

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	☒ Prospectively registered ☐ Protocol
Registration date 20/07/2007	Overall study status Stopped	☐ Statistical analysis plan ☐ Results
Last Edited 29/11/2011	Condition category Cancer	☐ Individual participant data ☐ Record updated in last year

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

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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).

Primary study design

Interventional

Study design

Phase I: Dose escalation study

Phase II: Randomised study of docetaxel (75 mg/m²) vs docetaxel (75 mg/m²) + RAD001 (at dose determined in phase I)

Study type(s)

Treatment

Health condition(s) or problem(s) studied

Advanced / recurrent or metastatic squamous cell carcinoma of the head and neck.

Interventions

Phase I: RAD001 and docetaxel (75 mg/m², 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/m²) vs docetaxel (75 mg/m²) + 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 $1.5 \times 10^9/L$
 - b. Platelets greater than or equal to $100 \times 10^9/L$
 - 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 $<1.5 \times \text{ULN}$ with alkaline phosphatase $<2.5 \times \text{ULN}$

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