

# WISTERIA: WEE1 inhibitor with cisplatin and radiotherapy

<b>Submission date</b> 20/02/2017	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
<b>Registration date</b> 21/02/2017	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 03/09/2024	<b>Condition category</b> Cancer	<input type="checkbox"/> Individual participant data

## 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>

## Study website

<https://www.birmingham.ac.uk/research/activity/mds/trials/crctu/trials/wisteria/index.aspx>

## Contact information

### Type(s)

Public

### Contact name

Mr Rhys Mant

### Contact details

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## Additional identifiers

### EudraCT/CTIS number

2015-003583-37

**IRAS number****ClinicalTrials.gov number**

NCT03028766

**Secondary identifying numbers**

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 chemoradiation (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

**Secondary study design**

Non randomised study

**Study setting(s)**

Hospital

**Study type(s)**

Treatment

**Participant information sheet**

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

**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 measure**

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

### **Secondary outcome measures**

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

### **Overall study start date**

01/09/2015

### **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),  $\geq 60$  ml/min at baseline calculated using local practice calculation. If this is  $\leq 60$  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)  $\geq 55\%$  by echocardiogram (ECHO) or Multiple Gated Acquisition Scan (MUGA, if ECHO is equivocal)
7. Normal liver and bone marrow function:
  - 7.1. Haemoglobin (Hb)  $\geq 10.0$  g/dL or  $\geq 100$  g/L
  - 7.2. Absolute neutrophil count (ANC)  $\geq 1.5 \times 10^9/L$
  - 7.3. Absolute platelet count  $\geq 100 \times 10^9/L$
  - 7.4. Aspartate transaminase (AST) or alanine aminotransferase (ALT)  $\leq 2.5$  upper limit of normal (ULN)
  - 7.5. Total bilirubin  $\leq 1.5$  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),  $\geq 60$  ml/min at baseline calculated using local practice calculation. If this is  $\leq 60$  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)  $\geq 55\%$  by echocardiogram (ECHO) or Multiple Gated Acquisition Scan (MUGA, if ECHO is equivocal)
7. Normal liver and bone marrow function:
  - 7.1. Haemoglobin (Hb)  $\geq 10.0$  g/dL or  $\geq 100$  g/L
  - 7.2. Absolute neutrophil count (ANC)  $\geq 1.5 \times 10^9/L$
  - 7.3. Absolute platelet count  $\geq 100 \times 10^9/L$
  - 7.4. Aspartate transaminase (AST) or alanine aminotransferase (ALT)  $\leq 2.5$  upper limit of normal (ULN)
  - 7.5. Total bilirubin  $\leq 1.5$  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

### **Age group**

Adult

### **Lower age limit**

18 Years

### **Upper age limit**

70 Years

**Sex**

Both

**Target number of participants**

Planned Sample Size: 42; UK Sample Size: 42

**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 ( $\geq$  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

England

Scotland

United Kingdom

## 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

**Sponsor details**  
Edgbaston  
Birmingham  
England  
United Kingdom  
B15 2TT  
+44 121 414 6788  
wisteria@trials.bham.ac.uk

**Sponsor type**  
University/education

**ROR**  
<https://ror.org/03angcq70>

## Funder(s)

**Funder type**  
Charity

**Funder Name**  
Cancer Research 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

Planned publication in a high-impact peer reviewed journal.

## Intention to publish date

01/04/2023

## 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](mailto: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?
<a href="#">Protocol article</a>	protocol	16/03/2020	17/02/2021	Yes	No
<a href="#">Basic results</a>	version 1.0a	16/02/2023	16/02/2023	No	No
<a href="#">HRA research summary</a>			28/06/2023	No	No
<a href="#">Results article</a>		29/01/2024	07/02/2024	Yes	No
<a href="#">Plain English results</a>			18/03/2024	No	Yes
<a href="#">Results article</a>	Results and lessons learned	29/01/2024	03/09/2024	Yes	No

