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PICCOLO Trial: Panitumumab, Irinotecan & Ciclosporin in COLOrectal cancer therapy

Submission date 13/12/2004	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 20/12/2004	**Overall study status** Completed	
Last Edited 26/09/2019	**Condition category** Cancer	

Plain English summary of protocol
http://cancerhelp.cancerresearchuk.org/trials/a-trial-looking-at-panitumumab-irinotecan-and-ciclosporin-for-advanced-bowel-cancer

Contact information

Type(s)
Scientific

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT00389870

Protocol serial number
Protocol version 3.0 18th June 2008

Study information

Scientific Title
A randomised clinical trial of treatment for fluorouracil-resistant advanced colorectal cancer comparing standard single-agent irinotecan versus irinotecan plus panitumumab and versus irinotecan plus ciclosporin

Acronym
PICCOLO (formerly CIVIC)

Study objectives
Current information as of 28/09/2010:
A multi-centre, open-label, randomised, controlled trial to show whether in patients with KRAS wild-type tumours the addition of panitumumab to irinotecan (IrPan), gives superior anti-cancer efficacy compared to standard irinotecan alone (Ir), and whether (regardless of tumour subtype) the modulation of irinotecan with ciclosporin (IrCs) offers non-inferior anti-cancer efficacy and reduced toxicity compared to Ir. A total of 1324 patients will be recruited.

Initial information at time of registration
PICCOLO is a multi-centre, open-label, randomised, controlled, 3-arm clinical trial with equal randomisation. A total of 1269 patients will be recruited. The PICCOLO Trial aims to establish whether the toxicity of irinotecan (Ir) therapy is reduced, without loss of efficacy, by modulation with ciclosporin (Cs) and whether the efficacy of irinotecan therapy is improved by the addition of panitumumab (Pan).

Ethics approval required
Old ethics approval format

Ethics approval(s)
The Newcastle & North Tyneside Research Ethics Committee 2, 19/07/2006

Study design
Randomised controlled trial

Primary study design
Interventional

Study type(s)
Treatment

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

Interventions
Amended 28/09/2010:
Patients will be recruited over 3 years and 6 months with 1 year follow up period.

Current information in October 2005:
1. Irinotecan (Ir)
2. Irinotecan plus panitumumab (IrPan)
3. Irinotecan plus ciclosporin (IrCs)
Patients will be recruited over 3 years with 1 year follow up period

Initial information at time of registration:
1. Irinotecan (IR)
2. Irinotecan with cyclosporin (IRC)
3. Irinotecan plus panitumumab (IRP)
4. Irinotecan with cyclosporin plus Panitumumab (IRCP)

Chief investigator: Professor Matt Seymour

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Irinotecan, panitumumab, ciclosporin

Primary outcome(s)
Ir vs IrCs comparison: proportion of patients progression-free 12 weeks after randomisation

Amended 28/09/10:
Ir vs IrPan comparison (patients with KRAS wildtype tumours not previously receiving an anti-EGRF targeted therapy cetuximab): overall survival (OS) from randomisation

Initial information at time of registration:
Ir vs IrPan comparison (patients not previously receiving cetuximab): overall survival (OS) from randomisation

Key secondary outcome(s))
Current infotmation as of 28/09/10:
Ir vs IrCs comparison:
1. Proportion of patients free from treatment failure at 12 weeks
2. Overall survival (OS) from randomisation
3. Research nurse-assessed toxicity (NCI-CTC[V3] grades): maximum toxicity grade per patient; rate per cycle; all-cause mortality within 60 days of randomisation; toxicity of primary interest is grade 3+ diarrhoea within 12 weeks of randomisation

Ir vs IrPan comparison (patients with KRAS wildtype tumours not previously receiving an anti-EGRF targeted therapy):
1. Proportion of patients progression-free 12 weeks from randomisation
2. Research nurse-assessed toxicity (NCI-CTC[V3] grades): maximum toxicity grade per patient; rate per cycle; all-cause mortality within 60 days of randomisation

Ir vs IrCs and Ir vs IrPan (patients with KRAS wildtype tumours not previously receiving an anti-EGRF targeted therapy) comparisons:
1. Progression-free survival (PFS) from randomisation
2. Best response by RECIST criteria at 1-year follow-up from randomisation
3. Patient-assessed symptom/QL/PA scores at 12 and 24 weeks

Exploratory Endpoints

Ir vs IrPan comparison (patients with KRAS wildtype tumours previously receiving an anti-EGRF targeted therapy):
1. Proportion of patients progression free 12 weeks after randomisation
2. Research nurse-assessed toxicity (NCI-CTC[V3] grades): maximum toxicity grade per patient; rate per cycle; all-cause mortality within 60 days of randomisation

