An Open-label, Non-randomised, Multicentre Study to Allow Continued Access to and Assess the Safety and Tolerability of AZD1775 for Patients Enrolled in AZD1775 Clinical Pharmacology Studies

Published: 11-07-2017
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To assess the safety of AZD1775 following oral dosing of the capsule formulation in patients with advanced solid tumours

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Miscellaneous and site unspecified neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON47273

Source
ToetsingOnline

Brief title
AZD1775 - Catch All

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
Cancer, Solid Tumour

Research involving

Human

Sponsors and support

Primary sponsor: Astra Zeneca
Source(s) of monetary or material Support: Pharmaceutical industry

Intervention

Keyword: Advanced solid Tumours, Continued Access

Outcome measures

Primary outcome

To examine the safety of AZD1775 as monotherapy in patients with advanced

malignancies

Secondary outcome

NA

Study description

Background summary

AZD1775 is an inhibitor of WEE1, a protein tyrosine kinase. WEE1 phosphorylates and
inhibits cyclin-dependent kinases 1 (CDK1) and 2 (CDK2), and is involved in regulation of the intra-S and G2 cell cycle checkpoints.

It is anticipated that AZD1775 will have independent anti-tumour activity in the absence of added chemotherapy, particularly in cancer cells that already have significantly higher levels of replication stress. In preclinical cancer cell models associated with high levels of endogenous replication stress resulting from a combination of G1/S checkpoint deficiencies due to p53 mutations or CDKN2A deletions and the over-expression of oncogenic drivers such as MYC, mutant KRAS or the amplification of Cyclin E, AZD1775 demonstrated significant single-agent anti-tumour activity.

Study objective

To assess the safety of AZD1775 following oral dosing of the capsule

formulation in patients with advanced solid tumours

Study design

This is an open-label, non-randomised study designed to provide continued access to AZD1775 for eligible patients with advanced solid tumours who have previously completed an AZD1775 clinical pharmacology study and to investigate the safety of a once daily monotherapy regimen of AZD1775 in patients with advanced solid tumours.

Intervention

The dose administered to patients will be 300 mg orally once a day on Days 1 to 5 and 8 to 12 of a 21-day cycle (ie, 5 days on and 2 days off for Weeks 1 and 2 of a 21-day cycle).
Patients will continue to receive AZD1775 as long as they are benefiting from treatment in the Investigator*s opinion and do not meet any other discontinuation criteria.

Study burden and risks

This study is designed to provide continued access to AZD1775 to patients who have
completed 1 of the parent clinical pharmacology studies and allow the continued evaluation of the safety and tolerability of the therapy in this cohort of patients. AstraZeneca considers that AZD1775 continues to demonstrate an overall acceptable benefit-risk balance to support its further clinical development.
The identified risks (expected events) for AZD1775 are described in Section 5.4 (EmergingSafety Profile) of the IB.

Contacts

Public
Astra Zeneca

NA NA
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SE
Scientific
Astra Zeneca

NA NA
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SE

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Has read and understands the informed consent form (ICF) and has given written informed consent prior to any study procedures.
2. Female or male aged *18 years.
3. Has completed 1 of the parent AZD1775 clinical pharmacology studies (ie, D6014C00002, D6014C00003, D6014C00004, D6014C00005, or D6014C00006) and in the Investigator*s opinion will continue to benefit from treatment with AZD1775. Patients who discontinue early from the parent study will be considered by the Sponsor and treating physician on a case-by-case basis.
4. Any prior radiation must have been completed at least 7 days prior to the start of study treatment, and patients must have recovered from any acute effects prior to the start of study treatment.
5. Eastern Cooperative Oncology Group (ECOG) Performance Status score of 0 to 1.
6. Baseline laboratory values within 7 days of study treatment initiation in the CA study:
* Absolute neutrophil count (ANC) *1500/*L.
* Haemoglobin *9 g/dL.
* Platelets *100,000/*L.
* Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) *3 x upper limit of normal (ULN) or *5 x ULN if known hepatic metastases.
* Serum bilirubin within normal limits or *1.5 x ULN in patients with liver metastases; or total bilirubin *3.0 x ULN with direct bilirubin within normal limits in patients with well documented Gilbert*s Syndrome.
* Serum creatinine *1.5 x ULN, or measured creatinine clearance (CrCl) calculated by Cockcroft-Gault method *45 mL/min (confirmation of creatinine clearance is only required when creatinine is >1.5 x ULN)

(CrCl (glomerular filtration rate) <= (140-age) x (weight/kg) x Fa) /
(72 x serum creatinine mg/dL) awhere F <= 0.85 for females and F <= 1 for males.
7. Female patients who are of non-childbearing potential and fertile women of childbearing potential (WoCBP) who agree to use adequate contraceptive measures that are in place during screening (or consent), for the duration of the study, and for 1 month after treatment stops; who are not breastfeeding; and who have a negative serum or urine pregnancy test prior to the start of study treatment.
8. Male patients must be willing to use barrier contraception (ie, condoms) for the duration of the study and for 3 months after study treatment discontinuation.
9. Willingness and ability to comply with the study and the follow-up procedures.

Exclusion criteria

1. Involvement in the planning and/or conduct of the study (applies to both AstraZeneca personnel and/or personnel at the study centre).
2. Previous enrolment and received study treatment in the present study. Patients can, however, be re-screened if the reason for the screen failure no longer exists.
3. Concurrent enrolment in another clinical study, unless it is an observational (non-interventional) clinical study or the follow-up period of an interventional study.
4. Must not have received another systemic anti-cancer therapy in the interval following participation in the AZD1775 clinical pharmacology study and the start of treatment on the CA protocol.
5. Not developed any clinical findings suggestive of brain metastasis. Patients continue to be neurological stable and remain off systemic corticosteroids following treatment of known brain metastases.
6. Did not tolerate AZD1775 in the parent study in the opinion of the Investigator.
7. Where a course of palliative radiotherapy was indicated, the last fraction must have been delivered before the start of study treatment on the CA study.
8. Major surgical procedures *28 days of beginning study treatment, or minor surgical procedures *7 days. No waiting period required following port-a-cath placement or other central venous access placement.
9. Grade >1 toxicities from prior therapy, according to the Common Terminology Criteria for Adverse Events (CTCAE), excluding alopecia or anorexia.
10. Continue to be able to swallow oral medication, did not undergo placement of a percutaneous endoscopic gastrostomy tube and did not require total parenteral nutrition.
11. Has had prescription or non-prescription drugs or other products known to be sensitive to CYP3A4 substrates or CYP3A4 substrates with a narrow therapeutic index, or to be moderate to strong inhibitors/inducers of CYP3A4 between the parent study and entry into this CA study. Co administration of aprepitant or fosaprepitant during this study is prohibited.
12. Has consumed herbal preparations between the parent study and entry into this CA study.
13. Has consumed grapefruit, grapefruit juice, Seville oranges, Seville orange

marmalade, or other products containing grapefruit or Seville oranges between the parent study and entry into the CA study.
14. Any known hypersensitivity or contraindication to AZD1775 or to the components thereof.
15. Any of the following cardiac diseases currently or within the last 6 months as defined by the New York Heart Association *Class 2:
* Unstable angina pectoris.
* Congestive heart failure.
* Acute myocardial infarction.
* Conduction abnormality not controlled with pacemaker or medication.
* Significant ventricular or supraventricular arrhythmias (patients with chronic rate-controlled atrial fibrillation in the absence of other cardiac abnormalities are eligible).
16. AZD1775 should not be given to patients who have a history of Torsades de pointes unless all risk factors that contributed to Torsades have been corrected. AZD1775 has not been studied in patients with ventricular arrhythmias or recent myocardial infarction.
17. Patient with mean resting QTc interval (specifically QTc calculated using the Fridericia formula [QTcF]) >450 ms for males and >470 ms for females from 3 electrocardiograms (ECGs) performed within 2 to 5 minutes apart during screening, or congenital long QT syndrome.
18. Pregnant or lactating female patients.
19. Serious, symptomatic active infection at the time of study entry, or another serious underlying medical condition that would impair the ability of the patient to receive study treatment.
20. Active infection with hepatitis B, hepatitis C, or human immunodeficiency virus (HIV).

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	07-10-2017
Enrollment:	14

Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	AZD1775
Generic name:	na

Ethics review

Approved WMO Date:	11-07-2017
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	01-09-2017
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	18-07-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-08-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	29-08-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	31-08-2018
Application type:	Amendment

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2016-001910-94-NL
CCMO	NL57526.056.17