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Identifying biomarkers to predict clinical benefit in patients with colorectal cancer treated with bevacizumab

Submission date 19/01/2010	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 31/08/2010	**Overall study status** Completed	
Last Edited 04/07/2019	**Condition category** Cancer	

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-study-looking-at-new-types-of-mri-scans-see-how-chemotherapy-affects-bowel-cancer-cells

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
08_CLPHA_55

Study information

Scientific Title
An assessment of imaging and circulating biomarkers in patients with metastatic colorectal carcinoma treated with the anti-vascular endothelial growth factor (anti-VEGF) antibody, bevacizumab

Acronym
TRAVASTIN-1

Study objectives
The purpose of the study is to identify biomarkers that can predict clinical benefit in patients treated with bevacizumab and chemotherapy for metastatic colorectal cancer. Our hypotheses are:
1. That a circulating biomarker at baseline or the percentage change in a parameter after single agent treatment will predict benefit in terms of progression-free survival (PFS)
2. That a circulating biomarker will correlate with stable disease or progression on maintenance therapy
3. That bevacizumab improves response rate and PFS in patients with recurrent colorectal cancer who have already been treated with induction and maintenance bevacizumab

Ethics approval required
Old ethics approval format

Ethics approval(s)
Central Manchester Ethics Committee, 15/06/2009, ref: 09/H1008/99

Study design
Single-centre phase II therapeutic exploratory study

Primary study design
Interventional

Secondary study design
Non randomised study

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
Metastatic colorectal cancer

Interventions

All patients will be treated initially with first line chemotherapy and bevacizumab. They will undergo imaging (dynamic contrast-enhanced magnetic resonance imaging [DCE MRI] and fluorothymidine positron emission tomography [FLT PET]), circulating (circulating endothelial cells, circulating angiomodulatory biomarkers, deoxyribonucleic acid [DNA] analysis) and tissue biomarker investigations.

The treatment will continue until disease progression at which point they will be randomised to receive second line chemotherapy with or without bevacizumab. The treatment will continue until further disease progression.

Intervention Type
Drug

Phase
Phase II

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

Primary outcome measure
To identify a biomarker or suite of biomarkers that predict clinical benefit in terms of PFS, in patients treated with bevacizumab for metastatic colorectal cancer.

Secondary outcome measures
1. To define biomarker(s) that detect progressive disease in patients treated with bevacizumab-containing regimens for metastatic colorectal cancer
2. To obtain preliminary data on the utility of biomarkers in patients who have been treated with cytotoxic chemotherapy and bevacizumab, followed by maintenance therapy who are then treated, at progression, with chemotherapy with or without bevacizumab

Overall study start date
01/11/2009

Completion date
01/09/2016

Eligibility

Key inclusion criteria
1. Aged greater than or equal to 18 years old, either sex
2. Signed informed consent and ability to comply with study protocol
3. Histologically confirmed colorectal cancer.
4. Previously untreated metastatic disease
5. Eastern Cooperative Oncology Group (ECOG) performance status 0 - 2
6. Life expectancy greater than 12 weeks
7. Adequate bone marrow function: absolute neutrophil count (ANC) more than 1.5 x 10^9/L; platelets more than or equal to 100 x 10^9/L; haemoglobin (Hb) more than or equal to 9 g/dL (can be post-transfusion)
8. International normalised ratio (INR) less than or equal to 1.5 and activited partial thromboplastin time (aPTT) less than or equal to 1.5 x upper limit of normal (ULN) within 7 days

prior to starting study treatment
9. Adequate liver function: serum bilirubin less than or equal to 1.5 x ULN except in case of known Gilbert syndrome; transaminases less than or equal to 2.5 x ULN in the absence of liver metastases or less than or equal to 5 x ULN in the presence of liver metastases
10. Adequate renal function: estimated glomerular filtration rate greater than or equal to 50 ml /min by the Wright Formula
11. Urine dipstick for proteinuria less than or equal to 2+. If urine dipstick is more than or equal to 2+, a 24-hour urine must demonstrate less than 1 g of protein in 24 hours
12. At least one metastatic deposit in the abdomen (including inguinal lymphadenopathy) liver, retroperitoneum, pelvis or thorax greater than or equal to 3 cm diameter
13. No contraindications to magnetic resonance imaging (MRI) scanning or allergy to gadolininum-containing contrast media

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
70 (out of this, 25 will be entered into the FLT PET protocol)

Key exclusion criteria
1. Surgery (including open biopsy) within 4 weeks prior to anticipated first dose of bevacizumab
2. Significant traumatic injury or radiotherapy during 4 weeks preceding potential first dose of bevacizumab
3. Adjuvant therapy within the previous 12 months
4. Patients with previous adjuvant exposure to oxaliplatin can only take part if it is more than 12 months since their last exposure to oxaliplatin and they have grade I or less, residual peripheral neuropathy
5. No previous exposure to VEGF inhibitors in the adjuvant setting
6. History or evidence upon physical examination of brain metastases. Evidence of spinal cord compression. Computed tomography (CT)/MRI of the brain is mandatory (within 4 weeks prior to randomisation) in case of clinical evidence of brain metastases.
7. Pregnant or breast-feeding women. Positive pregnancy test (serum or urine beta-human chorionic gonadotropin [ß-HCG]) for women of reproductive potential
8. Fertile woman of childbearing potential not using adequate contraception (oral contraceptives, intrauterine device or barrier method of contraception in conjunction with spermicidal jelly or surgically sterile)
9. Other malignancies within 5 years prior to randomisation, except for adequately treated carcinoma in situ of the cervix and/or basal cell skin cancer
10. Treatment with any other investigational agent, or participation in another clinical trial within 30 days prior to entering this trial
11. Known hypersensitivity to bevacizumab, 5-fluorouracil, capecitabine, oxaliplatin or irinotecan
12. Known dihydro-pyrimidine dehydrogenase deficiency

13. Non-healing wound, ulcer or bone fracture
14. Patients cannot enter the trial if they have developed a deep venous thrombosis (DVT) or commenced therapeutic anticoagulation for any other reason, e.g., atrial fibrillation (AF) within the 4 weeks preceding the trial. Patients with a known DVT or AF on stable therapeutic doses of low molecular weight heparin for greater than 4 weeks duration, can enter the trial.
15. Patients with haemorrhagic disorders
16. Poorly controlled hypertension (sustained blood pressure [BP] greater than 150/100 mmHg despite antihypertensive therapy
17. Previous cerebrovascular accident (CVA), transient ischaemic attack (TIA) or subarachnoid haemorrhage (SAH) within six months before trial entry
18. Clinically significant cardiovascular disease, for example:
18.1. Myocardial infarction or unstable angina within 6 months of trial entry
18.2. New York Heart Association (NYHA) grade 2 or worse congestive heart failure (CHF)
18.3. Poorly controlled cardiac arrhythmia despite medication
19. Current or recent (within 10 days prior to first dose of trial treatment) use of aspirin greater than or equal to 325 mg/day
20. Pre-existing sensory or motor neuropathy greater than or equal to grade 2, uncontrolled spinal cord compression, or
21. Carcinomatous meningitis or new evidence of brain or leptomeningeal disease
22. Predisposing colonic or small bowel disorders in which the symptoms are uncontrolled as indicated by baseline of greater than 3 loose stools daily
23. Prior history of chronic enteropathy, inflammatory enteropathy, chronic diarrhoea, unresolved bowel obstruction/sub-obstruction, extensive small intestine resection with chronic diarrhoea
24. History of anaphylaxis or known intolerance to atropine sulphate or loperamide or appropriate antiemetics to be administered in conjunction with chemotherapy
25. Patients with a colonic stent
26. Evidence of any other disease, metabolic dysfunction, physical examination finding or laboratory finding giving reasonable suspicion of a disease or condition that contra-indicates the use of an investigational drug or puts the patient at high risk for treatment-related complications

Date of first enrolment
01/11/2009

Date of final enrolment
01/09/2015

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
The Christie NHS Foundation Trust
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M20 4BX

Sponsor information

Organisation
The Christie NHS Foundation Trust (UK)

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Wilmslow Road
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Sponsor type
Hospital/treatment centre

Website
http://www.christie.nhs.uk/

ROR
https://ror.org/03v9efr22

Funder(s)

Funder type
Industry

Funder Name
Roche

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
The manuscript will be submitted to a journal for publication by December 2016.

Intention to publish date
31/12/2016

Individual participant data (IPD) sharing plan
Patient data will be anonymised and will be provided as subject number and as data in the manuscript.

IPD sharing plan summary
Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	07/11/2018	31/01/2019	Yes	No
Plain English results			04/07/2019	No	Yes
HRA research summary			28/06/2023	No	No