ISRCTN73814534 https://doi.org/10.1186/ISRCTN73814534

A phase I and randomised phase II study of docetaxel and RAD001 (Everolimus) in advanced / recurrent or metastatic squamous cell carcinoma of the head and neck

Submission date 06/06/2007	**Recruitment status** Stopped	[X] Prospectively registered [ ] Protocol [ ] Statistical analysis plan [ ] Results [ ] Individual participant data [ ] Record updated in last year
Registration date 20/07/2007	**Overall study status** Stopped	
Last Edited 29/11/2011	**Condition category** Cancer	

Plain English summary of protocol
http://www.cancerhelp.org.uk/trials/a-trial-looking-at-docetaxel-and-rad001-for-head-and-neck-cancer-that-has-spread-or-has-come-back-after-treatment

Contact information

Type(s)
Scientific

Contact name
Prof Chris Boshoff

Contact details
Wolfson Institute for Biomedical Research
The Cruiciform Building
Gower Street
London
United Kingdom
WC1E 6BT
dora@ctc.ucl.ac.uk

Additional identifiers

ClinicalTrials.gov (NCT)
NCT01313390

Protocol serial number
BRD/06/053

Study information

Scientific Title

Acronym
DORA

Study objectives
To determine the maximum tolerated dose of RAD001 (with docetaxel) in the phase I study and to use this dose in a randomised trial in the phase II setting.

As of 17/02/2011 the anticipated end date for this trial has been updated from 01/08/2009 to 01/06/2012.

Ethics approval required
Old ethics approval format

Ethics approval(s)
South West Research Ethics Committee on 12/03/2008 (ref: 07/H0206/68).

Study design
Phase I: Dose escalation study
Phase II: Randomised study of docetaxel (75 mg/m^2) vs docetaxel (75 mg/m^2) + RAD001 (at dose determined in phase I)

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Advanced / recurrent or metastsatic squamous cell carcinoma of the head and neck.

Interventions
Phase I: RAD001 and docetaxel (75 mg/m^2, intravenous). The starting dose of RAD001 is 10 mg orally and the dose will escalate by 10 mg to a maximum of 50 mg. At least 3 patients will be entered per cohort and if there is no adverse toxicity a further 3 patients are entered at the next dose level.

Phase II: Randomised study of docetaxel (75 mg/m^2) vs docetaxel (75 mg/m^2) + RAD001 (at dose determined in Phase I)

In both phases, docetaxel will be administered for a maximum of 6 cycles (18 weeks). RAD001 will then continue after chemotherapy has finished (duration depends on each patients condition)

Intervention Type
Drug

Phase
Phase I/II

Drug/device/biological/vaccine name(s)
Everolimus, docetaxel

Primary outcome(s)
Phase I:
1. To determine the safety and tolerability of the combination of RAD001 and docetaxel
2. To determine the maximum tolerated dose of RAD001 when combined with docetaxel

Phase II:
To examine the response rates in patients receiving the combination of docetaxel and RAD001 and those receiving docetaxel alone. Scans will be repeated after 2, 4 and 6 cycles. Tumour shrinkage on any scan will count as a response.

Key secondary outcome(s))
Phase I:
1. To investigate possible pharmacokinetic interactions between docetaxel and RAD001
2. To investigate the effect of RAD001 on downstream targets of mTOR in tumour

Phase II:
1. To examine the time to progression after docetaxel and RAD001
2. To perform a pilot study to attempt to identify predictors of response including evaluation of EGFR family member expression, mutations or amplifications. Also downstream targets of the EGFR pathway including phosphorylation of S6 and phosphorylation of AKT.

Completion date
01/06/2012

Reason abandoned (if study stopped)
Participant recruitment issue

Eligibility

Key inclusion criteria
1. Locally advanced or metastatic squamous cell carcinoma of the head and neck (histologically proven)
2. Estimated life expectancy of at least 12 weeks
3. Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1
4. Measurable disease by Response Evaluation Criteria in Solid Tumours (RECIST) criteria (NB: For the purposes of this study recurrent disease within a previous radiation field can be considered to be measurable)
5. Aged 18 years or over
6. Patient willing and able to give written informed consent
7. Haematological parameters within a week prior to study entry: -
7.1. Blood cell counts:
a. Absolute neutrophils greater than or equal to 1.5 x 10^9/L
b. Platelets greater than or equal to 100 x 10^9/L
c. Haemoglobin greater than or equal to 10 g/dl

7.2. Renal function:
a. Urea and creatinine within normal limits
7.3. Hepatic functions:
a. Serum bilirubin within normal limits
b. AST or ALT <1.5 x ULN with alkaline phosphatase <2.5 x ULN
8. Patients may have received one line of prior chemotherapy for locally advanced or metastatic disease (but not a taxane)
9. Patients may have received prior radiation therapy for locally advanced or metastatic disease (but must have completed the radiotherapy more than six months before recruitment)
10. Female patients potentially able to child bear should have a negative pregnancy test prior to commencing the study drugs, and agree to use an approved contraceptive method (Intrauterine Device [IUD], birth control pills or barrier device) during and for 3 months after the last dose of the study drugs. All male patients should take adequate contraceptive precautions during and up to 2 months after the last dose of the study drugs

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Potentially curable disease
2. Disease relapsed within 6 months of radiotherapy
3. Patients with locally advanced disease for whom radiotherapy is indicated
4. Previous chemotherapy for any cancer, except for head and neck cancer
5. Previous chemotherapy with a taxane
6. Previous therapy with any erbB inhibitors (except Cetuximab given with radiotherapy, as indicated in treatment algorithm)
7. Treatment within the last 4 weeks with any investigational drug
8. The current use of drugs which are known to inhibit CYP3A4 (except dexamethasone), or block P-glycoprotein, including grapefruit juice
9. Evidence of the presence of central nervous system metastases
10. Evidence of uncontrolled infection
11. Mental condition rendering the subject unable to understand the nature, scope and possible consequences of the study
12. History of hypersensitivity to docetaxel or any of its excipients
13. Pregnant or breast-feeding

Date of first enrolment
01/08/2007

Date of final enrolment
01/06/2012

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Wolfson Institute for Biomedical Research
London
United Kingdom
WC1E 6BT

Sponsor information

Organisation
University College London (UCL) (UK)

ROR
https://ror.org/02jx3x895

Funder(s)

Funder type
Industry

Funder Name
Novartis (International)

Alternative Name(s)
Novartis AG, Novartis International AG

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location

Switzerland

Funder Name
Sanofi-Aventis (International)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration