 57 and 85.

| <b>Number of subjects in period 1</b>  | Low dose KY1005 | High dose KY1005 | Placebo |
|--|-----------------|------------------|---------|
| Started                                | 29              | 30               | 30      |
| Completed                              | 20              | 22               | 17      |
| Not completed                          | 9               | 8                | 13      |
| Consent withdrawn by subject           | 6               | 5                | 3       |
| Adverse event, non-fatal               | -               | -                | 3       |
| Other                                  | 2               | 3                | 5       |
| Failure to meet randomisation criteria | 1               | -                | -       |
| Protocol deviation                     | -               | -                | 2       |

## Baseline characteristics

### Reporting groups

|                                |                  |
|--------------------------------|------------------|
| Reporting group title          | Low dose KY1005  |
| Reporting group description: - |                  |
| Reporting group title          | High dose KY1005 |
| Reporting group description: - |                  |
| Reporting group title          | Placebo          |
| Reporting group description: - |                  |

| Reporting group values                             | Low dose KY1005 | High dose KY1005 | Placebo |
|--|-----------------|------------------|---------|
| Number of subjects                                 | 29              | 30               | 30      |
| Age categorical                                    |                 |                  |         |
| Units: Subjects                                    |                 |                  |         |
| In utero   | 0               | 0                | 0       |
| Preterm newborn infants (gestational age < 37 wks) | 0               | 0                | 0       |
| Newborns (0-27 days)                               | 0               | 0                | 0       |
| Infants and toddlers (28 days-23 months)           | 0               | 0                | 0       |
| Children (2-11 years)                              | 0               | 0                | 0       |
| Adolescents (12-17 years)                          | 0               | 0                | 0       |
| Adults (18-64 years)                               | 28              | 30               | 30      |
| From 65-84 years                                   | 1               | 0                | 0       |
| 85 years and over                                  | 0               | 0                | 0       |
| Gender categorical                                 |                 |                  |         |
| Units: Subjects                                    |                 |                  |         |
| Female   | 13              | 14               | 11      |
| Male   | 16              | 16               | 19      |

| Reporting group values                             | Total |  |  |
|--|-------|--|--|
| Number of subjects                                 | 89    |  |  |
| Age categorical                                    |       |  |  |
| Units: Subjects                                    |       |  |  |
| In utero   | 0     |  |  |
| Preterm newborn infants (gestational age < 37 wks) | 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)                               | 88    |  |  |
| From 65-84 years                                   | 1     |  |  |
| 85 years and over                                  | 0     |  |  |
| Gender categorical                                 |       |  |  |
| Units: Subjects                                    |       |  |  |
| Female   | 38    |  |  |
| Male   | 51    |  |  |



## End points

### End points reporting groups

|                                |                  |
|--------------------------------|------------------|
| Reporting group title          | Low dose KY1005  |
| Reporting group description: - |                  |
| Reporting group title          | High dose KY1005 |
| Reporting group description: - |                  |
| Reporting group title          | Placebo          |
| Reporting group description: - |                  |

### Primary: Percentage change in EASI from Baseline to Day 113 (FAS)

|                          |  |
|--------------------------|--|
| End point title          | Percentage change in EASI from Baseline to Day 113 (FAS) |
| End point description:   |  |
| Full analysis set        |  |
| End point type           | Primary  |
| End point timeframe:     |  |
| From Baseline to Day 113 |  |

| End point values                             | Low dose KY1005           | High dose KY1005          | Placebo                   |  |
|--|---------------------------|---------------------------|---------------------------|--|
| Subject group type                           | Reporting group           | Reporting group           | Reporting group           |  |
| Number of subjects analysed                  | 27                        | 27                        | 24                        |  |
| Units: Percentage                            |                           |                           |                           |  |
| least squares mean (confidence interval 95%) | -80.12 (-95.55 to -64.68) | -69.97 (-85.04 to -54.90) | -49.37 (-66.02 to -32.72) |  |