Ir vs IrPan comparison (patients randomised to receive Ir or IrPan under Protocol version 1.0 who have mutant or unknown KRAS status, regardless of previous anti-EGRF targeted therapy):
1. Proportion of patients progression free 12 weeks after randomisation
2. Research nurse-assessed toxicity (NCI-CTC[V3] grades): maximum toxicity grade per patient; rate per cycle; all-cause mortality within 60 days of randomisation

Initial information at time of registration
Ir vs IrCs comparison:
1. Proportion of patients free from treatment failure at 12 weeks
2. Overall survival (OS) from randomisation
3. Research nurse-assessed toxicity (NCI-CTC[V3] grades): maximum toxicity grade per patient; rate per cycle; all-cause mortality within 60 days of randomisation; toxicity of primary interest is grade 3+ diarrhoea within 12 weeks of randomisation

Ir vs IrPan comparison (patients not previously receiving cetuximab):
1. Proportion of patients progression-free 12 weeks from randomisation
2. Research nurse-assessed toxicity (NCI-CTC[V3] grades): maximum toxicity grade per patient; rate per cycle; all-cause mortality within 60 days of randomisation

Ir vs IrCs and Ir vs IrPan (patients not previously receiving cetuximab) comparisons:
1. Progression-free survival (PFS) from randomisation
2. Best response by RECIST criteria at 1-year follow-up from randomisation
3. Patient-assessed symptom/QL/PA scores at 12 and 24 weeks

Exploratory Endpoints

Ir vs IrPan comparison (patients previously receiving cetuximab):
1. Proportion of patients progression free 12 weeks after randomisation
2. Research nurse-assessed toxicity (NCI-CTC[V3] grades): maximum toxicity grade per patient; rate per cycle; all-cause mortality within 60 days of randomisation

Completion date
28/02/2010

Eligibility

Key inclusion criteria
Current information as of 28/09/10:
1. Advanced colorectal cancer defined in either of the following ways:
1.1. Previous or current histologically confirmed primary adenocarcinoma of colon or rectum, together with clinical/radiological evidence of advanced/metastatic disease
1.2. Histologically/cytologically confirmed metastatic adenocarcinoma, together with clinical /radiological evidence of colorectal primary tumour
2. Unidimensionally measurable disease (please refer to RECIST criteria)
3. Prior fluoropyrimidine therapy, +/- oxaliplatin, +/- bevacizumab together with disease

progression during or after that treatment. Adjuvant therapy and/or prior therapy for advanced disease may have been given
4. Able to start trial treatment within 14 days of randomisation
5. WHO performance status of 0, 1 or 2 and a life expectancy of at least 12 weeks
6. Aged ≥18 years at time of consent
7. Adequate full blood count, defined as:
7.1. Haemoglobin (Hb) >10.0 g/dl
7.2. While Blood Count (WBC) >3.0 x109/l
7.3. Platelets >100 x109/l
8. Adequate renal biochemistry, defined as:
8.1. Glomerular Filtration Rate (GFR) calculated/measured by either
8.1.1. Cockcroft formula >50 ml/min
8.1.2. EDTA clearance >60ml/min
Or
8.2. Creatinine clearance measured by 24hr urine collection >60ml/min
9. Adequate hepatobiliary function
9.1. Total bilirubin < 25 umol/l
9.2. Alkaline Phosphatase (ALP) no more than 5x upper limit of normal (ULN)
9.3. Aspartate Aminotransferase (AST) and Alanine Aminotransferase (ALT) no more than 2.5 X ULN
9.4. No clinical or radiological evidence of biliary obstruction
9.5. No known history of Gilberts syndrome
10. If female and of child bearing potential, must have a negative pregnancy test within 72 hours before trial entry, is not breastfeeding and has agreed to take adequate, medically approved, contraceptive precautions (oral or barrier contraceptives under the supervision of a General Practioner or Family Planning Clinic) during and for 6 months after study treatment
11. If male with a partner of childbearing age, must agreed to use adequate, medically approved, contraceptive precautions (oral or barrier contraceptives under the supervision of a General Practioner or Family Planning Clinic) during and for 6 months after study treatment
12. Capable of reliable oral self-medication and toxicity reporting
13. Capable of completing Quality of Life questionnaires (The baseline Quality of Life questionnaire must be completed before randomisation)
14. In the opinion of the investigator: Is the patient capable of giving informed consent?

Initial information at time of registration:
1. Confirmed advanced colorectal adenocarcinoma
2. Unidimensionally measurable disease (RECIST criteria)
3. Prior fluoropyrimidine +/- oxaliplatin therapy, +/- bevacizumab with disease progression during or after that treatment (adjuvant therapy and/or prior therapy for advanced disease may have been given)
4. At least 3 weeks from most recent systemic anticancer therapy to planned start of trial treatment, and able to start trial treatment within 2 weeks of randomisation
5. WHO performance status of 0, 1 or 2, with estimated life expectancy of at least 12 weeks
6. Aged ≥18 years
7. Adequate full blood count: Hb >10.0 g/dl; WBC >3.0 x109/l; Plts >100 x109/l
8. Adequate renal biochemistry: GFR calculated by the Cockcroft formula >50 ml/min, or measured by EDTA clearance, >60mL/min
9. Adequate hepatobiliary function: total bilirubin < 25 umol/l, ALP no more than 5x upper limit of normal, AST and ALT no more than 2.5 X ULN, no clinical or radiological evidence of biliary obstruction, no known history of Gilberts syndrome
10. If female and of childbearing potential, must have a negative pregnancy test within 72 hours prior to trial entry, and not breastfeeding and agree to use adequate contraceptive precautions

during and for 6 months after study treatment
11. If male with a partner of childbearing potential, must agree to use adequate contraceptive precautions during and for 6 months after study treatment
12. Capable of completing Quality of Life questionnaires
13. Signed, informed consent from the patient

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
Current information as of 28/09/10:
1. Previous treatment with irinotecan
2. Patient has received any of the following:
2.1. Capecitabine within 14 days prior to randomisation
2.2. All other licensed cytotoxic drugs within 21 days prior to randomisation
2.3. Prior cetuximab, panitumumab or bevacizumab within 21 days prior to randomisation
2.4. Any experimental anticancer drug therapy including antibodies within 42 days prior to randomisation
3. Prior anaphylactic allergic reaction to any anti-EGFR
4. Ongoing requirement for ciclosporin or any contraindicated concomitant medication, namely diltiazem, verapamil, amiodarone or fluvoxamine. Note: any prescribed short-courses of antifungals or antibiotics would not make a patient ineligible but should be completed 5 days before starting trial therapy.
5. Concurrent or previous other cancer (excluding non-melanomatous skin cancer), unresolved bowel obstruction or uncontrolled infection, uncontrolled chronic enteropathy (e.g. Crohns disease, ulcerative colitis), or chronic diarrhoea (≥4 stools per day) of any cause
6. Major thoracic or abdominal surgery within the last 4 weeks
7. Known CNS metastases, carcinomatous meningitis or a recent history of seizures
8. Clinical/radiological evidence of interstitial pneumonitis, ulmonary fibrosis, pleural effusion or ascites causing grade ≥2 dyspnea
9. Any other condition, which, in the investigators opinion would make the patient unsuitable for participation in the trial

Initial information at time of registration:
1. Any previous treatment with irinotecan
2. Experimental drug therapy or any antibody therapy other than cetuximab, within 6 weeks before study enrolment
3. Systemic chemotherapy and/or cetuximab within 28 days before study enrollment
4. Prior anaphylactic allergic reaction to cetuximab

5. Ongoing requirement for ciclosporin or any contraindicated concomitant medication, namely: diltiazem, verapamil, amiodarone or fluvoxamine
6. Concurrent or previous other cancer (excluding non-melanomatous skin cancer), major thoracic or abdominal surgery within preceding four weeks, unresolved bowel obstruction or uncontrolled infection, chronic enteropathy (e.g. Crohns disease, ulcerative colitis), or chronic diarrhoea (≥4 stools per day) of any cause
7. Known CNS metastases, carcinomatous meningitis or recent history of seizures
8. Clinical or radiological evidence of interstitial pneumonitis, pulmonary fibrosis, pleural effusion or ascites causing grade ≥2 dyspnea
9. Incapable of reliable oral self-medication
10. Any other condition, which, in the investigators opinion would make the patient unsuitable for participation in the trial

Date of first enrolment
01/03/2006

Date of final enrolment
28/02/2010

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University of Leeds
Leeds
United Kingdom
LS2 9JT

Sponsor information

Organisation
University of Leeds (UK)

ROR
https://ror.org/024mrxd33

Funder(s)

Funder type
Research council

Funder Name
Clinical Trials Advisory and Awards Committee (CTAAC) (UK)

Funder Name
Amgen Ltd (UK)

Results and Publications

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?
Results article	results	01/07/2013		Yes	No
Results article	results	01/11/2013		Yes	No
Results article	results	01/05/2016		Yes	No
Plain English results				No	Yes