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	v2 (current)
This version publication date	22 February 2024
First version publication date	16 June 2022
Version creation reason	

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, information.center@astrazeneca.com
Scientific contact	Global Clinical Head, AstraZeneca Clinical Study Information Center, +1 87724094 79, information.center@astrazeneca.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	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: 46
Worldwide total number of subjects	46
EEA total number of subjects	46

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)	16
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	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

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.

Arm title	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	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) of each treatment period

Arm title	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 Prednisolone 5 mg/day for 3 consecutive days (Day 1 to 3) of each treatment period

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, Oral suspension
Routes of administration	Oral use

Dosage and administration details:

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

Number of subjects in period 1	Cohort 1	Cohort 2	Cohort 3
Started	28	9	9
Completed	27	8	9
Not completed	1	1	0
Consent withdrawn by subject	1	-	-
Positive SARS-CoV-2 for patient’s daughter	-	1	-

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	28	9	9
Age categorical Units: Subjects			
18 - 44 (years)	1	0	0
45 - 64 (years)	8	4	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	3	1
Male	24	6	8
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	1	0
White	26	8	9
More than one race	0	0	0
Unknown or Not Reported	0	0	0

Reporting group values	Total		
Number of subjects	46		
Age categorical Units: Subjects			
18 - 44 (years)	1		
45 - 64 (years)	15		
65 - 75 (years)	30		

Age Continuous Units: Years arithmetic mean standard deviation	 -		
Sex: Female, Male Units: Participants			
Female Male	8 38		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native Asian Native Hawaiian or Other Pacific Islander Black or African American White More than one race Unknown or Not Reported	0 1 0 2 43 0 0		

End points

End points 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	
Subject analysis set title	Cohort 1
Subject analysis set type	Full analysis
Subject analysis set 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	
Subject analysis set title	Cohort 2
Subject analysis set type	Full analysis
Subject analysis set 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	
Subject analysis set title	Cohort 3
Subject analysis set type	Full analysis
Subject analysis set 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	

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:

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).

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	Primary

End point timeframe:

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[1]
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[2]
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

Statistical analysis title	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[3]
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 (± 0.3114)	7.7870 (± 0.2517)	9999.9999 (± 9999.9999)	8.5730 (± 0.3114)
Prednisolone (n= 26,8,9)	10.0797 (± 0.3150)	8.8969 (± 0.2494)	7.4238 (± 0.2889)	10.0797 (± 0.3150)
Placebo	9999.9999 (± 9999.9999)	9999.9999 (± 9999.9999)	7.2638 (± 0.2888)	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: millimole/liter (mmol/L)				
least squares mean (standard error)				
AZD9567	7.7870 (± 0.2517)	9999.9999 (± 9999.9999)		
Prednisolone (n= 26,8,9)	8.8969 (± 0.2494)	7.4238 (± 0.2889)		
Placebo	9999.9999 (± 9999.9999)	7.2638 (± 0.2888)		

Statistical analyses

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[4]
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:
[4] - 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	< 0.001 [5]
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:
[5] - 8 patients were evaluated in this analysis

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[6]
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:
[6] - 27 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 glucose level in mmol/L was analysed to determine the effect of AZD9567 on CGM compared to prednisolone.
For the calculation of the rise in mean glucose levels, the baseline was the average of the values from -24 hours to first dosing on Day 1 of each period.

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:

Baseline and up to 72 hours (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 (± 0.2869)	0.4070 (± 0.2509)	9999.9999 (± 9999.9999)	1.2071 (± 0.2869)
Prednisolone (00 to 24 h) (n= 26,8,9)	2.7086 (± 0.2938)	1.2545 (± 0.2460)	0.3123 (± 0.1549)	2.7086 (± 0.2938)
Placebo (00 to 24 h)	9999.9999 (± 9999.9999)	9999.9999 (± 9999.9999)	-0.0477 (± 0.1547)	9999.9999 (± 9999.9999)
AZD9567 (24 to 48 h)	0.8011 (± 0.2978)	0.5428 (± 0.2483)	9999.9999 (± 9999.9999)	0.8011 (± 0.2978)
Prednisolone (24 to 48 h) (n= 26,8,9)	2.6653 (± 0.3044)	1.3206 (± 0.2448)	-0.2415 (± 0.2898)	2.6653 (± 0.3044)
Placebo (24 to 48 h)	9999.9999 (± 9999.9999)	9999.9999 (± 9999.9999)	-0.3260 (± 0.2894)	9999.9999 (± 9999.9999)
AZD9567 (48 to 72 h)	0.8529 (± 0.3210)	0.0744 (± 0.2714)	9999.9999 (± 9999.9999)	0.8529 (± 0.3210)
Prednisolone (48 to 72 h) (n= 26,8,9)	2.4527 (± 0.3274)	1.2174 (± 0.2664)	-0.2202 (± 0.2229)	2.4527 (± 0.3274)
Placebo (48 to 72 h)	9999.9999 (± 9999.9999)	9999.9999 (± 9999.9999)	-0.3500 (± 0.2224)	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 (00 to 24 hours [h])	0.4070 (± 0.2509)	9999.9999 (± 9999.9999)		
Prednisolone (00 to 24 h) (n= 26,8,9)	1.2545 (± 0.2460)	0.3123 (± 0.1549)		
Placebo (00 to 24 h)	9999.9999 (± 9999.9999)	-0.0477 (± 0.1547)		
AZD9567 (24 to 48 h)	0.5428 (± 0.2483)	9999.9999 (± 9999.9999)		
Prednisolone (24 to 48 h) (n= 26,8,9)	1.3206 (± 0.2448)	-0.2415 (± 0.2898)		
Placebo (24 to 48 h)	9999.9999 (± 9999.9999)	-0.3260 (± 0.2894)		
AZD9567 (48 to 72 h)	0.0744 (± 0.2714)	9999.9999 (± 9999.9999)		
Prednisolone (48 to 72 h) (n= 26,8,9)	1.2174 (± 0.2664)	-0.2202 (± 0.2229)		