### Statistical analyses

|   |                                |
|---|--------------------------------|
| Statistical analysis title              | Difference in LSM estimate     |
| Comparison groups                       | Low dose KY1005 v Placebo      |
| Number of subjects included in analysis | 51                             |
| Analysis specification                  | Pre-specified                  |
| Analysis type                           | superiority                    |
| P-value                                 | = 0.009                        |
| Method                                  | Mixed models analysis          |
| Parameter estimate                      | Mean difference (final values) |
| Point estimate                          | -30.75                         |
| Confidence interval                     |                                |
| level                                   | 95 %                           |
| sides                                   | 2-sided                        |
| lower limit                             | -53.43                         |
| upper limit                             | -8.06                          |
| Variability estimate                    | Standard error of the mean     |
| Dispersion value                        | 11.38                          |



|   |                                |
|---|--------------------------------|
| <b>Statistical analysis title</b>       | Difference in LSM estimate     |
| Comparison groups                       | Placebo v High dose KY1005     |
| Number of subjects included in analysis | 51                             |
| Analysis specification                  | Pre-specified                  |
| Analysis type                           | superiority                    |
| P-value                                 | = 0.072                        |
| Method                                  | Mixed models analysis          |
| Parameter estimate                      | Mean difference (final values) |
| Point estimate                          | -20.6                          |
| Confidence interval                     |                                |
| level                                   | 95 %                           |
| sides                                   | 2-sided                        |
| lower limit                             | -43.08                         |
| upper limit                             | 1.88                           |
| Variability estimate                    | Standard error of the mean     |
| Dispersion value                        | 11.27                          |

### Primary: Summary of TEAEs to Day 113

|                        |  |
|------------------------|--|
| End point title        | Summary of TEAEs to Day 113 <sup>[1]</sup> |
| End point description: |  |
| End point type         | Primary                                    |
| End point timeframe:   |  |
| To Day 113             |  |

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: Per protocol no statistical analyses were conducted on this end point.

| <b>End point values</b>                       | Low dose<br>KY1005 | High dose<br>KY1005 | Placebo         |  |
|---|--------------------|---------------------|-----------------|--|
| Subject group type                            | Reporting group    | Reporting group     | Reporting group |  |
| Number of subjects analysed                   | 29                 | 30                  | 29              |  |
| Units: Number of patients                     |                    |                     |                 |  |
| At least one TEAE                             | 18                 | 14                  | 20              |  |
| At least one related TEAE                     | 10                 | 6                   | 9               |  |
| At least one serious TEAE                     | 1                  | 0                   | 0               |  |
| At least one related serious TEAE             | 1                  | 0                   | 0               |  |
| At least one treatment-emergent AESI          | 0                  | 1                   | 0               |  |
| At least one related TEAE of special interest | 0                  | 0                   | 0               |  |

### Statistical analyses



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From first dose to Day 113

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 21.1 |
|--------------------|------|

### Reporting groups

|                       |                 |
|-----------------------|-----------------|
| Reporting group title | Low dose KY1005 |
|-----------------------|-----------------|

Reporting group description: -

|                       |                  |
|-----------------------|------------------|
| Reporting group title | High dose KY1005 |
|-----------------------|------------------|

Reporting group description: -

|                       |         |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description: -

| <b>Serious adverse events</b>                     | Low dose KY1005 | High dose KY1005 | Placebo        |
|---|-----------------|------------------|----------------|
| Total subjects affected by serious adverse events |                 |                  |                |
| subjects affected / exposed                       | 1 / 29 (3.45%)  | 0 / 30 (0.00%)   | 0 / 29 (0.00%) |
| number of deaths (all causes)                     | 0               | 0                | 0              |
| number of deaths resulting from adverse events    | 0               | 0                | 0              |
| Infections and infestations                       |                 |                  |                |
| Infected dermal cyst                              |                 |                  |                |
| subjects affected / exposed                       | 1 / 29 (3.45%)  | 0 / 30 (0.00%)   | 0 / 29 (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          |

