



## Clinical trial results:

### A Phase IIa Randomised, Double Blind, Multi-centre Study to Assess the Effect on Glucose Homeostasis of Two Dose Levels of AZD9567, Compared to Prednisolone, in Adults with Type 2 Diabetes

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2020-000931-35 |
| Trial protocol           | DE             |
| Global end of trial date | 09 June 2021   |

#### Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v1           |
| This version publication date  | 16 June 2022 |
| First version publication date | 16 June 2022 |

#### Trial information

##### Trial identification

|                       |             |
|-----------------------|-------------|
| Sponsor protocol code | D6470C00005 |
|-----------------------|-------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT04556760 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |                                                                                                                                                                                 |
|------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Sponsor organisation name    | AstraZeneca AB                                                                                                                                                                  |
| Sponsor organisation address | Södertälje, Södertälje, Sweden, 15185                                                                                                                                           |
| Public contact               | Global Clinical Head, AstraZeneca Clinical Study Information Center, +1 87724094 79, <a href="mailto:information.center@astrazeneca.com">information.center@astrazeneca.com</a> |
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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                       | 16 August 2021 |
| Is this the analysis of the primary completion data? | No             |
| Global end of trial reached?                         | Yes            |
| Global end of trial date                             | 09 June 2021   |
| Was the trial ended prematurely?                     | No             |

Notes:

## General information about the trial

Main objective of the trial:

To determine the pharmacodynamic effect of AZD9567 on glucose homeostasis compared to prednisolone.

Protection of trial subjects:

This study was performed in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with International Council for Harmonisation Good Clinical Practices (ICH-GCP), applicable regulatory requirements, and the AstraZeneca policy on Bioethics.

Background therapy: -

Evidence for comparator: -

|                                                           |                  |
|-----------------------------------------------------------|------------------|
| Actual start date of recruitment                          | 26 November 2020 |
| Long term follow-up planned                               | No               |
| Independent data monitoring committee (IDMC) involvement? | No               |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |             |
|--------------------------------------|-------------|
| Country: Number of subjects enrolled | Germany: 44 |
| Worldwide total number of subjects   | 44          |
| EEA total number of subjects         | 44          |

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)                      | 14 |
| From 65 to 84 years                       | 30 |
| 85 years and over                         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

This cross-over study was conducted in Germany between 26 November 2020 and 09 June 2021.

### Pre-assignment

Screening details:

The Screening period was of 14 days which may be extended up to a maximum of 28 days. Informed consent was obtained from all patients before performing any study tests or procedures. All the study assessments were performed as per the schedule of assessment.

### 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, Subject          |

### Arms

|                              |          |
|------------------------------|----------|
| Are arms mutually exclusive? | Yes      |
| Arm title                    | Cohort 1 |

Arm description:

Patients were randomised in a ratio of 1:1 to receive 72 mg AZD9567 followed by 40 mg prednisolone or 40 mg prednisolone followed by 72 mg AZD956

|                                        |                 |
|----------------------------------------|-----------------|
| Arm type                               | Experimental    |
| Investigational medicinal product name | AZD9567         |
| Investigational medicinal product code |                 |
| Other name                             |                 |
| Pharmaceutical forms                   | Oral suspension |
| Routes of administration               | Oral use        |

Dosage and administration details:

Patients received AZD9567 72 mg/day for 3 consecutive days (Day 1 to 3) of each treatment period.

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

Dosage and administration details:

Patients received Placebo for Prednisolone for 3 consecutive days (Day 1 to 3) for each treatment period.

|                                        |                     |
|----------------------------------------|---------------------|
| Investigational medicinal product name | Placebo for AZD9567 |
| Investigational medicinal product code |                     |
| Other name                             |                     |
| Pharmaceutical forms                   | Oral suspension     |
| Routes of administration               | Oral use            |

Dosage and administration details:

Patients received Placebo for AZD9567 for 3 consecutive days (Day 1 to 3) for each treatment period.

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

**Dosage and administration details:**

Patients received Prednisolone 40 mg/day for 3 consecutive days (Day 1 to 3) of each treatment period

|                  |          |
|------------------|----------|
| <b>Arm title</b> | Cohort 2 |
|------------------|----------|

**Arm description:**

Patients were randomised in a ratio of 1:1 to receive 40 mg AZD9567 followed by 20 mg prednisolone or 20 mg prednisolone followed by 40 mg AZD9567

|                                        |                 |
|----------------------------------------|-----------------|
| Arm type                               | Experimental    |
| Investigational medicinal product name | AZD9567         |
| Investigational medicinal product code |                 |
| Other name                             |                 |
| Pharmaceutical forms                   | Oral suspension |
| Routes of administration               | Oral use        |

**Dosage and administration details:**

Patients received AZD9567 40 mg/day for 3 consecutive days (Day 1 to 3) of each treatment period.

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

**Dosage and administration details:**

Patients received Placebo for Prednisolone for 3 consecutive days (Day 1 to 3) for each treatment period.

|                                        |                     |
|----------------------------------------|---------------------|
| Investigational medicinal product name | Placebo for AZD9567 |
| Investigational medicinal product code |                     |
| Other name                             |                     |
| Pharmaceutical forms                   | Oral suspension     |
| Routes of administration               | Oral use            |

**Dosage and administration details:**

Patients received Placebo for AZD9567 for 3 consecutive days (Day 1 to 3) for each treatment period.

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

**Dosage and administration details:**

Patients received Prednisolone 20 mg/day for 3 consecutive days (Day 1 to 3) for each treatment period.

|                  |          |
|------------------|----------|
| <b>Arm title</b> | Cohort 3 |
|------------------|----------|

**Arm description:**

Patients were randomised in a ratio of 1:1 to receive placebo followed by 5 mg prednisolone or 5 mg prednisolone followed by placebo

|                                        |              |
|----------------------------------------|--------------|
| Arm type                               | Placebo      |
| Investigational medicinal product name | Prednisolone |
| Investigational medicinal product code |              |
| Other name                             |              |
| Pharmaceutical forms                   | Capsule      |
| Routes of administration               | Oral use     |

**Dosage and administration details:**

Patients received 5 mg/day for 3 consecutive days (Day 1 to 3) for each treatment period.

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

Dosage and administration details:

Patients received Placebo for Prednisolone for 3 consecutive days (Day 1 to 3) for each treatment period.

|                                        |                     |
|----------------------------------------|---------------------|
| Investigational medicinal product name | Placebo for AZD9567 |
| Investigational medicinal product code |                     |
| Other name                             |                     |
| Pharmaceutical forms                   | Oral suspension     |
| Routes of administration               | Oral use            |

Dosage and administration details:

Patients received Placebo for 3 consecutive days (Day 1 to 3) for each treatment period.

| <b>Number of subjects in period 1</b> | Cohort 1 | Cohort 2 | Cohort 3 |
|---------------------------------------|----------|----------|----------|
| Started                               | 27       | 8        | 9        |
| Completed                             | 27       | 8        | 9        |

## Baseline characteristics

### Reporting groups

|                                                                                                                                                    |          |
|----------------------------------------------------------------------------------------------------------------------------------------------------|----------|
| Reporting group title                                                                                                                              | Cohort 1 |
| Reporting group description:                                                                                                                       |          |
| Patients were randomised in a ratio of 1:1 to receive 72 mg AZD9567 followed by 40 mg prednisolone or 40 mg prednisolone followed by 72 mg AZD956  |          |
| Reporting group title                                                                                                                              | Cohort 2 |
| Reporting group description:                                                                                                                       |          |
| Patients were randomised in a ratio of 1:1 to receive 40 mg AZD9567 followed by 20 mg prednisolone or 20 mg prednisolone followed by 40 mg AZD9567 |          |
| Reporting group title                                                                                                                              | Cohort 3 |
| Reporting group description:                                                                                                                       |          |
| Patients were randomised in a ratio of 1:1 to receive placebo followed by 5 mg prednisolone or 5 mg prednisolone followed by placebo               |          |

| Reporting group values                    | Cohort 1 | Cohort 2 | Cohort 3 |
|-------------------------------------------|----------|----------|----------|
| Number of subjects                        | 27       | 8        | 9        |
| Age categorical                           |          |          |          |
| Units: Subjects                           |          |          |          |
| 18 - 44 (years)                           | 0        | 0        | 0        |
| 45 - 64 (years)                           | 8        | 3        | 3        |
| 65 - 75 (years)                           | 19       | 5        | 6        |
| Age Continuous                            |          |          |          |
| Units: Years                              |          |          |          |
| arithmetic mean                           | 67.3     | 64.4     | 66.6     |
| standard deviation                        | ± 6.41   | ± 9.32   | ± 5.36   |
| Sex: Female, Male                         |          |          |          |
| Units: Participants                       |          |          |          |
| Female                                    | 4        | 2        | 1        |
| Male                                      | 23       | 6        | 8        |
| Race (NIH/OMB)                            |          |          |          |
| Units: Subjects                           |          |          |          |
| American Indian or Alaska Native          | 0        | 0        | 0        |
| Asian                                     | 0        | 0        | 0        |
| Native Hawaiian or Other Pacific Islander | 0        | 0        | 0        |
| Black or African American                 | 1        | 1        | 0        |
| White                                     | 26       | 7        | 9        |
| More than one race                        | 0        | 0        | 0        |
| Unknown or Not Reported                   | 0        | 0        | 0        |
| Ethnicity (NIH/OMB)                       |          |          |          |
| Units: Subjects                           |          |          |          |
| Hispanic or Latino                        | 0        | 0        | 0        |
| Not Hispanic or Latino                    | 27       | 8        | 9        |
| Unknown or Not Reported                   | 0        | 0        | 0        |

| Reporting group values | Total |  |  |
|------------------------|-------|--|--|
| Number of subjects     | 44    |  |  |

|                                           |    |  |  |
|-------------------------------------------|----|--|--|
| Age categorical                           |    |  |  |
| Units: Subjects                           |    |  |  |
| 18 - 44 (years)                           | 0  |  |  |
| 45 - 64 (years)                           | 14 |  |  |
| 65 - 75 (years)                           | 30 |  |  |
| Age Continuous                            |    |  |  |
| Units: Years                              |    |  |  |
| arithmetic mean                           |    |  |  |
| standard deviation                        | -  |  |  |
| Sex: Female, Male                         |    |  |  |
| Units: Participants                       |    |  |  |
| Female                                    | 7  |  |  |
| Male                                      | 37 |  |  |
| Race (NIH/OMB)                            |    |  |  |
| Units: Subjects                           |    |  |  |
| American Indian or Alaska Native          | 0  |  |  |
| Asian                                     | 0  |  |  |
| Native Hawaiian or Other Pacific Islander | 0  |  |  |
| Black or African American                 | 2  |  |  |
| White                                     | 42 |  |  |
| More than one race                        | 0  |  |  |
| Unknown or Not Reported                   | 0  |  |  |
| Ethnicity (NIH/OMB)                       |    |  |  |
| Units: Subjects                           |    |  |  |
| Hispanic or Latino                        | 0  |  |  |
| Not Hispanic or Latino                    | 44 |  |  |
| Unknown or Not Reported                   | 0  |  |  |

## End points

### End points reporting groups

|                                                                                                                                                                                         |               |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------|
| Reporting group title                                                                                                                                                                   | Cohort 1      |
| Reporting group description:<br>Patients were randomised in a ratio of 1:1 to receive 72 mg AZD9567 followed by 40 mg prednisolone or 40 mg prednisolone followed by 72 mg AZD956       |               |
| Reporting group title                                                                                                                                                                   | Cohort 2      |
| Reporting group description:<br>Patients were randomised in a ratio of 1:1 to receive 40 mg AZD9567 followed by 20 mg prednisolone or 20 mg prednisolone followed by 40 mg AZD9567      |               |
| Reporting group title                                                                                                                                                                   | Cohort 3      |
| Reporting group description:<br>Patients were randomised in a ratio of 1:1 to receive placebo followed by 5 mg prednisolone or 5 mg prednisolone followed by placebo                    |               |
| Subject analysis set title                                                                                                                                                              | Cohort 1      |
| Subject analysis set type                                                                                                                                                               | Full analysis |
| Subject analysis set description:<br>Patients were randomised in a ratio of 1:1 to receive 72 mg AZD9567 followed by 40 mg prednisolone or 40 mg prednisolone followed by 72 mg AZD956  |               |
| Subject analysis set title                                                                                                                                                              | Cohort 2      |
| Subject analysis set type                                                                                                                                                               | Full analysis |
| Subject analysis set description:<br>Patients were randomised in a ratio of 1:1 to receive 40 mg AZD9567 followed by 20 mg prednisolone or 20 mg prednisolone followed by 40 mg AZD9567 |               |
| Subject analysis set title                                                                                                                                                              | Cohort 3      |
| Subject analysis set type                                                                                                                                                               | Full analysis |
| Subject analysis set description:<br>Patients were randomised in a ratio of 1:1 to receive placebo followed by 5 mg prednisolone or 5 mg prednisolone followed by placebo               |               |

### Primary: Change from baseline in glucose area under the plasma concentration versus time curve from zero to 4 hours post-dose AUC(0-4)

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                                               |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | Change from baseline in glucose area under the plasma concentration versus time curve from zero to 4 hours post-dose AUC(0-4) |
| End point description:<br>The change from baseline in glucose AUC(0-4) was analysed to determine the Pharmacodynamic (PD) effect of AZD9567 compared to Prednisolone following a standardised Mixed meal tolerance test (MMTT).<br><br>The Subject Analysis set was added to report statistical analysis and this is the only option available in order to accommodate reporting of statistical data for cross over cohorts.<br><br>Here, arbitrary value 9999.9999 represent not applicable.<br><br>Full Analysis Set (FAS) consisted of all randomised patients who received at least 1 dose of study treatment. |                                                                                                                               |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Primary                                                                                                                       |
| End point timeframe:<br>On Days -1 (baseline), and Days 4 (Treatment period 1 and 2)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                               |



| End point values                           | Cohort 1                | Cohort 2                | Cohort 3                | Cohort 1                |
|--------------------------------------------|-------------------------|-------------------------|-------------------------|-------------------------|
| Subject group type                         | Reporting group         | Reporting group         | Reporting group         | Subject analysis set    |
| Number of subjects analysed                | 27                      | 8                       | 9                       | 27                      |
| Units: minute*millimole/liter (min*mmol/L) |                         |                         |                         |                         |
| least squares mean (standard error)        |                         |                         |                         |                         |
| AZD9567                                    | -190.0296 (± 63.8805)   | -182.7172 (± 149.8600)  | 9999.9999 (± 9999.9999) | -190.0296 (± 63.8805)   |
| Prednisolone                               | -57.0768 (± 63.8762)    | -40.6842 (± 141.7154)   | -184.9677 (± 88.9807)   | -57.0768 (± 63.8762)    |
| Placebo                                    | 9999.9999 (± 9999.9999) | 9999.9999 (± 9999.9999) | -311.8506 (± 88.5443)   | 9999.9999 (± 9999.9999) |

| End point values                           | Cohort 2                | Cohort 3                |  |  |
|--------------------------------------------|-------------------------|-------------------------|--|--|
| Subject group type                         | Subject analysis set    | Subject analysis set    |  |  |
| Number of subjects analysed                | 8                       | 9                       |  |  |
| Units: minute*millimole/liter (min*mmol/L) |                         |                         |  |  |
| least squares mean (standard error)        |                         |                         |  |  |
| AZD9567                                    | -182.7172 (± 149.8600)  | 9999.9999 (± 9999.9999) |  |  |
| Prednisolone                               | -40.6842 (± 141.7154)   | -184.9677 (± 88.9807)   |  |  |
| Placebo                                    | 9999.9999 (± 9999.9999) | -311.8506 (± 88.5443)   |  |  |

## Statistical analyses

|                                                                           |                                   |
|---------------------------------------------------------------------------|-----------------------------------|
| Statistical analysis title                                                | AZD9567 72mg vs Prednisolone 40mg |
| Statistical analysis description:                                         |                                   |
| Pairwise Comparison with Prednisolone (AZD9567 72mg vs Prednisolone 40mg) |                                   |
| Comparison groups                                                         | Cohort 1 v Cohort 1               |
| Number of subjects included in analysis                                   | 54                                |
| Analysis specification                                                    | Pre-specified                     |
| Analysis type                                                             | other <sup>[1]</sup>              |
| P-value                                                                   | = 0.036                           |
| Method                                                                    | Mixed models analysis             |
| Parameter estimate                                                        | Mean difference (final values)    |
| Point estimate                                                            | -132.95                           |
| Confidence interval                                                       |                                   |
| level                                                                     | 95 %                              |
| sides                                                                     | 2-sided                           |
| lower limit                                                               | -256.5                            |
| upper limit                                                               | -9.39                             |

Notes:

[1] - 27 patients were evaluated in this analysis

|                            |                             |
|----------------------------|-----------------------------|
| Statistical analysis title | Placebo vs Prednisolone 5mg |
|----------------------------|-----------------------------|

Statistical analysis description:

Pairwise Comparison with Prednisolone (Placebo vs Prednisolone 5mg)

|                                         |                                |
|-----------------------------------------|--------------------------------|
| Comparison groups                       | Cohort 3 v Cohort 3            |
| Number of subjects included in analysis | 18                             |
| Analysis specification                  | Pre-specified                  |
| Analysis type                           | other <sup>[2]</sup>           |
| P-value                                 | = 0.03                         |
| Method                                  | Mixed models analysis          |
| Parameter estimate                      | Mean difference (final values) |
| Point estimate                          | -126.88                        |
| Confidence interval                     |                                |
| level                                   | 95 %                           |
| sides                                   | 2-sided                        |
| lower limit                             | -236.04                        |
| upper limit                             | -17.72                         |

Notes:

[2] - 9 patients were evaluated in this analysis

|                                                                           |                                   |
|---------------------------------------------------------------------------|-----------------------------------|
| <b>Statistical analysis title</b>                                         | AZD9567 40mg vs Prednisolone 20mg |
| Statistical analysis description:                                         |                                   |
| Pairwise Comparison with Prednisolone (AZD9567 40mg vs Prednisolone 20mg) |                                   |
| Comparison groups                                                         | Cohort 2 v Cohort 2               |
| Number of subjects included in analysis                                   | 16                                |
| Analysis specification                                                    | Pre-specified                     |
| Analysis type                                                             | other <sup>[3]</sup>              |
| P-value                                                                   | = 0.432                           |
| Method                                                                    | Mixed models analysis             |
| Parameter estimate                                                        | Mean difference (final values)    |
| Point estimate                                                            | -142.03                           |
| Confidence interval                                                       |                                   |
| level                                                                     | 95 %                              |
| sides                                                                     | 2-sided                           |
| lower limit                                                               | -554.87                           |
| upper limit                                                               | 270.8                             |

Notes:

[3] - 8 patients were evaluated in this analysis

**Secondary: Mean daily glucose at 48 – 72 hours treatment as determined from multiple measures via the Continuous Glucose Monitoring (CGM) system**

|                 |                                                                                                                                       |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Mean daily glucose at 48 – 72 hours treatment as determined from multiple measures via the Continuous Glucose Monitoring (CGM) system |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------------|

End point description:

The mean daily glucose was analysed to determine the effect of AZD9567 on CGM compared to prednisolone.

