Impact of trials in rare cancers: the ABC trials

Marian Duggan, Senior Trial Coordinator

Cancer Research UK & UCL Cancer Trials Centre

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Outline

• Rare cancers & challenges
• Biliary tract cancer
• ABC-01/ABC-02 trials
• Impact
• Portfolio of trials
• Summary
Rare cancer

http://www.rarecancerseurope.org/About-Rare-Cancers

• Fewer than 6 in 100,000 people are diagnosed with it each year
Challenges of conducting trials in rare cancers

• Longer to recruit
• International
• Cost more money
• Most practice-changing clinical trials require large populations of patients in order to produce statistically robust results relating to moderate treatment effects
• Standard practice may vary
Biliary tract cancer

**Function:** facilitates the storage and release of bile to aid the breakdown of fats
Biliary tract cancer

• 3% of all GI cancers globally ¹

• UK annual incidence
  – Cholangiocarcinoma | 1600 cases ²
    (Incidence is 1-2 per 100,000 population per year in the UK³)
  – Gallbladder cancer | 650 cases ⁴

In the early 2000’s, there was no standard chemotherapy for patients with locally advanced or metastatic biliary tract cancer.
ABC-01 trial

- Randomised phase II study
  - Arm A: Gemcitabine 1000mg/m²
  - Arm B: Cisplatin 25mg/m² & Gemcitabine 1000mg/m²

- First-line, patients with advanced Biliary Tract Cancer

- Primary endpoint: Progression Free Survival at 6 months

- Accrual: Feb 2002 – May 2004; n=86 patients
Results of ABC-01

Activity of Cis-Gem combination appeared superior

- Improved 6-mo Progression Free Survival (57.1 vs. 47.7%)
- Improved median Time to progression (8.0 vs. 4.0 mths)
- Improved Response Rate (24 vs. 15%)
- Improved tumour control rate (76 vs. 58%)

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ABC-02 trial

- ABC-01 extended into ABC-02
- May 2005 – Sep 2008 (n=324)
- 34 sites open in the UK
- Primary endpoint: Overall Survival
ABC-02 - Results: Overall Survival

<table>
<thead>
<tr>
<th>Treatment arm</th>
<th>Gem</th>
<th>Gem + Cis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>n=206</td>
<td>n=204</td>
</tr>
<tr>
<td>Deaths n(%)</td>
<td>141 (68.5)</td>
<td>122 (59.8)</td>
</tr>
<tr>
<td>Median survival (mo)</td>
<td>8.3</td>
<td>11.7</td>
</tr>
<tr>
<td>Log rank p value</td>
<td>0.002</td>
<td></td>
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<tr>
<td>Hazard ratio (95% CI)</td>
<td>0.70 (0.54, 0.89)</td>
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</tbody>
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Impact of results

• First demonstration of survival benefit in advanced Biliary tract cancer

• Benefit gained with no clinically significant added toxicity

• Large, collaborative, randomised studies in patients in rare cancers are feasible

• Cisplatin & Gemcitabine is recommended as a worldwide standard of care and the backbone for further studies
International impact

• ABC-02 publication- cited 1017 times since April 2010
• Cis/Gem adopted in the following guidelines:
  – British Society of Gastroenterology (BSG)
  – European Association for the Study of the Liver (EASL)
  – International Liver Cancer Association (ILCA)
  – National Comprehensive Cancer Network (NCCN, USA)
• 31 clinical trials are open or in development consequent on findings from the ABC-02 study;
  – using cisplatin/gemcitabine as a comparator (n=3),
  – studies with additional therapy coupled to cisplatin/gemcitabine (n=16)
  – second-line studies following failure with cisplatin/gemcitabine (n=6) in advanced disease

7 Valle JW, McNamara MG, Backen AC, Hubner RA; Manchester Academic Health Science Centre Conference; 2014
International impact

- An international collaborative group (International Biliary Tract Collaborators [IBTCC]) has been established following the results of ABC-02
Portfolio of trials

+ Cediranib or Placebo

ABC-03 trial: phase II randomised blinded trial

Cis/Gem
ABC-03 trial

ABC-03 Final Accrual
April 2011 - September 2012

No difference in Progression Free Survival or Overall Survival between the cediranib and placebo-treated patients

Lancet Oncol, Volume 16, No. 8, p967–978, August 2015
Portfolio of trials

ABC-03 trial: phase II randomised blinded trial
+ Cediranib or Placebo

ABC-07 trial: Feasibility/phase II
Vs 6 cycles of Cis/Gem +Stereotactic Body Radiotherapy

ABC-04 trial: phase 1b
+ Selumetinib

Recommended phase II dose - 75mg bd
13 pts in 12 months

BMC Cancer 2016:153
Summary

• First large scale UK led trial in biliary tract cancer

• Demonstrated that trials in rare cancers is possible

• Results from such trials can have clinical impact internationally

• Results of the ABC-02 trial have provided an important foundation on which clinical trials are being designed
Questions

• **Contacts**
  
  Marian.Duggan@ucl.ac.uk (until 27\textsuperscript{th} May) or Sandy Beare
  S.beare@ucl.ac.uk

• **Lead Investigators:**
  Prof John Bridgwater (UCL)
  Prof Juan Valle (Christie)

• **Making a impact in rarer cancers – the ABC02 trial**
  Prof John Bridgewater