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

| <b>Non-serious adverse events</b>                     | Low dose KY1005  | High dose KY1005 | Placebo          |
|---|------------------|------------------|------------------|
| Total subjects affected by non-serious adverse events |                  |                  |                  |
| subjects affected / exposed                           | 18 / 29 (62.07%) | 14 / 30 (46.67%) | 20 / 29 (68.97%) |
| Vascular disorders                                    |                  |                  |                  |
| Orthostatic hypotension                               |                  |                  |                  |
| subjects affected / exposed                           | 0 / 29 (0.00%)   | 1 / 30 (3.33%)   | 0 / 29 (0.00%)   |
| occurrences (all)                                     | 0                | 1                | 0                |
| Hypertension  |                  |                  |                  |

|   |                     |                     |                     |
|---|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)        | 1 / 29 (3.45%)<br>1 | 1 / 30 (3.33%)<br>1 | 0 / 29 (0.00%)<br>0 |
| General disorders and administration<br>site conditions |                     |                     |                     |
| Influenza like illness                                  |                     |                     |                     |
| subjects affected / exposed                             | 0 / 29 (0.00%)      | 2 / 30 (6.67%)      | 1 / 29 (3.45%)      |
| occurrences (all)                                       | 0                   | 3                   | 1                   |
| Pyrexia   |                     |                     |                     |
| subjects affected / exposed                             | 2 / 29 (6.90%)      | 0 / 30 (0.00%)      | 0 / 29 (0.00%)      |
| occurrences (all)                                       | 2                   | 0                   | 0                   |
| Asthenia  |                     |                     |                     |
| subjects affected / exposed                             | 0 / 29 (0.00%)      | 0 / 30 (0.00%)      | 1 / 29 (3.45%)      |
| occurrences (all)                                       | 0                   | 0                   | 1                   |
| Drug ineffective  |                     |                     |                     |
| subjects affected / exposed                             | 0 / 29 (0.00%)      | 0 / 30 (0.00%)      | 1 / 29 (3.45%)      |
| occurrences (all)                                       | 0                   | 0                   | 1                   |
| Malaise   |                     |                     |                     |
| subjects affected / exposed                             | 0 / 29 (0.00%)      | 0 / 30 (0.00%)      | 1 / 29 (3.45%)      |
| occurrences (all)                                       | 0                   | 0                   | 1                   |
| Immune system disorders                                 |                     |                     |                     |
| Food allergy  |                     |                     |                     |
| subjects affected / exposed                             | 0 / 29 (0.00%)      | 1 / 30 (3.33%)      | 0 / 29 (0.00%)      |
| occurrences (all)                                       | 0                   | 1                   | 0                   |
| Reproductive system and breast<br>disorders             |                     |                     |                     |
| Menometrorrhagia  |                     |                     |                     |
| subjects affected / exposed                             | 0 / 29 (0.00%)      | 0 / 30 (0.00%)      | 1 / 29 (3.45%)      |
| occurrences (all)                                       | 0                   | 0                   | 1                   |
| Menorrhagia   |                     |                     |                     |
| subjects affected / exposed                             | 0 / 29 (0.00%)      | 0 / 30 (0.00%)      | 1 / 29 (3.45%)      |
| occurrences (all)                                       | 0                   | 0                   | 1                   |
| Respiratory, thoracic and mediastinal<br>disorders      |                     |                     |                     |
| Asthma  |                     |                     |                     |
| subjects affected / exposed                             | 0 / 29 (0.00%)      | 1 / 30 (3.33%)      | 0 / 29 (0.00%)      |
| occurrences (all)                                       | 0                   | 1                   | 0                   |
| Cough   |                     |                     |                     |

|  |                     |                     |                     |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)   | 0 / 29 (0.00%)<br>0 | 1 / 30 (3.33%)<br>1 | 0 / 29 (0.00%)<br>0 |
| Rhinitis allergic<br>subjects affected / exposed<br>occurrences (all)                                    | 0 / 29 (0.00%)<br>0 | 1 / 30 (3.33%)<br>1 | 0 / 29 (0.00%)<br>0 |
| Oropharyngeal pain<br>subjects affected / exposed<br>occurrences (all)                                   | 0 / 29 (0.00%)<br>0 | 1 / 30 (3.33%)<br>1 | 1 / 29 (3.45%)<br>1 |
| Psychiatric disorders<br>Depressed mood<br>subjects affected / exposed<br>occurrences (all)              | 0 / 29 (0.00%)<br>0 | 0 / 30 (0.00%)<br>0 | 1 / 29 (3.45%)<br>1 |
| Insomnia<br>subjects affected / exposed<br>occurrences (all)   | 0 / 29 (0.00%)<br>0 | 1 / 30 (3.33%)<br>2 | 0 / 29 (0.00%)<br>0 |
| Mood altered<br>subjects affected / exposed<br>occurrences (all)   | 0 / 29 (0.00%)<br>0 | 0 / 30 (0.00%)<br>0 | 1 / 29 (3.45%)<br>1 |
| Investigations<br>Alanine aminotransferase increased<br>subjects affected / exposed<br>occurrences (all) | 1 / 29 (3.45%)<br>1 | 2 / 30 (6.67%)<br>2 | 1 / 29 (3.45%)<br>1 |
| Aspartate aminotransferase increased<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 29 (0.00%)<br>0 | 2 / 30 (6.67%)<br>2 | 0 / 29 (0.00%)<br>0 |
| Gamma-glutamyltransferase increased<br>subjects affected / exposed<br>occurrences (all)                  | 1 / 29 (3.45%)<br>1 | 0 / 30 (0.00%)<br>0 | 1 / 29 (3.45%)<br>1 |
| Blood creatine phosphokinase increased<br>subjects affected / exposed<br>occurrences (all)               | 1 / 29 (3.45%)<br>1 | 0 / 30 (0.00%)<br>0 | 0 / 29 (0.00%)<br>0 |
| Blood potassium increased<br>subjects affected / exposed<br>occurrences (all)                            | 0 / 29 (0.00%)<br>0 | 0 / 30 (0.00%)<br>0 | 1 / 29 (3.45%)<br>1 |
| Blood urine present  |                     |                     |                     |

|  |                |                 |                |
|--|----------------|-----------------|----------------|
| subjects affected / exposed                    | 1 / 29 (3.45%) | 0 / 30 (0.00%)  | 0 / 29 (0.00%) |
| occurrences (all)                              | 1              | 0               | 0              |
| Haematocrit increased                          |                |                 |                |
| subjects affected / exposed                    | 1 / 29 (3.45%) | 0 / 30 (0.00%)  | 0 / 29 (0.00%) |
| occurrences (all)                              | 1              | 0               | 0              |
| Hepatic enzyme increased                       |                |                 |                |
| subjects affected / exposed                    | 1 / 29 (3.45%) | 0 / 30 (0.00%)  | 0 / 29 (0.00%) |
| occurrences (all)                              | 1              | 0               | 0              |
| Red blood cells urine positive                 |                |                 |                |
| subjects affected / exposed                    | 1 / 29 (3.45%) | 0 / 30 (0.00%)  | 0 / 29 (0.00%) |
| occurrences (all)                              | 1              | 0               | 0              |
| Urine analysis abnormal                        |                |                 |                |
| subjects affected / exposed                    | 0 / 29 (0.00%) | 1 / 30 (3.33%)  | 0 / 29 (0.00%) |
| occurrences (all)                              | 0              | 1               | 0              |
| Weight decreased                               |                |                 |                |
| subjects affected / exposed                    | 0 / 29 (0.00%) | 0 / 30 (0.00%)  | 1 / 29 (3.45%) |
| occurrences (all)                              | 0              | 0               | 1              |
| Injury, poisoning and procedural complications |                |                 |                |
| Wound  |                |                 |                |
| subjects affected / exposed                    | 1 / 29 (3.45%) | 0 / 30 (0.00%)  | 0 / 29 (0.00%) |
| occurrences (all)                              | 1              | 0               | 0              |
| Nervous system disorders                       |                |                 |                |
| Headache                                       |                |                 |                |
| subjects affected / exposed                    | 0 / 29 (0.00%) | 3 / 30 (10.00%) | 1 / 29 (3.45%) |
| occurrences (all)                              | 0              | 12              | 2              |
| Formication                                    |                |                 |                |
| subjects affected / exposed                    | 1 / 29 (3.45%) | 0 / 30 (0.00%)  | 0 / 29 (0.00%) |
| occurrences (all)                              | 1              | 0               | 0              |
| Somnolence                                     |                |                 |                |
| subjects affected / exposed                    | 0 / 29 (0.00%) | 1 / 30 (3.33%)  | 0 / 29 (0.00%) |
| occurrences (all)                              | 0              | 1               | 0              |
| Blood and lymphatic system disorders           |                |                 |                |
| Iron deficiency anaemia                        |                |                 |                |
| subjects affected / exposed                    | 2 / 29 (6.90%) | 0 / 30 (0.00%)  | 0 / 29 (0.00%) |
| occurrences (all)                              | 2              | 0               | 0              |
| Ear and labyrinth disorders                    |                |                 |                |

|  |                     |                     |                     |
|--|---------------------|---------------------|---------------------|
| Vertigo<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 29 (0.00%)<br>0 | 0 / 30 (0.00%)<br>0 | 2 / 29 (6.90%)<br>2 |
| Ear pain<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 29 (0.00%)<br>0 | 0 / 30 (0.00%)<br>0 | 1 / 29 (3.45%)<br>1 |
| Eye disorders  |                     |                     |                     |
| Conjunctival haemorrhage<br>subjects affected / exposed<br>occurrences (all) | 0 / 29 (0.00%)<br>0 | 1 / 30 (3.33%)<br>1 | 0 / 29 (0.00%)<br>0 |
| Conjunctivitis allergic<br>subjects affected / exposed<br>occurrences (all)  | 0 / 29 (0.00%)<br>0 | 1 / 30 (3.33%)<br>1 | 0 / 29 (0.00%)<br>0 |
| Eyelid cyst<br>subjects affected / exposed<br>occurrences (all)              | 0 / 29 (0.00%)<br>0 | 1 / 30 (3.33%)<br>1 | 0 / 29 (0.00%)<br>0 |
| Ulcerative keratitis<br>subjects affected / exposed<br>occurrences (all)     | 0 / 29 (0.00%)<br>0 | 1 / 30 (3.33%)<br>1 | 0 / 29 (0.00%)<br>0 |
| Gastrointestinal disorders   |                     |                     |                     |
| Abdominal distension<br>subjects affected / exposed<br>occurrences (all)     | 0 / 29 (0.00%)<br>0 | 0 / 30 (0.00%)<br>0 | 1 / 29 (3.45%)<br>1 |
| Abdominal pain lower<br>subjects affected / exposed<br>occurrences (all)     | 0 / 29 (0.00%)<br>0 | 0 / 30 (0.00%)<br>0 | 1 / 29 (3.45%)<br>1 |
| Abdominal pain upper<br>subjects affected / exposed<br>occurrences (all)     | 0 / 29 (0.00%)<br>0 | 0 / 30 (0.00%)<br>0 | 1 / 29 (3.45%)<br>1 |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)                | 0 / 29 (0.00%)<br>0 | 1 / 30 (3.33%)<br>1 | 0 / 29 (0.00%)<br>0 |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 29 (0.00%)<br>0 | 0 / 30 (0.00%)<br>0 | 1 / 29 (3.45%)<br>1 |
| Skin and subcutaneous tissue disorders                                       |                     |                     |                     |

|  |                      |                      |                       |
|--|----------------------|----------------------|-----------------------|
| Dermatitis atopic<br>subjects affected / exposed<br>occurrences (all)                              | 3 / 29 (10.34%)<br>3 | 4 / 30 (13.33%)<br>5 | 9 / 29 (31.03%)<br>16 |
| Hyperhidrosis<br>subjects affected / exposed<br>occurrences (all)                                  | 0 / 29 (0.00%)<br>0  | 2 / 30 (6.67%)<br>2  | 0 / 29 (0.00%)<br>0   |
| Eczema<br>subjects affected / exposed<br>occurrences (all)   | 0 / 29 (0.00%)<br>0  | 0 / 30 (0.00%)<br>0  | 1 / 29 (3.45%)<br>3   |
| Erythema<br>subjects affected / exposed<br>occurrences (all)                                       | 0 / 29 (0.00%)<br>0  | 0 / 30 (0.00%)<br>0  | 1 / 29 (3.45%)<br>1   |
| Pain of skin<br>subjects affected / exposed<br>occurrences (all)                                   | 0 / 29 (0.00%)<br>0  | 1 / 30 (3.33%)<br>1  | 0 / 29 (0.00%)<br>0   |
| Pruritus allergic<br>subjects affected / exposed<br>occurrences (all)                              | 0 / 29 (0.00%)<br>0  | 0 / 30 (0.00%)<br>0  | 1 / 29 (3.45%)<br>1   |
| Rash<br>subjects affected / exposed<br>occurrences (all)   | 0 / 29 (0.00%)<br>0  | 0 / 30 (0.00%)<br>0  | 1 / 29 (3.45%)<br>1   |
| Skin erosion<br>subjects affected / exposed<br>occurrences (all)                                   | 1 / 29 (3.45%)<br>1  | 0 / 30 (0.00%)<br>0  | 0 / 29 (0.00%)<br>0   |
| Swelling face<br>subjects affected / exposed<br>occurrences (all)                                  | 0 / 29 (0.00%)<br>0  | 1 / 30 (3.33%)<br>1  | 0 / 29 (0.00%)<br>0   |
| Renal and urinary disorders<br>Nephrolithiasis<br>subjects affected / exposed<br>occurrences (all) | 0 / 29 (0.00%)<br>0  | 0 / 30 (0.00%)<br>0  | 1 / 29 (3.45%)<br>1   |
| Endocrine disorders<br>Hyperprolactinaemia<br>subjects affected / exposed<br>occurrences (all)     | 0 / 29 (0.00%)<br>0  | 0 / 30 (0.00%)<br>0  | 1 / 29 (3.45%)<br>1   |
| Musculoskeletal and connective tissue disorders  |                      |                      |                       |



|                                   |                 |                 |                 |
|-----------------------------------|-----------------|-----------------|-----------------|
| Back pain                         |                 |                 |                 |
| subjects affected / exposed       | 0 / 29 (0.00%)  | 0 / 30 (0.00%)  | 2 / 29 (6.90%)  |
| occurrences (all)                 | 0               | 0               | 2               |
| Musculoskeletal pain              |                 |                 |                 |
| subjects affected / exposed       | 1 / 29 (3.45%)  | 0 / 30 (0.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)                 | 1               | 0               | 0               |
| Neck pain                         |                 |                 |                 |
| subjects affected / exposed       | 0 / 29 (0.00%)  | 1 / 30 (3.33%)  | 0 / 29 (0.00%)  |
| occurrences (all)                 | 0               | 1               | 0               |
| Spinal pain                       |                 |                 |                 |
| subjects affected / exposed       | 0 / 29 (0.00%)  | 1 / 30 (3.33%)  | 0 / 29 (0.00%)  |
| occurrences (all)                 | 0               | 1               | 0               |
| Infections and infestations       |                 |                 |                 |
| Nasopharyngitis                   |                 |                 |                 |
| subjects affected / exposed       | 2 / 29 (6.90%)  | 3 / 30 (10.00%) | 6 / 29 (20.69%) |
| occurrences (all)                 | 2               | 3               | 9               |
| Folliculitis                      |                 |                 |                 |
| subjects affected / exposed       | 1 / 29 (3.45%)  | 2 / 30 (6.67%)  | 1 / 29 (3.45%)  |
| occurrences (all)                 | 1               | 5               | 1               |
| Upper respiratory tract infection |                 |                 |                 |
| subjects affected / exposed       | 3 / 29 (10.34%) | 0 / 30 (0.00%)  | 1 / 29 (3.45%)  |
| occurrences (all)                 | 3               | 0               | 1               |
| Skin infection                    |                 |                 |                 |
| subjects affected / exposed       | 1 / 29 (3.45%)  | 1 / 30 (3.33%)  | 0 / 29 (0.00%)  |
| occurrences (all)                 | 1               | 1               | 0               |
| Tonsillitis                       |                 |                 |                 |
| subjects affected / exposed       | 1 / 29 (3.45%)  | 0 / 30 (0.00%)  | 1 / 29 (3.45%)  |
| occurrences (all)                 | 1               | 0               | 1               |
| Bacterial infection               |                 |                 |                 |
| subjects affected / exposed       | 1 / 29 (3.45%)  | 0 / 30 (0.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)                 | 1               | 0               | 0               |
| Bronchitis                        |                 |                 |                 |
| subjects affected / exposed       | 1 / 29 (3.45%)  | 0 / 30 (0.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)                 | 1               | 0               | 0               |
| Conjunctivitis                    |                 |                 |                 |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 30 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| Furuncle                    |                |                |                |
| subjects affected / exposed | 0 / 29 (0.00%) | 1 / 30 (3.33%) | 0 / 29 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Herpes simplex              |                |                |                |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 30 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| Infected dermal cyst        |                |                |                |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 30 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| Periodontitis               |                |                |                |
| subjects affected / exposed | 0 / 29 (0.00%) | 1 / 30 (3.33%) | 0 / 29 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Pharyngitis                 |                |                |                |
| subjects affected / exposed | 0 / 29 (0.00%) | 1 / 30 (3.33%) | 0 / 29 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Rash pustular               |                |                |                |
| subjects affected / exposed | 0 / 29 (0.00%) | 1 / 30 (3.33%) | 0 / 29 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Skin bacterial infection    |                |                |                |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 30 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| Tooth infection             |                |                |                |
| subjects affected / exposed | 0 / 29 (0.00%) | 1 / 30 (3.33%) | 0 / 29 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Urinary tract infection     |                |                |                |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 30 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| Vulvovaginal candidiasis    |                |                |                |
| subjects affected / exposed | 0 / 29 (0.00%) | 1 / 30 (3.33%) | 0 / 29 (0.00%) |
| occurrences (all)           | 0              | 2              | 0              |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date              | Amendment   |
|-------------------|---|
| 27 September 2018 | Amendment of exclusion criterion related to recommended washout of systemic immunosuppressive or immunomodulatory drugs<br>Addition of lower weight limit<br>Amendment of exclusion criterion related to anaemia<br>Revision of guidance regarding the adequacy of double barrier contraceptive methods<br>Revision of liver function test criteria in relation to the permanent discontinuation of IMP<br>Establishment of consistent safety follow up for all study participants that covers 4 to 5 half-lives of IMP.<br>Revision of code break process in the event of a medical emergency  |
| 19 June 2019      | Corrected previous omission in synopsis<br>Clarification that change in immunohistochemistry of K16 would be measured by a qualified pathologist<br>Clarification that Cmax would be determined after all infusions.<br>Reduction of Follow-up Period to Day 253 for all patients<br>Clarification of the personnel who would be blinded<br>Reduction of washout period for systemic Cyclosporin A to within 3 weeks of Baseline<br>Clarification of Total bilirubin >ULN (except in circumstances where Gilbert's Syndrome can be confirmed)<br>Clarification of the duration of birth control measures<br>Clarification of the rules for replacement of patients and dosing<br>Clarification of rules around dosing if a dose needs to be temporarily discontinued<br>Investigator Assessments to be performed by the same Assessor<br>One repeat of safety laboratory tests and vital signs and more flexibility for rescreening<br>Clarification of timing of baseline biopsy<br>Clarification of the type of assay to be used for Inflammatory Proteomic Analysis<br>Reduction in blood volume required during study extension<br>Further clarification of the FAS population<br>Further clarification and detail provided on PK analysis<br>Where previously used incorrectly the term Monitor or Medical Monitor was replaced by Study Monitor<br>Replacement of Amendment 1 by Summary of Protocol Amendments |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

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

The study was not prospectively powered. Any P values presented are nominal.

Notes: