

# Dynamic contrast enhanced magnetic resonance imaging (DCE-MRI) assessment of the vascular changes induced with bevacizumab alone and in combination with interferon-alpha in patients with advanced renal cell carcinoma

<b>Submission date</b> 11/03/2009	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 23/04/2009	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 13/10/2017	<b>Condition category</b> Cancer	<input type="checkbox"/> Individual participant data <input type="checkbox"/> Record updated in last year

**Plain English summary of protocol**  
Not provided at time of registration

## Contact information

**Type(s)**  
Scientific

**Contact name**  
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## Additional identifiers

**EudraCT/CTIS number**

**IRAS number**

**ClinicalTrials.gov number**

**Secondary identifying numbers**

RD2007-114

## **Study information**

### **Scientific Title**

Dynamic contrast enhanced magnetic resonance imaging (DCE-MRI) assessment of the vascular changes induced with bevacizumab alone and in combination with interferon-alpha in patients with advanced renal cell carcinoma: a phase II, open labelled, randomised, multicentre trial

### **Study objectives**

The trial aims to answer:

1. Whether bevacizumab induced changes in DCE-MRI vascular parameters are significantly enhanced by interferon-alpha
2. To establish whether there is an interferon (IFN) dose response in potentiating bevacizumab induced changes in dynamic contrast enhanced magnetic resonance imaging (DCE-MRI) vascular parameters
3. If the DCE-MRI vascular parameter changes correlate to the tumour response, progression free survival and changes of other biomarkers

### **Ethics approval required**

Old ethics approval format

### **Ethics approval(s)**

National Research Ethics Service, Charing Cross Research Ethics Committee, 19/01/2009, ref: 09/H0711/6

### **Study design**

Phase II open labelled randomised multicentre trial

### **Primary study design**

Interventional

### **Secondary study design**

Randomised controlled trial

### **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**

Advanced or metastatic renal cell carcinoma

**Interventions**

Patients will be randomised to one of the following:

Arm A: Bevacizumab 10 mg/kg every 2 weeks

Arm B: Bevacizumab 10 mg/kg every 2 weeks + interferon alpha 2a (IFN-a2a) 3MU three times per week (t.i.w.)

Arm C: Bevacizumab 10 mg/kg every 2 weeks + IFN-a2a 9 MU t.i.w.

All patients will continue on their randomised treatment regimen until the first tumour assessment at week 8. At this point the decision to introduce or modify the IFN dosage will be at the discretion of the investigator. Treatment with both study drugs will continue until disease progression, unacceptable toxicity, or consent is withdrawn. Patients in all arms will undergo two baseline DCE-MRI scans in the week pre-treatment and then further scans at weeks 2, and 6 weeks post-commencement of bevacizumab. Tumour response will be assessed by RECIST criteria via computed tomography (CT) scans at baseline, 8 weeks and three-monthly thereafter.

**Intervention Type**

Drug

**Phase**

Phase II

**Drug/device/biological/vaccine name(s)**

Bevacizumab, interferon alpha 2a

**Primary outcome measure**

DCE-MRI defined changes in Ktrans after 6 weeks of bevacizumab monotherapy or bevacizumab and low or standard dose IFN-alpha.

**Secondary outcome measures**

1. Vascular endpoints: intra-arm change in vascular permeability (Ktrans) and tumour hypoxia at 2 and 6 weeks post-commencement of treatment
2. Efficacy endpoints: best overall response, progression free survival, time to progression, measured during follow up analyses
3. Safety endpoints: treatment duration of bevacizumab and IFN, treatment withdrawal, dose modification, incidence of adverse events, measured during follow up analyses
4. Surrogate biomarker analysis: peripheral blood analysis of circulating endothelial cells (CEC), circulating endothelial progenitors (CEP) and proangiogenic monocytic cells; angiogenic factors (e.g. vascular endothelial growth factor [VEGF]) and hypoxia regulated markers, measured during follow up analyses
5. Correlation of DCE-MRI defined changes in Ktrans with clinical response, measured during follow up analyses
6. Correlation of DCE-MRI defined changes in Ktrans with surrogate biomarkers, measured during follow up analyses
7. Analysis of Diffusion MRI and BOLD MRI changes and comparison with other pharmacodynamic markers, measured during follow up analyses

**Overall study start date**

06/04/2009

**Completion date**

28/02/2010

## Eligibility

**Key inclusion criteria**

1. Male or female subjects greater than or equal to 18 years
2. Patients with previously untreated metastatic (stage IV) or locally advanced (inoperable stage III) renal cell carcinoma (RCC)
3. Subject with histologically and/or cytologically confirmed advanced RCC, of which a majority component of conventional clear-cell type is mandatory. Tumours of mixed histology should be categorised by the predominant cell type.
4. Good or intermediate prognosis disease as defined by Motzer score
5. Response Evaluation Criteria In Solid Tumors (RECIST) measurable lesion(s), which must be amenable to DCE-MRI scanning
6. Life expectancy of at least 12 weeks
7. Eastern Co-operative Oncology Group (ECOG) performance status 0 - 2
8. Adequate haematological function:
  - 8.1. Absolute neutrophil count (ANC) greater than or equal to  $1.5 \times 10^9/l$ , and
  - 8.2. Platelet count greater than or equal to  $100 \times 10^9/l$ , and
  - 8.3. Haemoglobin greater than or equal to 8 g/dl (may be transfused to maintain or exceed this level)
9. Adequate liver function:
  - 9.1. Total bilirubin less than 1.5 x upper limit of normal (ULN), and
  - 9.2. Aspartate aminotransferase (AST), alanine aminotransferase (ALT) less than 2.5 x ULN in patients without liver metastases; less than 5 x ULN in patients with liver metastases
10. Adequate renal function:
  - 10.1. Serum creatinine less than or equal to 1.5 x ULN, and
  - 10.2. Urine dipstick for proteinuria less than 2+. Patients discovered to have greater than or equal to 2+ proteinuria on dipstick urinalysis at baseline should undergo a 24-hour urine collection and must demonstrate less than 1 g of protein in 24 hours
11. International normalised ratio (INR) less than or equal to 1.5 within 7 days prior to enrolment. Anticoagulation is allowed if target INR is less than 3 and INR is therapeutic on a stable dose of coumarin-type anticoagulation, or if subject is on a stable dose of low molecular weight (LMW) heparin for greater than 2 weeks at time of enrolment
12. Women of childbearing age must have a negative pregnancy test and must use adequate contraception during the treatment phase of the study and for 9 months afterwards. Women who wish to breastfeed are not eligible for the study

**Participant type(s)**

Patient

**Age group**

Adult

**Lower age limit**

18 Years

**Sex**

Both

**Target number of participants**

30 patients, 10 in each arm

**Key exclusion criteria**

1. Diagnosis of brain metastasis
2. Major surgery (including open biopsy) or radiation therapy within 28 days prior to enrolment (palliative radiotherapy to painful bone lesions is allowed within 14 days prior to enrolment). Subjects must have recovered from prior surgery (greater than 28 days) and radiation (greater than 28 days - 14 days if palliative radiotherapy to painful bone lesions)
3. Core biopsy or other minor surgical procedure, excluding placement of a vascular access device, within 7 days prior to enrolment
4. Significant cardiovascular disease defined as congestive heart failure (New York Heart Association [NYHA] class II, III or IV), unstable angina pectoris, or myocardial infarction within 6 months prior to enrolment
5. Inadequately controlled hypertension (defined as a blood pressure of greater than 150 mmHg systolic and/or greater than 100 mmHg diastolic on medication), or any prior history of hypertensive crisis or hypertensive encephalopathy
6. History of stroke or transient ischaemic attack within 6 months prior to enrolment
7. Significant vascular disease (e.g., aortic aneurysm, aortic dissection), or symptomatic peripheral vascular disease
8. Evidence or history of recurrent thromboembolism (more than one episode of deep vein thrombosis [DVT]/pulmonary embolism [PE]) during the past 6 months, bleeding diathesis or coagulopathy
9. Chronic daily intake of aspirin greater than 325 mg/day or clopidogrel greater than 75 mg/day, or steroids (prednisone greater than 12.5 mg/day or dexamethasone greater than 2 mg/day), excluding inhaled steroids
10. History of abdominal or tracheo-oesophageal fistula, gastrointestinal perforation, or intra-abdominal abscess within 6 months prior to study enrolment
11. Serious, non-healing wound, ulcer, or bone fracture
12. Pregnant or breast-feeding mothers
13. No contraindication to MRI scanning e.g. no history of claustrophobia, metal fragment implantation
14. Current active second malignancy other than non-melanoma skin cancers and post-treatment for localised prostate cancer. Patients are not considered to have a currently active malignancy if they are in complete remission for greater than 3 years prior to study
15. Patients with a history of allergic reactions to contrast agents
16. Patients with gross ascites
17. Seizure disorder requiring medication
18. Human immunodeficiency virus (HIV)/hepatitis B/hepatitis C/other infection greater than common toxicity criteria grade 2 (CTC 2); active clinically serious bacterial or fungal infections (greater than CTC 2)
19. Other investigational drug during trial or within 30 days
20. Any other significant medical illness or medically significant abnormal laboratory finding that would, in the investigator's judgment, make the patient inappropriate for this study, or would increase the risk associated with the patients' participation in the study

**Date of first enrolment**

06/04/2009

**Date of final enrolment**

28/02/2010

# Locations

## Countries of recruitment

England

United Kingdom

## Study participating centre

**Mount Vernon Cancer Centre**

Middlesex

United Kingdom

HA6 2RN

# Sponsor information

## Organisation

East and North Hertfordshire NHS Trust (UK)

## Sponsor details

Research and Development Department

The Clock Tower

Mount Vernon Cancer Centre

Northwood

Middlesex

England

United Kingdom

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## Sponsor type

Hospital/treatment centre

## Website

<http://www.enherts-pct.nhs.uk/>

## ROR

<https://ror.org/02ryc4y44>

# Funder(s)

## Funder type

Industry

**Funder Name**

Roche - educational grant and free IMP supply

**Alternative Name(s)**

F. Hoffmann-La Roche Ltd, F. Hoffmann-La Roche & Co, F. Hoffmann-La Roche AG, Roche Holding AG, Roche Holding Ltd, Roche Holding, Roche Holding A.G., Roche Holding, Limited, F. Hoffmann-La Roche & Co.

**Funding Body Type**

Government organisation

**Funding Body Subtype**

For-profit companies (industry)

**Location**

Switzerland

## 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?
<a href="#">HRA research summary</a>			28/06/2023	No	No