

Dose escalation study of Olaparib in addition to cisplatin based concurrent chemoradiotherapy for patients with high risk locally advanced squamous cell carcinoma of the head and neck (HNSCC)

Submission date 28/10/2011	Recruitment status Stopped	☒ Prospectively registered ☐ Protocol
Registration date 28/10/2011	Overall study status Stopped	☐ Statistical analysis plan ☐ Results
Last Edited 16/10/2012	Condition category Cancer	☐ Individual participant data ☐ Record updated in last year

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

Contact name
Miss Dymphna Lee

Contact details
Cancer Research UK & UCL Cancer Trials Centre
90 Tottenham Court Road
London
United Kingdom
W1T 4TJ
ORCA@ctc.ucl.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)
2010-023599-24

Protocol serial number
11024

Study information

Scientific Title

A phase I/II study of Olaparib in addition to cisplatin based concurrent chemoradiotherapy for patients with high risk locally advanced squamous cell carcinoma of the head and neck (HNSCC)

Acronym

ORCA

Study objectives

Head and neck squamous cell carcinoma (HNSCC) is the 6th most common cancer in the world, accounting for >7500 of recorded cases in the UK (2006 data). Currently the standard treatment for high risk locally advanced HNSCC is cisplatin chemotherapy alongside high dose radiotherapy, however local recurrence rates are high at approximately 80%. This means there is a real need to look at improving local disease control in this group of patients.

The purpose of this Phase I trial is to assess how olaparib, a Poly (ADP-ribose) polymerase (PARP) inhibitor is tolerated when added to standard chemoradiotherapy (CRT) treatment. This is a dose escalation trial which aims to find out the recommended dose and the best dosing schedule for olaparib in combination with cisplatin based CRT. Patients will be recruited from sites in the UK and the total number recruited will depend on the outcome of the dose escalation (expected to be around 40).

This study is funded by Cancer Research UK and Astra Zeneca.

A placebo controlled, randomised Phase II trial will follow once the recommended dose of olaparib has been established.

Ethics approval required

Old ethics approval format

Ethics approval(s)

London City and East REC, ref:11/LO/1618 approval pending

Primary study design

Interventional

Study design

Non-randomised; Interventional; Design type: Treatment

Study type(s)

Treatment

Health condition(s) or problem(s) studied

Topic: National Cancer Research Network; Subtopic: Head and Neck Cancer; Disease: Head and Neck

Interventions

The patient numbers in this dose escalation phase I are estimated and will depend on the frequency and severity of adverse events. A modified continual reassessment method (mCRM)

design will be used to maximise the information gathered across different cohorts. We aim to minimise patient delay by enrolling patients in parallel into all cohorts within the same dose band.

This is a single arm study.

The trial treatment will involve 2 cycles of induction chemotherapy which will consist of cisplatin and 5-FU (fluorouracil) chemotherapy. This will be followed by olaparib plus cisplatin based chemoradiotherapy for a further 7 weeks.

Induction chemotherapy (6 weeks)

Cisplatin 80mg/m² i.v. on day 1 and 5-FU 1000mg/m²/day i.v. on day 1-4 (continuous infusion) of a 21 day cycle

Chemoradiotherapy (8 weeks)

Cisplatin will be given at a dose of 35mg/m² i.v. on day 1 of each week and radiotherapy of 70Gy in 2Gy fractions on day 1-5. Olaparib will be started one week prior to chemoradiotherapy and continued until the end of chemoradiotherapy.

This trial involves a dose escalation of olaparib. The first cohort dose will be 25mg bd (twice daily) for 3 consecutive days, and the maximum dose cohort will be 125mg bd for 5 consecutive days. Patients will be allocated the next available cohort upon entering the study.

Total duration of treatment for this study is 14 weeks, and the follow up is for 2 years post end of treatment.

As of 29/05/2012, the the above study was closed early due to issues surrounding the development and formulation of olaparib. No patients were recruited.

Intervention Type

Drug

Phase

Phase I/II

Drug/device/biological/vaccine name(s)

Olaparib

Primary outcome(s)

To assess the frequency of Dose Limiting Toxicities (DLTs) and adverse events.

Key secondary outcome(s)

1. Other efficacy endpoints: complete response rate (cRR)
2. Time to loco-regional and any progression

Completion date

01/12/2015

Reason abandoned (if study stopped)

Lack of staff/facilities/resources

Eligibility

Key inclusion criteria

1. Histologically confirmed high risk locally advanced HNSCC (TNM staging T(any) N2 or N3 M0, bulky T3 or T4 N(any) M0) who would normally be offered cisplatin-based radical chemoradiotherapy
2. Estimated life expectancy of at least 12 weeks
3. WHO performance status of 0 or 1
4. Aged more than or equal to 18 years
5. Adequate organ function:
 - 5.1. Absolute neutrophils $=1.5 \times 10^9/L$
 - 5.2. Platelets $=100 \times 10^9/L$
 - 5.3. Haemoglobin $=10g/dl$ (to be maintained above $12g/dl$ whilst on CRT treatment)
 - 5.4. Creatinine $=1.5 \times ULN$
 - 5.5. Glomerular filtration rate (GFR) $=60 \text{ ml/min}$
 - 5.6. Serum bilirubin $=1.25 \times ULN$
 - 5.7. Aspartate aminotransferase (AST) or alanine aminotransferase (ALT) $=2.5 \times ULN$
6. Patients willing to use contraception for the duration of the trial and for six months post treatment
7. Able to give informed consent
8. Patient is willing and able to comply with the protocol for the duration of the study, including the treatment plan investigations required and follow up visits; Target Gender: Male & Female ; Lower Age Limit 18 years

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

18 Years

Sex

All

Key exclusion criteria

1. Head & neck cancers of the following types: Nasopharyngeal and paranasal sinus tumours, oral cavity tumours (tumours of the oral cavity)
2. Human Papilloma Virus positive oropharyngeal tumours (tonsillar and tongue base tumours)
3. Confirmed distant metastatic disease
4. Previous chemotherapy or radiotherapy for the treatment of HNSCC tumour
5. Previous therapy with a PARP inhibitor
6. Previous chemotherapy, immunotherapy or radiotherapy within the last 28 days prior to registration
7. Prior history of malignancy, except for basal cell or squamous cell carcinoma of the skin, carcinoma in situ of the cervix, breast or prostate, and unless the patient has been free of

malignancy for a period of 3 years prior to first dose of trial drug

8. Women who are pregnant or lactating

9. Pre-existing gastrointestinal disorders that may interfere with the delivery or absorption of trial drugs

10. Peripheral neuropathy > Grade 2 (lower grade neuropathy considered significant by treating clinician may be considered an exclusion criterion)

11. Significant hearing difficulties (patients with mildly impaired hearing must be made aware of potential ototoxicity)

12. Any serious and/or unstable pre-existing medical, psychiatric or other condition that, in the treating clinician's judgement, could interfere with patient safety or obtaining informed consent

13. Known hepatitis B or C infection

14. Immunocompromised patients [e.g. Known human immunodeficiency virus (HIV) positive status]

15. Active uncontrolled infection

16. The current use of drugs which are known to inhibit Cytochrome P450 3A4 (CYP3A4) which cannot be discontinued for the duration of trial treatment

Date of first enrolment

01/12/2011

Date of final enrolment

01/12/2015

Locations

Countries of recruitment

United Kingdom

England

Study participating centre

Cancer Research UK & UCL Cancer Trials Centre

London

United Kingdom

W1T 4TJ

Sponsor information

Organisation

University College London (UK)

ROR

<https://ror.org/02jx3x895>

Funder(s)

Funder type

Industry

Funder Name

AstraZeneca (UK)

Alternative Name(s)

AstraZeneca PLC, Pearl Therapeutics, AZ

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, 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

IPD sharing plan summary

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
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[HRA research summary](#)

[Study website](#)

Study website

11/11/2025

28/06/2023

11/11/2025

No

No

No

Yes