Placebo (48 to 72 h)	9999.9999 (± 9999.9999)	-0.3500 (± 0.2224)		

Statistical analyses

Statistical analysis title	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[7]
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

Statistical analysis title	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[8]
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

Statistical analysis title	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[9]
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

Statistical analysis title	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[10]
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

Statistical analysis title	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[11]
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

Statistical analysis title	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

Statistical analysis title	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[12]
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

Statistical analysis title	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[13]
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

Statistical analysis title	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[14]
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

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[15]
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

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	
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

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	= 0.802
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

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

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	< 0.001
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

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[16]
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

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[17]
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

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[18]
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

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[19]
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

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	= 0.865
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[20]
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

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[21]
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:

[21] - 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	other[22]
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:

[22] - 8 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

	polypeptide [GIP])

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[23]
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

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[24]
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

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[25]
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

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[26]
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

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[27]
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

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[28]
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 (ΔI10/ΔG10)

End point title	Change from baseline in ratio of insulin to glucose level between 10 and 0 minutes (ΔI10/ΔG10)

End point description:

Effects of AZD9567 on ΔI10/ΔG10 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 (± 0.6632)	9999.9999 (± 9999.9999)	9999.9999 (± 9999.9999)	-0.5249 (± 0.6632)
Prednisolone (n= 18,8,5)	0.0774 (± 0.6674)	9999.9999 (± 9999.9999)	-0.8153 (± 0.8305)	0.0774 (± 0.6674)
Placebo (n=27,8,7)	9999.9999 (± 9999.9999)	9999.9999 (± 9999.9999)	-0.3532 (± 0.6893)	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: Ratio				
least squares mean (standard error)				
AZD9567 (n= 16,8,9)	9999.9999 (± 9999.9999)	9999.9999 (± 9999.9999)		
Prednisolone (n= 18,8,5)	9999.9999 (± 9999.9999)	-0.8153 (± 0.8305)		
Placebo (n=27,8,7)	9999.9999 (± 9999.9999)	-0.3532 (± 0.6893)		

Statistical analyses

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[29]
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

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	= 0.531
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

Secondary: Change from baseline in ratio of insulin to glucose level between 30 and 0 minutes [ΔI30/ΔG30])

End point title	Change from baseline in ratio of insulin to glucose level between 30 and 0 minutes [ΔI30/ΔG30])

End point description:

Effects of AZD9567 on ΔI30/ΔG30 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 (± 0.0726)	0.1824 (± 0.0773)	9999.9999 (± 9999.9999)	0.1203 (± 0.0726)
Prednisolone (n= 24,6,8)	0.0530 (± 0.0755)	0.0943 (± 0.1264)	-0.1047 (± 0.0665)	0.0530 (± 0.0755)
Placebo	9999.9999 (± 9999.9999)	9999.9999 (± 9999.9999)	0.0209 (± 0.0599)	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: Ratio				
least squares mean (standard error)				
AZD9567 (n= 25,8,9)	0.1824 (± 0.0773)	9999.9999 (± 9999.9999)		
Prednisolone (n= 24,6,8)	0.0943 (± 0.1264)	-0.1047 (± 0.0665)		
Placebo	9999.9999 (± 9999.9999)	0.0209 (± 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[30]
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

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[31]
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

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[32]
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 (ΔC10/ΔG10)

End point title	Change from baseline in ratio of C-peptide to glucose level between 10 and 0 minutes (ΔC10/ΔG10)

End point description:

Effects of AZD9567 on ΔC10/ΔG10 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 (± 0.0095)	0.0059 (± 0.0041)	9999.9999 (± 9999.9999)	-0.0004 (± 0.0095)
Prednisolone (n= 20,4,6)	-0.0103 (± 0.0092)	0.0026 (± 0.0047)	-0.0033 (± 0.0064)	-0.0103 (± 0.0092)
Placebo (n= 27,8,7)	9999.9999 (± 9999.9999)	9999.9999 (± 9999.9999)	-0.0024 (± 0.0057)	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: Ratio				
least squares mean (standard error)				
AZD9567 (n= 17,6,9)	0.0059 (± 0.0041)	9999.9999 (± 9999.9999)		
Prednisolone (n= 20,4,6)	0.0026 (± 0.0047)	-0.0033 (± 0.0064)		
Placebo (n= 27,8,7)	9999.9999 (± 9999.9999)	-0.0024 (± 0.0057)		

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	= 0.226
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

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[33]
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

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[34]
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 (ΔC30/ΔG30)

End point title	Change from baseline in ratio of C-peptide to glucose level between 30 and 0 minutes (ΔC30/ΔG30)

End point description:

Effects of AZD9567 on ΔC30/ΔG30 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 (± 0.0005)	0.0007 (± 0.0005)	9999.9999 (± 9999.9999)	0.0012 (± 0.0005)
Prednisolone	0.0005 (± 0.0005)	0.0004 (± 0.0005)	-0.0010 (± 0.0005)	0.0005 (± 0.0005)
Placebo	9999.9999 (± 9999.9999)	9999.9999 (± 9999.9999)	0.0002 (± 0.0005)	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: Ratio				
least squares mean (standard error)				
AZD9567	0.0007 (± 0.0005)	9999.9999 (± 9999.9999)		
Prednisolone	0.0004 (± 0.0005)	-0.0010 (± 0.0005)		
Placebo	9999.9999 (± 9999.9999)	0.0002 (± 0.0005)		

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	= 0.357
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

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[35]
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

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[36]
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 (± 4.30)	9999.9999 (± 9999.9999)		
Prednisolone	4.92 (± 4.29)	-2.49 (± 9.08)		
Placebo	9999.9999 (± 9999.9999)	-2.85 (± 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	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

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[37]
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

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 (± 20.4)	9999.9999 (± 9999.9999)		
Prednisolone	17.6 (± 20.3)	-18.1 (± 21.4)		
Placebo	9999.9999 (± 9999.9999)	12.9 (± 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[38]
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	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[39]
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:

[39] - 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	other[40]
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:

[40] - 8 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)[41]

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)][42]

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 (± 41.32)	17790 (± 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)][43]

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 (± 30.45)	9914 (± 35.06)		

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:

[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: 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: Apparent volume of distribution following extravascular administration (Vz/F)

End point title	Apparent volume of distribution following extravascular administration (Vz/F)[45]

End point description:

Vz/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:

[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: Liter				
arithmetic mean (standard deviation)	45.11 (± 11.39)	41.75 (± 14.19)		

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)[46]

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:

[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: Liter/hour (L/h)				
arithmetic mean (standard deviation)	4.766 (± 1.896)	4.924 (± 2.098)		

Statistical analyses

No statistical analyses for this end point

Secondary: Terminal elimination half-life (t½λz)

End point title	Terminal elimination half-life (t½λz)[47]

End point description:

t½λz 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: hours				
arithmetic mean (standard deviation)	6.99 (± 1.44)	6.16 (± 1.08)		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum observed drug concentration (Cmax)

End point title	Maximum observed drug concentration (Cmax)[48]

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:

[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: nmol/L				
geometric mean (geometric coefficient of variation)	4501 (± 26.90)	2939 (± 31.50)		

Statistical analyses

No statistical analyses for this end point

Secondary: Tumour necrosis factor alpha (TNFα) concentrations

End point title	Tumour necrosis factor alpha (TNFα) concentrations[49]

End point description:

Relationship between AZD9567 exposure and inhibition of LPS-stimulated TNFα release for high and low dose comparison (Cohort 1 and Cohort 2) was assessed. LPS-stimulated TNFα 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 (± 15413.92)	23525.0 (± 15260.57)		
Prednisolone (0h) (n= 26,8)	21361.5 (± 18124.60)	12385.0 (± 11835.31)		
AZD9567 (1h) (n= 26,8)	9100.2 (± 6248.93)	8122.5 (± 5303.16)		
Prednisolone (1h) (n=25,8)	3581.1 (± 3642.93)	3617.5 (± 1552.62)		
AZD9567 (2h) (n= 26,8)	8170.7 (± 5053.69)	8098.0 (± 7709.06)		
Prednisolone (2h) (n= 26,8)	1648.2 (± 1109.64)	1421.1 (± 591.80)		
AZD9567 (4h)	7534.6 (± 4519.50)	8898.8 (± 5249.73)		
Prednisolone (4h)	2293.1 (± 1329.60)	4292.0 (± 3207.76)		
AZD9567 (8h)	10674.4 (± 7731.94)	13023.8 (± 8946.33)		
Prednisolone (8h) (n= 26,8)	4585.7 (± 4453.61)	7247.5 (± 2889.87)		
AZD9567 (12h)	13332.5 (± 10831.44)	14695.0 (± 11422.87)		
Prednisolone (12h)	12415.5 (± 9474.44)	16790.0 (± 8010.23)		
AZD9567 (24h)	22136.7 (± 13414.45)	19741.3 (± 11048.74)		
Prednisolone (24h)	23292.9 (± 15548.12)	20920.0 (± 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[50]
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

