

NCRI Bladder Cancer Clinical Studies Group

Membership of the Group rotated in July 2006. 8 members left the Group and 7 new members were appointed. The Group had an interim review by the NCRN on the 16th June. The key strengths of the Group and issues which the Group need to address, as identified by the Review Panel, are attached as an appendix.

Portfolio and accrual

There are currently 7 open trials that are actively recruiting and 2 in set up. The BCON study, one of the largest radiotherapy studies of muscle invasive bladder cancer ever, has just completed recruitment. CTAAC have given approval for continuation of the BC2001 study and It is hopeful that many patients that would have been available for BCON can now be recruited into BC2001.

The ODMIT C study for multicentre, prospective, randomised study to assess the value of intravesical Mitomycin C and to bladder tumours following nephro-ureterectomy for TCC of the upper urinary tract has reached its recruitment number and has closed.

The BSO6 study of pT 1G3 NxM0 has also closed, the first abstract has reported showing no difference in outcome and indeed in general terms, the outcome of patients with this lesion was poor in comparison with reported studies of radical surgery in the world literature.

The EORTC studies of 30986 and 30994 for chemotherapy in patients with advanced metastatic disease remain open and the studies of advice MCM5 and the Pittsburgh study and radiotherapy with weekly Gemcitabine which had been restricted to single or relatively few centres continue to recruit, albeit slowly.

ADVICE is a feasibility study of molecular markers in patients with muscle invasive translational cell carcinoma of the bladder entered into new adjuvant chemotherapy trial.

The BOXIT study, superficial bladder cancer, has received approval and is waiting MREC approval. The SPARE trial involving systemic chemotherapy and comparison of surgery versus bladder preserving treatment with radiotherapy has been approved by CTAAC and the grant award letter will be released once an EU directive sponsorship letter has been received in the CTAAC office. Hopefully it will be recruiting having had MREC approval, in the Autumn.

The accrual had increased in 2005/2006 to 4.3% but given that this was predominantly to muscle invasive bladder cancer studies, the recruitment is nearer 10% of incident muscle invasive disease. However, in the absence of a superficial bladder cancer study, this still falls short of a desired recruitment.

Subgroups

The Group has established two subgroups, the Penile Cancer Subgroup chaired by Dr Jim Barber and the Chemotherapy Subgroup chaired by Dr Ben Mead. The Penile Cancer Subgroup has met and has mapped out parameters for future studies which they hope will involve a sentinel node study surgically and will look for new agents to treat these patients in a phase II setting.

The Chemotherapy Subgroup has also met twice and are pursuing the new molecules via contacts in the pharmaceutical industry in the hope that some phase II

studies in metastatic or locally advanced bladder cancer can be initiated. It is hopeful that a positive outcome will be reported and studies being prepared by the next meeting in the Autumn.

Strategy

The Chairman has responded to the interim review and particular as to whether or not the Group should merge with other urological groups. The three year strategy will likely go in one of two directions;

1. The desired recruitment in the next twelve months will occur, newer phase II studies will become activated and from these quality of life studies as well as incorporation of a Health Economics model will occur and will need to be elaborated over the next three years.
2. Although these studies may start they will stagger and recruit poorly and there would be little to make a case not to re-organize and re-integrate the bladder studies group into a larger urological grouping.

Bladder Group Portfolio

Acronym	Title of Trial	PI(s)	Status
ADVICE Study	A Feasibility study of molecular markers in patients with muscle invasive transitional cell carcinoma of the bladder entered into Neo-adjuvant chemotherapy trial	Professor Nicholas James	Open
BA11 [EORTC 30987]	Randomised phase III study comparing Paclitaxel/Cisplatin/ Gemcitabine and Cisplatin/Gemcitabine in metastatic or locally advanced urothelial cancer without prior systemic therapy	Dr Michael Leahy	Closed
BC2001	2x2 Factorial Randomised Phase III Study comparing Standard versus Reduced Volume Radiotherapy with and without synchronous Chemotherapy in Muscle Invasive Bladder Cancer	Dr Robert Huddart, Dr Nick James	Open
BCON	A Multicentre Randomised Trial of Radical Radiotherapy with Carbogen in the Radical Radiotherapy of Locally Advanced Bladder Cancer	Dr Peter Hoskin	Closed
BCPP (incorporating SELENIB)	Bladder Cancer Prognosis Programme		In Set-up
BOXIT	Randomised trial of Wx-2 inhibitors vs no inhibitors in intermediate and high risk patients who go onto standard BCG maintenance regimes	Mr John Kelly	In Set-up
BS06	A Randomised Study of Radical Radiotherapy in the Management of pT1G3 NxM0 Transitional Cell Carcinoma of the Bladder	Dr Stephen Harland	Closed
CPT11 and Cisplatin for penile carcinoma	International multicentre trial of Irinotecan (CPT11) and Cisplatin (CDDP) in metastatic or locally advanced penile carcinoma (EORTC 30992).	Professor Tim Oliver	Closed
EORTC 30986	Randomised phase II/III study assessing Gemcitabine/Carboplatin and Methotrexate/Carboplatin/Vinblastine in previously untreated patients with advanced urothelial cancer ineligible for Cisplatin based chemotherapy	Dr John Graham	Open

EORTC 30994	Randomized phase III trial comparing immediate versus deferred chemotherapy after radical cystectomy in patients with pT3-pT4, and/or N+M0 transitional cell carcinoma (TCC) of the bladder	Dr Michael Leahy	Open
Gem v Mv	Randomised phase II study of Gemcitabine (Gem) or Methotrexate and Vinblastine (Mv) in advanced transitional cell carcinoma of the urothelium	Dr Poulam Patel, Professor Peter Selby	Open
MCM5	Evaluation of urinary MCM5 as a diagnostic agent in genito-urinary malignancy.	Mr JD Kelly	Open
ODMIT C	A multicentre, prospective, randomised study to the value of a single dose of intravesical mitomycin in preventing the development of bladder tumours following nephroureterectomy for transitional cell carcinoma of the upper urinary tract	Mr Ralph Beard	Closed
Pittsburgh	Pittsburgh study	Mr Raj Persad	Open
RT with Weekly GEM (temp acronym)	Phase II study of radiotherapy with concurrent weekly gemcitabine in muscle-invasive bladder cancer.	Dr Richard Cowan	Open

Mr Peter Whelan, Chair

Appendix 1: Key issues from the Interim Progress Review, May 2006

The Group needs to consider:

- Increasing the overall size of the membership
- Increasing the number of medical oncologists on the Group
- Increasing the number of members with expertise in translational studies, biologically targeted agents and qualitative studies
- The establishment of a Penile Cancer Subgroup
- The possibility of combining with one or more other urological Clinical Studies Groups, and the Chair to discuss this with the chairs of the other urological Clinical Studies Groups (Prostate, Renal, Testis)
- Re-instating a joint annual meeting with the other three urological cancer clinical studies groups (possibly with an overnight stay)
- The analysis and publication of the results from the BS06 trial, which finished recruiting two years ago
- Substantially increasing accrual to trials, which is significantly below target
- Developing a simple pragmatic trial, possibly in superficial disease, to generate momentum within the group since seven of the eleven currently open trials are due to finish in 2005
- The resubmission of the MeGLA and EPIMEC trials to CTAAC
- Developing further trials in advanced/metastatic disease
- Developing links with international groups in addition to the existing ones with the EORTC
- Collaborating with the new development groups