BILCAP: A randomised clinical trial evaluating adjuvant capecitabine compared to expectant treatment alone following surgery for biliary tract cancer

Trial development group: Prof J Primrose (Chief Investigator), Dr John Bridgewater, Dr D Cunningham, Dr J Dunn, Mr J Garden, Prof. P. Johnson, Prof J Neoptolemas, Mr G Poston, Mr D Sherlock, Dr J Valle, Dr H Wassan on behalf of the NCRI Upper GI CSG

Rationale for the study: Currently the benefit of adjuvant treatment following surgery for biliary tract cancer remains unclear although there are now data to support adjuvant chemotherapy in bowel and pancreatic malignancy. The best available evidence suggests that in this setting a fluoropyrimidine such as capecitabine may be the best option. This study aims to evaluate adjuvant chemotherapy with capecitabine in patients who have undergone complete macroscopic resection for biliary tract cancer, compared to expectant treatment alone. The primary endpoint will be 2-year survival, and secondary endpoints progression 5-year survival, relapse free interval, toxicity, Quality of Life and Health Economics.

Study Design
A two-arm, multi-centre phase III randomised study for patients having undergone a macroscopically complete surgical resection of a biliary tract cancer.

Eligible patients will be randomised between:

Control: Observation
Treatment: Capecitabine 1250mg/m² given PO twice a day on day 1 to 14 of a 3 weekly cycle for 24 weeks (8 cycles).

Further treatment as indicated on progression

Study Aim
To investigate the role of adjuvant capecitabine in the treatment of macroscopically complete surgical resection of biliary tract cancer.

Primary Endpoint
• 2-year survival

Secondary Endpoints
• 5-year survival
• Relapse free interval
• Toxicity
• Quality of Life
• Health Care Economics

Study organisation
• The trial will recruit 360 patients within the UK over 3 years
• Planned completion of accrual is September 2008
• Planned completion of 2 year follow-up September 2010 and publication
• Study completion of 5 year follow-up September 2013
• Co-ordinated by the Cancer Research UK Trials Unit in Birmingham.
• NCRN trial funded by Cancer Research UK

Inclusion & Exclusion Criteria

Inclusion Criteria
• Histologically confirmed biliary tract cancer (intrahepatic or extrahepatic) or cholangiocarcinoma or muscle invasive gallbladder cancer (not a resection that involves the pancreas) who have undergone macroscopically complete resection with curative intent.
• Adequate renal function: serum urea and serum creatinine < 1.5 times ULN and glomerular filtration rate ≥ 60 ml/min a (measured by creatinine clearance or EDTA or by using the Cockcroft formula).
• Adequate haematological function: HB ≥ 10g/dl, WBC ≥ 3.0 x 10⁹/L, ANC ≥ 1.5 x 10⁹/L, Platelet count ≥ 100,000/mm³
• Adequate liver function: bilirubin <50 µmol/L, ALT or AST ≤ 5 x ULN,
• Adequate surgical biliary drainage - no evidence of infection
• Age ≥ 18 years
• ECOG performance status ≤ 2
• Not of childbearing potential or must use approved contraception
• Written informed consent

Exclusion Criteria
• Pancreatic or periampullary cancer, mucosal gallbladder cancer
• Incomplete recovery from previous surgery or unresolved biliary tree obstruction
• Use of other investigational agents during the study or within 4 weeks of planned entry to the study
• History of second malignancy within 5 years of trial entry, except cervical carcinoma-in-situ or non-melanotic skin cancer.
• Previous chemotherapy, radiotherapy, biological or hormone therapy given for biliary tract cancer
• Serious co-existing medical condition including a potential serious infection.
• Evidence of significant clinical disorder or laboratory finding which, in the opinion of the investigator makes it undesirable for the patient to participate in the trial
• Psychological, familial, sociological or geographical factors considered likely to prevent compliance with the protocol.
• Any other serious uncontrolled medical conditions
• Any pregnant or breastfeeding women

For Further Information
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