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[51]
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:

[51] - 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	other[52]
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:
[52] - 8 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:

The HOMA-IR was calculated based on glucose and insulin measured prior to MMTT.

HOMA-IR= Glucose(mmol/L) x Insulin (mU/L) / 22.5

HOMA-IR score estimates the degree of insulin resistance.
Higher range indicates greater insulin resistance (i.e. high diabetes risk), while lower range indicates insulin sensitivity (i.e. low diabetes risk)

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: 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

Secondary: HOMA-insulin sensitivity (HOMA-S)

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

End point description:

Insulin sensitivity is a term used to indicate the responsiveness of the peripheral tissue cells to insulin, and their resultant capacity to uptake glucose out of the bloodstream.
HOMA-S score estimates the degree of insulin sensitivity.
HOMA-S was calculated as the reciprocal of HOMA-IR.

Higher values indicates greater insulin sensitivity (i.e. low diabetes risk), while lower values indicates insulin resistance (i.e. high diabetes risk)

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

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 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: 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 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: 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 2: AZD9567 40mg	Cohort 3: Prednisolone 5mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 27 (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			

Serious adverse events	Cohort 1:	Cohort 2:	Cohort 3: Placebo

	Prednisolone 40mg	Prednisolone 20mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 27 (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 %

Non-serious adverse events	Cohort 1: AZD9567 72mg	Cohort 2: AZD9567 40mg	Cohort 3: Prednisolone 5mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 27 (14.81%)	2 / 8 (25.00%)	0 / 9 (0.00%)
Investigations			
Blood pressure increased			
subjects affected / exposed	0 / 27 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 27 (0.00%)	1 / 8 (12.50%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Dizziness			
subjects affected / exposed	0 / 27 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Administration site phlebitis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Catheter site related reaction			
subjects affected / exposed	0 / 27 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Catheter site erythema			
subjects affected / exposed	0 / 27 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	1 / 27 (3.70%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Mucosal inflammation			

subjects affected / exposed	0 / 27 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Haematochezia			
subjects affected / exposed	0 / 27 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 27 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	1 / 27 (3.70%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 27 (0.00%)	1 / 8 (12.50%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 27 (3.70%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Conjunctivitis			
subjects affected / exposed	1 / 27 (3.70%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Cellulitis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 27 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Hypoglycaemia			
subjects affected / exposed	0 / 27 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Cohort 1: Prednisolone 40mg	Cohort 2: Prednisolone 20mg	Cohort 3: Placebo
Total subjects affected by non-serious			

adverse events			
subjects affected / exposed	7 / 27 (25.93%)	5 / 8 (62.50%)	1 / 9 (11.11%)
Investigations			
Blood pressure increased			
subjects affected / exposed	0 / 27 (0.00%)	1 / 8 (12.50%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 27 (3.70%)	2 / 8 (25.00%)	0 / 9 (0.00%)
occurrences (all)	1	2	0
Dizziness			
subjects affected / exposed	1 / 27 (3.70%)	1 / 8 (12.50%)	0 / 9 (0.00%)
occurrences (all)	1	1	0
General disorders and administration site conditions			
Administration site phlebitis			
subjects affected / exposed	1 / 27 (3.70%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Catheter site related reaction			
subjects affected / exposed	0 / 27 (0.00%)	1 / 8 (12.50%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Catheter site erythema			
subjects affected / exposed	1 / 27 (3.70%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Fatigue			
subjects affected / exposed	0 / 27 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Mucosal inflammation			
subjects affected / exposed	1 / 27 (3.70%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Haematochezia			
subjects affected / exposed	0 / 27 (0.00%)	1 / 8 (12.50%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Diarrhoea			
subjects affected / exposed	0 / 27 (0.00%)	0 / 8 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Renal and urinary disorders			

Pollakiuria			
subjects affected / exposed	0 / 27 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 27 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Cellulitis			
subjects affected / exposed	1 / 27 (3.70%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	1 / 27 (3.70%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Hypoglycaemia			
subjects affected / exposed	1 / 27 (3.70%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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: