AstraZeneca

Clinical Study Report Synopsis

Drug Substance	AZD7295
Study Code	D1820C00001
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A Phase I, Randomised, Double-Blind, Placebo-Controlled Study to Assess the Safety, Tolerability and Pharmacokinetics of AZD7295 following Single and Multiple Ascending Oral Dose Administration in Healthy Male Japanese Subjects

Study dates:	First subject enrolled: 22 December 2008 Last subject completed: 05 May 2009
Phase of development:	Clinical Pharmacology (1)

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

Study centre(s)

This study was conducted at one study centre in Japan.

Publications

None at the time of writing this report.

Objectives and criteria for evaluation

The primary objective of the study was to investigate the safety and tolerability of single and multiple oral doses of AZD7295 in healthy male Japanese subjects.

The secondary objective of the study was to investigate the pharmacokinetics of AZD7295 after single and multiple oral administration of AZD7295 to healthy male Japanese subjects.

Study design

This was a 2-Part, Randomised, Double-Blind, Placebo-Controlled Study to assess the safety, tolerability and pharmacokinetics of AZD7295 following single and multiple oral administration of ascending doses to healthy male Japanese subjects.

Target healthy subject population and sample size

A maximum of sixty-two subjects were planned to take part in this study. Each level in SAD Part (Cohort 1 - 4) was to consist of 8 healthy male Japanese subjects with 6 subjects receiving active drug and 2 receiving placebo. Each level in MAD Part (Cohort 5 – 7) was to consist of 10 healthy male Japanese subjects, 8 receiving active drug and 2 receiving placebo.

In total, 42 Japanese healthy male subjects were randomised into the study at 1 study site. In SAD Part, 32 subjects were randomized to dose administration with AZD7295 (n=6) or placebo (n=2) in each of 4 cohorts. In MAD Part, 10 subjects were randomized to dose administration with AZD7295 (n=8) or placebo (n=2) in 1 cohort. All subjects randomised to treatment completed the study.

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

AZD7295 (batch number P7808, P7973) and placebo (batch number P7807) were provided as oral solution. In SAD Part, AZD7295 and placebo were administered as a single dose of 90, 270, 500 and 700 mg. In MAD Part, AZD7295 and placebo were administered three times daily as a dose of 233 mg.

Duration of treatment

SAD Part: Single dose

MAD Part: Three times daily for 6 continuous days

Statistical methods

The sample size was based on experience with previous studies and was determined without formal statistical consideration or formal power calculations.

The data were summarized using descriptive statistics. Dose proportionality was analysed by using the power model approach.

Subject population

In total, 42 Japanese healthy male subjects were randomised into the study at 1 study site. All subjects randomised to treatment completed the study. None of the protocol deviations led to exclusion of the subjects from the analysis of safety and PK. The safety analysis included all randomised healthy subjects. In the study, no stopping criteria were met.

Summary of pharmacokinetic results

C_{max} increased slightly less than proportionally to the dose whereas AUC increased proportionally to the dose. The reason for the increase in C_{max} being slightly less than dose proportionally may be due to saturation of absorption. This is reflected in the later t_{max} values at higher doses. In general, exposure (AUC, C_{max}) of AZD7295 increased proportionally to dose. Plasma concentration of AZD7295 reached steady state at Day 4 based on trough concentration. As elimination half-life at steady state was similar to that at SAD part, it seems multiple dosing was not likely to alter elimination phase of AZD7295 significantly. CL/F appeared to be constant within the investigated dosing range.

Summary of safety results

In total, 13 adverse events were observed in 9 subjects. In SAD part, 9 AEs were observed in 6 subjects. And in MAD part, 4 AEs were observed in 3 subjects. The intensities of AEs were all mild. All events related to study treatment were resolved by the end of the study. The most common AEs in subjects treated with AZD7295 were nausea (5 of 24 subjects [20.8%]) in SAD part and headache (2 of 8 subjects [25.0%]) in MAD part. In SAD part, product quality issue (bitter taste in mouth) was observed in both placebo (1 of 8 subjects [12.5%]) and AZD7295 (1 of 24 subjects [4.2%]) group. There were no deaths, other serious adverse events (SAEs), discontinuations due to adverse events (DAEs), or any other significant adverse event (OAEs) in the study