Clinical Study Report Synopsis

Drug Substance	AZD7325
Study Code	D1140C00018
Edition Number	1
Date	11 MAR 2010

A Randomized, Open-label, Two-way Crossover Study to Determine the Effects of Co-administration of AZD7325 and a Monophasic Oral Contraceptive Containing Ethinyl Estradiol and Norgestimate in Healthy Female Subjects

Study dates: First subject enrolled: 11 MAY 2009
Last subject last visit: 17 SEP 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 center: Quintiles Phase I Services, Overland Park, Kansas, United States.

Publications

None at the time of writing this report.

Objectives and criteria for evaluation

Table S1 Primary and secondary objectives and outcome variables

Objectives	Outcome variables	Type
Primary	**Primary**	
To evaluate the effect of repeated doses of AZD7325 on the pharmacokinetics of ORTHOCYCLEN®, a monophasic oral contraceptive, by assessment of $C_{ss,max}$ and AUC_{tau} of ethinyl estradiol, norelgestromin, and levonorgestrel on Study Day 21.	Not collected	Pharmacokinetic
Secondary	**Secondary**	
To characterize the pharmacokinetics of progesterone, luteinising hormone, follicle-stimulating hormone, and sex hormone binding globulin following dosing with monophasic oral contraceptive (ORTHO-CYCLEN®) alone and following coadministration with AZD7325.	Not collected	Pharmacokinetic
To characterize the steady-state pharmacokinetics of AZD7325.	Not collected	Pharmacokinetic
To examine the safety and tolerability of AZD7325 in combination with the monophasic oral contraceptive (ORTHO-CYCLEN®).	Collection of adverse events, clinical laboratory data, vital signs, and electrocardiograms	Safety
Exploratory		
Retrospective genetic analyses may have been performed if sufficient samples were donated and exploratory analysis justified by study data.	Not collected	
Measure 4-beta-hydroxy-cholesterol, an endogenous marker of CYP 3A4 activity on Day -1 and at predose on Day 21.	Not collected	

Study design

This study was conducted as an open-label, randomized, two-way crossover, with an enrollment of approximately 56 healthy female volunteers for at least 28 volunteers to complete the study. The study consisted of a two-cycle (28 days each) stabilization period

(run in) with the oral contraceptive, followed by 2 treatment periods (28 days each) of the oral contraceptive (ORTHO-CYCLEN®) in the presence (Treatment A = oral contraceptive + AZD7325) and absence (Treatment B = oral contraceptive alone) of the drug AZD7325.

Target subject population and sample size

The aim was to include healthy, premenopausal, nonpregnant, nonbreastfeeding female volunteers of 18 to 45 years of age who were greater than 6 months postpartum at the time of randomization with a body mass index between 18 and 30 kg/m^2.

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

AZD7325 – 5 mg tablets
15 mg (3 tablets), orally, twice daily

ORTHO-CYCLEN®
1 active tablet orally, once every morning

Duration of treatment

The overall duration of the study was to be approximately 5 months, inclusive of screening, stabilization, and treatment periods. This study was terminated early because AstraZeneca has discontinued the AZD7325 development program.

Statistical methods

Statistical methods planned in the protocol were not used. Data listings are provided for safety parameters (adverse events and laboratory values) and summary tables are provided for demographics and adverse events.

Subject population

The first subject was enrolled on 11 May 2009 and the last subject completed the study on 17 September 2009. Twenty-one volunteers were enrolled and 4 volunteers were randomized and received treatment.

Summary of efficacy results

Efficacy data are not available.

Summary of pharmacokinetic results

No samples were analyzed; therefore, pharmacokinetic data are not available.

Summary of safety results

There were no deaths, serious adverse events, or discontinuations due to adverse events. There were no other significant adverse events reported during the study. Clinical laboratory, vital sign, and electrocardiogram data were not summarized and are presented for individual volunteers in data listings.