

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
Registration date 31/08/2010	Overall study status Completed	☐ Statistical analysis plan ☒ Results
Last Edited 04/07/2019	Condition category Cancer	☐ Individual participant data

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

Contact name

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Additional identifiers

Protocol serial number

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

Primary study design

Interventional

Study design

Single-centre phase II therapeutic exploratory study

Study type(s)

Treatment

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(s)

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.

Key secondary outcome(s)

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

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 $1.5 \times 10^9/L$; platelets more than or equal to $100 \times 10^9/L$; 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 activated 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 gadolinium-containing contrast media

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

18 Years

Sex

All

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 [β -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

United Kingdom

England

Study participating centre

The Christie NHS Foundation Trust

Manchester

United Kingdom

M20 4BX

Sponsor information

Organisation

The Christie NHS Foundation Trust (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., Roche Holdings, Inc.

Funding Body Type

Government organisation

Funding Body Subtype

For-profit companies (industry)

Location

Switzerland

Results and Publications

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
HRA research summary			28/06/2023	No	No
Plain English results			04/07/2019	No	Yes