The Subject Analysis set was added to report statistical analysis and this is the only option available in order to accommodate reporting of statistical data for cross over cohorts.

Here, arbitrary value 9999.9999 represent not applicable.

Full Analysis Set (FAS) consisted of all randomised patients who received at least 1 dose of study treatment.

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

End point timeframe:

On Days 2 and 3 (Treatment period 1 and 2)

| End point values                    | Cohort 1                     | Cohort 2                     | Cohort 3                     | Cohort 1                     |
|-------------------------------------|------------------------------|------------------------------|------------------------------|------------------------------|
| Subject group type                  | Reporting group              | Reporting group              | Reporting group              | Subject analysis set         |
| Number of subjects analysed         | 27                           | 8                            | 9                            | 27                           |
| Units: millimole/liter (mmol/L)     |                              |                              |                              |                              |
| least squares mean (standard error) |                              |                              |                              |                              |
| AZD9567                             | 8.5730 ( $\pm$ 0.3114)       | 7.7870 ( $\pm$ 0.2517)       | 9999.9999 ( $\pm$ 9999.9999) | 8.5730 ( $\pm$ 0.3114)       |
| Prednisolone (n= 26,8,9)            | 10.0797 ( $\pm$ 0.3150)      | 8.8969 ( $\pm$ 0.2494)       | 7.4238 ( $\pm$ 0.2889)       | 10.0797 ( $\pm$ 0.3150)      |
| Placebo                             | 9999.9999 ( $\pm$ 9999.9999) | 9999.9999 ( $\pm$ 9999.9999) | 7.2638 ( $\pm$ 0.2888)       | 9999.9999 ( $\pm$ 9999.9999) |

| End point values                    | Cohort 2                     | Cohort 3                     |  |  |
|-------------------------------------|------------------------------|------------------------------|--|--|
| Subject group type                  | Subject analysis set         | Subject analysis set         |  |  |
| Number of subjects analysed         | 8                            | 9                            |  |  |
| Units: millimole/liter (mmol/L)     |                              |                              |  |  |
| least squares mean (standard error) |                              |                              |  |  |
| AZD9567                             | 7.7870 ( $\pm$ 0.2517)       | 9999.9999 ( $\pm$ 9999.9999) |  |  |
| Prednisolone (n= 26,8,9)            | 8.8969 ( $\pm$ 0.2494)       | 7.4238 ( $\pm$ 0.2889)       |  |  |
| Placebo                             | 9999.9999 ( $\pm$ 9999.9999) | 7.2638 ( $\pm$ 0.2888)       |  |  |

## Statistical analyses

|                                                                            |                                   |
|----------------------------------------------------------------------------|-----------------------------------|
| Statistical analysis title                                                 | AZD9567 72mg vs Prednisolone 40mg |
| Statistical analysis description:                                          |                                   |
| Pairwise Comparisons with Prednisolone (AZD9567 72mg vs Prednisolone 40mg) |                                   |
| Comparison groups                                                          | Cohort 1 v Cohort 1               |
| Number of subjects included in analysis                                    | 54                                |
| Analysis specification                                                     | Pre-specified                     |
| Analysis type                                                              | other <sup>[4]</sup>              |
| P-value                                                                    | < 0.001                           |
| Method                                                                     | Mixed models analysis             |
| Parameter estimate                                                         | Mean difference (final values)    |
| Point estimate                                                             | -1.5                              |
| Confidence interval                                                        |                                   |
| level                                                                      | 95 %                              |
| sides                                                                      | 2-sided                           |
| lower limit                                                                | -2.08                             |
| upper limit                                                                | -0.93                             |

Notes:

[4] - 27 patients were evaluated in this analysis

|                                                                      |                                |
|----------------------------------------------------------------------|--------------------------------|
| <b>Statistical analysis title</b>                                    | Placebo vs Prednisolone 5mg    |
| Statistical analysis description:                                    |                                |
| Pairwise Comparisons with Prednisolone (Placebo vs Prednisolone 5mg) |                                |
| Comparison groups                                                    | Cohort 3 v Cohort 3            |
| Number of subjects included in analysis                              | 18                             |
| Analysis specification                                               | Pre-specified                  |
| Analysis type                                                        | other <sup>[5]</sup>           |
| P-value                                                              | = 0.547                        |
| Method                                                               | Mixed models analysis          |
| Parameter estimate                                                   | Mean difference (final values) |
| Point estimate                                                       | -0.16                          |
| Confidence interval                                                  |                                |
| level                                                                | 95 %                           |
| sides                                                                | 2-sided                        |
| lower limit                                                          | -0.69                          |
| upper limit                                                          | 0.37                           |

Notes:

[5] - 9 patients were evaluated in this analysis

|                                                                            |                                   |
|----------------------------------------------------------------------------|-----------------------------------|
| <b>Statistical analysis title</b>                                          | AZD9567 40mg vs Prednisolone 20mg |
| Statistical analysis description:                                          |                                   |
| Pairwise Comparisons with Prednisolone (AZD9567 40mg vs Prednisolone 20mg) |                                   |
| Comparison groups                                                          | Cohort 2 v Cohort 2               |
| Number of subjects included in analysis                                    | 16                                |
| Analysis specification                                                     | Pre-specified                     |
| Analysis type                                                              |                                   |
| P-value                                                                    | < 0.001 <sup>[6]</sup>            |
| Method                                                                     | Mixed models analysis             |
| Parameter estimate                                                         | Mean difference (final values)    |
| Point estimate                                                             | -1.1                              |
| Confidence interval                                                        |                                   |
| level                                                                      | 95 %                              |
| sides                                                                      | 2-sided                           |
| lower limit                                                                | -1.72                             |
| upper limit                                                                | -0.49                             |

Notes:

[6] - 8 patients were evaluated in this analysis

### **Secondary: Rise in mean daily glucose over 24-hour periods from start of IMP dosing (0 – 24 hours, 24 – 48 hours, 48 – 72 hours)**

|                 |                                                                                                                       |
|-----------------|-----------------------------------------------------------------------------------------------------------------------|
| End point title | Rise in mean daily glucose over 24-hour periods from start of IMP dosing (0 – 24 hours, 24 – 48 hours, 48 – 72 hours) |
|-----------------|-----------------------------------------------------------------------------------------------------------------------|

End point description:

The mean daily glucose was analysed to determine the effect of AZD9567 on CGM compared to prednisolone.

The Subject Analysis set was added to report statistical analysis and this is the only option available in order to accommodate reporting of statistical data for cross over cohorts.

Here, arbitrary value 9999.9999 represent not applicable.

|                                            |           |
|--------------------------------------------|-----------|
| End point type                             | Secondary |
| End point timeframe:                       |           |
| On Days 1, 2, 3 (Treatment period 1 and 2) |           |

| End point values                      | Cohort 1                     | Cohort 2                     | Cohort 3                     | Cohort 1                     |
|---------------------------------------|------------------------------|------------------------------|------------------------------|------------------------------|
| Subject group type                    | Reporting group              | Reporting group              | Reporting group              | Subject analysis set         |
| Number of subjects analysed           | 27                           | 8                            | 9                            | 27                           |
| Units: mmol/L                         |                              |                              |                              |                              |
| least squares mean (standard error)   |                              |                              |                              |                              |
| AZD9567 (00 to 24 hours [h])          | 1.2071 ( $\pm$ 0.2869)       | 0.4070 ( $\pm$ 0.2509)       | 9999.9999 ( $\pm$ 9999.9999) | 1.2071 ( $\pm$ 0.2869)       |
| Prednisolone (00 to 24 h) (n= 26,8,9) | 2.7086 ( $\pm$ 0.2938)       | 1.2545 ( $\pm$ 0.2460)       | 0.3123 ( $\pm$ 0.1549)       | 2.7086 ( $\pm$ 0.2938)       |
| Placebo (00 to 24 h)                  | 9999.9999 ( $\pm$ 9999.9999) | 9999.9999 ( $\pm$ 9999.9999) | -0.0477 ( $\pm$ 0.1547)      | 9999.9999 ( $\pm$ 9999.9999) |
| AZD9567 (24 to 48 h)                  | 0.8011 ( $\pm$ 0.2978)       | 0.5428 ( $\pm$ 0.2483)       | 9999.9999 ( $\pm$ 9999.9999) | 0.8011 ( $\pm$ 0.2978)       |
| Prednisolone (24 to 48 h) (n= 26,8,9) | 2.6653 ( $\pm$ 0.3044)       | 1.3206 ( $\pm$ 0.2448)       | -0.2415 ( $\pm$ 0.2898)      | 2.6653 ( $\pm$ 0.3044)       |
| Placebo (24 to 48 h)                  | 9999.9999 ( $\pm$ 9999.9999) | 9999.9999 ( $\pm$ 9999.9999) | -0.3260 ( $\pm$ 0.2894)      | 9999.9999 ( $\pm$ 9999.9999) |
| AZD9567 (48 to 72 h)                  | 0.8529 ( $\pm$ 0.3210)       | 0.0744 ( $\pm$ 0.2714)       | 9999.9999 ( $\pm$ 9999.9999) | 0.8529 ( $\pm$ 0.3210)       |
| Prednisolone (48 to 72 h) (n= 26,8,9) | 2.4527 ( $\pm$ 0.3274)       | 1.2174 ( $\pm$ 0.2664)       | -0.2202 ( $\pm$ 0.2229)      | 2.4527 ( $\pm$ 0.3274)       |
| Placebo (48 to 72 h)                  | 9999.9999 ( $\pm$ 9999.9999) | 9999.9999 ( $\pm$ 9999.9999) | -0.3500 ( $\pm$ 0.2224)      | 9999.9999 ( $\pm$ 9999.9999) |

| End point values                      | Cohort 2                     | Cohort 3                     |  |  |
|---------------------------------------|------------------------------|------------------------------|--|--|
| Subject group type                    | Subject analysis set         | Subject analysis set         |  |  |
| Number of subjects analysed           | 8                            | 9                            |  |  |
| Units: mmol/L                         |                              |                              |  |  |
| least squares mean (standard error)   |                              |                              |  |  |
| AZD9567 (00 to 24 hours [h])          | 0.4070 ( $\pm$ 0.2509)       | 9999.9999 ( $\pm$ 9999.9999) |  |  |
| Prednisolone (00 to 24 h) (n= 26,8,9) | 1.2545 ( $\pm$ 0.2460)       | 0.3123 ( $\pm$ 0.1549)       |  |  |
| Placebo (00 to 24 h)                  | 9999.9999 ( $\pm$ 9999.9999) | -0.0477 ( $\pm$ 0.1547)      |  |  |
| AZD9567 (24 to 48 h)                  | 0.5428 ( $\pm$ 0.2483)       | 9999.9999 ( $\pm$ 9999.9999) |  |  |
| Prednisolone (24 to 48 h) (n= 26,8,9) | 1.3206 ( $\pm$ 0.2448)       | -0.2415 ( $\pm$ 0.2898)      |  |  |
| Placebo (24 to 48 h)                  | 9999.9999 ( $\pm$ 9999.9999) | -0.3260 ( $\pm$ 0.2894)      |  |  |
| AZD9567 (48 to 72 h)                  | 0.0744 ( $\pm$ 0.2714)       | 9999.9999 ( $\pm$ 9999.9999) |  |  |
| Prednisolone (48 to 72 h) (n= 26,8,9) | 1.2174 ( $\pm$ 0.2664)       | -0.2202 ( $\pm$ 0.2229)      |  |  |

|                      |                              |                         |  |  |
|----------------------|------------------------------|-------------------------|--|--|
| Placebo (48 to 72 h) | 9999.9999 ( $\pm$ 9999.9999) | -0.3500 ( $\pm$ 0.2224) |  |  |
|----------------------|------------------------------|-------------------------|--|--|

## Statistical analyses

|                                                                                         |                                                |
|-----------------------------------------------------------------------------------------|------------------------------------------------|
| <b>Statistical analysis title</b>                                                       | AZD9567 72mg vs Prednisolone 40mg [00 to 24 h] |
| Statistical analysis description:                                                       |                                                |
| Pairwise Comparisons with Prednisolone (AZD9567 72mg vs Prednisolone 40mg [00 to 24 h]) |                                                |
| Comparison groups                                                                       | Cohort 1 v Cohort 1                            |
| Number of subjects included in analysis                                                 | 54                                             |
| Analysis specification                                                                  | Pre-specified                                  |
| Analysis type                                                                           | other <sup>[7]</sup>                           |
| P-value                                                                                 | < 0.001                                        |
| Method                                                                                  | Mixed models analysis                          |
| Parameter estimate                                                                      | Mean difference (final values)                 |
| Point estimate                                                                          | -1.5                                           |
| Confidence interval                                                                     |                                                |
| level                                                                                   | 95 %                                           |
| sides                                                                                   | 2-sided                                        |
| lower limit                                                                             | -2.22                                          |
| upper limit                                                                             | -0.77                                          |

Notes:

[7] - 27 patients were evaluated in this analysis

|                                                                                         |                                                |
|-----------------------------------------------------------------------------------------|------------------------------------------------|
| <b>Statistical analysis title</b>                                                       | AZD9567 72mg vs Prednisolone 40mg [24 to 48 h] |
| Statistical analysis description:                                                       |                                                |
| Pairwise Comparisons with Prednisolone (AZD9567 72mg vs Prednisolone 40mg [24 to 48 h]) |                                                |
| Comparison groups                                                                       | Cohort 1 v Cohort 1                            |
| Number of subjects included in analysis                                                 | 54                                             |
| Analysis specification                                                                  | Pre-specified                                  |
| Analysis type                                                                           | other <sup>[8]</sup>                           |
| P-value                                                                                 | < 0.001                                        |
| Method                                                                                  | Mixed models analysis                          |
| Parameter estimate                                                                      | Mean difference (final values)                 |
| Point estimate                                                                          | -1.86                                          |
| Confidence interval                                                                     |                                                |
| level                                                                                   | 95 %                                           |
| sides                                                                                   | 2-sided                                        |
| lower limit                                                                             | -2.56                                          |
| upper limit                                                                             | -1.16                                          |

Notes:

[8] - 27 patients were evaluated in this analysis

|                                                                                         |                                                |
|-----------------------------------------------------------------------------------------|------------------------------------------------|
| <b>Statistical analysis title</b>                                                       | AZD9567 72mg vs Prednisolone 40mg [48 to 72 h] |
| Statistical analysis description:                                                       |                                                |
| Pairwise Comparisons with Prednisolone (AZD9567 72mg vs Prednisolone 40mg [48 to 72 h]) |                                                |
| Comparison groups                                                                       | Cohort 1 v Cohort 1                            |

|                                         |                                |
|-----------------------------------------|--------------------------------|
| Number of subjects included in analysis | 54                             |
| Analysis specification                  | Pre-specified                  |
| Analysis type                           | other <sup>[9]</sup>           |
| P-value                                 | < 0.001                        |
| Method                                  | Mixed models analysis          |
| Parameter estimate                      | Mean difference (final values) |
| Point estimate                          | -1.59                          |
| Confidence interval                     |                                |
| level                                   | 95 %                           |
| sides                                   | 2-sided                        |
| lower limit                             | -2.3                           |
| upper limit                             | -0.89                          |

Notes:

[9] - 27 patients were evaluated in this analysis

|                                                                                         |                                                |
|-----------------------------------------------------------------------------------------|------------------------------------------------|
| <b>Statistical analysis title</b>                                                       | AZD9567 40mg vs Prednisolone 20mg [00 to 24 h] |
| Statistical analysis description:                                                       |                                                |
| Pairwise Comparisons with Prednisolone (AZD9567 40mg vs Prednisolone 20mg [00 to 24 h]) |                                                |
| Comparison groups                                                                       | Cohort 2 v Cohort 2                            |
| Number of subjects included in analysis                                                 | 16                                             |
| Analysis specification                                                                  | Pre-specified                                  |
| Analysis type                                                                           | other <sup>[10]</sup>                          |
| P-value                                                                                 | = 0.013                                        |
| Method                                                                                  | Mixed models analysis                          |
| Parameter estimate                                                                      | Mean difference (final values)                 |
| Point estimate                                                                          | -0.84                                          |
| Confidence interval                                                                     |                                                |
| level                                                                                   | 95 %                                           |
| sides                                                                                   | 2-sided                                        |
| lower limit                                                                             | -1.44                                          |
| upper limit                                                                             | -0.24                                          |

Notes:

[10] - 8 patients were evaluated in this analysis

|                                                                                         |                                                |
|-----------------------------------------------------------------------------------------|------------------------------------------------|
| <b>Statistical analysis title</b>                                                       | AZD9567 40mg vs Prednisolone 20mg [24 to 48 h] |
| Statistical analysis description:                                                       |                                                |
| Pairwise Comparisons with Prednisolone (AZD9567 40mg vs Prednisolone 20mg [24 to 48 h]) |                                                |
| Comparison groups                                                                       | Cohort 2 v Cohort 2                            |
| Number of subjects included in analysis                                                 | 16                                             |
| Analysis specification                                                                  | Pre-specified                                  |
| Analysis type                                                                           | other <sup>[11]</sup>                          |
| P-value                                                                                 | = 0.061                                        |
| Method                                                                                  | Mixed models analysis                          |
| Parameter estimate                                                                      | Mean difference (final values)                 |
| Point estimate                                                                          | -0.77                                          |
| Confidence interval                                                                     |                                                |
| level                                                                                   | 95 %                                           |
| sides                                                                                   | 2-sided                                        |
| lower limit                                                                             | -1.6                                           |
| upper limit                                                                             | 0.04                                           |

Notes:

[11] - 8 patients were evaluated in this analysis

|                                                                                    |                                           |
|------------------------------------------------------------------------------------|-------------------------------------------|
| <b>Statistical analysis title</b>                                                  | Placebo vs Prednisolone 5 mg [00 to 24 h] |
| Statistical analysis description:                                                  |                                           |
| Pairwise Comparisons with Prednisolone (Placebo vs Prednisolone 5 mg [00 to 24 h]) |                                           |
| Comparison groups                                                                  | Cohort 3 v Cohort 3                       |
| Number of subjects included in analysis                                            | 18                                        |
| Analysis specification                                                             | Pre-specified                             |
| Analysis type                                                                      | other <sup>[12]</sup>                     |
| P-value                                                                            | = 0.125                                   |
| Method                                                                             | Mixed models analysis                     |
| Parameter estimate                                                                 | Mean difference (final values)            |
| Point estimate                                                                     | -0.36                                     |
| Confidence interval                                                                |                                           |
| level                                                                              | 95 %                                      |
| sides                                                                              | 2-sided                                   |
| lower limit                                                                        | -0.83                                     |
| upper limit                                                                        | 0.11                                      |

Notes:

[12] - 9 patients were evaluated in this analysis

|                                                                                         |                                                |
|-----------------------------------------------------------------------------------------|------------------------------------------------|
| <b>Statistical analysis title</b>                                                       | AZD9567 40mg vs Prednisolone 20mg [48 to 72 h] |
| Statistical analysis description:                                                       |                                                |
| Pairwise Comparisons with Prednisolone (AZD9567 40mg vs Prednisolone 20mg [48 to 72 h]) |                                                |
| Comparison groups                                                                       | Cohort 2 v Cohort 2                            |
| Number of subjects included in analysis                                                 | 16                                             |
| Analysis specification                                                                  | Pre-specified                                  |
| Analysis type                                                                           |                                                |
| P-value                                                                                 | = 0.003                                        |
| Method                                                                                  | Mixed models analysis                          |
| Parameter estimate                                                                      | Mean difference (final values)                 |
| Point estimate                                                                          | -1.14                                          |
| Confidence interval                                                                     |                                                |
| level                                                                                   | 95 %                                           |
| sides                                                                                   | 2-sided                                        |
| lower limit                                                                             | -1.76                                          |
| upper limit                                                                             | -0.52                                          |

|                                                                                    |                                           |
|------------------------------------------------------------------------------------|-------------------------------------------|
| <b>Statistical analysis title</b>                                                  | Placebo vs Prednisolone 5 mg [24 to 48 h] |
| Statistical analysis description:                                                  |                                           |
| Pairwise Comparisons with Prednisolone (Placebo vs Prednisolone 5 mg [24 to 48 h]) |                                           |
| Comparison groups                                                                  | Cohort 3 v Cohort 3                       |



|                                         |                                |
|-----------------------------------------|--------------------------------|
| Number of subjects included in analysis | 18                             |
| Analysis specification                  | Pre-specified                  |
| Analysis type                           | other <sup>[13]</sup>          |
| P-value                                 | = 0.84                         |
| Method                                  | Mixed models analysis          |
| Parameter estimate                      | Mean difference (final values) |
| Point estimate                          | -0.08                          |
| Confidence interval                     |                                |
| level                                   | 95 %                           |
| sides                                   | 2-sided                        |
| lower limit                             | -0.97                          |
| upper limit                             | 0.8                            |

Notes:

[13] - 9 patients were evaluated in this analysis

|                                                                                    |                                           |
|------------------------------------------------------------------------------------|-------------------------------------------|
| <b>Statistical analysis title</b>                                                  | Placebo vs Prednisolone 5 mg [48 to 72 h] |
| Statistical analysis description:                                                  |                                           |
| Pairwise Comparisons with Prednisolone (Placebo vs Prednisolone 5 mg [48 to 72 h]) |                                           |
| Comparison groups                                                                  | Cohort 3 v Cohort 3                       |
| Number of subjects included in analysis                                            | 18                                        |
| Analysis specification                                                             | Pre-specified                             |
| Analysis type                                                                      | other <sup>[14]</sup>                     |
| P-value                                                                            | = 0.571                                   |
| Method                                                                             | Mixed models analysis                     |
| Parameter estimate                                                                 | Mean difference (final values)            |
| Point estimate                                                                     | -0.12                                     |
| Confidence interval                                                                |                                           |
| level                                                                              | 95 %                                      |
| sides                                                                              | 2-sided                                   |
| lower limit                                                                        | -0.64                                     |
| upper limit                                                                        | 0.38                                      |

Notes:

[14] - 9 patients were evaluated in this analysis

## Secondary: Change from baseline in fasting glucose

|                                                                                                                                                                                       |                                         |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------|
| End point title                                                                                                                                                                       | Change from baseline in fasting glucose |
| End point description:                                                                                                                                                                |                                         |
| Pharmacodynamic effects (fasting glucose) of AZD9567 following a MMTT were evaluated as compared to prednisolone.                                                                     |                                         |
| The Subject Analysis set was added to report statistical analysis and this is the only option available in order to accommodate reporting of statistical data for cross over cohorts. |                                         |
| Here, arbitrary value 9999.9999 represent not applicable.                                                                                                                             |                                         |
| FAS consisted of all randomised patients who received at least 1 dose of study treatment.                                                                                             |                                         |
| End point type                                                                                                                                                                        | Secondary                               |
| End point timeframe:                                                                                                                                                                  |                                         |
| On Day -1 (Baseline), and Day 4 (Treatment period 1 and 2)                                                                                                                            |                                         |

| End point values                    | Cohort 1                | Cohort 2                | Cohort 3                | Cohort 1                |
|-------------------------------------|-------------------------|-------------------------|-------------------------|-------------------------|
| Subject group type                  | Reporting group         | Reporting group         | Reporting group         | Subject analysis set    |
| Number of subjects analysed         | 27                      | 8                       | 9                       | 27                      |
| Units: mmol/L                       |                         |                         |                         |                         |
| least squares mean (standard error) |                         |                         |                         |                         |
| AZD9567                             | -1.14 (± 0.17)          | -0.95 (± 0.36)          | 9999.9999 (± 9999.9999) | -1.14 (± 0.17)          |
| Prednisolone                        | -1.06 (± 0.17)          | -0.91 (± 0.35)          | -1.15 (± 0.20)          | -1.06 (± 0.17)          |
| Placebo                             | 9999.9999 (± 9999.9999) | 9999.9999 (± 9999.9999) | -1.15 (± 0.20)          | 9999.9999 (± 9999.9999) |

| End point values                    | Cohort 2                | Cohort 3                |  |  |
|-------------------------------------|-------------------------|-------------------------|--|--|
| Subject group type                  | Subject analysis set    | Subject analysis set    |  |  |
| Number of subjects analysed         | 8                       | 9                       |  |  |
| Units: mmol/L                       |                         |                         |  |  |
| least squares mean (standard error) |                         |                         |  |  |
| AZD9567                             | -0.95 (± 0.36)          | 9999.9999 (± 9999.9999) |  |  |
| Prednisolone                        | -0.91 (± 0.35)          | -1.15 (± 0.20)          |  |  |
| Placebo                             | 9999.9999 (± 9999.9999) | -1.15 (± 0.20)          |  |  |

## Statistical analyses

|                                                                            |                                   |
|----------------------------------------------------------------------------|-----------------------------------|
| <b>Statistical analysis title</b>                                          | AZD9567 72mg vs Prednisolone 40mg |
| Statistical analysis description:                                          |                                   |
| Pairwise Comparisons with Prednisolone (AZD9567 72mg vs Prednisolone 40mg) |                                   |
| Comparison groups                                                          | Cohort 1 v Cohort 1               |
| Number of subjects included in analysis                                    | 54                                |
| Analysis specification                                                     | Pre-specified                     |
| Analysis type                                                              | other <sup>[15]</sup>             |
| P-value                                                                    | = 0.753                           |
| Method                                                                     | Mixed models analysis             |
| Parameter estimate                                                         | Mean difference (final values)    |
| Point estimate                                                             | -0.07                             |
| Confidence interval                                                        |                                   |
| level                                                                      | 95 %                              |
| sides                                                                      | 2-sided                           |
| lower limit                                                                | -0.55                             |
| upper limit                                                                | 0.4                               |

Notes:

[15] - 27 patients were evaluated in this analysis

|                                                                            |                                   |
|----------------------------------------------------------------------------|-----------------------------------|
| <b>Statistical analysis title</b>                                          | AZD9567 40mg vs Prednisolone 20mg |
| Statistical analysis description:                                          |                                   |
| Pairwise Comparisons with Prednisolone (AZD9567 40mg vs Prednisolone 20mg) |                                   |
| Comparison groups                                                          | Cohort 2 v Cohort 2               |

|                                         |                                |
|-----------------------------------------|--------------------------------|
| Number of subjects included in analysis | 16                             |
| Analysis specification                  | Pre-specified                  |
| Analysis type                           |                                |
| P-value                                 | = 0.802                        |
| Method                                  | Mixed models analysis          |
| Parameter estimate                      | Mean difference (final values) |
| Point estimate                          | -0.04                          |
| Confidence interval                     |                                |
| level                                   | 95 %                           |
| sides                                   | 2-sided                        |
| lower limit                             | -0.46                          |
| upper limit                             | 0.37                           |

|                                                                      |                                |
|----------------------------------------------------------------------|--------------------------------|
| <b>Statistical analysis title</b>                                    | Placebo vs Prednisolone 5mg    |
| Statistical analysis description:                                    |                                |
| Pairwise Comparisons with Prednisolone (Placebo vs Prednisolone 5mg) |                                |
| Comparison groups                                                    | Cohort 3 v Cohort 3            |
| Number of subjects included in analysis                              | 18                             |
| Analysis specification                                               | Pre-specified                  |
| Analysis type                                                        |                                |
| P-value                                                              | = 0.985                        |
| Method                                                               | Mixed models analysis          |
| Parameter estimate                                                   | Mean difference (final values) |
| Point estimate                                                       | 0                              |
| Confidence interval                                                  |                                |
| level                                                                | 95 %                           |
| sides                                                                | 2-sided                        |
| lower limit                                                          | -0.37                          |
| upper limit                                                          | 0.37                           |

### **Secondary: Change from baseline AUC(0-4) on hormones related to glucose homeostasis (Insulin)**

|                 |                                                                                    |
|-----------------|------------------------------------------------------------------------------------|
| End point title | Change from baseline AUC(0-4) on hormones related to glucose homeostasis (Insulin) |
|-----------------|------------------------------------------------------------------------------------|

End point description:

Effects of AZD9567 on insulin AUC(0-4) were assessed following MMTT compared to prednisolone.

Here, arbitrary value 9999.9999 represent not applicable.

FAS consisted of all randomised patients who received at least 1 dose of study treatment.

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

End point timeframe:

On Day -1 (Baseline), and Day 4 (Treatment period 1 and 2)

| End point values                           | Cohort 1                 | Cohort 2                 | Cohort 3                | Cohort 1                 |
|--------------------------------------------|--------------------------|--------------------------|-------------------------|--------------------------|
| Subject group type                         | Reporting group          | Reporting group          | Reporting group         | Subject analysis set     |
| Number of subjects analysed                | 27                       | 8                        | 9                       | 27                       |
| Units: minute*picomole/liter (min*pmole/L) |                          |                          |                         |                          |
| least squares mean (standard error)        |                          |                          |                         |                          |
| AZD9567 (n= 21,8,9)                        | 15319.3857 (± 4165.9135) | 13413.1929 (± 4791.9873) | 9999.9999 (± 9999.9999) | 15319.3857 (± 4165.9135) |
| Prednisolone (n= 23,7,9)                   | -5179.3659 (± 3989.2683) | 10091.7869 (± 5461.2631) | 4915.4115 (± 7049.5460) | -5179.3659 (± 3989.2683) |
| Placebo                                    | 9999.9999 (± 9999.9999)  | 9999.9999 (± 9999.9999)  | 2216.5532 (± 7049.0432) | 9999.9999 (± 9999.9999)  |

| End point values                           | Cohort 2                 | Cohort 3                |  |  |
|--------------------------------------------|--------------------------|-------------------------|--|--|
| Subject group type                         | Subject analysis set     | Subject analysis set    |  |  |
| Number of subjects analysed                | 8                        | 9                       |  |  |
| Units: minute*picomole/liter (min*pmole/L) |                          |                         |  |  |
| least squares mean (standard error)        |                          |                         |  |  |
| AZD9567 (n= 21,8,9)                        | 13413.1929 (± 4791.9873) | 9999.9999 (± 9999.9999) |  |  |
| Prednisolone (n= 23,7,9)                   | 10091.7869 (± 5461.2631) | 4915.4115 (± 7049.5460) |  |  |
| Placebo                                    | 9999.9999 (± 9999.9999)  | 2216.5532 (± 7049.0432) |  |  |

## Statistical analyses

|                                                                            |                                   |
|----------------------------------------------------------------------------|-----------------------------------|
| <b>Statistical analysis title</b>                                          | AZD9567 72mg vs Prednisolone 40mg |
| Statistical analysis description:                                          |                                   |
| Pairwise Comparisons with Prednisolone (AZD9567 72mg vs Prednisolone 40mg) |                                   |
| Comparison groups                                                          | Cohort 1 v Cohort 1               |
| Number of subjects included in analysis                                    | 54                                |
| Analysis specification                                                     | Pre-specified                     |
| Analysis type                                                              |                                   |
| P-value                                                                    | < 0.001                           |
| Method                                                                     | Mixed models analysis             |
| Parameter estimate                                                         | Mean difference (final values)    |
| Point estimate                                                             | 20498.7                           |
| Confidence interval                                                        |                                   |
| level                                                                      | 95 %                              |
| sides                                                                      | 2-sided                           |
| lower limit                                                                | 10819.2                           |
| upper limit                                                                | 30178.2                           |

|                                   |                             |
|-----------------------------------|-----------------------------|
| <b>Statistical analysis title</b> | Placebo vs Prednisolone 5mg |
|-----------------------------------|-----------------------------|

Statistical analysis description:

Pairwise Comparisons with Prednisolone (Placebo vs Prednisolone 5mg)

|                                         |                                |
|-----------------------------------------|--------------------------------|
| Comparison groups                       | Cohort 3 v Cohort 3            |
| Number of subjects included in analysis | 18                             |
| Analysis specification                  | Pre-specified                  |
| Analysis type                           | other <sup>[16]</sup>          |
| P-value                                 | = 0.521                        |
| Method                                  | Mixed models analysis          |
| Parameter estimate                      | Mean difference (final values) |
| Point estimate                          | -2698.8                        |
| Confidence interval                     |                                |
| level                                   | 95 %                           |
| sides                                   | 2-sided                        |
| lower limit                             | -14849                         |
| upper limit                             | 9451.3                         |

Notes:

[16] - 9 patients were evaluated in this analysis

|                                                                            |                                   |
|----------------------------------------------------------------------------|-----------------------------------|
| <b>Statistical analysis title</b>                                          | AZD9567 40mg vs Prednisolone 20mg |
| Statistical analysis description:                                          |                                   |
| Pairwise Comparisons with Prednisolone (AZD9567 40mg vs Prednisolone 20mg) |                                   |
| Comparison groups                                                          | Cohort 2 v Cohort 2               |
| Number of subjects included in analysis                                    | 16                                |
| Analysis specification                                                     | Pre-specified                     |
| Analysis type                                                              | other <sup>[17]</sup>             |
| P-value                                                                    | = 0.659                           |
| Method                                                                     | Mixed models analysis             |
| Parameter estimate                                                         | Mean difference (final values)    |
| Point estimate                                                             | 3321.4                            |
| Confidence interval                                                        |                                   |
| level                                                                      | 95 %                              |
| sides                                                                      | 2-sided                           |
| lower limit                                                                | -12975.8                          |
| upper limit                                                                | 19618.6                           |

Notes:

[17] - 8 patients were evaluated in this analysis

**Secondary: Change from baseline AUC(0-4) on hormones related to glucose homeostasis (Glucagon)**

|                 |                                                                                     |
|-----------------|-------------------------------------------------------------------------------------|
| End point title | Change from baseline AUC(0-4) on hormones related to glucose homeostasis (Glucagon) |
|-----------------|-------------------------------------------------------------------------------------|

End point description:

Effects of AZD9567 on glucagon AUC(0-4) were assessed following MMTT in comparison to prednisolone.

Here, arbitrary value 9999.9999 represent not applicable.

FAS consisted of all randomised patients who received at least 1 dose of study treatment.

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

End point timeframe:

On Day -1 (Baseline), and Day 4 (Treatment period 1 and 2)

| End point values                    | Cohort 1                | Cohort 2                | Cohort 3                | Cohort 1                |
|-------------------------------------|-------------------------|-------------------------|-------------------------|-------------------------|
| Subject group type                  | Reporting group         | Reporting group         | Reporting group         | Subject analysis set    |
| Number of subjects analysed         | 27                      | 8                       | 9                       | 27                      |
| Units: min*pmol/L                   |                         |                         |                         |                         |
| least squares mean (standard error) |                         |                         |                         |                         |
| AZD9567                             | -36.9846 (± 216.5777)   | 552.0634 (± 213.9300)   | 9999.9999 (± 9999.9999) | -36.9846 (± 216.5777)   |
| Prednisolone                        | 965.6018 (± 216.6054)   | 511.0798 (± 213.5970)   | 259.9835 (± 298.9801)   | 965.6018 (± 216.6054)   |
| Placebo                             | 9999.9999 (± 9999.9999) | 9999.9999 (± 9999.9999) | 361.3971 (± 348.5104)   | 9999.9999 (± 9999.9999) |

| End point values                    | Cohort 2                | Cohort 3                |  |  |
|-------------------------------------|-------------------------|-------------------------|--|--|
| Subject group type                  | Subject analysis set    | Subject analysis set    |  |  |
| Number of subjects analysed         | 8                       | 9                       |  |  |
| Units: min*pmol/L                   |                         |                         |  |  |
| least squares mean (standard error) |                         |                         |  |  |
| AZD9567                             | 552.0634 (± 213.9300)   | 9999.9999 (± 9999.9999) |  |  |
| Prednisolone                        | 511.0798 (± 213.5970)   | 259.9835 (± 298.9801)   |  |  |
| Placebo                             | 9999.9999 (± 9999.9999) | 361.3971 (± 348.5104)   |  |  |

## Statistical analyses

|                                                                            |                                   |
|----------------------------------------------------------------------------|-----------------------------------|
| <b>Statistical analysis title</b>                                          | AZD9567 72mg vs Prednisolone 40mg |
| Statistical analysis description:                                          |                                   |
| Pairwise Comparisons with Prednisolone (AZD9567 72mg vs Prednisolone 40mg) |                                   |
| Comparison groups                                                          | Cohort 1 v Cohort 1               |
| Number of subjects included in analysis                                    | 54                                |
| Analysis specification                                                     | Pre-specified                     |
| Analysis type                                                              | other <sup>[18]</sup>             |
| P-value                                                                    | = 0.003                           |
| Method                                                                     | Mixed models analysis             |
| Parameter estimate                                                         | Mean difference (final values)    |
| Point estimate                                                             | -1002.58                          |
| Confidence interval                                                        |                                   |
| level                                                                      | 95 %                              |
| sides                                                                      | 2-sided                           |
| lower limit                                                                | -1620.21                          |
| upper limit                                                                | -384.95                           |

Notes:

[18] - 27 patients were evaluated in this analysis

|                                                                      |                                |
|----------------------------------------------------------------------|--------------------------------|
| <b>Statistical analysis title</b>                                    | Placebo vs Prednisolone 5mg    |
| Statistical analysis description:                                    |                                |
| Pairwise Comparisons with Prednisolone (Placebo vs Prednisolone 5mg) |                                |
| Comparison groups                                                    | Cohort 3 v Cohort 3            |
| Number of subjects included in analysis                              | 18                             |
| Analysis specification                                               | Pre-specified                  |
| Analysis type                                                        | other <sup>[19]</sup>          |
| P-value                                                              | = 0.754                        |
| Method                                                               | Mixed models analysis          |
| Parameter estimate                                                   | Mean difference (final values) |
| Point estimate                                                       | 101.41                         |
| Confidence interval                                                  |                                |
| level                                                                | 95 %                           |
| sides                                                                | 2-sided                        |
| lower limit                                                          | -628.8                         |
| upper limit                                                          | 831.63                         |

Notes:

[19] - 9 patients were evaluated in this analysis

|                                                                            |                                   |
|----------------------------------------------------------------------------|-----------------------------------|
| <b>Statistical analysis title</b>                                          | AZD9567 40mg vs Prednisolone 20mg |
| Statistical analysis description:                                          |                                   |
| Pairwise Comparisons with Prednisolone (AZD9567 40mg vs Prednisolone 20mg) |                                   |
| Comparison groups                                                          | Cohort 2 v Cohort 2               |
| Number of subjects included in analysis                                    | 16                                |
| Analysis specification                                                     | Pre-specified                     |
| Analysis type                                                              |                                   |
| P-value                                                                    | = 0.865                           |
| Method                                                                     | Mixed models analysis             |
| Parameter estimate                                                         | Mean difference (final values)    |
| Point estimate                                                             | 40.98                             |
| Confidence interval                                                        |                                   |
| level                                                                      | 95 %                              |
| sides                                                                      | 2-sided                           |
| lower limit                                                                | -526.69                           |
| upper limit                                                                | 608.66                            |

### **Secondary: Change from baseline AUC(0-4) on hormones related to glucose homeostasis (Glucagon-like peptide-1 [GLP-1])**

|                 |                                                                                                            |
|-----------------|------------------------------------------------------------------------------------------------------------|
| End point title | Change from baseline AUC(0-4) on hormones related to glucose homeostasis (Glucagon-like peptide-1 [GLP-1]) |
|-----------------|------------------------------------------------------------------------------------------------------------|

End point description:

Effects of AZD9567 on GLP-1 AUC(0-4) were assessed following MMTT in comparison to prednisolone.

The Subject Analysis set was added to report statistical analysis and this is the only option available in order to accommodate reporting of statistical data for cross over cohorts.

Here, arbitrary value 9999.9999 represent not applicable.

FAS consisted of all randomised patients who received at least 1 dose of study treatment.

|                                                            |           |
|------------------------------------------------------------|-----------|
| End point type                                             | Secondary |
| End point timeframe:                                       |           |
| On Day -1 (Baseline), and Day 4 (Treatment period 1 and 2) |           |

| End point values                    | Cohort 1                | Cohort 2                | Cohort 3                | Cohort 1                |
|-------------------------------------|-------------------------|-------------------------|-------------------------|-------------------------|
| Subject group type                  | Reporting group         | Reporting group         | Reporting group         | Subject analysis set    |
| Number of subjects analysed         | 27                      | 8                       | 9                       | 27                      |
| Units: min*pmol/L                   |                         |                         |                         |                         |
| least squares mean (standard error) |                         |                         |                         |                         |
| AZD9567                             | 615.9803 (± 328.8418)   | 322.5690 (± 454.2028)   | 9999.9999 (± 9999.9999) | 615.9803 (± 328.8418)   |
| Prednisolone                        | 1841.8853 (± 328.8877)  | 789.5492 (± 450.2548)   | 575.6726 (± 318.1088)   | 1841.8853 (± 328.8877)  |
| Placebo                             | 9999.9999 (± 9999.9999) | 9999.9999 (± 9999.9999) | 200.3565 (± 317.6326)   | 9999.9999 (± 9999.9999) |

| End point values                    | Cohort 2                | Cohort 3                |  |  |
|-------------------------------------|-------------------------|-------------------------|--|--|
| Subject group type                  | Subject analysis set    | Subject analysis set    |  |  |
| Number of subjects analysed         | 8                       | 9                       |  |  |
| Units: min*pmol/L                   |                         |                         |  |  |
| least squares mean (standard error) |                         |                         |  |  |
| AZD9567                             | 322.5690 (± 454.2028)   | 9999.9999 (± 9999.9999) |  |  |
| Prednisolone                        | 789.5492 (± 450.2548)   | 575.6726 (± 318.1088)   |  |  |
| Placebo                             | 9999.9999 (± 9999.9999) | 200.3565 (± 317.6326)   |  |  |

## Statistical analyses

|                                                                            |                                   |
|----------------------------------------------------------------------------|-----------------------------------|
| Statistical analysis title                                                 | AZD9567 72mg vs Prednisolone 40mg |
| Statistical analysis description:                                          |                                   |
| Pairwise Comparisons with Prednisolone (AZD9567 72mg vs Prednisolone 40mg) |                                   |
| Comparison groups                                                          | Cohort 1 v Cohort 1               |
| Number of subjects included in analysis                                    | 54                                |
| Analysis specification                                                     | Pre-specified                     |
| Analysis type                                                              | other <sup>[20]</sup>             |
| P-value                                                                    | = 0.004                           |
| Method                                                                     | Mixed models analysis             |
| Parameter estimate                                                         | Mean difference (final values)    |
| Point estimate                                                             | -1225.9                           |



|                     |          |
|---------------------|----------|
| Confidence interval |          |
| level               | 95 %     |
| sides               | 2-sided  |
| lower limit         | -2007.22 |
| upper limit         | -444.58  |

Notes:

[20] - 27 patients were evaluated in this analysis

|                                                                            |                                   |
|----------------------------------------------------------------------------|-----------------------------------|
| <b>Statistical analysis title</b>                                          | AZD9567 40mg vs Prednisolone 20mg |
| Statistical analysis description:                                          |                                   |
| Pairwise Comparisons with Prednisolone (AZD9567 40mg vs Prednisolone 20mg) |                                   |
| Comparison groups                                                          | Cohort 2 v Cohort 2               |
| Number of subjects included in analysis                                    | 16                                |
| Analysis specification                                                     | Pre-specified                     |
| Analysis type                                                              | other <sup>[21]</sup>             |
| P-value                                                                    | = 0.313                           |
| Method                                                                     | Mixed models analysis             |
| Parameter estimate                                                         | Mean difference (final values)    |
| Point estimate                                                             | -466.98                           |
| Confidence interval                                                        |                                   |
| level                                                                      | 95 %                              |
| sides                                                                      | 2-sided                           |
| lower limit                                                                | -1521.5                           |
| upper limit                                                                | 587.54                            |

Notes:

[21] - 8 patients were evaluated in this analysis

|                                                                      |                                |
|----------------------------------------------------------------------|--------------------------------|
| <b>Statistical analysis title</b>                                    | Placebo vs Prednisolone 5mg    |
| Statistical analysis description:                                    |                                |
| Pairwise Comparisons with Prednisolone (Placebo vs Prednisolone 5mg) |                                |
| Comparison groups                                                    | Cohort 3 v Cohort 3            |
| Number of subjects included in analysis                              | 18                             |
| Analysis specification                                               | Pre-specified                  |
| Analysis type                                                        | other <sup>[22]</sup>          |
| P-value                                                              | = 0.404                        |
| Method                                                               | Mixed models analysis          |
| Parameter estimate                                                   | Mean difference (final values) |
| Point estimate                                                       | -375.31                        |
| Confidence interval                                                  |                                |
| level                                                                | 95 %                           |
| sides                                                                | 2-sided                        |
| lower limit                                                          | -1433.62                       |
| upper limit                                                          | 682.99                         |

Notes:

[22] - 9 patients were evaluated in this analysis

### **Secondary: Change from baseline AUC(0-4) on hormones related to glucose homeostasis (Glucose-dependent insulin releasing polypeptide [GIP])**

|                 |                                                                                                               |
|-----------------|---------------------------------------------------------------------------------------------------------------|
| End point title | Change from baseline AUC(0-4) on hormones related to glucose homeostasis (Glucose-dependent insulin releasing |
|-----------------|---------------------------------------------------------------------------------------------------------------|

End point description:

Effects of AZD9567 on GIP AUC(0-4) were assessed following MMTT in comparison to prednisolone.

The Subject Analysis set was added to report statistical analysis and this is the only option available in order to accommodate reporting of statistical data for cross over cohorts.

Here, arbitrary value 9999.9999 represent not applicable.

FAS consisted of all randomised patients who received at least 1 dose of study treatment.

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

End point timeframe:

|                                                            |
|------------------------------------------------------------|
| On Day -1 (Baseline), and Day 4 (Treatment period 1 and 2) |
|------------------------------------------------------------|

| End point values                    | Cohort 1                | Cohort 2                | Cohort 3                | Cohort 1                |
|-------------------------------------|-------------------------|-------------------------|-------------------------|-------------------------|
| Subject group type                  | Reporting group         | Reporting group         | Reporting group         | Subject analysis set    |
| Number of subjects analysed         | 27                      | 8                       | 9                       | 27                      |
| Units: min*pmol/L                   |                         |                         |                         |                         |
| least squares mean (standard error) |                         |                         |                         |                         |
| AZD9567                             | 3658.9885 (± 584.5079)  | 3842.9307 (± 1303.1553) | 9999.9999 (± 9999.9999) | 3658.9885 (± 584.5079)  |
| Prednisolone (n= 26,8,9)            | 3293.3563 (± 596.7472)  | 3654.6947 (± 1289.5516) | 3271.5164 (± 823.9967)  | 3293.3563 (± 596.7472)  |
| Placebo                             | 9999.9999 (± 9999.9999) | 9999.9999 (± 9999.9999) | 2210.0670 (± 827.7335)  | 9999.9999 (± 9999.9999) |

| End point values                    | Cohort 2                | Cohort 3                |  |  |
|-------------------------------------|-------------------------|-------------------------|--|--|
| Subject group type                  | Subject analysis set    | Subject analysis set    |  |  |
| Number of subjects analysed         | 8                       | 9                       |  |  |
| Units: min*pmol/L                   |                         |                         |  |  |
| least squares mean (standard error) |                         |                         |  |  |
| AZD9567                             | 3842.9307 (± 1303.1553) | 9999.9999 (± 9999.9999) |  |  |
| Prednisolone (n= 26,8,9)            | 3654.6947 (± 1289.5516) | 3271.5164 (± 823.9967)  |  |  |
| Placebo                             | 9999.9999 (± 9999.9999) | 2210.0670 (± 827.7335)  |  |  |

## Statistical analyses

|                            |                                   |
|----------------------------|-----------------------------------|
| Statistical analysis title | AZD9567 72mg vs Prednisolone 40mg |
|----------------------------|-----------------------------------|

Statistical analysis description:

Pairwise Comparisons with Prednisolone (AZD9567 72mg vs Prednisolone 40mg)

|                   |                     |
|-------------------|---------------------|
| Comparison groups | Cohort 1 v Cohort 1 |
|-------------------|---------------------|

|                                         |                                |
|-----------------------------------------|--------------------------------|
| Number of subjects included in analysis | 54                             |
| Analysis specification                  | Pre-specified                  |
| Analysis type                           | other <sup>[23]</sup>          |
| P-value                                 | = 0.608                        |
| Method                                  | Mixed models analysis          |
| Parameter estimate                      | Mean difference (final values) |
| Point estimate                          | 365.63                         |
| Confidence interval                     |                                |
| level                                   | 95 %                           |
| sides                                   | 2-sided                        |
| lower limit                             | -1097.79                       |
| upper limit                             | 1829.06                        |

Notes:

[23] - 27 patients were evaluated in this analysis

|                                                                      |                                |
|----------------------------------------------------------------------|--------------------------------|
| <b>Statistical analysis title</b>                                    | Placebo vs Prednisolone 5mg    |
| Statistical analysis description:                                    |                                |
| Pairwise Comparisons with Prednisolone (Placebo vs Prednisolone 5mg) |                                |
| Comparison groups                                                    | Cohort 3 v Cohort 3            |
| Number of subjects included in analysis                              | 18                             |
| Analysis specification                                               | Pre-specified                  |
| Analysis type                                                        | other <sup>[24]</sup>          |
| P-value                                                              | = 0.381                        |
| Method                                                               | Mixed models analysis          |
| Parameter estimate                                                   | Mean difference (final values) |
| Point estimate                                                       | -1061.44                       |
| Confidence interval                                                  |                                |
| level                                                                | 95 %                           |
| sides                                                                | 2-sided                        |
| lower limit                                                          | -3588.22                       |
| upper limit                                                          | 1465.32                        |

Notes:

[24] - 9 patients were evaluated in this analysis

|                                                                            |                                   |
|----------------------------------------------------------------------------|-----------------------------------|
| <b>Statistical analysis title</b>                                          | AZD9567 40mg vs Prednisolone 20mg |
| Statistical analysis description:                                          |                                   |
| Pairwise Comparisons with Prednisolone (AZD9567 40mg vs Prednisolone 20mg) |                                   |
| Comparison groups                                                          | Cohort 2 v Cohort 2               |
| Number of subjects included in analysis                                    | 16                                |
| Analysis specification                                                     | Pre-specified                     |
| Analysis type                                                              | other <sup>[25]</sup>             |
| P-value                                                                    | = 0.897                           |
| Method                                                                     | Mixed models analysis             |
| Parameter estimate                                                         | Mean difference (final values)    |
| Point estimate                                                             | 188.23                            |
| Confidence interval                                                        |                                   |
| level                                                                      | 95 %                              |
| sides                                                                      | 2-sided                           |
| lower limit                                                                | -3214.33                          |
| upper limit                                                                | 3590.8                            |

Notes:

[25] - 8 patients were evaluated in this analysis

## Secondary: Change from baseline in AUC(0-4) on C-peptide

|                 |                                               |
|-----------------|-----------------------------------------------|
| End point title | Change from baseline in AUC(0-4) on C-peptide |
|-----------------|-----------------------------------------------|

End point description:

Effects of AZD9567 on C-peptide AUC(0-4) were assessed through a MMTT in comparison to prednisolone.

The Subject Analysis set was added to report statistical analysis and this is the only option available in order to accommodate reporting of statistical data for cross over cohorts.

Here, arbitrary value 9999.9999 represent not applicable.

FAS consisted of all randomised patients who received at least 1 dose of study treatment.

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

End point timeframe:

On Day -1 (Baseline), and Day 4 (Treatment period 1 and 2)

| End point values                      | Cohort 1                | Cohort 2                | Cohort 3                | Cohort 1                |
|---------------------------------------|-------------------------|-------------------------|-------------------------|-------------------------|
| Subject group type                    | Reporting group         | Reporting group         | Reporting group         | Subject analysis set    |
| Number of subjects analysed           | 27                      | 8                       | 9                       | 27                      |
| Units: minute*nanomole/L (min*nmol/L) |                         |                         |                         |                         |
| least squares mean (standard error)   |                         |                         |                         |                         |
| AZD9567                               | 85.3305 (± 13.4279)     | 82.1134 (± 22.9858)     | 9999.9999 (± 9999.9999) | 85.3305 (± 13.4279)     |
| Prednisolone                          | 24.9094 (± 13.4282)     | 55.6606 (± 22.6155)     | 24.7245 (± 22.2183)     | 24.9094 (± 13.4282)     |
| Placebo                               | 9999.9999 (± 9999.9999) | 9999.9999 (± 9999.9999) | 0.7002 (± 22.0424)      | 9999.9999 (± 9999.9999) |

| End point values                      | Cohort 2                | Cohort 3                |  |  |
|---------------------------------------|-------------------------|-------------------------|--|--|
| Subject group type                    | Subject analysis set    | Subject analysis set    |  |  |
| Number of subjects analysed           | 8                       | 9                       |  |  |
| Units: minute*nanomole/L (min*nmol/L) |                         |                         |  |  |
| least squares mean (standard error)   |                         |                         |  |  |
| AZD9567                               | 82.1134 (± 22.9858)     | 9999.9999 (± 9999.9999) |  |  |
| Prednisolone                          | 55.6606 (± 22.6155)     | 24.7245 (± 22.2183)     |  |  |
| Placebo                               | 9999.9999 (± 9999.9999) | 0.7002 (± 22.0424)      |  |  |

## Statistical analyses

|                                                                            |                                   |
|----------------------------------------------------------------------------|-----------------------------------|
| <b>Statistical analysis title</b>                                          | AZD9567 72mg vs Prednisolone 40mg |
| Statistical analysis description:                                          |                                   |
| Pairwise Comparisons with Prednisolone (AZD9567 72mg vs Prednisolone 40mg) |                                   |
| Comparison groups                                                          | Cohort 1 v Cohort 1               |
| Number of subjects included in analysis                                    | 54                                |
| Analysis specification                                                     | Pre-specified                     |
| Analysis type                                                              | other <sup>[26]</sup>             |
| P-value                                                                    | < 0.001                           |
| Method                                                                     | Mixed models analysis             |
| Parameter estimate                                                         | Mean difference (final values)    |
| Point estimate                                                             | 60.42                             |
| Confidence interval                                                        |                                   |
| level                                                                      | 95 %                              |
| sides                                                                      | 2-sided                           |
| lower limit                                                                | 29.49                             |
| upper limit                                                                | 91.35                             |

Notes:

[26] - 27 patients were evaluated in this analysis

|                                                                      |                                |
|----------------------------------------------------------------------|--------------------------------|
| <b>Statistical analysis title</b>                                    | Placebo vs Prednisolone 5mg    |
| Statistical analysis description:                                    |                                |
| Pairwise Comparisons with Prednisolone (Placebo vs Prednisolone 5mg) |                                |
| Comparison groups                                                    | Cohort 3 v Cohort 3            |
| Number of subjects included in analysis                              | 18                             |
| Analysis specification                                               | Pre-specified                  |
| Analysis type                                                        | other <sup>[27]</sup>          |
| P-value                                                              | = 0.282                        |
| Method                                                               | Mixed models analysis          |
| Parameter estimate                                                   | Mean difference (final values) |
| Point estimate                                                       | -24.02                         |
| Confidence interval                                                  |                                |
| level                                                                | 95 %                           |
| sides                                                                | 2-sided                        |
| lower limit                                                          | -74.07                         |
| upper limit                                                          | 26.02                          |

Notes:

[27] - 9 patients were evaluated in this analysis

|                                                                            |                                   |
|----------------------------------------------------------------------------|-----------------------------------|
| <b>Statistical analysis title</b>                                          | AZD9567 40mg vs Prednisolone 20mg |
| Statistical analysis description:                                          |                                   |
| Pairwise Comparisons with Prednisolone (AZD9567 40mg vs Prednisolone 20mg) |                                   |
| Comparison groups                                                          | Cohort 2 v Cohort 2               |
| Number of subjects included in analysis                                    | 16                                |
| Analysis specification                                                     | Pre-specified                     |
| Analysis type                                                              | other <sup>[28]</sup>             |
| P-value                                                                    | = 0.432                           |
| Method                                                                     | Mixed models analysis             |
| Parameter estimate                                                         | Mean difference (final values)    |
| Point estimate                                                             | 26.45                             |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -44.94  |
| upper limit         | 97.84   |

Notes:

[28] - 8 patients were evaluated in this analysis

## Secondary: Change from baseline in ratio of insulin to glucose level between 10 and 0 minutes ( $\Delta I10/\Delta G10$ )

|                 |                                                                                                                |
|-----------------|----------------------------------------------------------------------------------------------------------------|
| End point title | Change from baseline in ratio of insulin to glucose level between 10 and 0 minutes ( $\Delta I10/\Delta G10$ ) |
|-----------------|----------------------------------------------------------------------------------------------------------------|

End point description:

Effects of AZD9567 on  $\Delta I10/\Delta G10$  of beta cell function from the MMTT compared to Prednisolone was evaluated.

The Subject Analysis set was added to report statistical analysis and this is the only option available in order to accommodate reporting of statistical data for cross over cohorts.

Here, arbitrary value 9999.9999 represent not applicable.

FAS consisted of all randomised patients who received at least 1 dose of study treatment.

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

End point timeframe:

On Day -1 (Baseline), and Day 4 (Treatment period 1 and 2)

| End point values                    | Cohort 1                     | Cohort 2                     | Cohort 3                     | Cohort 1                     |
|-------------------------------------|------------------------------|------------------------------|------------------------------|------------------------------|
| Subject group type                  | Reporting group              | Reporting group              | Reporting group              | Subject analysis set         |
| Number of subjects analysed         | 27                           | 8                            | 9                            | 27                           |
| Units: Ratio                        |                              |                              |                              |                              |
| least squares mean (standard error) |                              |                              |                              |                              |
| AZD9567 (n= 16,8,9)                 | -0.5249 ( $\pm$ 0.6632)      | 9999.9999 ( $\pm$ 9999.9999) | 9999.9999 ( $\pm$ 9999.9999) | -0.5249 ( $\pm$ 0.6632)      |
| Prednisolone (n= 18,8,5)            | 0.0774 ( $\pm$ 0.6674)       | 9999.9999 ( $\pm$ 9999.9999) | -0.8153 ( $\pm$ 0.8305)      | 0.0774 ( $\pm$ 0.6674)       |
| Placebo (n=27,8,7)                  | 9999.9999 ( $\pm$ 9999.9999) | 9999.9999 ( $\pm$ 9999.9999) | -0.3532 ( $\pm$ 0.6893)      | 9999.9999 ( $\pm$ 9999.9999) |

| End point values                    | Cohort 2                     | Cohort 3                     |  |  |
|-------------------------------------|------------------------------|------------------------------|--|--|
| Subject group type                  | Subject analysis set         | Subject analysis set         |  |  |
| Number of subjects analysed         | 8                            | 9                            |  |  |
| Units: Ratio                        |                              |                              |  |  |
| least squares mean (standard error) |                              |                              |  |  |
| AZD9567 (n= 16,8,9)                 | 9999.9999 ( $\pm$ 9999.9999) | 9999.9999 ( $\pm$ 9999.9999) |  |  |
| Prednisolone (n= 18,8,5)            | 9999.9999 ( $\pm$ 9999.9999) | -0.8153 ( $\pm$ 0.8305)      |  |  |
| Placebo (n=27,8,7)                  | 9999.9999 ( $\pm$ 9999.9999) | -0.3532 ( $\pm$ 0.6893)      |  |  |

## Statistical analyses

|                                                                                                                 |                                   |
|-----------------------------------------------------------------------------------------------------------------|-----------------------------------|
| <b>Statistical analysis title</b>                                                                               | AZD9567 72mg vs Prednisolone 40mg |
| Statistical analysis description:<br>Pairwise Comparisons with Prednisolone (AZD9567 72mg vs Prednisolone 40mg) |                                   |
| Comparison groups                                                                                               | Cohort 1 v Cohort 1               |
| Number of subjects included in analysis                                                                         | 54                                |
| Analysis specification                                                                                          | Pre-specified                     |
| Analysis type                                                                                                   |                                   |
| P-value                                                                                                         | = 0.531                           |
| Method                                                                                                          | Mixed models analysis             |
| Parameter estimate                                                                                              | Mean difference (final values)    |
| Point estimate                                                                                                  | -0.6                              |
| Confidence interval                                                                                             |                                   |
| level                                                                                                           | 95 %                              |
| sides                                                                                                           | 2-sided                           |
| lower limit                                                                                                     | -2.54                             |
| upper limit                                                                                                     | 1.34                              |

|                                                                                                           |                                |
|-----------------------------------------------------------------------------------------------------------|--------------------------------|
| <b>Statistical analysis title</b>                                                                         | Placebo vs Prednisolone 5mg    |
| Statistical analysis description:<br>Pairwise Comparisons with Prednisolone (Placebo vs Prednisolone 5mg) |                                |
| Comparison groups                                                                                         | Cohort 3 v Cohort 3            |
| Number of subjects included in analysis                                                                   | 18                             |
| Analysis specification                                                                                    | Pre-specified                  |
| Analysis type                                                                                             | other <sup>[29]</sup>          |
| P-value                                                                                                   | = 0.682                        |
| Method                                                                                                    | Mixed models analysis          |
| Parameter estimate                                                                                        | Mean difference (final values) |
| Point estimate                                                                                            | 0.46                           |
| Confidence interval                                                                                       |                                |
| level                                                                                                     | 95 %                           |
| sides                                                                                                     | 2-sided                        |
| lower limit                                                                                               | -2.09                          |
| upper limit                                                                                               | 3.01                           |

Notes:

[29] - 9 patients were evaluated in this analysis

## Secondary: Change from baseline in ratio of insulin to glucose level between 30 and 0 minutes [ $\Delta I30/\Delta G30$ ]

|                 |                                                                                                                |
|-----------------|----------------------------------------------------------------------------------------------------------------|
| End point title | Change from baseline in ratio of insulin to glucose level between 30 and 0 minutes [ $\Delta I30/\Delta G30$ ] |
|-----------------|----------------------------------------------------------------------------------------------------------------|

End point description:

Effects of AZD9567 on  $\Delta I30/\Delta G30$  of beta cell function from the MMTT compared to Prednisolone was evaluated.

The Subject Analysis set was added to report statistical analysis and this is the only option available in order to accommodate reporting of statistical data for cross over cohorts.

Here, arbitrary value 9999.9999 represent not applicable.

FAS consisted of all randomised patients who received at least 1 dose of study treatment.

|                                                            |           |
|------------------------------------------------------------|-----------|
| End point type                                             | Secondary |
| End point timeframe:                                       |           |
| On Day -1 (Baseline), and Day 4 (Treatment period 1 and 2) |           |

| End point values                    | Cohort 1                     | Cohort 2                     | Cohort 3                     | Cohort 1                     |
|-------------------------------------|------------------------------|------------------------------|------------------------------|------------------------------|
| Subject group type                  | Reporting group              | Reporting group              | Reporting group              | Subject analysis set         |
| Number of subjects analysed         | 27                           | 8                            | 9                            | 27                           |
| Units: Ratio                        |                              |                              |                              |                              |
| least squares mean (standard error) |                              |                              |                              |                              |
| AZD9567 (n= 25,8,9)                 | 0.1203 ( $\pm$ 0.0726)       | 0.1824 ( $\pm$ 0.0773)       | 9999.9999 ( $\pm$ 9999.9999) | 0.1203 ( $\pm$ 0.0726)       |
| Prednisolone (n= 24,6,8)            | 0.0530 ( $\pm$ 0.0755)       | 0.0943 ( $\pm$ 0.1264)       | -0.1047 ( $\pm$ 0.0665)      | 0.0530 ( $\pm$ 0.0755)       |
| Placebo                             | 9999.9999 ( $\pm$ 9999.9999) | 9999.9999 ( $\pm$ 9999.9999) | 0.0209 ( $\pm$ 0.0599)       | 9999.9999 ( $\pm$ 9999.9999) |

| End point values                    | Cohort 2                     | Cohort 3                     |  |  |
|-------------------------------------|------------------------------|------------------------------|--|--|
| Subject group type                  | Subject analysis set         | Subject analysis set         |  |  |
| Number of subjects analysed         | 8                            | 9                            |  |  |
| Units: Ratio                        |                              |                              |  |  |
| least squares mean (standard error) |                              |                              |  |  |
| AZD9567 (n= 25,8,9)                 | 0.1824 ( $\pm$ 0.0773)       | 9999.9999 ( $\pm$ 9999.9999) |  |  |
| Prednisolone (n= 24,6,8)            | 0.0943 ( $\pm$ 0.1264)       | -0.1047 ( $\pm$ 0.0665)      |  |  |
| Placebo                             | 9999.9999 ( $\pm$ 9999.9999) | 0.0209 ( $\pm$ 0.0599)       |  |  |

## Statistical analyses

|                                                                            |                                   |
|----------------------------------------------------------------------------|-----------------------------------|
| Statistical analysis title                                                 | AZD9567 72mg vs Prednisolone 40mg |
| Statistical analysis description:                                          |                                   |
| Pairwise Comparisons with Prednisolone (AZD9567 72mg vs Prednisolone 40mg) |                                   |
| Comparison groups                                                          | Cohort 1 v Cohort 1               |



|                                         |                                |
|-----------------------------------------|--------------------------------|
| Number of subjects included in analysis | 54                             |
| Analysis specification                  | Pre-specified                  |
| Analysis type                           | other <sup>[30]</sup>          |
| P-value                                 | = 0.526                        |
| Method                                  | Mixed models analysis          |
| Parameter estimate                      | Mean difference (final values) |
| Point estimate                          | 0.06                           |
| Confidence interval                     |                                |
| level                                   | 95 %                           |
| sides                                   | 2-sided                        |
| lower limit                             | -0.15                          |
| upper limit                             | 0.28                           |

Notes:

[30] - 27 patients were evaluated in this analysis

|                                                                      |                                |
|----------------------------------------------------------------------|--------------------------------|
| <b>Statistical analysis title</b>                                    | Placebo vs Prednisolone 5mg    |
| Statistical analysis description:                                    |                                |
| Pairwise Comparisons with Prednisolone (Placebo vs Prednisolone 5mg) |                                |
| Comparison groups                                                    | Cohort 3 v Cohort 3            |
| Number of subjects included in analysis                              | 18                             |
| Analysis specification                                               | Pre-specified                  |
| Analysis type                                                        | other <sup>[31]</sup>          |
| P-value                                                              | = 0.166                        |
| Method                                                               | Mixed models analysis          |
| Parameter estimate                                                   | Mean difference (final values) |
| Point estimate                                                       | 0.12                           |
| Confidence interval                                                  |                                |
| level                                                                | 95 %                           |
| sides                                                                | 2-sided                        |
| lower limit                                                          | -0.06                          |
| upper limit                                                          | 0.31                           |

Notes:

[31] - 9 patients were evaluated in this analysis

|                                                                            |                                   |
|----------------------------------------------------------------------------|-----------------------------------|
| <b>Statistical analysis title</b>                                          | AZD9567 40mg vs Prednisolone 20mg |
| Statistical analysis description:                                          |                                   |
| Pairwise Comparisons with Prednisolone (AZD9567 40mg vs Prednisolone 20mg) |                                   |
| Comparison groups                                                          | Cohort 2 v Cohort 2               |
| Number of subjects included in analysis                                    | 16                                |
| Analysis specification                                                     | Pre-specified                     |
| Analysis type                                                              | other <sup>[32]</sup>             |
| P-value                                                                    | = 0.569                           |
| Method                                                                     | Mixed models analysis             |
| Parameter estimate                                                         | Mean difference (final values)    |
| Point estimate                                                             | 0.08                              |
| Confidence interval                                                        |                                   |
| level                                                                      | 95 %                              |
| sides                                                                      | 2-sided                           |
| lower limit                                                                | -0.26                             |
| upper limit                                                                | 0.44                              |

Notes:

[32] - 8 patients were evaluated in this analysis

## Secondary: Change from baseline in ratio of C-peptide to glucose level between 10 and 0 minutes ( $\Delta C10/\Delta G10$ )

|                 |                                                                                                                  |
|-----------------|------------------------------------------------------------------------------------------------------------------|
| End point title | Change from baseline in ratio of C-peptide to glucose level between 10 and 0 minutes ( $\Delta C10/\Delta G10$ ) |
|-----------------|------------------------------------------------------------------------------------------------------------------|

End point description:

Effects of AZD9567 on  $\Delta C10/\Delta G10$  of beta cell function from the MMTT compared to Prednisolone was evaluated.

The Subject Analysis set was added to report statistical analysis and this is the only option available in order to accommodate reporting of statistical data for cross over cohorts.

Here, arbitrary value 9999.9999 represent not applicable.

FAS consisted of all randomised patients who received at least 1 dose of study treatment.

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

End point timeframe:

On Day -1 (Baseline), and Day 4 (Treatment period 1 and 2)

| End point values                    | Cohort 1                     | Cohort 2                     | Cohort 3                     | Cohort 1                     |
|-------------------------------------|------------------------------|------------------------------|------------------------------|------------------------------|
| Subject group type                  | Reporting group              | Reporting group              | Reporting group              | Subject analysis set         |
| Number of subjects analysed         | 27                           | 8                            | 9                            | 27                           |
| Units: Ratio                        |                              |                              |                              |                              |
| least squares mean (standard error) |                              |                              |                              |                              |
| AZD9567 (n= 17,6,9)                 | -0.0004 ( $\pm$ 0.0095)      | 0.0059 ( $\pm$ 0.0041)       | 9999.9999 ( $\pm$ 9999.9999) | -0.0004 ( $\pm$ 0.0095)      |
| Prednisolone (n= 20,4,6)            | -0.0103 ( $\pm$ 0.0092)      | 0.0026 ( $\pm$ 0.0047)       | -0.0033 ( $\pm$ 0.0064)      | -0.0103 ( $\pm$ 0.0092)      |
| Placebo (n= 27,8,7)                 | 9999.9999 ( $\pm$ 9999.9999) | 9999.9999 ( $\pm$ 9999.9999) | -0.0024 ( $\pm$ 0.0057)      | 9999.9999 ( $\pm$ 9999.9999) |

| End point values                    | Cohort 2                     | Cohort 3                     |  |  |
|-------------------------------------|------------------------------|------------------------------|--|--|
| Subject group type                  | Subject analysis set         | Subject analysis set         |  |  |
| Number of subjects analysed         | 8                            | 9                            |  |  |
| Units: Ratio                        |                              |                              |  |  |
| least squares mean (standard error) |                              |                              |  |  |
| AZD9567 (n= 17,6,9)                 | 0.0059 ( $\pm$ 0.0041)       | 9999.9999 ( $\pm$ 9999.9999) |  |  |
| Prednisolone (n= 20,4,6)            | 0.0026 ( $\pm$ 0.0047)       | -0.0033 ( $\pm$ 0.0064)      |  |  |
| Placebo (n= 27,8,7)                 | 9999.9999 ( $\pm$ 9999.9999) | -0.0024 ( $\pm$ 0.0057)      |  |  |

## Statistical analyses

|                                                                            |                                   |
|----------------------------------------------------------------------------|-----------------------------------|
| <b>Statistical analysis title</b>                                          | AZD9567 72mg vs Prednisolone 40mg |
| Statistical analysis description:                                          |                                   |
| Pairwise Comparisons with Prednisolone (AZD9567 72mg vs Prednisolone 40mg) |                                   |
| Comparison groups                                                          | Cohort 1 v Cohort 1               |
| Number of subjects included in analysis                                    | 54                                |
| Analysis specification                                                     | Pre-specified                     |
| Analysis type                                                              |                                   |
| P-value                                                                    | = 0.226                           |
| Method                                                                     | Mixed models analysis             |
| Parameter estimate                                                         | Mean difference (final values)    |
| Point estimate                                                             | 0.01                              |
| Confidence interval                                                        |                                   |
| level                                                                      | 95 %                              |
| sides                                                                      | 2-sided                           |
| lower limit                                                                | -0.0072                           |
| upper limit                                                                | 0.0271                            |

|                                                                      |                                |
|----------------------------------------------------------------------|--------------------------------|
| <b>Statistical analysis title</b>                                    | Placebo vs Prednisolone 5mg    |
| Statistical analysis description:                                    |                                |
| Pairwise Comparisons with Prednisolone (Placebo vs Prednisolone 5mg) |                                |
| Comparison groups                                                    | Cohort 3 v Cohort 3            |
| Number of subjects included in analysis                              | 18                             |
| Analysis specification                                               | Pre-specified                  |
| Analysis type                                                        | other <sup>[33]</sup>          |
| P-value                                                              | = 0.917                        |
| Method                                                               | Mixed models analysis          |
| Parameter estimate                                                   | Mean difference (final values) |
| Point estimate                                                       | 0.0009                         |
| Confidence interval                                                  |                                |
| level                                                                | 95 %                           |
| sides                                                                | 2-sided                        |
| lower limit                                                          | -0.0189                        |
| upper limit                                                          | 0.0207                         |

Notes:

[33] - 9 patients were evaluated in this analysis

|                                                                            |                                   |
|----------------------------------------------------------------------------|-----------------------------------|
| <b>Statistical analysis title</b>                                          | AZD9567 40mg vs Prednisolone 20mg |
| Statistical analysis description:                                          |                                   |
| Pairwise Comparisons with Prednisolone (AZD9567 40mg vs Prednisolone 20mg) |                                   |
| Comparison groups                                                          | Cohort 2 v Cohort 2               |
| Number of subjects included in analysis                                    | 16                                |
| Analysis specification                                                     | Pre-specified                     |
| Analysis type                                                              | other <sup>[34]</sup>             |
| P-value                                                                    | = 0.619                           |
| Method                                                                     | Mixed models analysis             |
| Parameter estimate                                                         | Mean difference (final values)    |
| Point estimate                                                             | 0.0033                            |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -0.0128 |
| upper limit         | 0.0195  |

Notes:

[34] - 8 patients were evaluated in this analysis

### Secondary: Change from baseline in ratio of C-peptide to glucose level between 30 and 0 minutes ( $\Delta C30/\Delta G30$ )

|                 |                                                                                                                  |
|-----------------|------------------------------------------------------------------------------------------------------------------|
| End point title | Change from baseline in ratio of C-peptide to glucose level between 30 and 0 minutes ( $\Delta C30/\Delta G30$ ) |
|-----------------|------------------------------------------------------------------------------------------------------------------|

End point description:

Effects of AZD9567 on  $\Delta C30/\Delta G30$  of beta cell function from the MMTT compared to Prednisolone was evaluated.

