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CINATRA: Chromosomal Instability and Anti-Tubulin Response Assessment

Submission date 05/03/2008	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 21/04/2008	**Overall study status** Completed	
Last Edited 25/10/2022	**Condition category** Cancer	

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-patupilone-for-people-with-advanced-bowel-cancer

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
CCR 2983

Study information

Scientific Title
A phase 2 study of Epo906/patupilone in metastatic colorectal carcinoma in patients with microsatellite instability or chromosomal instability previously treated with irinotecan, oxaliplatin and fluoropyrimidines

Acronym
CINATRA

Study objectives
To determine the anti-tumour activity of Epo906 administered to patients with metastatic colorectal cancer previously treated with irinotecan, oxaliplatin and fluoropyrimidines.

As of 19/03/2009 this record has been updated to include an amended overall trial start date; the initial start date at the time of registration was 01/05/2008.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Hertfordshire Research Ethics Committee, 13/05/2008

Study design
Phase II single-arm interventional study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Metastatic colorectal cancer

Interventions
This trial aims to find out whether Epo906 has activity in the two main types of colorectal cancer: cancers with a near normal DNA content (i.e. unselected patients [Cohort A]; microsatellite instability) and cancers with a continuously changing DNA content (Cohort B; chromosomal instability). The first part of the trial will assess the activity of Epo906 in all patients (Cohort A). In the second part of the study, only patients who have tumours with a near normal DNA content will be treated (Cohort B).

Cohort A (75 unselected patients; microsatellite instability): Epo906/patupilone is given intravenously (iv) at a dose of 8 mg/m^2 over 20 minutes on day 1 of a 21-day cycle, after pre-medication with iv dexamethasone and metoclopramide. Patients will receive 8 cycles (8 doses) unless there is evidence of disease progression or unacceptable toxicity.

Cohort B (35 patients selected for microsatellite instability): As above

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)

Epo906/patupilone

Primary outcome(s)
Twelve-week progression free survival (PFS). This will be measured by comparing a CT scan of the thorax/abdomen and pelvis at baseline (Within 28 days of starting treatment) to a second CT scan performed after 12 weeks from trial registration, evaluated by RECIST criteria.

Key secondary outcome(s))
1. To determine the effect of CIN and MSI on the efficacy (response rate and progression-free survival [PFS]) of Epo906 as an anticancer agent, assuming that MSI+ colorectal cancer patients will benefit more than CIN+ colorectal cancer patients
2. To describe the safety of Epo906 and quality of life benefits associated with treatment
3. To correlate specific genetic variation with outcome following EPO906 therapy, in particular with reference to adenomatous polyposis coli (APC) gene status (MSI+ APCwt versus MSI APCmutant versus CIN). Other genetic analysis will include but not be limited to, b-catenin, Kras, or Braf mutations; copy number polymorphisms; loss of heterozygosity (LOH)
4. To retrospectively assess the response to prior treatment in relation to MSI and CIN status, particularly with reference to response to irinotecan and oxaliplatin containing regimens

The following assessments will be carried out:
a. Overall survival (Time from trial registration to death from any cause), response rate (Proportion of patients with complete or partial response as their best response as measured by RECIST criteria), tumour control rate (Total number of patients with best response measured by RECIST criteria as complete response, partial response or stable disease)
b. Twelve-week PFS stratified by MSI and CIN status, tested by flow immunohistochemistry, flow cytometry and DNA analysis of tumour sample
c. Response rate stratified by MSI and CIN status, tested by flow immunohistochemistry, flow cytometry and DNA analysis of tumour sample
d. Incidence of serious toxicity with Epo906 therapy, measured by CTCAE version 3.0
e. Quality of life parameters, measured by EORTC QLQ-C30 and QLQ-CR38 questionnaires at baseline, prior to cycles 2 and 5 and at the end of treatment
f. To retrospectively assess response to prior treatments according to MSI and CIN status, tested by flow immunohistochemistry, flow cytometry and DNA analysis of tumour sample

