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Fibroblast growth factor receptors (FGFR) Inhibition for Epithelial Solid Tumours

Submission date 24/08/2011	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 14/10/2011	**Overall study status** Completed	
Last Edited 26/10/2021	**Condition category** Cancer	

Plain English summary of protocol
http://www.cancerresearchuk.org/cancer-help/trials/a-trial-of-azd4547-alongside-chemotherapy-for-solid-tumours-such-as-bladder-cancer-fiesta

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2011-004072-10

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers

MO11/9803

Study information

Scientific Title
Fibroblast growth factor receptors (FGFR) Inhibition for Epithelial Solid Tumours: a phase Ib trial of AZD4547 in combination with gemcitabine and cisplatin

Acronym
FIESTA

Study objectives
This study aims to investigate, for the first time in man, the combination of gemcitabine /cisplatin (GC) with AZD4547. As GC is a standard-of-care for both neoadjuvant and first-line palliative chemotherapy, the three-drug combination of AZD4547 plus GC (AGC) therefore has the potential for improving outcomes in both disease settings.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

Study design
Dose escalation cohort trial followed by a randomised expansion cohort

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Epithelial Solid Tumours

Interventions
AZD4547 with Gemcitabine and Cisplatin with increasing doses of AZD4547 during the Dose Escalation Cohort. Randomisation between AZD4547 with Gemcitabine and Cisplatin, and Gemcitabine and Cisplatin alone in the Randomised Expansion Cohort

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
AZD4547, cisplatin, gemcitabine

Primary outcome measure
1. Dose-escalation cohort:
1.1. Dose-Limiting Toxicities (DLTs), Maximum Tolerated Dose (MTD) of AZD4547 in combination with GC
1.2. Recommended Dose for Sustained Tolerability (RDST) for use in the randomized expansion cohort of this trial and in subsequent studies.
2. Randomised expansion cohort:
2.1. Relative proportions of participants experiencing any grade 3/4 CTCAE v4.02 toxicity within first cycle of treatment of AGC and GC regimens.

Secondary outcome measures
No secondary outcome measures

Overall study start date
01/02/2012

Completion date
01/07/2017

Eligibility

Key inclusion criteria
1. Provision of written informed consent
2. Age 25 years or greater
3. Histologically confirmed locally advanced / metastatic non-haematological malignancy
3.1. Dose-escalation cohort
3.2. Any locally-advanced and/or metastatic malignancy for which no recognised standard treatment is available (including tumours refractory to previous standard therapies), and for whom gemcitabine and cisplatin would be appropriate treatment. Any number of previous lines of therapy are permitted OR
3.3. Locally advanced and/or metastatic transitional cell carcinoma, of the urinary tract, as in the randomised expansion cohort
3.4. Dose expansion cohort-Locally advanced and/or metastatic transitional cell carcinoma (pure or mixed histology) of (upper or lower) urinary tract, including bladder cancer. No prior systemic therapy for locally advanced or metastatic disease - patients who have received prior neoadjuvant or adjuvant chemotherapy for potentially-curable urothelial cancer (up to 4 cycles), completed at least 6 months prior to first documented disease progression, will be eligible
4. Radiologically measurable disease (randomised expansion cohort only)
4.1. T4b Nany Many, Tany N2-3 Many or Tany Nany M1 TCC of the urinary tract (as above), not amenable to curative treatment with surgery or radiotherapy
5. Fit to receive cisplatin-containing combination chemotherapy

6. Minimum life expectancy of 18 weeks
7. WHO Performance Status 0-1
8. Adequate renal function [glomerular filtration rate (GFR) greater than or equal to 60ml/min, uncorrected for surface area and measured by isotopic means]
9. Adequate bone marrow function (absolute neutrophil count greater than or equal to 1.5 x 109 /L and platelets greater than or equal to 100 x 109/L at screening)
10. Adequate liver function i.e. plasma bilirubin less than or equal to 1.5 x ULN (upper limit of normal), and ALT and ALP less than or equal to 2.5 x ULN (ALP less than or equal to 5 x ULN in case of liver metastases), at screening
11. Prothrombin time (PT) or International Normalized Ratio (INR) less than or equal to 1.5
12. Serum total calcium and/or phosphate less than or equal to ULN

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
44

Total final enrolment
28

Key exclusion criteria
1. Being considered for subsequent radical treatment with the possibility of cure
2. Prior treatments with any of the following, prior to first dose of study treatment:
2.1. AZD4547
2.2. Any investigational agents or study drugs from a previous clinical study within 30 days
2.3. Any other chemotherapy, immunotherapy or anticancer agents within 3 weeks
2.4. Major surgery within 4 weeks
2.5. Radiotherapy
2.5.1. With a wide field of radiation or involving >30% of total bone marrow volume, within 4 weeks
2.5.2. With a limited field of radiation, for palliation, within 2 weeks
3. Any unresolved toxicities from prior therapy greater than Common Terminology Criteria for Adverse Events (CTCAE) grade 1 (with the exception of alopecia) at the time of registration
4. Any of the following pre-existing conditions
4.1. Other malignant disease
4.1.1. Previous malignancy other than non-melanoma skin cancer, cervical carcinoma in situ or incidental localised prostate cancer
4.1.2. Previously-identified central nervous system (CNS) metastases unless asymptomatic, treated and stable and not requiring steroids for at least 4 weeks prior to start of study treatment
4.2. Infections: Clinically significant bacterial or fungal infection

4.2.1 Known active viral infection with: human immunodeficiency virus (HIV), hepatitis B or C virus
4.3. Gastro-intestinal: Previous bowel resection or other condition which might preclude adequate absorption of AZD4547
4.4. Other: any evidence of severe or uncontrolled systemic diseases, including uncontrolled hypertension, active bleeding diatheses
5. Any of the following ophthalmological criteria:
5.1. Current evidence or previous history of retinal pigmented epithelium detachment (RPED)
5.2. Previous laser treatment or intra-ocular injection for treatment of macular degeneration
5.3. Current evidence or previous history of dry or wet age-related macular degeneration
5.4. Current evidence or previous history of retinal vein occlusion (RVO)
5.5. Patients with uncontrolled glaucoma or intra-ocular pressure greater than or equal to 21mm Hg at screening.
6. Women who are pregnant or breast feeding - women of child-bearing potential must have a negative pregnancy test performed within 7 days prior to the start of study treatment
7. Men or women who are not prepared to practise methods of contraception of proven efficacy
8. Any patient who, in the judgment of the investigator, is unlikely to comply with study procedures, restrictions or requirements

Date of first enrolment
01/02/2012

Date of final enrolment
30/09/2016

Locations

Countries of recruitment
United Kingdom

Study participating centre
Southampton Hospitals NHS Trust
Southampton
United Kingdom
SO16 6YD

Study participating centre
Clatterbridge Cancer Centre
Wirral
United Kingdom
CH63 4JY

Study participating centre
Beatson West of Scotland Cancer Centre
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St Bart's Hospital
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EC1A 7BE

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CF14 2TL

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St James' University Hospital
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Sponsor information

Organisation
University of Leeds (UK)

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Sponsor type
University/education

Website
http://www.leeds.ac.uk/

ROR

https://ror.org/024mrxd33

Funder(s)

Funder type
Industry

Funder Name
AstraZeneca (UK)

Alternative Name(s)
AstraZeneca PLC, Pearl Therapeutics

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

Funder Name
Cancer Research UK (CRUK) (UK)

Alternative Name(s)
CR_UK, Cancer Research UK - London, CRUK

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Results and Publications

Publication and dissemination plan
To be confirmed at a later date

Intention to publish date

Individual participant data (IPD) sharing plan

Not provided at time of registration

IPD sharing plan summary

Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results		31/08/2019	26/10/2021	No	No