The Subject Analysis set was added to report statistical analysis and this is the only option available in order to accommodate reporting of statistical data for cross over cohorts.

Here, arbitrary value 9999.9999 represent not applicable.

FAS consisted of all randomised patients who received at least 1 dose of study treatment.

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

End point timeframe:

On Day -1 (Baseline), and Day 4 (Treatment period 1 and 2)

| End point values                    | Cohort 1                     | Cohort 2                     | Cohort 3                     | Cohort 1                     |
|-------------------------------------|------------------------------|------------------------------|------------------------------|------------------------------|
| Subject group type                  | Reporting group              | Reporting group              | Reporting group              | Subject analysis set         |
| Number of subjects analysed         | 27                           | 8                            | 9                            | 27                           |
| Units: Ratio                        |                              |                              |                              |                              |
| least squares mean (standard error) |                              |                              |                              |                              |
| AZD9567                             | 0.0012 ( $\pm$ 0.0005)       | 0.0007 ( $\pm$ 0.0005)       | 9999.9999 ( $\pm$ 9999.9999) | 0.0012 ( $\pm$ 0.0005)       |
| Prednisolone                        | 0.0005 ( $\pm$ 0.0005)       | 0.0004 ( $\pm$ 0.0005)       | -0.0010 ( $\pm$ 0.0005)      | 0.0005 ( $\pm$ 0.0005)       |
| Placebo                             | 9999.9999 ( $\pm$ 9999.9999) | 9999.9999 ( $\pm$ 9999.9999) | 0.0002 ( $\pm$ 0.0005)       | 9999.9999 ( $\pm$ 9999.9999) |

| End point values                    | Cohort 2                     | Cohort 3                     |  |  |
|-------------------------------------|------------------------------|------------------------------|--|--|
| Subject group type                  | Subject analysis set         | Subject analysis set         |  |  |
| Number of subjects analysed         | 8                            | 9                            |  |  |
| Units: Ratio                        |                              |                              |  |  |
| least squares mean (standard error) |                              |                              |  |  |
| AZD9567                             | 0.0007 ( $\pm$ 0.0005)       | 9999.9999 ( $\pm$ 9999.9999) |  |  |
| Prednisolone                        | 0.0004 ( $\pm$ 0.0005)       | -0.0010 ( $\pm$ 0.0005)      |  |  |
| Placebo                             | 9999.9999 ( $\pm$ 9999.9999) | 0.0002 ( $\pm$ 0.0005)       |  |  |

## Statistical analyses

|                                                                            |                                   |
|----------------------------------------------------------------------------|-----------------------------------|
| <b>Statistical analysis title</b>                                          | AZD9567 72mg vs Prednisolone 40mg |
| Statistical analysis description:                                          |                                   |
| Pairwise Comparisons with Prednisolone (AZD9567 72mg vs Prednisolone 40mg) |                                   |
| Comparison groups                                                          | Cohort 1 v Cohort 1               |
| Number of subjects included in analysis                                    | 54                                |
| Analysis specification                                                     | Pre-specified                     |
| Analysis type                                                              |                                   |
| P-value                                                                    | = 0.357                           |
| Method                                                                     | Mixed models analysis             |
| Parameter estimate                                                         | Mean difference (final values)    |
| Point estimate                                                             | 0.0007                            |
| Confidence interval                                                        |                                   |
| level                                                                      | 95 %                              |
| sides                                                                      | 2-sided                           |
| lower limit                                                                | -0.0008                           |
| upper limit                                                                | 0.0022                            |

|                                                                      |                                |
|----------------------------------------------------------------------|--------------------------------|
| <b>Statistical analysis title</b>                                    | Placebo vs Prednisolone 5mg    |
| Statistical analysis description:                                    |                                |
| Pairwise Comparisons with Prednisolone (Placebo vs Prednisolone 5mg) |                                |
| Comparison groups                                                    | Cohort 3 v Cohort 3            |
| Number of subjects included in analysis                              | 18                             |
| Analysis specification                                               | Pre-specified                  |
| Analysis type                                                        | other <sup>[35]</sup>          |
| P-value                                                              | = 0.096                        |
| Method                                                               | Mixed models analysis          |
| Parameter estimate                                                   | Mean difference (final values) |
| Point estimate                                                       | 0.0012                         |
| Confidence interval                                                  |                                |
| level                                                                | 95 %                           |
| sides                                                                | 2-sided                        |
| lower limit                                                          | -0.0002                        |
| upper limit                                                          | 0.0026                         |

Notes:

[35] - 9 patients were evaluated in this analysis

|                                                                            |                                   |
|----------------------------------------------------------------------------|-----------------------------------|
| <b>Statistical analysis title</b>                                          | AZD9567 40mg vs Prednisolone 20mg |
| Statistical analysis description:                                          |                                   |
| Pairwise Comparisons with Prednisolone (AZD9567 40mg vs Prednisolone 20mg) |                                   |
| Comparison groups                                                          | Cohort 2 v Cohort 2               |

|                                         |                                |
|-----------------------------------------|--------------------------------|
| Number of subjects included in analysis | 16                             |
| Analysis specification                  | Pre-specified                  |
| Analysis type                           | other <sup>[36]</sup>          |
| P-value                                 | = 0.676                        |
| Method                                  | Mixed models analysis          |
| Parameter estimate                      | Mean difference (final values) |
| Point estimate                          | 0.0003                         |
| Confidence interval                     |                                |
| level                                   | 95 %                           |
| sides                                   | 2-sided                        |
| lower limit                             | -0.0012                        |
| upper limit                             | 0.0017                         |

Notes:

[36] - 8 patients were evaluated in this analysis

## Secondary: Change from baseline in 24-hour urinary potassium concentration

|                 |                                                                 |
|-----------------|-----------------------------------------------------------------|
| End point title | Change from baseline in 24-hour urinary potassium concentration |
|-----------------|-----------------------------------------------------------------|

End point description:

The concentration of potassium in urine was measured over 24 hours to determine the effect of AZD9567 on urinary potassium (U-K) excretion compared to prednisolone.

The Subject Analysis set was added to report statistical analysis and this is the only option available in order to accommodate reporting of statistical data for cross over cohorts.

Here, arbitrary value 9999.9999 represent not applicable.

FAS consisted of all randomised patients who received at least 1 dose of study treatment.

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

End point timeframe:

On Day -1 (Baseline), and Day 4 (Treatment period 1 and 2)

| End point values                    | Cohort 1                | Cohort 2                | Cohort 3                | Cohort 1                |
|-------------------------------------|-------------------------|-------------------------|-------------------------|-------------------------|
| Subject group type                  | Reporting group         | Reporting group         | Reporting group         | Subject analysis set    |
| Number of subjects analysed         | 27                      | 8                       | 9                       | 27                      |
| Units: mmol/day                     |                         |                         |                         |                         |
| least squares mean (standard error) |                         |                         |                         |                         |
| AZD9567                             | -2.92 (± 3.27)          | -6.05 (± 4.30)          | 9999.9999 (± 9999.9999) | -2.92 (± 3.27)          |
| Prednisolone                        | -1.19 (± 3.27)          | 4.92 (± 4.29)           | -2.49 (± 9.08)          | -1.19 (± 3.27)          |
| Placebo                             | 9999.9999 (± 9999.9999) | 9999.9999 (± 9999.9999) | -2.85 (± 9.07)          | 9999.9999 (± 9999.9999) |

| End point values                    | Cohort 2             | Cohort 3             |  |  |
|-------------------------------------|----------------------|----------------------|--|--|
| Subject group type                  | Subject analysis set | Subject analysis set |  |  |
| Number of subjects analysed         | 8                    | 9                    |  |  |
| Units: mmol/day                     |                      |                      |  |  |
| least squares mean (standard error) |                      |                      |  |  |

|              |                              |                              |  |  |
|--------------|------------------------------|------------------------------|--|--|
| AZD9567      | -6.05 ( $\pm$ 4.30)          | 9999.9999 ( $\pm$ 9999.9999) |  |  |
| Prednisolone | 4.92 ( $\pm$ 4.29)           | -2.49 ( $\pm$ 9.08)          |  |  |
| Placebo      | 9999.9999 ( $\pm$ 9999.9999) | -2.85 ( $\pm$ 9.07)          |  |  |

## Statistical analyses

| Statistical analysis title                                                 | AZD9567 72mg vs Prednisolone 40mg |
|----------------------------------------------------------------------------|-----------------------------------|
| Statistical analysis description:                                          |                                   |
| Pairwise Comparisons with Prednisolone (AZD9567 72mg vs Prednisolone 40mg) |                                   |
| Comparison groups                                                          | Cohort 1 v Cohort 1               |
| Number of subjects included in analysis                                    | 54                                |
| Analysis specification                                                     | Pre-specified                     |
| Analysis type                                                              |                                   |
| P-value                                                                    | = 0.646                           |
| Method                                                                     | Mixed models analysis             |
| Parameter estimate                                                         | Mean difference (final values)    |
| Point estimate                                                             | -1.73                             |
| Confidence interval                                                        |                                   |
| level                                                                      | 95 %                              |
| sides                                                                      | 2-sided                           |
| lower limit                                                                | -9.4                              |
| upper limit                                                                | 5.95                              |

| Statistical analysis title                                           | Placebo vs Prednisolone 5mg    |
|----------------------------------------------------------------------|--------------------------------|
| Statistical analysis description:                                    |                                |
| Pairwise Comparisons with Prednisolone (Placebo vs Prednisolone 5mg) |                                |
| Comparison groups                                                    | Cohort 3 v Cohort 3            |
| Number of subjects included in analysis                              | 18                             |
| Analysis specification                                               | Pre-specified                  |
| Analysis type                                                        | other <sup>[37]</sup>          |
| P-value                                                              | = 0.932                        |
| Method                                                               | Mixed models analysis          |
| Parameter estimate                                                   | Mean difference (final values) |
| Point estimate                                                       | -0.35                          |
| Confidence interval                                                  |                                |
| level                                                                | 95 %                           |
| sides                                                                | 2-sided                        |
| lower limit                                                          | -10.32                         |
| upper limit                                                          | 9.61                           |

Notes:

[37] - 9 patients were evaluated in this analysis

| Statistical analysis title | AZD9567 40mg vs Prednisolone 20mg |
|----------------------------|-----------------------------------|
|----------------------------|-----------------------------------|

Statistical analysis description:

Pairwise Comparisons with Prednisolone (AZD9567 40mg vs Prednisolone 20mg)

|                                         |                                |
|-----------------------------------------|--------------------------------|
| Comparison groups                       | Cohort 2 v Cohort 2            |
| Number of subjects included in analysis | 16                             |
| Analysis specification                  | Pre-specified                  |
| Analysis type                           |                                |
| P-value                                 | = 0.11                         |
| Method                                  | Mixed models analysis          |
| Parameter estimate                      | Mean difference (final values) |
| Point estimate                          | -10.97                         |
| Confidence interval                     |                                |
| level                                   | 95 %                           |
| sides                                   | 2-sided                        |
| lower limit                             | -25.39                         |
| upper limit                             | 3.44                           |

### Secondary: Change from baseline in 24-hour urinary sodium concentration

|                 |                                                              |
|-----------------|--------------------------------------------------------------|
| End point title | Change from baseline in 24-hour urinary sodium concentration |
|-----------------|--------------------------------------------------------------|

End point description:

The concentration of sodium in urine was measured over 24 hours to determine the effect of AZD9567 on urinary-sodium (U-Na) excretion compared to prednisolone.

The Subject Analysis set was added to report statistical analysis and this is the only option available in order to accommodate reporting of statistical data for cross over cohorts.

Here, arbitrary value 9999.9999 represent not applicable.

FAS consisted of all randomised patients who received at least 1 dose of study treatment.

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

End point timeframe:

On Day -1 (Baseline), and Day 4 (Treatment period 1 and 2)

| End point values                    | Cohort 1                | Cohort 2                | Cohort 3                | Cohort 1                |
|-------------------------------------|-------------------------|-------------------------|-------------------------|-------------------------|
| Subject group type                  | Reporting group         | Reporting group         | Reporting group         | Subject analysis set    |
| Number of subjects analysed         | 27                      | 8                       | 9                       | 27                      |
| Units: mmol/day                     |                         |                         |                         |                         |
| least squares mean (standard error) |                         |                         |                         |                         |
| AZD9567                             | 17.4 (± 11.0)           | 39.9 (± 20.4)           | 9999.9999 (± 9999.9999) | 17.4 (± 11.0)           |
| Prednisolone                        | 9.7 (± 11.0)            | 17.6 (± 20.3)           | -18.1 (± 21.4)          | 9.7 (± 11.0)            |
| Placebo                             | 9999.9999 (± 9999.9999) | 9999.9999 (± 9999.9999) | 12.9 (± 21.3)           | 9999.9999 (± 9999.9999) |

| End point values                    | Cohort 2             | Cohort 3             |  |  |
|-------------------------------------|----------------------|----------------------|--|--|
| Subject group type                  | Subject analysis set | Subject analysis set |  |  |
| Number of subjects analysed         | 8                    | 9                    |  |  |
| Units: mmol/day                     |                      |                      |  |  |
| least squares mean (standard error) |                      |                      |  |  |



|              |                              |                              |  |  |
|--------------|------------------------------|------------------------------|--|--|
| AZD9567      | 39.9 ( $\pm$ 20.4)           | 9999.9999 ( $\pm$ 9999.9999) |  |  |
| Prednisolone | 17.6 ( $\pm$ 20.3)           | -18.1 ( $\pm$ 21.4)          |  |  |
| Placebo      | 9999.9999 ( $\pm$ 9999.9999) | 12.9 ( $\pm$ 21.3)           |  |  |

## Statistical analyses

| Statistical analysis title                                                 | AZD9567 72mg vs Prednisolone 40mg |
|----------------------------------------------------------------------------|-----------------------------------|
| Statistical analysis description:                                          |                                   |
| Pairwise Comparisons with Prednisolone (AZD9567 72mg vs Prednisolone 40mg) |                                   |
| Comparison groups                                                          | Cohort 1 v Cohort 1               |
| Number of subjects included in analysis                                    | 54                                |
| Analysis specification                                                     | Pre-specified                     |
| Analysis type                                                              | other <sup>[38]</sup>             |
| P-value                                                                    | = 0.533                           |
| Method                                                                     | Mixed models analysis             |
| Parameter estimate                                                         | Mean difference (final values)    |
| Point estimate                                                             | 7.6                               |
| Confidence interval                                                        |                                   |
| level                                                                      | 95 %                              |
| sides                                                                      | 2-sided                           |
| lower limit                                                                | -17.4                             |
| upper limit                                                                | 32.7                              |

Notes:

[38] - 27 patients were evaluated in this analysis

| Statistical analysis title                                                 | AZD9567 40mg vs Prednisolone 20mg |
|----------------------------------------------------------------------------|-----------------------------------|
| Statistical analysis description:                                          |                                   |
| Pairwise Comparisons with Prednisolone (AZD9567 40mg vs Prednisolone 20mg) |                                   |
| Comparison groups                                                          | Cohort 2 v Cohort 2               |
| Number of subjects included in analysis                                    | 16                                |
| Analysis specification                                                     | Pre-specified                     |
| Analysis type                                                              | other <sup>[39]</sup>             |
| P-value                                                                    | = 0.311                           |
| Method                                                                     | Mixed models analysis             |
| Parameter estimate                                                         | Mean difference (final values)    |
| Point estimate                                                             | 22.3                              |
| Confidence interval                                                        |                                   |
| level                                                                      | 95 %                              |
| sides                                                                      | 2-sided                           |
| lower limit                                                                | -26.7                             |
| upper limit                                                                | 71.3                              |

Notes:

[39] - 8 patients were evaluated in this analysis

| Statistical analysis title | Placebo vs Prednisolone 5mg |
|----------------------------|-----------------------------|
|----------------------------|-----------------------------|

Statistical analysis description:

Pairwise Comparisons with Prednisolone (Placebo vs Prednisolone 5mg)

|                                         |                                |
|-----------------------------------------|--------------------------------|
| Comparison groups                       | Cohort 3 v Cohort 3            |
| Number of subjects included in analysis | 18                             |
| Analysis specification                  | Pre-specified                  |
| Analysis type                           | other <sup>[40]</sup>          |
| P-value                                 | = 0.204                        |
| Method                                  | Mixed models analysis          |
| Parameter estimate                      | Mean difference (final values) |
| Point estimate                          | 31                             |
| Confidence interval                     |                                |
| level                                   | 95 %                           |
| sides                                   | 2-sided                        |
| lower limit                             | -21.9                          |
| upper limit                             | 83.9                           |

Notes:

[40] - 9 patients were evaluated in this analysis

### Secondary: Area under the plasma concentration versus time curve from zero to the last quantifiable concentration (AUClast)

|                 |                                                                                                                                  |
|-----------------|----------------------------------------------------------------------------------------------------------------------------------|
| End point title | Area under the plasma concentration versus time curve from zero to the last quantifiable concentration (AUClast) <sup>[41]</sup> |
|-----------------|----------------------------------------------------------------------------------------------------------------------------------|

End point description:

AUClast of AZD9567 following once daily dosing was evaluated.

Pharmacokinetic analysis set (PKAS) consisted of all patients in the FAS with at least 1 quantifiable AZD9567 concentration and no important protocol deviations, or adverse events (AEs) considered to have an effect upon PK.

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

End point timeframe:

On Days 3, 4, 30, and 31 (Pre-dose, Post-dose 0.25, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 12, 24, 30 hours)

Notes:

[41] - 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: Statistical Analysis was not performed for the endpoint

| End point values                                    | Cohort 1        | Cohort 2        |  |  |
|-----------------------------------------------------|-----------------|-----------------|--|--|
| Subject group type                                  | Reporting group | Reporting group |  |  |
| Number of subjects analysed                         | 27              | 8               |  |  |
| Units: hour*nanomole/liter (h*nmol/L)               |                 |                 |  |  |
| geometric mean (geometric coefficient of variation) | 34400 (± 42.97) | 18410 (± 46.06) |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Area under the plasma concentration versus time curve from zero to 24 hours post-dose [AUC(0-24)]

|                 |                                                                                                                   |
|-----------------|-------------------------------------------------------------------------------------------------------------------|
| End point title | Area under the plasma concentration versus time curve from zero to 24 hours post-dose [AUC(0-24)] <sup>[42]</sup> |
|-----------------|-------------------------------------------------------------------------------------------------------------------|

End point description:

AUC(0-24) of AZD9567 following once daily dosing was evaluated.

PKAS consisted of all patients in the FAS with at least 1 quantifiable AZD9567 concentration and no important protocol deviations, or AEs considered to have an effect upon PK.

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

End point timeframe:

On Days 3, 4, 30, and 31 (Pre-dose, Post-dose 0.25, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 12, 24, 30 hours)

Notes:

[42] - 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: Statistical Analysis was not performed for the endpoint

| End point values                                    | Cohort 1             | Cohort 2             |  |  |
|-----------------------------------------------------|----------------------|----------------------|--|--|
| Subject group type                                  | Reporting group      | Reporting group      |  |  |
| Number of subjects analysed                         | 27                   | 8                    |  |  |
| Units: h*nmol/L                                     |                      |                      |  |  |
| geometric mean (geometric coefficient of variation) | 32920 ( $\pm$ 41.32) | 17790 ( $\pm$ 44.86) |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Area under the plasma concentration versus time curve from zero to 6 hours post-dose [AUC(0-6)]

|                 |                                                                                                                 |
|-----------------|-----------------------------------------------------------------------------------------------------------------|
| End point title | Area under the plasma concentration versus time curve from zero to 6 hours post-dose [AUC(0-6)] <sup>[43]</sup> |
|-----------------|-----------------------------------------------------------------------------------------------------------------|

End point description:

AUC(0-6) of AZD9567 following once daily dosing was evaluated.

PKAS consisted of all patients in the FAS with at least 1 quantifiable AZD9567 concentration and no important protocol deviations, or AEs considered to have an effect upon PK.

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

End point timeframe:

On Days 3, 4, 30, and 31 (Pre-dose, Post-dose 0.25, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 12, 24, 30 hours)

Notes:

[43] - 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: Statistical Analysis was not performed for the endpoint

| End point values                                    | Cohort 1             | Cohort 2            |  |  |
|-----------------------------------------------------|----------------------|---------------------|--|--|
| Subject group type                                  | Reporting group      | Reporting group     |  |  |
| Number of subjects analysed                         | 27                   | 8                   |  |  |
| Units: h*nmol/L                                     |                      |                     |  |  |
| geometric mean (geometric coefficient of variation) | 17050 ( $\pm$ 30.45) | 9914 ( $\pm$ 35.06) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Maximum observed drug concentration (Cmax)

|                 |                                                            |
|-----------------|------------------------------------------------------------|
| End point title | Maximum observed drug concentration (Cmax) <sup>[44]</sup> |
|-----------------|------------------------------------------------------------|

End point description:

Cmax of AZD9567 following once daily dosing was evaluated.

PKAS consisted of all patients in the FAS with at least 1 quantifiable AZD9567 concentration and no important protocol deviations, or AEs considered to have an effect upon PK.

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

End point timeframe:

On Days 3, 4, 30, and 31 (Pre-dose, Post-dose 0.25, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 12, 24, 30 hours)

Notes:

[44] - 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: Statistical Analysis was not performed for the endpoint

| End point values                                    | Cohort 1        | Cohort 2        |  |  |
|-----------------------------------------------------|-----------------|-----------------|--|--|
| Subject group type                                  | Reporting group | Reporting group |  |  |
| Number of subjects analysed                         | 27              | 8               |  |  |
| Units: nmol/L                                       |                 |                 |  |  |
| geometric mean (geometric coefficient of variation) | 4501 (± 26.90)  | 2939 (± 31.50)  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Time to reach maximum observed drug concentration (tmax)

|                 |                                                   |
|-----------------|---------------------------------------------------|
| End point title | Time to reach maximum observed drug concentration |
|-----------------|---------------------------------------------------|

End point description:

Tmax of AZD9567 following once daily dosing was evaluated.

PKAS consisted of all patients in the FAS with at least 1 quantifiable AZD9567 concentration and no important protocol deviations, or AEs considered to have an effect upon PK.

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

End point timeframe:

On Days 3, 4, 30, and 31 (Pre-dose, Post-dose 0.25, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 12, 24, 30 hours)

Notes:

[45] - 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: Statistical Analysis was not performed for the endpoint

| End point values              | Cohort 1            | Cohort 2            |  |  |
|-------------------------------|---------------------|---------------------|--|--|
| Subject group type            | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed   | 27                  | 8                   |  |  |
| Units: hours                  |                     |                     |  |  |
| median (full range (min-max)) | 0.50 (0.25 to 1.50) | 0.50 (0.50 to 1.00) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Terminal elimination half-life ( $t_{1/2\lambda z}$ )

|                 |                                                                       |
|-----------------|-----------------------------------------------------------------------|
| End point title | Terminal elimination half-life ( $t_{1/2\lambda z}$ ) <sup>[46]</sup> |
|-----------------|-----------------------------------------------------------------------|

End point description:

$t_{1/2\lambda z}$  of AZD9567 following once daily dosing was evaluated.

PKAS consisted of all patients in the FAS with at least 1 quantifiable AZD9567 concentration and no important protocol deviations, or AEs considered to have an effect upon PK.

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

End point timeframe:

On Days 3, 4, 30, and 31 (Pre-dose, Post-dose 0.25, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 12, 24, 30 hours)

Notes:

[46] - 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: Statistical Analysis was not performed for the endpoint

| End point values                     | Cohort 1           | Cohort 2           |  |  |
|--------------------------------------|--------------------|--------------------|--|--|
| Subject group type                   | Reporting group    | Reporting group    |  |  |
| Number of subjects analysed          | 27                 | 8                  |  |  |
| Units: hours                         |                    |                    |  |  |
| arithmetic mean (standard deviation) | 6.99 ( $\pm$ 1.44) | 6.16 ( $\pm$ 1.08) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Apparent total body clearance of drug from plasma after extravascular (CL/F)

|                 |                                                                                              |
|-----------------|----------------------------------------------------------------------------------------------|
| End point title | Apparent total body clearance of drug from plasma after extravascular (CL/F) <sup>[47]</sup> |
|-----------------|----------------------------------------------------------------------------------------------|

End point description:

CL/F of AZD9567 following once daily dosing was evaluated.

PKAS consisted of all patients in the FAS with at least 1 quantifiable AZD9567 concentration and no important protocol deviations, or AEs considered to have an effect upon PK.

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

End point timeframe:

On Days 3, 4, 30, and 31 (Pre-dose, Post-dose 0.25, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 12, 24, 30 hours)

Notes:

[47] - 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: Statistical Analysis was not performed for the endpoint

| End point values                     | Cohort 1             | Cohort 2             |  |  |
|--------------------------------------|----------------------|----------------------|--|--|
| Subject group type                   | Reporting group      | Reporting group      |  |  |
| Number of subjects analysed          | 27                   | 8                    |  |  |
| Units: Liter/hour (L/h)              |                      |                      |  |  |
| arithmetic mean (standard deviation) | 4.766 ( $\pm$ 1.896) | 4.924 ( $\pm$ 2.098) |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Apparent volume of distribution following extravascular administration (V<sub>z</sub>/F)

|                 |                                                                                                            |
|-----------------|------------------------------------------------------------------------------------------------------------|
| End point title | Apparent volume of distribution following extravascular administration (V <sub>z</sub> /F) <sup>[48]</sup> |
|-----------------|------------------------------------------------------------------------------------------------------------|

End point description:

V<sub>z</sub>/F of AZD9567 was derived using standard non-compartmental methods using WinNonLin version 8.1 or higher (Certara).

PKAS consisted of all patients in the FAS with at least 1 quantifiable AZD9567 concentration and no important protocol deviations, or AEs considered to have an effect upon PK.

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

End point timeframe:

On Days 3, 4, 30, and 31 (Pre-dose, Post-dose 0.25, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 12, 24, 30 hours)

Notes:

[48] - 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: Statistical Analysis was not performed for the endpoint

| End point values                     | Cohort 1             | Cohort 2             |  |  |
|--------------------------------------|----------------------|----------------------|--|--|
| Subject group type                   | Reporting group      | Reporting group      |  |  |
| Number of subjects analysed          | 27                   | 8                    |  |  |
| Units: Liter                         |                      |                      |  |  |
| arithmetic mean (standard deviation) | 45.11 ( $\pm$ 11.39) | 41.75 ( $\pm$ 14.19) |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Tumour necrosis factor alpha (TNF $\alpha$ ) concentrations

|                 |                                                                             |
|-----------------|-----------------------------------------------------------------------------|
| End point title | Tumour necrosis factor alpha (TNF $\alpha$ ) concentrations <sup>[49]</sup> |
|-----------------|-----------------------------------------------------------------------------|

End point description:

Relationship between AZD9567 exposure and inhibition of LPS-stimulated TNF $\alpha$  release for high and low dose comparison (Cohort 1 and Cohort 2) was assessed. LPS-stimulated TNF $\alpha$  concentration was measured.

FAS consisted of all randomised patients who received at least 1 dose of study treatment.

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

End point timeframe:

On Days 3 (Treatment period 1 and 2)

Notes:

[49] - 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: Statistical Analysis was not performed for the endpoint

| End point values                     | Cohort 1                  | Cohort 2                  |  |  |
|--------------------------------------|---------------------------|---------------------------|--|--|
| Subject group type                   | Reporting group           | Reporting group           |  |  |
| Number of subjects analysed          | 27                        | 8                         |  |  |
| Units: nanogram/liter (ng/L)         |                           |                           |  |  |
| arithmetic mean (standard deviation) |                           |                           |  |  |
| AZD9567 (0h) (n= 26,8)               | 21000.1 ( $\pm$ 15413.92) | 23525.0 ( $\pm$ 15260.57) |  |  |
| Prednisolone (0h) (n= 26,8)          | 21361.5 ( $\pm$ 18124.60) | 12385.0 ( $\pm$ 11835.31) |  |  |
| AZD9567 (1h) (n= 26,8)               | 9100.2 ( $\pm$ 6248.93)   | 8122.5 ( $\pm$ 5303.16)   |  |  |
| Prednisolone (1h) (n=25,8)           | 3581.1 ( $\pm$ 3642.93)   | 3617.5 ( $\pm$ 1552.62)   |  |  |
| AZD9567 (2h) (n= 26,8)               | 8170.7 ( $\pm$ 5053.69)   | 8098.0 ( $\pm$ 7709.06)   |  |  |
| Prednisolone (2h) (n= 26,8)          | 1648.2 ( $\pm$ 1109.64)   | 1421.1 ( $\pm$ 591.80)    |  |  |
| AZD9567 (4h)                         | 7534.6 ( $\pm$ 4519.50)   | 8898.8 ( $\pm$ 5249.73)   |  |  |
| Prednisolone (4h)                    | 2293.1 ( $\pm$ 1329.60)   | 4292.0 ( $\pm$ 3207.76)   |  |  |
| AZD9567 (8h)                         | 10674.4 ( $\pm$ 7731.94)  | 13023.8 ( $\pm$ 8946.33)  |  |  |
| Prednisolone (8h) (n= 26,8)          | 4585.7 ( $\pm$ 4453.61)   | 7247.5 ( $\pm$ 2889.87)   |  |  |
| AZD9567 (12h)                        | 13332.5 ( $\pm$ 10831.44) | 14695.0 ( $\pm$ 11422.87) |  |  |
| Prednisolone (12h)                   | 12415.5 ( $\pm$ 9474.44)  | 16790.0 ( $\pm$ 8010.23)  |  |  |
| AZD9567 (24h)                        | 22136.7 ( $\pm$ 13414.45) | 19741.3 ( $\pm$ 11048.74) |  |  |
| Prednisolone (24h)                   | 23292.9 ( $\pm$ 15548.12) | 20920.0 ( $\pm$ 14802.66) |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from baseline AUC(04) on hormones related to glucose homeostasis (Free fatty acids)

|                 |                                                                                            |
|-----------------|--------------------------------------------------------------------------------------------|
| End point title | Change from baseline AUC(04) on hormones related to glucose homeostasis (Free fatty acids) |
|-----------------|--------------------------------------------------------------------------------------------|

End point description:

Effects of AZD9567 on free fatty acids were evaluated following a MMTT compared to prednisolone.

The Subject Analysis set was added to report statistical analysis and this is the only option available in order to accommodate reporting of statistical data for cross over cohorts.

Here, arbitrary value 9999.9999 represent not applicable.

FAS consisted of all randomised patients who received at least 1 dose of study treatment.

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

End point timeframe:

On Day -1 (Baseline), and Day 4 (Treatment period 1 and 2)

| End point values                    | Cohort 1                | Cohort 2                | Cohort 3                | Cohort 1                |
|-------------------------------------|-------------------------|-------------------------|-------------------------|-------------------------|
| Subject group type                  | Reporting group         | Reporting group         | Reporting group         | Subject analysis set    |
| Number of subjects analysed         | 27                      | 8                       | 9                       | 27                      |
| Units: min*mmol/L                   |                         |                         |                         |                         |
| least squares mean (standard error) |                         |                         |                         |                         |
| AZD9567                             | -18.1304 (± 1.7543)     | -14.0582 (± 3.7038)     | 9999.9999 (± 9999.9999) | -18.1304 (± 1.7543)     |
| Prednisolone                        | -14.1238 (± 1.7542)     | -19.8117 (± 3.7060)     | -4.1625 (± 3.7212)      | -14.1238 (± 1.7542)     |
| Placebo                             | 9999.9999 (± 9999.9999) | 9999.9999 (± 9999.9999) | 4.8995 (± 3.7153)       | 9999.9999 (± 9999.9999) |

| End point values                    | Cohort 2                | Cohort 3                |  |  |
|-------------------------------------|-------------------------|-------------------------|--|--|
| Subject group type                  | Subject analysis set    | Subject analysis set    |  |  |
| Number of subjects analysed         | 8                       | 9                       |  |  |
| Units: min*mmol/L                   |                         |                         |  |  |
| least squares mean (standard error) |                         |                         |  |  |
| AZD9567                             | -14.0582 (± 3.7038)     | 9999.9999 (± 9999.9999) |  |  |
| Prednisolone                        | -19.8117 (± 3.7060)     | -4.1625 (± 3.7212)      |  |  |
| Placebo                             | 9999.9999 (± 9999.9999) | 4.8995 (± 3.7153)       |  |  |

## Statistical analyses

|                                                                            |                                   |
|----------------------------------------------------------------------------|-----------------------------------|
| Statistical analysis title                                                 | AZD9567 72mg vs Prednisolone 40mg |
| Statistical analysis description:                                          |                                   |
| Pairwise Comparisons with Prednisolone (AZD9567 72mg vs Prednisolone 40mg) |                                   |
| Comparison groups                                                          | Cohort 1 v Cohort 1               |



|                                         |                                |
|-----------------------------------------|--------------------------------|
| Number of subjects included in analysis | 54                             |
| Analysis specification                  | Pre-specified                  |
| Analysis type                           | other <sup>[50]</sup>          |
| P-value                                 | = 0.103                        |
| Method                                  | Mixed models analysis          |
| Parameter estimate                      | Mean difference (final values) |
| Point estimate                          | -4                             |
| Confidence interval                     |                                |
| level                                   | 95 %                           |
| sides                                   | 2-sided                        |
| lower limit                             | -8.88                          |
| upper limit                             | 0.87                           |

Notes:

[50] - 27 patients were evaluated in this analysis

|                                                                            |                                   |
|----------------------------------------------------------------------------|-----------------------------------|
| <b>Statistical analysis title</b>                                          | AZD9567 40mg vs Prednisolone 20mg |
| Statistical analysis description:                                          |                                   |
| Pairwise Comparisons with Prednisolone (AZD9567 40mg vs Prednisolone 20mg) |                                   |
| Comparison groups                                                          | Cohort 2 v Cohort 2               |
| Number of subjects included in analysis                                    | 16                                |
| Analysis specification                                                     | Pre-specified                     |
| Analysis type                                                              | other <sup>[51]</sup>             |
| P-value                                                                    | = 0.005                           |
| Method                                                                     | Mixed models analysis             |
| Parameter estimate                                                         | Mean difference (final values)    |
| Point estimate                                                             | 5.7535                            |
| Confidence interval                                                        |                                   |
| level                                                                      | 95 %                              |
| sides                                                                      | 2-sided                           |
| lower limit                                                                | 2.6034                            |
| upper limit                                                                | 8.9036                            |

Notes:

[51] - 8 patients were evaluated in this analysis

|                                                                      |                                |
|----------------------------------------------------------------------|--------------------------------|
| <b>Statistical analysis title</b>                                    | Placebo vs Prednisolone 5mg    |
| Statistical analysis description:                                    |                                |
| Pairwise Comparisons with Prednisolone (Placebo vs Prednisolone 5mg) |                                |
| Comparison groups                                                    | Cohort 3 v Cohort 3            |
| Number of subjects included in analysis                              | 18                             |
| Analysis specification                                               | Pre-specified                  |
| Analysis type                                                        | other <sup>[52]</sup>          |
| P-value                                                              | = 0.023                        |
| Method                                                               | Mixed models analysis          |
| Parameter estimate                                                   | Mean difference (final values) |
| Point estimate                                                       | 9.06                           |
| Confidence interval                                                  |                                |
| level                                                                | 95 %                           |
| sides                                                                | 2-sided                        |
| lower limit                                                          | 1.67                           |
| upper limit                                                          | 16.44                          |

Notes:

[52] - 9 patients were evaluated in this analysis

### Secondary: Homeostatic model assessment- insulin resistance (HOMA-IR)

|                 |                                                            |
|-----------------|------------------------------------------------------------|
| End point title | Homeostatic model assessment- insulin resistance (HOMA-IR) |
|-----------------|------------------------------------------------------------|

End point description:

Pharmacodynamic effects of AZD9567 on HOMA-IR were evaluated following a MMTT compared to prednisolone.

Here, arbitrary value 9999.9999 represent not applicable.

FAS consisted of all randomised patients who received at least 1 dose of study treatment.

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

End point timeframe:

On Day -1 (Baseline), and Day 4 (Treatment period 1 and 2)

| End point values                     | Cohort 1                | Cohort 2                | Cohort 3                |  |
|--------------------------------------|-------------------------|-------------------------|-------------------------|--|
| Subject group type                   | Reporting group         | Reporting group         | Reporting group         |  |
| Number of subjects analysed          | 27                      | 8                       | 9                       |  |
| Units: Change from Baseline          |                         |                         |                         |  |
| arithmetic mean (standard deviation) |                         |                         |                         |  |
| AZD9567 (n= 26,8,9)                  | -0.4406 (± 1.9875)      | -0.1738 (± 0.7576)      | 9999.9999 (± 9999.9999) |  |
| Prednisolone (n= 25,8,9)             | -0.7023 (± 1.5896)      | 0.0721 (± 0.9606)       | -0.5662 (± 0.7364)      |  |
| Placebo                              | 9999.9999 (± 9999.9999) | 9999.9999 (± 9999.9999) | -0.9280 (± 0.8173)      |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: HOMA-insulin sensitivity (HOMA-S)

|                 |                                   |
|-----------------|-----------------------------------|
| End point title | HOMA-insulin sensitivity (HOMA-S) |
|-----------------|-----------------------------------|

End point description:

Pharmacodynamic effects of AZD9567 on HOMA-S were evaluated following a MMTT compared to prednisolone.

Here, arbitrary value 9999.9999 represent not applicable.

FAS consisted of all randomised patients who received at least 1 dose of study treatment.

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

End point timeframe:

On Day -1 (Baseline), and Day 4 (Treatment period 1 and 2)

| End point values                     | Cohort 1                | Cohort 2                | Cohort 3                |  |
|--------------------------------------|-------------------------|-------------------------|-------------------------|--|
| Subject group type                   | Reporting group         | Reporting group         | Reporting group         |  |
| Number of subjects analysed          | 27                      | 8                       | 9                       |  |
| Units: Change from Baseline          |                         |                         |                         |  |
| arithmetic mean (standard deviation) |                         |                         |                         |  |
| AZD9567 (n= 26,8,9)                  | 0.0134 (± 0.2352)       | -0.0360 (± 0.1990)      | 9999.9999 (± 9999.9999) |  |
| Prednisolone (n= 25,8,9)             | 0.0328 (± 0.1400)       | -0.0799 (± 0.2077)      | 0.0750 (± 0.0949)       |  |
| Placebo                              | 9999.9999 (± 9999.9999) | 9999.9999 (± 9999.9999) | 0.1468 (± 0.0930)       |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of participants with adverse events

|                                                                                                                                                                                    |                                            |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------|
| End point title                                                                                                                                                                    | Number of participants with adverse events |
| End point description:                                                                                                                                                             |                                            |
| Safety and tolerability of AZD9567 was assessed.                                                                                                                                   |                                            |
| IP: Investigational product                                                                                                                                                        |                                            |
| Safety Analysis Set (SAF) consisted of all patients who were randomised to one of the 2 sequence groups within the cohort and have received at least 1 dose of study intervention. |                                            |
| End point type                                                                                                                                                                     | Secondary                                  |
| End point timeframe:                                                                                                                                                               |                                            |
| From screening up to 79 days                                                                                                                                                       |                                            |

| End point values                                | Cohort 1        | Cohort 2        | Cohort 3        |  |
|-------------------------------------------------|-----------------|-----------------|-----------------|--|
| Subject group type                              | Reporting group | Reporting group | Reporting group |  |
| Number of subjects analysed                     | 27              | 8               | 9               |  |
| Units: Participants                             |                 |                 |                 |  |
| Any Adverse Event (AE)                          | 10              | 5               | 1               |  |
| Any AE with outcome = death                     | 0               | 0               | 0               |  |
| Any SAE (including events with outcome = death) | 0               | 0               | 0               |  |
| Any AE leading to discontinuation of IP         | 0               | 0               | 0               |  |
| Any AE leading to drug interruption             | 0               | 0               | 0               |  |
| Any AE leading to withdrawal from study         | 0               | 0               | 0               |  |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From Screening up to Final/ end of treatment visit (Day 79).

Adverse event reporting additional description:

Safety Analysis Set (SAF) consisted of all patients who were randomised to one of the 2 sequence groups within the cohort and have received at least 1 dose of study intervention. The SAF was analysed according to actual treatment.

Three additional arms were created to capture Adverse Events for each treatment within the cohort.

|                 |                |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 24.0 |
|--------------------|------|

### Reporting groups

|                       |                        |
|-----------------------|------------------------|
| Reporting group title | Cohort 1: AZD9567 72mg |
|-----------------------|------------------------|

Reporting group description:

Patients were randomised in a ratio of 1:1 to receive 72 mg AZD9567 followed by 40 mg prednisolone or 40 mg prednisolone followed by 72 mg AZD956

|                       |                             |
|-----------------------|-----------------------------|
| Reporting group title | Cohort 1: Prednisolone 40mg |
|-----------------------|-----------------------------|

Reporting group description:

Patients were randomised in a ratio of 1:1 to receive 72 mg AZD9567 followed by 40 mg prednisolone or 40 mg prednisolone followed by 72 mg AZD956

|                       |                             |
|-----------------------|-----------------------------|
| Reporting group title | Cohort 2: Prednisolone 20mg |
|-----------------------|-----------------------------|

Reporting group description:

Patients were randomised in a ratio of 1:1 to receive 40 mg AZD9567 followed by 20 mg prednisolone or 20 mg prednisolone followed by 40 mg AZD956

|                       |                            |
|-----------------------|----------------------------|
| Reporting group title | Cohort 3: Prednisolone 5mg |
|-----------------------|----------------------------|

Reporting group description:

Patients were randomised in a ratio of 1:1 to receive placebo followed by 5 mg prednisolone or 5 mg prednisolone followed by placebo

|                       |                        |
|-----------------------|------------------------|
| Reporting group title | Cohort 2: AZD9567 40mg |
|-----------------------|------------------------|

Reporting group description:

Patients were randomised in a ratio of 1:1 to receive 40 mg AZD9567 followed by 20 mg prednisolone or 20 mg prednisolone followed by 40 mg AZD9567

|                       |                   |
|-----------------------|-------------------|
| Reporting group title | Cohort 3: Placebo |
|-----------------------|-------------------|

Reporting group description:

Patients were randomised in a ratio of 1:1 to receive placebo followed by 5 mg prednisolone or 5 mg prednisolone followed by placebo

| Serious adverse events                            | Cohort 1: AZD9567 72mg | Cohort 1: Prednisolone 40mg | Cohort 2: Prednisolone 20mg |
|---------------------------------------------------|------------------------|-----------------------------|-----------------------------|
| Total subjects affected by serious adverse events |                        |                             |                             |
| subjects affected / exposed                       | 0 / 27 (0.00%)         | 0 / 27 (0.00%)              | 0 / 8 (0.00%)               |
| number of deaths (all causes)                     | 0                      | 0                           | 0                           |
| number of deaths resulting from adverse events    |                        |                             |                             |

| Serious adverse events | Cohort 3: | Cohort 2: AZD9567 | Cohort 3: Placebo |
|------------------------|-----------|-------------------|-------------------|
|------------------------|-----------|-------------------|-------------------|

|                                                   | Prednisolone 5mg | 40mg          |               |
|---------------------------------------------------|------------------|---------------|---------------|
| Total subjects affected by serious adverse events |                  |               |               |
| subjects affected / exposed                       | 0 / 9 (0.00%)    | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| number of deaths (all causes)                     | 0                | 0             | 0             |
| number of deaths resulting from adverse events    |                  |               |               |

Frequency threshold for reporting non-serious adverse events: 0 %

| <b>Non-serious adverse events</b>                     | Cohort 1: AZD9567<br>72mg | Cohort 1:<br>Prednisolone 40mg | Cohort 2:<br>Prednisolone 20mg |
|-------------------------------------------------------|---------------------------|--------------------------------|--------------------------------|
| Total subjects affected by non-serious adverse events |                           |                                |                                |
| subjects affected / exposed                           | 4 / 27 (14.81%)           | 7 / 27 (25.93%)                | 5 / 8 (62.50%)                 |
| Investigations                                        |                           |                                |                                |
| Blood pressure increased                              |                           |                                |                                |
| subjects affected / exposed                           | 0 / 27 (0.00%)            | 0 / 27 (0.00%)                 | 1 / 8 (12.50%)                 |
| occurrences (all)                                     | 0                         | 0                              | 1                              |
| Nervous system disorders                              |                           |                                |                                |
| Dizziness                                             |                           |                                |                                |
| subjects affected / exposed                           | 0 / 27 (0.00%)            | 1 / 27 (3.70%)                 | 1 / 8 (12.50%)                 |
| occurrences (all)                                     | 0                         | 1                              | 1                              |
| Headache                                              |                           |                                |                                |
| subjects affected / exposed                           | 0 / 27 (0.00%)            | 1 / 27 (3.70%)                 | 2 / 8 (25.00%)                 |
| occurrences (all)                                     | 0                         | 1                              | 2                              |
| General disorders and administration site conditions  |                           |                                |                                |
| Administration site phlebitis                         |                           |                                |                                |
| subjects affected / exposed                           | 0 / 27 (0.00%)            | 1 / 27 (3.70%)                 | 0 / 8 (0.00%)                  |
| occurrences (all)                                     | 0                         | 1                              | 0                              |
| Catheter site erythema                                |                           |                                |                                |
| subjects affected / exposed                           | 0 / 27 (0.00%)            | 1 / 27 (3.70%)                 | 0 / 8 (0.00%)                  |
| occurrences (all)                                     | 0                         | 1                              | 0                              |
| Fatigue                                               |                           |                                |                                |
| subjects affected / exposed                           | 1 / 27 (3.70%)            | 0 / 27 (0.00%)                 | 0 / 8 (0.00%)                  |
| occurrences (all)                                     | 1                         | 0                              | 0                              |
| Mucosal inflammation                                  |                           |                                |                                |
| subjects affected / exposed                           | 0 / 27 (0.00%)            | 1 / 27 (3.70%)                 | 0 / 8 (0.00%)                  |
| occurrences (all)                                     | 0                         | 1                              | 0                              |
| Catheter site related reaction                        |                           |                                |                                |

|                                                  |                     |                     |                     |
|--------------------------------------------------|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all) | 0 / 27 (0.00%)<br>0 | 0 / 27 (0.00%)<br>0 | 1 / 8 (12.50%)<br>1 |
| Gastrointestinal disorders                       |                     |                     |                     |
| Haematochezia                                    |                     |                     |                     |
| subjects affected / exposed                      | 0 / 27 (0.00%)      | 0 / 27 (0.00%)      | 1 / 8 (12.50%)      |
| occurrences (all)                                | 0                   | 0                   | 1                   |
| Diarrhoea                                        |                     |                     |                     |
| subjects affected / exposed                      | 0 / 27 (0.00%)      | 0 / 27 (0.00%)      | 0 / 8 (0.00%)       |
| occurrences (all)                                | 0                   | 0                   | 0                   |
| Renal and urinary disorders                      |                     |                     |                     |
| Pollakiuria                                      |                     |                     |                     |
| subjects affected / exposed                      | 1 / 27 (3.70%)      | 0 / 27 (0.00%)      | 0 / 8 (0.00%)       |
| occurrences (all)                                | 1                   | 0                   | 0                   |
| Musculoskeletal and connective tissue disorders  |                     |                     |                     |
| Back pain                                        |                     |                     |                     |
| subjects affected / exposed                      | 0 / 27 (0.00%)      | 0 / 27 (0.00%)      | 0 / 8 (0.00%)       |
| occurrences (all)                                | 0                   | 0                   | 0                   |
| Infections and infestations                      |                     |                     |                     |
| Conjunctivitis                                   |                     |                     |                     |
| subjects affected / exposed                      | 1 / 27 (3.70%)      | 0 / 27 (0.00%)      | 0 / 8 (0.00%)       |
| occurrences (all)                                | 1                   | 0                   | 0                   |
| Cellulitis                                       |                     |                     |                     |
| subjects affected / exposed                      | 0 / 27 (0.00%)      | 1 / 27 (3.70%)      | 0 / 8 (0.00%)       |
| occurrences (all)                                | 0                   | 1                   | 0                   |
| Nasopharyngitis                                  |                     |                     |                     |
| subjects affected / exposed                      | 1 / 27 (3.70%)      | 0 / 27 (0.00%)      | 0 / 8 (0.00%)       |
| occurrences (all)                                | 1                   | 0                   | 0                   |
| Metabolism and nutrition disorders               |                     |                     |                     |
| Hyperglycaemia                                   |                     |                     |                     |
| subjects affected / exposed                      | 0 / 27 (0.00%)      | 1 / 27 (3.70%)      | 0 / 8 (0.00%)       |
| occurrences (all)                                | 0                   | 1                   | 0                   |
| Hypoglycaemia                                    |                     |                     |                     |
| subjects affected / exposed                      | 0 / 27 (0.00%)      | 1 / 27 (3.70%)      | 0 / 8 (0.00%)       |
| occurrences (all)                                | 0                   | 1                   | 0                   |

|                                        |                               |                           |                   |
|----------------------------------------|-------------------------------|---------------------------|-------------------|
| <b>Non-serious adverse events</b>      | Cohort 3:<br>Prednisolone 5mg | Cohort 2: AZD9567<br>40mg | Cohort 3: Placebo |
| Total subjects affected by non-serious |                               |                           |                   |

|                                                      |               |                |                |
|------------------------------------------------------|---------------|----------------|----------------|
| adverse events                                       |               |                |                |
| subjects affected / exposed                          | 0 / 9 (0.00%) | 2 / 8 (25.00%) | 1 / 9 (11.11%) |
| Investigations                                       |               |                |                |
| Blood pressure increased                             |               |                |                |
| subjects affected / exposed                          | 0 / 9 (0.00%) | 0 / 8 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                                    | 0             | 0              | 0              |
| Nervous system disorders                             |               |                |                |
| Dizziness                                            |               |                |                |
| subjects affected / exposed                          | 0 / 9 (0.00%) | 0 / 8 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                                    | 0             | 0              | 0              |
| Headache                                             |               |                |                |
| subjects affected / exposed                          | 0 / 9 (0.00%) | 1 / 8 (12.50%) | 0 / 9 (0.00%)  |
| occurrences (all)                                    | 0             | 1              | 0              |
| General disorders and administration site conditions |               |                |                |
| Administration site phlebitis                        |               |                |                |
| subjects affected / exposed                          | 0 / 9 (0.00%) | 0 / 8 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                                    | 0             | 0              | 0              |
| Catheter site erythema                               |               |                |                |
| subjects affected / exposed                          | 0 / 9 (0.00%) | 0 / 8 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                                    | 0             | 0              | 0              |
| Fatigue                                              |               |                |                |
| subjects affected / exposed                          | 0 / 9 (0.00%) | 0 / 8 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                                    | 0             | 0              | 0              |
| Mucosal inflammation                                 |               |                |                |
| subjects affected / exposed                          | 0 / 9 (0.00%) | 0 / 8 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                                    | 0             | 0              | 0              |
| Catheter site related reaction                       |               |                |                |
| subjects affected / exposed                          | 0 / 9 (0.00%) | 0 / 8 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                                    | 0             | 0              | 0              |
| Gastrointestinal disorders                           |               |                |                |
| Haematochezia                                        |               |                |                |
| subjects affected / exposed                          | 0 / 9 (0.00%) | 0 / 8 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                                    | 0             | 0              | 0              |
| Diarrhoea                                            |               |                |                |
| subjects affected / exposed                          | 0 / 9 (0.00%) | 0 / 8 (0.00%)  | 1 / 9 (11.11%) |
| occurrences (all)                                    | 0             | 0              | 1              |
| Renal and urinary disorders                          |               |                |                |

|                                                                                                                                                                                                                                                    |                                                                        |                                                                        |                                                                        |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------|------------------------------------------------------------------------|------------------------------------------------------------------------|
| Pollakiuria<br>subjects affected / exposed<br>occurrences (all)                                                                                                                                                                                    | 0 / 9 (0.00%)<br>0                                                     | 0 / 8 (0.00%)<br>0                                                     | 0 / 9 (0.00%)<br>0                                                     |
| Musculoskeletal and connective tissue disorders<br>Back pain<br>subjects affected / exposed<br>occurrences (all)                                                                                                                                   | 0 / 9 (0.00%)<br>0                                                     | 1 / 8 (12.50%)<br>1                                                    | 0 / 9 (0.00%)<br>0                                                     |
| Infections and infestations<br>Conjunctivitis<br>subjects affected / exposed<br>occurrences (all)<br><br>Cellulitis<br>subjects affected / exposed<br>occurrences (all)<br><br>Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all) | 0 / 9 (0.00%)<br>0<br><br>0 / 9 (0.00%)<br>0<br><br>0 / 9 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0<br><br>0 / 8 (0.00%)<br>0<br><br>0 / 8 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0<br><br>0 / 9 (0.00%)<br>0<br><br>0 / 9 (0.00%)<br>0 |
| Metabolism and nutrition disorders<br>Hyperglycaemia<br>subjects affected / exposed<br>occurrences (all)<br><br>Hypoglycaemia<br>subjects affected / exposed<br>occurrences (all)                                                                  | 0 / 9 (0.00%)<br>0<br><br>0 / 9 (0.00%)<br>0                           | 0 / 8 (0.00%)<br>0<br><br>0 / 8 (0.00%)<br>0                           | 0 / 9 (0.00%)<br>0<br><br>0 / 9 (0.00%)<br>0                           |



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

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

Arbitrary value 9999.9999 represent not applicable due to Placebo/AZD9567 was not administered in that cohort.

For Outcome measure MMTT derived first phase insulin response (I10/G10]), in cohort 2, convergence was not met thus no data was available.

Notes: