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WISTERIA: WEE1 inhibitor with cisplatin and radiotherapy

Submission date	Recruitment status	[X] Prospectively registered
20/02/2017	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
21/02/2017	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
03/09/2024	Cancer	

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-of-azd1775-for-head-and-neck-cancer-wisteria

Contact information

Type(s)
Public

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Additional identifiers

Clinical Trials Information System (CTIS)
2015-003583-37

ClinicalTrials.gov (NCT)
NCT03028766

Protocol serial number
32918

Study information

Scientific Title
A Phase I trial of WEE1 inhibition with chemotherapy and radiotherapy as adjuvant treatment, and a window of opportunity trial with cisplatin in patients with head and neck cancer

Acronym
WISTERIA

Study objectives
The aim of this study is to determine how effective and safe it is to combine AZD1775 with cisplatin in the pre-operative setting (Group A) and with post-operative cisplatin based chemo-radiation (Group B) in patients with head and neck cancer.

Ethics approval required
Old ethics approval format

Ethics approval(s)
West Midlands – Edgbaston REC, 18/01/2017, ref: 16/WM/0501

Study design
Non-randomized; Interventional; Design type: Treatment, Drug, Radiotherapy

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Head and neck cancer

Interventions
Current interventions as of 04/05/2018:
Patients who have been diagnosed with cancer of the oral cavity, larynx or hypopharynx and are due to undergo surgery will be allocated to Group A. Patients who have been diagnosed with cancer of the oral cavity, larynx or hypopharynx, have undergone surgery and will require radiotherapy afterwards due to being considered to be at risk of relapse after surgery will be allocated to Group B.

Group A: Patients will receive the cohort specified dose of AZD1775, twice a day for the first 3 days of each week for 2 weeks. Patients will receive cisplatin at the start of the second week of treatment. Patients in this group will commence surgery within 42 days of commencing pre-operative chemotherapy. Patients will be followed-up clinically for 3 months.

Group B: Patients will receive the cohort specified dose of AZD1775, twice a day for 3 days, on Weeks 1, 2, 4 and 5. Patients will receive cisplatin at the start of each week of treatment for 5

weeks. Intensity Modulated Radiotherapy will be delivered 5 days a week (once daily, Monday to Friday) for 6 weeks commencing within 3 months of surgery. Patients will be followed up clinically for 12 months.

Previous interventions:
Patients who have been diagnosed with cancer of the oral cavity, larynx or hypopharynx and are due to undergo surgery will be allocated to Group A. Patients who have been diagnosed with cancer of the oral cavity, larynx or hypopharynx, have undergone surgery and will require radiotherapy afterwards due to being considered to be at risk of relapse after surgery will be allocated to Group B.

Group A: Patients will receive the cohort specified dose of AZD1775, twice a day for the first 3 days of each week for 2 weeks. Patients will receive cisplatin at the start of the second week of treatment. Patients in this group will commence surgery within 42 days of commencing pre-operative chemotherapy. Patients will be followed-up clinically for 3 months.

Group B: Patients will receive the cohort specified dose of AZD1775, twice a day for 3 days, for 5 weeks. Patients will receive cisplatin at the start of each week of treatment for 5 weeks. Intensity Modulated Radiotherapy will be delivered 5 days a week (once daily, Monday to Friday) for 6 weeks commencing within 42 days of surgery. Patients will be followed up clinically for 12 months.

Intervention Type
Other

Phase
Phase I

Primary outcome(s)
1. Recommended dose(s) of AZD1775. For Group A this is measured as the highest safe dose of AZD1775 in combination with cisplatin with a predefined target Dose Limiting Toxicity probability of 25% for up to 42 days from start of treatment. For Group B this is measured as the maximum tolerated dose of AZD1775 in combination with cisplatin/radiotherapy with a target DLT of 30% for up to 12 weeks from the start of treatment.
2. Safety profile of AZD1775 for Group A and Group B is assessed by reporting of all adverse events, serious adverse events, suspected unexpected adverse reactions, deaths, deviations and withdrawal as assessed by the Safety Committee from registration, while on treatment and during follow up periods

Key secondary outcome(s))
Disease-free survival is measured as the time from trial entry to date of disease recurrence, progression or patient death until end of follow up period

Completion date
03/02/2021

Eligibility

Key inclusion criteria
Current inclusion criteria as of 04/05/2018:
1. Histologically confirmed diagnosis of oral, laryngeal or hypopharyngeal squamous cell

carcinoma
2. Multi-Disciplinary Team (MDT) recommendation for surgical resection with curative intent
3. Eastern Cooperative Oncology Group (ECOG) performance status 0/1
4. Aged between 18 and 70 years
5. Creatinine clearance, measured by Glomerular Filtration Rate (GFR), > = 60 ml/min at baseline calculated using local practice calculation. If this is < = 60 ml/min then an isotopic GFR may be carried out and must be > 60 ml/min
6. Acceptable cardiac function. If significant cardiac history, then required for patient to have Left Ventricular Ejection Fraction (LVEF) > = 55% by echocardiogram (ECHO) or Multiple Gated Acquisition Scan (MUGA, if ECHO is equivocal)
7. Normal liver and bone marrow function:
7.1. Haemoglobin (Hb) > = 10.0 g/dL or > = 100 g/L
7.2. Absolute neutrophil count (ANC) > = 1.5 x 109/L
7.3. Absolute platelet count > = 100 x 109/L
7.4. Aspartate transaminase (AST) or alanine aminotransferase (ALT) < = 2.5 upper limit of normal (ULN)
7.5. Total bilirubin < = 1.5 ULN (except for patients with known Gilbert's syndrome)
8. Male and female participants must agree to take appropriate measures to prevent pregnancy. Contraceptive measures should be used for 2 weeks prior to trial entry, during the trial and for at least 6 months after last receiving treatment. Acceptable methods of contraception include total abstinence (if this is the patient's usual and preferred lifestyle choice), tubal ligation, combined oral, transdermal or intra-vaginal hormonal contraceptives, medroxyprogesterone injections (e.g. Depo-Provera), copper-banded intra-uterine devices; hormone impregnated intra-uterine systems and vasectomised partners. All methods of contraception (with the exception of total abstinence) should be used in combination with the use of a condom by their male sexual partner for intercourse.

9. Inclusion criteria Group A – in addition to general criteria:
Accessible tumours for re-biopsy under local anaesthetic or via ultrasound guided biopsy

10. Inclusion criteria Group B – in addition to general criteria:
10.1. High-risk histopathological features after surgical resection, i.e. nodal extra-capsular spread and/or tissue resection margin <1 mm as agreed at MDT
10.2. Patients who have previously registered to Group A can be considered for inclusion in Group B

Previous inclusion criteria:
1. Histologically confirmed diagnosis of oral, laryngeal or hypopharyngeal squamous cell carcinoma
2. Multi-Disciplinary Team (MDT) recommendation for surgical resection with curative intent
3. Eastern Cooperative Oncology Group (ECOG) performance status 0/1
4. Aged between 18 and 70 years
5. Creatinine clearance, measured by Glomerular Filtration Rate (GFR), > = 60 ml/min at baseline calculated using local practice calculation. If this is < = 60 ml/min then an isotopic GFR may be carried out and must be > 60 ml/min
6. Acceptable cardiac function. If significant cardiac history, then required for patient to have Left Ventricular Ejection Fraction (LVEF) > = 55% by echocardiogram (ECHO) or Multiple Gated Acquisition Scan (MUGA, if ECHO is equivocal)
7. Normal liver and bone marrow function:
7.1. Haemoglobin (Hb) > = 10.0 g/dL or > = 100 g/L
7.2. Absolute neutrophil count (ANC) > = 1.5 x 109/L
7.3. Absolute platelet count > = 100 x 109/L

7.4. Aspartate transaminase (AST) or alanine aminotransferase (ALT) < = 2.5 upper limit of normal (ULN)
7.5. Total bilirubin < = 1.5 ULN (except for patients with known Gilbert's syndrome)
8. Male and female participants must agree to take appropriate measures to prevent pregnancy. Contraceptive measures should be used for 2 weeks prior to trial entry, during the trial and for at least 6 months after last receiving treatment. Acceptable methods of contraception include total abstinence (if this is the patient's usual and preferred lifestyle choice), tubal ligation, combined oral, transdermal or intra-vaginal hormonal contraceptives, medroxyprogesterone injections (e.g. Depo-Provera), copper-banded intra-uterine devices; hormone impregnated intra-uterine systems and vasectomised partners. All methods of contraception (with the exception of total abstinence) should be used in combination with the use of a condom by their male sexual partner for intercourse.

Inclusion criteria Group A – in addition to general criteria:
Accessible tumours for re-biopsy under local anaesthetic, e.g. oral cancer

Inclusion criteria Group B – in addition to general criteria:
High-risk histopathological features after surgical resection, i.e. nodal extra-capsular spread and /or tissue resection margin < 1 mm as agreed at MDT

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
70 years

Sex
All

Total final enrolment
9

Key exclusion criteria
1. Any previous treatment for the same cancer, or previous head and neck malignancy, apart from laser excision of carcinoma in situ, with minimal residual functional deficit
2. Patients with cancer of the oropharynx will not be included
3. Any metastatic disease from any primary site
4. Use of an Investigational Medicinal Product concurrently or within 4 weeks of starting this trial
5. Uncontrolled intercurrent illness, which will interfere with the patient's participation in the trial, e.g.:
5.1. Myocardial infarction within 6 months
5.2. Congestive cardiac failure

5.3. Unstable angina
5.4. Symptomatic cardiomyopathy
5.5. Chronic infections
5.6. Active peptic ulcer or liver disease
5.7. Serious psychiatric condition limiting ability to comply with trial protocol
6. Clinical evidence of current heart failure (> = New York Heart Association (NYHA) Class II)
7. Clinical evidence of atrial fibrillation (with heart rate > 100 bpm, within 6 months prior to starting treatment)
8. Unstable ischaemic heart disease (Myocardial Infarction within 6 months prior to trial entry or angina requiring the use of nitrates greater than once weekly)
9. Active gastro-intestinal disease that might limit absorption of study drug, e.g. coeliac disease, Crohn's disease, ulcerative colitis, pancreatic insufficiency
10. Evidence of any psychological, familial, sociological or geographical condition potentially hampering protocol compliance
11. Participation in another interventional clinical trial whilst taking part in this trial
12. Patients who are unable to discontinue any prohibited drug and unable to tolerate a washout period for at least 14 days prior to trial entry
13. Clinical judgement by the Investigator that the patient should not participate in the study
14. Known hypersensitivity to the study drugs or active substances or excipients of the preparations
15. Pregnant or lactating patients
16. Significant pre-existing neuropathy which currently interferes with the patient's daily life
17. Mean resting corrected QTc interval using the Fridericia formula (QTcF) > 450 msec (male) and > 470 msec (female) (as calculated per institutional standards) obtained from 3 electrocardiograms (ECGs) 2-5 minutes apart at study entry, or congenital long QT syndrome
18. Inability to swallow oral medications

Date of first enrolment
22/06/2017

Date of final enrolment
31/10/2019

Locations

Countries of recruitment
United Kingdom

England

Scotland

Study participating centre
Queen Elizabeth Hospital Birmingham
Mindelsohn Way
Birmingham
United Kingdom
B15 2TH

Study participating centre
Royal Marsden Hospital
Fulham Road
London
United Kingdom
SW3 6JJ

Study participating centre
University College London Hospital
235 Euston Road
London
United Kingdom
NW1 2PG

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

Study participating centre
Beatson West of Scotland Cancer
1053 Great Western Road
Glasgow
United Kingdom
G12 0YN

Study participating centre
St James's University Hospital
Leeds Teaching Hospitals NHS Trust
Beckett St
Leeds
United Kingdom
LS9 7TF

Sponsor information

Organisation
University of Birmingham

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Charity

Funder Name
Cancer Research UK

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

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
Current IPD sharing statement as of 28/10/2022:
Scientifically sound proposals from appropriately qualified researchers will be considered for data sharing. Requests should be made by returning a Data Sharing Request Form to newbusiness@trials.bham.ac.uk; this captures the research requirements, statistical analysis plan, and intended publication schedule. Requests will be reviewed by the Cancer Research UK Clinical Trials Unit (CRCTU) Directors in discussion with the Chief Investigator (CI), Trial Management Group (TMG) and independent Trial Safety Committee (TSC). They will consider the scientific validity of the request, qualifications of the researchers, CI, TMG & TSC views, consent arrangements, practicality of anonymizing the requested data & contractual obligations. If supportive of the request, and where not already obtained, Sponsor consent for data transfer will be sought before notifying applicants of the outcome. It is anticipated that applicants will be notified within 3 months of receipt of the original request.

Previous IPD sharing statement:
The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		29/01/2024	07/02/2024	Yes	No
Results article	Results and lessons learned	29/01/2024	03/09/2024	Yes	No
Protocol article	protocol	16/03/2020	17/02/2021	Yes	No
Basic results	version 1.0a	16/02/2023	16/02/2023	No	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Plain English results			18/03/2024	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes