Clinical Study Report Synopsis	
Drug Substance	AZD1402 (elarekibep)
Study Code	D2912C00003
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A Two-part Phase IIa Randomised, Double-blind, Placebo-controlled, Dose-ranging, Multi-centre Study to Assess Efficacy and Safety of Inhaled AZD1402 Administered as a Dry Powder Twice Daily for Four Weeks in Adults with Asthma on Medium-to-High Dose Inhaled Corticosteroids

Study dates: First subject enrolled: 21 April 2021
Last subject last visit: 20 July 2023
The analyses presented in this report are based on a clinical data lock date of 19 October 2023.

Phase of development: Therapeutic exploratory (IIa)

International Co-ordinating Investigator: PPD

Sponsor's Responsible Medical Officer: PPD

This study was performed in compliance with Good Clinical Practice, including the archiving of essential documents.

Study centres

The study was planned to be conducted at approximately 76 study centres (Part 1: 8 study centres and Part 2: 68 study centres) in about 8 to 10 countries. The study was conducted at 63 study centres in 10 countries before discontinuing enrolment and stopping dosing on 21 June 2023.

Publications

None at the time of writing this report.

Objectives and criteria for evaluation

Table S1 Objectives and Endpoints (Part 1)

Objectives	Outcome Measures
Primary	
• To evaluate the safety and tolerability of AZD1402 compared to Placebo at different dose levels in adults with asthma controlled on medium dose ICS-LABA	**Primary safety endpoint:** • AEs/AESIs/SAEs with a particular focus on infection, eosinophilia, and hypersensitivity-like events • Vital signs • Changes in clinical chemistry, haematology, and coagulation parameters • Immuno-biomarkers (including but not limited to cytokines, CRP, immunoglobulins including IgE) • ECGs • FEV_1 • FeNO
Secondary	
• To investigate the PK profile and immunogenicity of AZD1402, and associated effects on safety	• PK parameters (full profile in all patients) • ADAs

Exploratory objectives are not included in the CSR Synopsis but can be found in the CSR.

Abbreviations: ADAs = anti-drug antibodies; AE = adverse event; AESI = adverse event of special interest; CSR = clinical study report; CRP = C-reactive protein; ECG = electrocardiogram; FeNO = fractional exhaled nitric oxide; FEV_1 = forced expiratory volume in 1 second; ICS = inhaled corticosteroids; IgE = immunoglobulin E; LABA = long-acting beta agonist; PK = pharmacokinetics; SAE = serious adverse event.

Table S2 Objectives and Endpoints (Part 2)

Objectives	Outcome Measures
Primary	
• To investigate the efficacy of inhaled AZD1402 compared to Placebo in adults with asthma who are uncontrolled on medium-to-high dose ICS-LABA	**Primary efficacy endpoint:** • Change from baseline in pre-bronchodilator FEV_1 at Week 4
Secondary	
• To further investigate the efficacy of AZD1402 compared to Placebo in adults with asthma who are uncontrolled on medium-to-high dose ICS-LABA	• Change from baseline in pre-bronchodilator FEV_1 average over the 4-week Treatment Period. • Change from baseline in ACQ-6 at Week 4 and average over the Treatment Period. • Proportion of patients with a decrease in ACQ-6 score of ≥ 0.5 from baseline to Week 4. • Change from baseline in average morning PEF over the Treatment Period. • Change from baseline in average evening PEF over the Treatment Period. • Change from baseline in daily average asthma symptom score (AM/PM) over the Treatment Period.
• To investigate the effect of AZD1402 compared to Placebo on airway inflammation in adults with asthma who are uncontrolled on medium-to-high dose ICS-LABA	• Change from baseline in FeNO (in-clinic) at Week 4 and average over the Treatment Period
• To investigate the PK profile and immunogenicity of AZD1402, and associated effects on safety	• PK parameters (sparse in all, full profile in a subset of patients in each treatment arm) • ADAs
• To evaluate the safety and tolerability of AZD1402 compared to Placebo in adults with asthma who are uncontrolled on medium-to-high dose ICS-LABA	• AEs/AESIs/SAEs with a particular focus on infection, eosinophilia, and hypersensitivity-like events • Vital signs • Changes in clinical chemistry, haematology, and coagulation parameters • Immuno-biomarkers (including but not limited to cytokines, CRP, immunoglobulins including IgE) • ECGs • FEV_1 • FeNO

Exploratory objectives are not included in the CSR Synopsis but can be found in the CSR.

Abbreviations: ACQ-6 = Asthma Control Questionnaire-6; AE = adverse event; AESI = adverse event of special interest; ADAs = anti-drug antibodies; AM = before noon (antemeridiem); CRP = C-reactive protein; CSR = clinical study report; ECG = electrocardiogram; FeNO = fractional exhaled nitric oxide; FEV_1 = forced expiratory volume in 1 second; ICS = inhaled corticosteroids; IgE = immunoglobulin E; LABA = long-acting beta agonist; PEF = peak expiratory flow; PK = pharmacokinetics; PM = after noon (post-meridiem); SAE = serious adverse event.

Study design

This was a randomised, Placebo-controlled, double-blinded, multi-centre, 2-part study to assess the efficacy and safety of inhaled AZD1402 (elarekibep). Part 1 was performed in a Lead-in Cohort for each dose level to evaluate the safety and pharmacokinetics (PK) in a population with asthma controlled on medium dose inhaled corticosteroids long-acting beta-adrenoceptor agonist (ICS-LABA) before progressing to at-home dosing in adults with asthma who were uncontrolled on medium-to-high dose ICS-LABA in Part 2. Part 2 was initiated following evaluation of safety and PK in Part 1a. The investigational product (IP) in both parts of the study was administered CCI using the CCI dry powder inhaler (DPI) for a period of 4 weeks.

A Lead-in Dose Progression and Escalation Cohort approach with 3 dose levels was selected to confirm Phase I data dose response observations and further evaluate safety and PK in adults with asthma controlled on medium dose ICS. The Part 1a safety cohort was completed before progressing to at-home dosing in adults with asthma uncontrolled on medium-to-high dose ICS-LABA in Part 2.

Part 1

Part 1 of the study was randomised, double-blind, Placebo-controlled, and conducted in parallel for the 2 CCI dose levels (Part 1a) followed by an unblinded safety review and escalation to the CCI dose (Part 1b) dependent on the outcome of the safety review. Data evaluated in the safety review was unblinded; however, blinding was maintained for patients and Investigators. The total sample size for Part 1 was estimated to be 45 patients.

Part 1a was planned to consist of 30 patients who were randomised 1:1:1 to receive 1 of the 2 CCI AZD1402 DPI doses (CCI or CCI mg) or Placebo in parallel. Part 1b was planned to consist of 15 patients who were randomised 2:1 to receive the CCI AZD1402 DPI dose (CCI mg) or Placebo. Due to logistical reasons, the randomisation in Part 1 was stratified by site in Australia and Germany.

Part 1a Lead-in Cohort

- AZD1402 inhalation CCI mg CCI
- AZD1402 inhalation CCI mg CCI
- Placebo inhalation CCI

Part 1b Lead-in Cohort

- AZD1402 inhalation CCI mg CCI
- Placebo inhalation CCI

Part 2

Part 2 was randomised, double-blind, Placebo-controlled and was planned to include approximately 165 patients to evaluate 2 inhaled dose levels [redacted] and [redacted] mg) of AZD1402 against Placebo. Approximately 5 patients were planned to be randomised to [redacted] mg and 80 patients per arm were planned to be randomised to [redacted] mg and Placebo, respectively. The number of patients enrolled in the [redacted] mg dose depended on the enrolment rate and the randomisation ratio changed during the study. Patients were randomised 2:1 (active to Placebo) whilst the [redacted] mg arm was ongoing. Once the [redacted] mg had stopped recruiting and randomisation continued in the [redacted] mg and Placebo arms, the randomisation ratio was 1:1 (active to Placebo).

Apart from the scheduled clinic visits, the 4 weeks of dosing in Part 2 of the study was at-home. Part 2 started after the unblinded safety review for Part 1a. Part 2 included:

- AZD1402 inhalation [redacted] mg [redacted]
- AZD1402 inhalation [redacted] mg [redacted]
- Placebo inhalation [redacted]

Patients in both parts of the study received a handheld e-Diary device which they were required to complete [redacted] during the entire duration of the study.

AstraZeneca decided to discontinue enrolment and stop dosing on 21 June 2023. The decision was based on new cynomolgus monkey lung findings from a non-clinical 13-week good laboratory practice toxicology study with DPI-formulated elarekibep that did not support a chronic dosing development plan (Report No. 8489001).

The 13-week non-human primate study included 3 active dose cohorts. There were no clinical observations across any of the doses but there were respiratory tract pathology findings. These findings included inflammation-mediated lung tissue damage, which did not appear to be dose related.

Whilst there was no immediate safety risk to patients in the study, the decision was made to stop all AZD1402 dosing in ongoing clinical studies since these findings do not support long-term use and progression to later-stage development.

Target subject population and sample size

Part 1

The target population was adults with asthma (age 18 to 75 years, inclusive) who were adequately controlled on a stable medium dose ICS-LABA and additional rescue medication as needed, Asthma Control Questionnaire-6 (ACQ-6) score ≤ 1.0 and pre-bronchodilator forced expiratory volume in one second (FEV_1) $\geq 70\%$, and with no exacerbation requiring

systemic treatment or hospitalisation/emergency department visit for asthma during the 12 months prior to study start.

Part 2

The target population was adult patients (age 18 to 75 years, inclusive) with physician diagnosed uncontrolled asthma treated with medium-to-high dose ICS (total daily dose > 400 µg of budesonide dry powder formulation or equivalent) with LABA, as maintenance treatment, for at least 6 months prior to Visit 1 was included. ICS-LABA and any additional asthma maintenance controller medications (eg, leukotriene receptor inhibitors, theophylline, long-acting muscarinic antagonist, and chromones) must have been stable for at least 4 weeks prior to Visit 1.

Approximately 45 patients were planned to be randomised to Part 1 of the study and approximately 165 patients were planned to be randomised to Part 2 of the study.

Investigational product and comparators: dosage, mode of administration and batch numbers

AZD1402 is an inhalation powder CCI for oral inhalation, provided centrally by AstraZeneca as CCI mg, CCI mg, CCI mg doses.

Placebo is an inhalation powder CCI for oral inhalation, provided centrally by AstraZeneca.

19 batches of AZD1402 and 5 batches of Placebo were used in this study. Individual batch numbers and further information are included in the clinical study report.

Duration of treatment

The entire study period for each patient in both Parts 1 and 2, was approximately 3.5 months; a 2-week Screening Period, a 4-week Run-in Period, 4 weeks of Treatment Period, and 4 weeks of Follow-up Period.

Statistical methods

Analyses were performed by Parexel, except for the determination of AZD1402 in serum, anti-drug antibody (ADA) bioanalysis and the derivation of PK parameters, which were performed by bioanalytical test sites and PK vendor operated on behalf of AstraZeneca Research and Development.

All variables, if not otherwise specified, were summarised by each Part (Part 1 and Part 2), study treatment group (dose level of AZD1402 or Placebo) and AZD1402 overall (when required), using descriptive statistics, tables and/or figures, as applicable.

Continuous data were in general summarised in terms of the mean, standard deviation (SD), median, minimum, maximum, and number of observations. Continuous data that were expected to be skewed were presented in terms of the maximum, upper quartile, median, lower quartile, min and number of observations. The same level of precision was used for means, SD, Standard Error, and Confidence intervals (CIs).

These summaries were provided by timepoint of assessment as appropriate.

Categorical data were summarised in terms of the number of patients providing data at the relevant time point (n), frequency counts and percentages. Changes from baseline in categorical data were summarised using shift tables where appropriate.

All CIs were 2-sided 95% CIs, unless stated otherwise, and presented to one more decimal place than the raw data recorded in the database. If a model was used to estimate the treatment difference, the corresponding CI was presented. Otherwise, the unadjusted CI was presented. Nominal p-values could have also been presented.

Descriptive statistics for calculated PK parameters and fractional exhaled nitric oxide (FeNO) included: n, mean, SD, geometric mean, coefficient of variation, median, minimum and maximum values except for observed time, for which n, median, minimum and maximum were calculated.

The geometric coefficient of variation % will be calculated as SQRT(es^2-1)*100 where s is the SD of the log-transformed values.

The treatment comparisons of interest are the different doses of AZD1402 versus Placebo. No formal comparisons between the different AZD1402 doses were conducted.

All statistical analyses were conducted using SAS® version 9.4. PK parameters were calculated using Phoenix® WinNonlin version 8.3.5 or a later version in a secure and validated environment.

Study population

Part 1:

A total of 94 patients signed the study informed consent form (ICF) and were screened for enrolment. A total of 50 patients were randomised to Part 1 of the study and all 50 patients started treatment. Forty-five (90.0%) patients completed treatment. Forty-eight (96.0%) patients completed the study, ie, completed all protocol scheduled assessments up to the Follow-up visit. Five (10.0%) patients had at least 1 disruption due to the global/country situation.

