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Multicentre international study of capecitabine ± bevacizumab as adjuvant treatment of colorectal cancer

Submission date 01/12/2003	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 10/12/2003	**Overall study status** Completed	
Last Edited 02/09/2022	**Condition category** Cancer	

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-capecitabine-with-or-without-bevacizumab-for-colorectal-cancer

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number

N/A

Study information

Scientific Title
Multicentre international study of capecitabine ± bevacizumab as adjuvant treatment of colorectal cancer

Acronym
QUASAR 2

Study objectives
Study hypothesis added as of 18/07/2007:
Treatment with a combination of capecitabine plus bevacizumab results in better disease-free survival (DFS) than treatment with capecitabine alone.

Please note that the trial title provided at time of registration was "QUASAR 2 Multicentre international study of capecitabine +/- bevacizumab as adjuvant treatment of colon cancer". The current trial title was added as of 02/07/2007.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Metropolitan Multi-centre Research Ethics Committee, 03/09/2004, ref: 04/MRE11/18

Study design
Randomised controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Colorectal cancer

Interventions
Randomised to:
Arm A (standard arm)
Capecitabine 1250 mg/m^2, twice daily 12 hours apart (total daily dose 2500 mg/m^2) for 14 days (max 2500 mg twice a day [bd] [total daily dose 5000 mg]).
Treatment is repeated every 3 weeks for a total of eight cycles (24 weeks). One cycle = 3 weeks.

Arm B (experimental arm)
Capecitabine 1250 mg/m^2 twice daily, 12 hours apart (total daily dose 2500 mg/m^2) for 14 days (max 2500 mg twice daily [max total daily dose 5000 mg]).Treatment is repeated every 3 weeks for a total of eight cycles (24 weeks). One cycle = 3 weeks.
Bevacizumab 7.5 mg/kg will be administered initially over a 90 (±15) minute period on day 1. The

infusion will be repeated every 3 weeks for a total of 16 cycles (48 weeks). One cycle = three weeks.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Capecitabine, bevacizumab

Primary outcome(s)
Primary outcome measure added as of 28/06/2007:
Disease-free survival at 3 years.

Key secondary outcome(s))
Secondary outcome measures added as of 28/06/2007:
1. Disease-free survival for stage III patients at 3 years
2. Overall survival at 5 years
3. Side effect profiles
4. Translational science

Completion date
31/12/2011

Eligibility

Key inclusion criteria
Inclusion criteria amended as of 02/07/2007:
1. Histologically proven stage III (stage T2, T3 or T4) and stage II (any one or more of the following - stage T4, lymphatic invasion, vascular invasion, peritoneal involvement, poor differentiation) colorectal cancer (expected ratio 70% : 30%). N.B Patients can be Stage II, T3 as long as they have one of the other poor prognostic features. For the purposes of stratification, rectal cancers will be anything below the peritoneal reflection.
2. Patients must have undergone complete resection of the primary tumour without evidence of residual disease.
3. Patients must be randomised to start treatment a minimum of 28 days and maximum of 70 days* after surgery (If a subject has had a major surgical procedure, open biopsy, or significant traumatic injury within 28 days prior to study treatment start, or there is the anticipated need for major surgical procedure during the course of the study they are not eligible).
4. World Health Organization Performance Status 0 or 1.
5. Male or female outpatients age 18 years.
6. Written informed consent given.
7. Life expectancy of greater than or equal to 5 years, in terms of non-cancer-related morbidity.

*Calculation of these dates is based on date of surgery being day 1.

Inclusion criteria provided at time of registration:
1. Histologically proven stage III and high risk stage II (any of the following - stage T4, or lymphatic invasion, vascular invasion, peritoneal involvement) colon cancer (expected ratio 70%:

30%)
2. Patients must have undergone complete resection of the primary tumour without evidence of residual disease
3. Patients must be randomised to start treatment a minimum of 28 days and maximum of 70 days after surgery. (If a subject has had a major surgical procedure, open biopsy, or significant traumatic injury within 28 days prior to study treatment start, or there is the anticipated need for major surgical procedure during the course of the study they are not eligible).
4. World Health Organisation (WHO) Performance Status 0 or 1
5. Male or female outpatients age ≥18 years
6. Written informed consent given
7. Life expectancy of ≥5 years

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
1952

Key exclusion criteria
Exclusion criteria amended as of 02/07/2007:
1. Previous chemotherapy, immunotherapy or infra-diaphragmatic radiotherapy.
2. Received any investigational drug or agent/procedure (i.e. participation in another treatment trial) within 4 weeks of randomisation.
3. Moderate or severe renal impairment (creatinine clearance <30 ml/min [calculated according to Cockroft-Gault formula]).
4. Any of the following laboratory values (tests must not have been carried out more than 2 weeks prior to randomisation):
a. Absolute Neutrophil Count (ANC) <1.5 x 109/L
b. Platelet count < 100 x 109/L
c. Total bilirubin > 1.5 Upper Limit of Normal (ULN)
d. Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST) > 2.5 x ULN
e. Alkaline phosphatase > 2.5 x ULN
5. Patients requiring chronic use of full dose oral or parenteral anticoagulants, high dose aspirin (>325 mg/day), anti-platelet drugs or known bleeding diathesis. Low dose aspirin is allowed.
6. Proteinuria > 500 mg/24 hours.
7. Known coagulopathy.
8. Clinically significant cardiovascular disease (i.e. active; or <12 months since e.g. cerebrovascular accident, myocardial infarction, unstable angina, New York Heart Association (NYHA) grade II or greater congestive heart failure, serious cardiac arrhythmia requiring

medication; or uncontrolled hypertension).
9. Concomitant treatment with sorivudine or its chemically related analogues such as brivudine.
10. Pregnant (positive pregnancy test within 7 days of starting treatment), or lactating women.
11. Sexually active patients of child bearing potential not using adequate contraception (male and female)**.
12. Previous malignancies other than adequately treated in situ carcinoma of the uterine cervix or basal or squamous cell carcinoma of the skin, unless there has been a disease free interval of at least 10 years.
13. Lack of physical integrity of the upper gastrointestinal tract, malabsorption syndrome or inability to take oral medication.
14. Chronic inflammatory bowel disease and/or bowel obstruction and/or active peptic ulcer.
15. History of uncontrolled seizures, central nervous system disorders or psychiatric disability judged by the investigator to be clinically significant precluding informed consent or interfering with compliance for oral drug intake.
16. Patients with known allergy to Chinese hamster ovary cell proteins or other recombinant human or humanized antibodies or to any excipients of bevacizumab formulation; or to any other study drugs.

** Women of childbearing potential randomised to receive bevacizumab are required to have a serum pregnancy test at baseline (i.e. prior to starting treatment). Postmenopausal women must have been amenorrheic for at least 12 months to be considered of non-childbearing potential.

Exclusion criteria provided at time of registration:
1. Previous chemotherapy or immunotherapy
2. Received any investigational drug or agent/procedure i.e. participation in another treatment trial within four weeks of randomisation
3. Moderate or severe renal impairment (creatinine clearance ≤30 ml/min [calculated according to Cockroft-Gault formula])
4. Any of the following laboratory values (tests should not have been carried out more than two weeks prior to randomisation):
4.1. Absolute neutrophil count (ANC) <1.5 x 10^9/l
4.2. Platelet count <100 x 10^9/l
4.3. Total bilirubin >1.5 Upper Limit of Normal (ULN)
4.4. Alanine aminotransferase (ALT), aspartate aminotransferase (AST) >2.5 x ULN
4.5. Alkaline phosphatase >2.5 x ULN
5. Subjects requiring chronic use of full dose oral or parenteral anticoagulants, high dose aspirin (>325 mg/day), anti-platelet drugs or known bleeding diathesis. Low dose aspirin is allowed.
6. Proteinuria >500 mg/24 hours
7. Known coagulopathy
8. Clinically significant cardiovascular disease (i.e. active; or <12 months since e.g. cerebrovascular accident, myocardial infarction, unstable angina, New York Heart Association [NYHA] grade II or greater congestive heart failure, serious cardiac arrhythmia requiring medication; or uncontrolled hypertension)
9. Concomitant treatment with sorivudine or its chemically related analogues such as brivudine
10. Pregnant (positive pregnancy test within seven days of starting treatment), or lactating women
11. Sexually active patients of child bearing potential not using adequate contraception (male and female)
12. Previous malignancies other than adequately treated in situ carcinoma of the uterine cervix or basal or squamous cell carcinoma of the skin, unless there has been a disease-free interval of at least ten years
13. Lack of physical integrity of the upper gastrointestinal tract, malabsorption syndrome or

inability to take oral medication
14. Chronic inflammatory bowel disease and/or bowel obstruction and/or active peptic ulcer
15. History of uncontrolled seizures, central nervous system disorders or psychiatric disability judged by the investigator to be clinically significant precluding informed consent or interfering with compliance for oral drug intake
16. Known dihydropyrimidine dehydrogenase (DPD) deficiency
17. Patients with known allergy to Chinese hamster ovary cell proteins or other recombinant human or humanized antibodies or to any excipients of bevacizumab formulation; or to any other study drugs
18. Women of childbearing potential randomised to receive bevacizumab are required to have a serum pregnancy test at baseline (i.e. prior to starting treatment). Postmenopausal women must have been amenorrheic for at least 12 months to be considered of non-childbearing potential.

Date of first enrolment
01/07/2005

Date of final enrolment
31/12/2011

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University of Oxford
Oxford
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OX3 7DQ

Sponsor information

Organisation
University of Oxford (UK)

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Industry

Funder Name
Hoffman La Roche Inc. (ref: MO17092) (International)

Results and Publications

Individual participant data (IPD) sharing plan
Not provided at time of registration

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/11/2016		Yes	No
Plain English results			02/09/2022	No	Yes