Completion date
01/05/2012

Eligibility

Key inclusion criteria
1. Male or female
2. 18 years of age or older
3. Histologically confirmed metastatic or locally recurrent carcinoma of the colon or rectum
4. Prior therapy with oxaliplatin, a fluoropyrimidine, and irinotecan for colorectal cancer. If a patient has previously received raltitrexed, this would be considered as equivalent to fluoropyrimidine treatment
5. Availability of paraffin embedded tumour tissue for analysis of microsatellite instability (MSI) status and chromosomal instability (CIN)
6. Life expectancy of 12 weeks or greater
7. Eastern Cooperative Oncology Group (ECOG) performance status 0 or 1
8. Clinically and/or radiographically documented measurable disease according to the Response

Evaluation Criteria In Solid Tumours (RECIST), with at least one unidimensionally lesion measuring 10mm or greater by spiral CT or 20mm or greater by conventional (non-spiral) computerised tomography (CT)
9. Adequate liver function:
9.1. Serum aspartate aminotransferase (AST) less than or equal to 5 x upper limit of normal (ULN)
9.2. Serum alanine aminotransferase (ALT) less than or equal to 5 x ULN
9.3. Serum alkaline phosphatase (ALP) less than 5 x ULN
9.4. Total serum bilirubin less than 1.5 x ULN
9.5. Prothrombin time (PT) less than or equal to 1.5 x ULN
10. Adequate haematological function:
10.1. Absolute neutrophil count (ANC) greater than or equal to 1.0 x 10^9/L
10.2. Platelets greater than or equal to 100 x 10^9/L
10.3. Haemoglobin greater than or equal to 9.0 g/dL
11. Serum creatinine clearance of greater than 50 ml/min according to the Cockcroft-Gault calculation or measured glomerular filtration rate of greater than 50 ml/min
12. Willingness and ability to comply with scheduled visits, treatment plans, laboratory tests, and other study procedures
13. Prior radiotherapy or colostomy are allowed. A marker lesion may not be in a previously irradiated area, unless there has been documented disease progression in that area since radiotherapy.
14. Signed and dated informed consent document indicating that the patient (or legally acceptable representative) has been informed of all pertinent aspects prior to enrolment
15. For Cohort B, all patients must have tumours which are microsatellite instability (MSI) positive by immunohistochemistry (IHC)
16. Patients must be willing to undertake adequate contraceptive methods or remain sexually abstinent for the duration of study treatment and for at least 28 days after receiving the last dose of study drug

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
29

Key exclusion criteria
1. Persistent toxicity from previous treatment. Neurotoxicity from prior oxaliplatin must have resolved to at least grade 1.
2. Diagnosis of or treatment for any second malignancy within the last 5 years, except for adequately treated basal cell or squamous cell carcinoma of the skin, or adequately treated in-

situ cervical cancer
3. Any of the following within the 12 months prior to study drug administration:
3.1. Myocardial infarction or severe/unstable angina
3.2. Coronary/peripheral artery bypass graft
3.3. Symptomatic congestive heart failure
3.4. Cerebrovascular accident or transient ischaemic attack
3.5. Pulmonary embolism
4. Pregnancy or breastfeeding
5. Other severe acute or chronic medical or psychiatric condition, or laboratory abnormality that may increase the risk associated with study participation or study drug administration, or may interfere with the interpretation of study results, and in the judgment of the investigator would make the patient inappropriate for entry into this study
6. Clinically significant neuropathy that could be worsened by study treatment

Date of first enrolment
10/12/2008

Date of final enrolment
01/05/2010

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Royal Marsden Hospital
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Sponsor information

Organisation
The Royal Marsden Hospital NHS Foundation Trust (UK)

ROR
https://ror.org/0008wzh48

Funder(s)

Funder type

Government

Funder Name
The Royal Marsden Hospital NHS Foundation Trust (UK)

Funder Name
Novartis Pharmaceuticals (UK) - supported in conjunction with Professor Cunningham's Charitable Research Fund (UK)

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	01/10/2013		Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Plain English results			25/10/2022	No	Yes