The demographics and baseline characteristics data were as per inclusion and exclusion criteria and as expected for this study population. There were no notable differences in baseline characteristics between the different dose levels and Placebo.

Part 2:

A total of 147 patients signed the study ICF and were screened for enrolment. A total of 22 patients were randomised to Part 1 of the study and all 22 patients started treatment. Twenty (90.9%) patients completed the study, ie, completed all protocol scheduled assessments up to the Follow-up visit. Twenty (90.9%) patients completed treatment. None of the patients had a disruption due to the global/country situation and none of the patients withdrew due to the global/country situation.

The demographics and baseline characteristics data were as per inclusion and exclusion criteria and as expected for this study population. There were no notable differences in baseline characteristics between the different dose levels and Placebo.

Summary of efficacy results

Part 1:

Part 1 was not designed to draw any efficacy conclusions.

Part 2:

Primary objective:

- At Week 4, FEV_1 (L) in-clinic spirometry results from the mixed model repeated measure (MMRM) model showed that the [redacted] mg AZD1402 group had the highest least square (LS) mean difference (95% CI) compared to Placebo of 0.1960 L (0.0143, 0.3778) with a p-value of 0.035. The number of patients in treatment groups were too few to consider that the study provided conclusive results.
- No other important trends were observed in change from baseline from the MMRM model at each week for the different treatment groups over the 4-week Treatment Period.

Secondary objectives:

- At Week 4, FEV_1 (L) in-clinic spirometry results showed that both the [redacted] and [redacted] mg AZD1402 groups had a higher change from baseline compared to the Placebo group. The change from baseline for the [redacted] mg AZD1402 group was the highest. No other important trends were observed in change from baseline results in the in-clinic or at-home assessments for the different treatment groups over the 4-week Treatment Period.
- At Week 4, both the [redacted] and [redacted] mg AZD1402 treatment groups had a lower ACQ-6 score than the Placebo group. At Week 4, no other important trends were observed in change from baseline results for the different treatment groups over the average Treatment

Period. Over the Treatment Period, based on ACQ-6 scores, the AZD1402 group had more responders than the Placebo group with 3 responders in the [redacted] mg AZD1402 group and 7 responders in the [redacted] mg AZD1402 group.

- No important trends were observed in change from baseline in average morning and evening peak expiratory flow results for the different treatment groups over the Treatment Period.
- No important trends were observed in change from baseline in daily average asthma symptom score (before noon [ante meridiem]/after noon [post-meridiem]) results for the different treatment groups over the average Treatment Period.
- At Week 4, FeNO (ppb) in-clinic results from the MMRM model showed that the [redacted] mg AZD1402 group had the highest percentage change from baseline (95% CI) compared to Placebo of -15.43 ppb (-55.57, 60.96) with a p-value of 0.596 although not statistically significant. No important trends were observed from the MMRM model at each week for the different treatment groups over the 4-week Treatment Period.

Summary of pharmacokinetic results

Following DPI administration AZD1402 was steadily absorbed with a median time to reach peak or maximum observed concentration or response following drug administration (tmax) between 3.000 hours and 4.017 hours (overall range was between 0.00 hours and 8.02 hours) with no apparent trend with dose or study day. AZD1402 serum concentration remained quantifiable on Day 28 throughout the dosing interval at the [redacted] and [redacted] mg dose levels.

Following maximum observed serum (peak) drug concentration (Cmax), serum concentrations declined in a multiphasic manner with a half-life associated with terminal slope of a semi-logarithmic concentration-time curve (t½λz) estimates generally between 4.44 hours and 17.1 hours. One patient at the [redacted] mg dose level had quantifiable concentrations until Day 56 and a long t½λz (> 1000 hours). Although this result was atypical the PK parameters were not excluded from statistics since the regression was acceptable. All adjusted R-squared were > 0.8, however and gave confidence that the half-life estimates were reliable. However, the majority of t½λz values were estimated over an interval of < 3 half-lives which may indicate that the terminal phase was fully characterised.

Accumulation was observed following multiple dosing. Accumulation ratio for and area under serum concentration-time curve in the dosing interval τ (AUCτ) (Rac [AUC]), where calculable, ranged between 1.75 and 13.7. Accumulation ratio for Cmax (Rac [Cmax]) ranged between 0.793 and 20.2. Steady state was generally reached by Day 28 at all doses.

Inter-patient variability in Cmax, area under the serum concentration-curve from zero to the last quantifiable concentration (AUClast) and AUCτ was generally high (> 40%).

The increase in exposure with dose (all data) was sub-proportional on Day 28. The 3-fold increase in dose from [redacted] mg to [redacted] mg resulted in a 1.99-fold increase in geometric mean AUCτ

and a 2.62-fold increase in geometric mean Cmax and the 3.33-fold increase in dose from [redacted] mg to [redacted] mg resulted in a 2.85-fold increase in geometric mean AUCτ and a 2.96-fold increase in geometric mean Cmax. Overall, the 10-fold increase in dose resulted in a 5.66-fold increase in geometric mean AUCτ and a 7.77-fold increase in geometric mean Cmax.

PK data from Part 2 were similar to Part 1.

Summary of safety results

Part 1:

- There were no serious adverse events (SAEs) with the outcome of death, other SAEs, or treatment emergent adverse events (TEAEs) leading to withdrawal from the study reported in Part 1 of the study.
- Twenty (58.8%) patients in the total AZD1402 group and 8 (50.0%) patients in the Placebo group experienced at least one TEAE.
- Two (5.9%) patients in the total AZD1402 group (1 [10.0%] patient that received [redacted] mg AZD1402 and 1 [7.7%] patient that received [redacted] mg AZD1402), and 1 (6.3%) patient that received Placebo had a TEAE leading to discontinuation of the IP.
- The most frequently reported TEAEs were reported in the system organ class (SOC) of Respiratory, thoracic and mediastinal disorders (12 [35.3%] patients in the AZD1402 group and 5 [31.3%] patients in the Placebo group).
- Most of the TEAEs reported by patients were considered to be of mild intensity. Seven (20.6%) patients reported TEAEs of moderate intensity in the total AZD1402 group and 1 (6.3%) patient in the Placebo group. One (7.7%) patient reported an TEAE considered to be of severe intensity in the [redacted] mg AZD1402 group as assessed by the Investigator.
- TEAEs that were considered possibly related to the IP as assessed by the Investigator were reported in 4 (11.8%) patients in the total AZD1402 group and none in the Placebo group.
- TEAEs leading to discontinuation of IP were reported by 2 (5.9%) patients in the total AZD1402 group and 1 (6.3%) patient in the Placebo group.
- Adverse events of special interest (AESIs) were reported by 17 (50.0%) patients in the total AZD1402 group and by 8 (50.0%) patients in the Placebo group.
- Twenty-eight out of thirty-four patients in the total AZD1402 group and none in the Placebo group were treatment emergent ADA (TE-ADA) positive. Sixteen (57.1%) out of these 28 patients in the total AZD1402 group reported at least one TEAE. Of these, 4 out of 10 (40.0%) patients were in the [redacted] mg AZD1402 group, 6 out of 10 (60.0%) patients were in the [redacted] mg AZD1402 group, and 6 out of 8 (75.0%) patients were in the [redacted] mg AZD1402 group. No patients were TE-ADA negative. Five out of thirty-four patients in the total AZD1402 group and all 16 patients in the Placebo group were ADA negative. Three (60.0%) out of these 5 patients in the total AZD1402 group and 8 (50.0%) patients in the Placebo group reported at least one TEAE.

- In Part 1, 55.1% patients (27 out of 49 patients with any ADA result at baseline and/or post-baseline) were classified as ADA persistently positive, with equal prevalence of ADA persistently positive in [redacted] and [redacted] mg group (90.9% [10 out of 11 patients] and 90.0% [9 out of 10 patients], correspondingly) and lower incidence in [redacted] mg group (66.7% [8 out of 12 patients]) and 0% in the Placebo group.
- An increase from baseline for high-sensitivity C-reactive protein (hs-CRP) was observed at Day 16 in the [redacted] mg AZD1402 group, and at Day 12 in both the [redacted] and [redacted] mg AZD1402 group, and none in the Placebo group. These increases in hs-CRP were not associated with TEAEs.
- No important trends for changes from baseline were observed for interferon gamma and Interleukin 8 (IL-8) across the treatment groups. Immunoglobulin A (IgA), Immunoglobulin E (IgE), Immunoglobulin G (IgG), Immunoglobulin M (IgM), Interleukin 1 Beta, Interleukin 10 (IL-10), Interleukin 12 (IL-12), Interleukin 13 (IL-13), Interleukin 2 (IL-2), Interleukin 4 (IL-4), Interleukin 6 (IL-6), Tryptase, and Tumour Necrosis Factor (TNF) results remained relatively unchanged from baseline across the treatment groups with some increases and decreases in change from baseline, but none were considered clinically important.
- No results met the limits for clinical significance in laboratory parameters, vital signs, and 12-lead electrocardiogram (ECG) results change from baseline.
- No important trends for changes were observed in FEV_1 and FeNO results.

Part 2:

- There were no SAEs with the outcome of death, TEAEs leading to discontinuation of IP or TEAEs leading to withdrawal from the study reported in Part 2 of the study.
- Eight (61.5%) patients in the total AZD1402 group and 6 (66.7%) patients in the Placebo group experienced at least one TEAE.
- One (7.7%) patient in the total AZD1402 that received [redacted] mg AZD1402 had a SAE, with preferred term (PT) Asthma (SOC Respiratory, thoracic and mediastinal disorders)
- The most frequently reported TEAEs were reported in the SOC of Respiratory, thoracic and mediastinal disorders.
- Most of the TEAEs were considered to be of mild intensity (4 [30.8%] patients in the total AZD1402 group and 5 [55.6%] patients in the Placebo group). Three (23.1%) patients reported moderate TEAEs in the total AZD1402 group and 1 (11.1%) patient in the Placebo group. One (7.7%) patient that received [redacted] mg AZD1402, patient reported an TEAE considered to be of severe intensity in the total AZD1402 group.
- TEAEs with PT Cough that were considered possibly related to the IP as assessed by the Investigator were reported by 1 (7.7%) patient in the total AZD1402 group, that received [redacted] mg group, and 4 (44.4%) patients in the Placebo group.
- AESIs were reported by 4 (30.8%) patients in the total AZD1402 group and 5 (55.6%) patients in the Placebo group.
- Ten out of 13 patients in the total AZD1402 group and none in the Placebo group were TE-ADA positive. Seven (70%) patients out of these 10 patients in the total AZD1402 group and none in the Placebo group reported at least one TEAE. Of these, 3 out of

4 (75.0%) patients were in the [redacted] mg AZD1402 group and 4 out of 6 (66.7%) patients of these patients were in the [redacted] mg AZD1402 group. No patients were TE-ADA negative in Part 2. Three out of 13 patients in the total AZD1402 group (all received [redacted] mg AZD1402) and all patients in the Placebo group were in the category of ADA negative. One out of these 3 patients in the total AZD1402 group and 6 out of these 9 patients in the Placebo group reported at least one TEAE.

- In Part 2, 45.5% (10 out of 22 of patients with any ADA result at baseline and/or post-baseline) of all patients were classified as ADA persistently positive, with higher prevalence of ADA positive in [redacted] mg group versus [redacted] mg (100% [4 out of 4 patients] and 66.7% [6 out of 9 patients], correspondingly) and 0% in the Placebo group.
- Although there were other fluctuations in laboratory parameters, vital signs, and 12-lead ECG results in change from baseline, and some of these were outside of the normal range, none of these met the limits for clinical significance.
- No important trends for changes from baseline were observed for hs-CRP, interferon gamma, IL-8 across the treatment groups.
- IgA, IgE, IgG, IgM, IL-1 Beta, IL-10, IL-12, IL-13, IL-2, IL-4, IL-6, Tryptase, and TNF results remained relatively unchanged from baseline across the treatment groups with some increases and decreases in change from baseline, but none were considered clinically important.
- No important trends for changes were observed in FEV_1 and FeNO result.

Conclusions

- In general, AZD1402 was clinically well-tolerated and with no identified short-term safety concerns.
- There were no clinically significant findings regarding changes in haematology, clinical chemistry values, urinalysis, ECG or vital signs.
- At Week 4, the [redacted] mg AZD1402 group had the highest LS mean difference (95% CI) compared to Placebo of 0.1960 (0.0143, 0.3778) with a p-value of 0.035. Due to fewer evaluable study participants than the target sample size conclusions about the efficacy of AZD1402 could not be drawn.
- AZD1402 was steadily absorbed following DPI administration with a median tmax of approximately 3 to 4 hours post-dose.
- Geometric mean t½λz ranged between 7.668 hours and 20.17 hours.
- Accumulation was observed upon multiple dosing which exceeded that predicted by t½λz and τ.
- Intersubject variability in Cmax, AUClast and AUCτ was generally high, > 40%.
- There was no clear difference in PK parameters between ADA negative and TE-ADA positive patients at the [redacted] mg dose level.
- The PK results were similar between Part 1 and Part 2.