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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	[X] 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

Study website
http://www.ctc.ucl.ac.uk/TrialDetails.aspx?TrialID=59

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2010-023599-24

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
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

Study design
Non-randomised; Interventional; Design type: Treatment

Primary study design
Interventional

Secondary study design
Non randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please contact ORCA@ctc.ucl.ac.uk to request a patient information sheet

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

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

Overall study start date
01/12/2011

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 x 10*9/L
5.2. Platelets =100 x 10*9/L
5.3. Haemoglobin =10g/dl (to be maintained above 12g/dl whilst on CRT treatment)
5.4. Creatinine =1.5 x ULN
5.5. Glomerular filtration rate (GFR) =60 ml/min
5.6. Serum bilirubin = 1.25 x ULN
5.7. Aspartate aminotransferase (AST) or alanine aminotransferase (ALT) = 2.5 x 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

Age group
Adult

Lower age limit

18 Years

Sex
Both

Target number of participants
Planned Sample Size: 60; UK Sample Size: 60;

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 clinicians judgement, could interfere with patient safety or obtaining informed consent
13. Known hepatitis B or C infection
14. Immunocompromised patients [e.g. Known human imunodeficiency 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
England

United Kingdom

Study participating centre
Cancer Research UK & UCL Cancer Trials Centre
London
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Sponsor information

Organisation
University College London (UK)

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Sponsor type
University/education

ROR
https://ror.org/02jx3x895

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
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No