AstraZeneca

Clinical Study Report Synopsis

Drug Substance	AZD1656
Study Code	D1020C00008
Edition Number	1
Date	10 December 2009

An open, single-centre, single group, Phase I study to assess the absorption, distribution, metabolism and excretion (ADME) of AZD1656 after oral administration of ^{14}C-labelled AZD1656 to Type II Diabetes Mellitus patients

Study dates: First subject enrolled: 30 July 2009
Last subject last visit: 1 September 2009

Phase of development: Clinical pharmacology (I)

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

Study centre(s)

The study was conducted at 1 centre: AstraZeneca Clinical Pharmacology Unit, Macclesfield, Cheshire, UK.

Publications

None at the time of writing this report.

Objectives and criteria for evaluation

Table S 1 Primary and secondary objectives and outcome variables

Objectives	Outcome variables	Type
Primary	**Primary**	
To evaluate the absorption, distribution, metabolism and excretion of AZD1656 and its metabolite/s, after administration of a single oral dose of ^{14}C-labelled AZD1656 by assessment of recovery, rate and routes of excretion of total radioactivity, metabolic profile and pharmacokinetic variables in patients with type 2 diabetes mellitus (T2DM).	Total recovery of radioactive dose, rate and routes of excretion of total radioactivity, metabolic profile. AZD1656: AUC, AUC_{0-t}, C_{max}, t_{max}, $t_{1/2,}$ Ae, CL/F, CL_R and Vz/F. AZ12555623: AUC, AUC_{0-t}, C_{max}, t_{max}, $t_{1/2}$, Ae and CL_R Total radioactivity: AUC, AUC_{0-t}, C_{max}, t_{max} and $t_{1/2}$	Pharmaco-kinetic
Secondary	**Secondary**	
To describe the safety and tolerability of AZD1656 after oral administration of a single dose of ^{14}C-labelled AZD1656.	Adverse events, blood pressure, pulse, electrocardiogram, laboratory variables and plasma glucose.	Safety
To identify metabolites, if possible[a]	Not applicable	Pharmaco-kinetic
Exploratory	**Exploratory**	
To collect and store DNA for future exploratory research into genes that may influence drug response ie, distribution (PK profile), safety, tolerability and efficacy of AZD1656 treatment[a]	Pharmacogenetic biomarkers	Pharmaco-genetic

DNA= Deoxyribonucleic acid
a Reported separately from this CSR

Study design

This was an open, single-centre, single group, phase I study to evaluate the absorption, distribution, metabolism and excretion (ADME) of AZD1656 and its metabolite/s.

After administration of a single oral 40 mg dose of AZD1656 ^{14}C-labelled solution, recovery of radioactive molecules in urine and faeces continued 168 hours (7 days) post-dose at the clinic, and for a maximum of 7 days in the following outpatient period for subjects who were still excreting >1% of the administered dose within a 120-144 hour time span after intake of investigational product (IP).

Target subject population

Male T2DM patients (henceforth called subjects) treated with a stable dose of metformin alone or in combination with 1 other oral antidiabetic drug for at least 3 months before enrolment.

Investigational product and comparator(s): dosage, mode of administration and batch numbers

The details of the IP are given in Table S 2.

Table S 2 Details of investigational product and other study treatments

Investigational product	Dosage form, strength, dosing schedule, and route of administration	Manufacturer	Formulation number	Batch number
AZD1656 ^{14}C (0.17 MBq/mL)	Oral solution 2 mg/ml, single dose 40 mg	AstraZeneca R&D Mölndal, Sweden	D0900063	09-001779AZ

Duration of treatment

Single dose.

Statistical methods

The data were summarised using descriptive statistics. Estimates and confidence intervals of the true geometric mean were calculated for the relevant PK variables.

Subject population

Six (6) subjects, 5 white and 1 subject described as “Chilean”, between 42 and 57 years of age, were included into the study. All 6 subjects completed the study according to protocol.

Summary of pharmacokinetic results

See conclusions.

Summary of safety results

There were no adverse events (AEs) with fatal outcome, other serious AEs (SAE) or other significant AEs. AEs, the majority of which were of mild intensity, were reported for 5 subjects. The most common AEs were administration site conditions. There were no clinically relevant treatment-related changes or trends in any laboratory variables, blood pressure or pulse rate. There were no abnormalities in ECG, changes in mean weight or abnormal physical findings at follow-up compared to baseline.