BILCAP: A randomized clinical trial evaluating adjuvant chemotherapy with capecitabine compared to expectant treatment alone following curative surgery for biliary tract cancer

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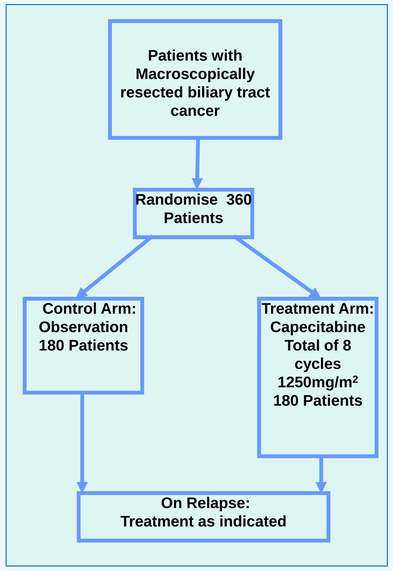
Introduction/ Abstract

BILCAP is a multi-centre prospective, randomised phase III trial investigating the role of adjuvant chemotherapy with oral fluoropyrimidine (capecitabine) in patients following potentially curative surgical resection of a biliary tract cancer. BILCAP is a multi-centre prospective, randomised phase III trial investigating the role of adjuvant chemotherapy with oral fluoropyrimidine (capecitabine) in patients following potentially curative surgical resection of a biliary tract cancer. Patients who have undergone macroscopically complete surgical resection are randomised to receive either adjuvant chemotherapy with capecitabine or observation.

Background

Biliary tract tumours are relatively rare, accounting for 0.7% of malignant tumours in adults, with approximately 1200 new cases registered each year in England and Wales. The 1-year and 5-year survival is poor at 22% and 9% respectively (Cancer Survival Trends in England and Wales 1971 – 1995). Approximately 15-20% of cases are suitable for surgical resection but the outlook remains poor with survival at 5 years approximately 15% (Cancer Survival Trends in England and Wales 1971 – 1995 Most tumours are advanced at presentation and are unsuitable for surgical resection. The BILCAP study, developed by the Hepatobiliary group of the NCRI Upper GI Clinical Studies Group, was designed to determine the benefit of adjuvant therapy following surgery. As such it aims to deliver a key NCRN objective, practise changing outcomes in uncommon cancers. Funding was approved by Cancer Research UK in March 2005 for a phase III, non-commercial trial in patients with resectable biliary tract cancer.

Trial Design



Aims and Objectives

The primary outcome measure is overall survival . To detect an increase in 2 year survival from 20 to 32%, with 2-sided significance level of 5% and 80% power, 360 patients (270 events) are to be randomised

BILCAP Outcome Measures

Primary

- **Overall Survival**

Secondary

- **Relapse free survival**
- **Toxicity**
- **Quality of life (QoL)**
- **Health economics**

Main Inclusion Criteria

Patients with histologically confirmed:

- ❖**intrahepatic cholangiocarcinoma**
- ❖**extrahepatic/hilar cholangiocarcinoma**
- ❖**lower common bile duct cholangiocarcinoma**
- ❖**muscle invasive gallbladder cancer**

Radical and macroscopically complete surgery which includes liver resection, pancreatic resection or, less commonly, both.

ECOG Performance Status ≤ 2

Adequate renal, haematological and liver function

Age 18 years or over

Main Exclusion Criteria

Pancreatic or ampullary cancer

Mucosal gallbladder cancer

Incomplete recovery from previous surgery or unresolved biliary tree obstruction

Any previous chemotherapy or radiotherapy for biliary tract cancer

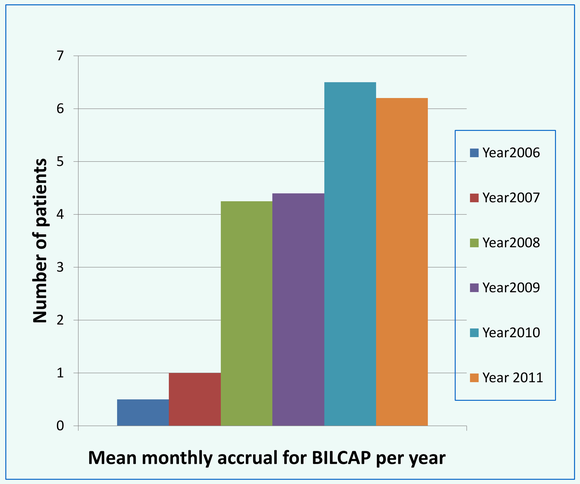
BILCAP Timelines

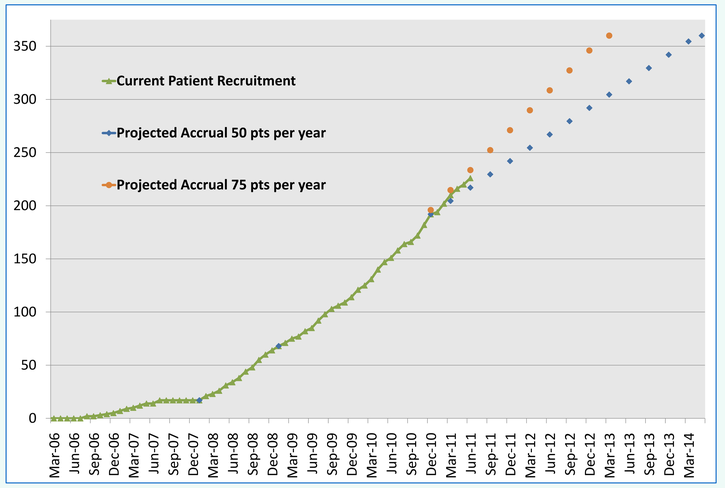
- **First centre opened March 2006**
- **1st patient recruited July 2006**
- **Accrual completion Q1 2013**
- **Primary analysis 2015**

Study Recruitment

Trial recruitment,, remains very strong. 225 of 360 patients have been successfully recruited to date.

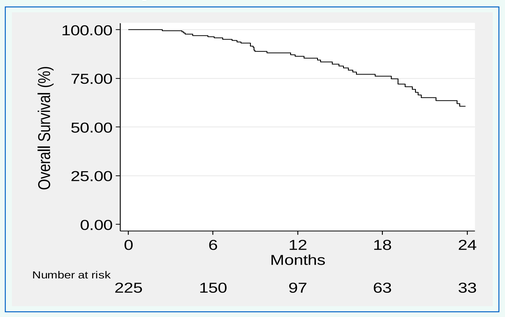
With approximately 200 resections for biliary tract cancer per year in the UK, BILCAP has recruited more than 25% of all resected patients in the UK for the last 3 years and 36% in 2010 (51pts in 2008, 53 pts in 2009 and 73 patients in 2010). Recruitment in 2011 currently is on target to surpass the number of patients recruited in 2010.





Survival and Toxicity

❖**At the time of this interim analysis 41 (18%) patients had died within 24 months.**
❖**Median FU of alive patients is 9.3 (IQR 2.8, 18.5) months and as such the survival curves are not stable beyond this time point.**
❖**12 month survival rate of 86.4% (95%CI 79.6, 91.0) at the time of this interim analysis.**



- ❖ **100 (Capecitabine) patients have returned 571 treatment forms**
- ❖ **No grade 4 toxicities observed to date**
- ❖ **Toxicities within expected levels**
- ❖ **Hand-foot and GI toxicities most prevalent, as anticipated**

Toxicity	Grades 1&2 % pts	Grades 3&4* % pts	Overall
Fatigue	71%	13%	84%
Fever	13%	0%	13%
Weight loss	13%	0%	13%
Hand-foot reaction	65%	15%	80%
Diarrhea	54%	10%	64%
Mucositis/stomatitis	41%	1%	42%
Nausea	48%	1%	49%
Vomiting	20%	0%	20%
Other	60%	16%	76%

Conclusions

BILCAP is the most successful adjuvant study in biliary tract cancer and is on target to complete accrual early in 2013. The main focus for the Trials Management Group is to demonstrate the relative success in the UK and open the trial internationally. The results of BILCAP will define the international standard of care for patients with resected biliary tract cancer.

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