

NCRI Testis Clinical Studies Group

Introduction

The past year has been a period of reflection and re-direction for the Testis CSG following the Group's triennial review this year that supported the direction the Group is pursuing with a greater emphasis on translational and survivorship issues.

The year saw the launch of the first randomized trial in seminoma surveillance (TRISST study, CI Dr Johnathan Joffe) and approval for funding of a translational study in stage I NSGCT (CI, Dr Janet Shipley).

Membership and structure

The Group currently consists of 16 scientific members. The most significant changes in the last year has been the appointment of Dr Jonathan Joffe as the Chair, who after a run in period will take over chairmanship of the Group from summer 2009, and the establishment of a QoL/Survivorship Subgroup under the chairmanship of Dr Jeff White. We are also pleased to welcome Mr Hugh Stevenson as our new consumer representative.

Portfolio and accrual

494 patients were recruited to Testis studies in 2008/09. With a UK incidence 2002-4 of 1899 this reflects 26% of incidence cases. 81 (4.3%) patients entered randomized trials up from 55 (2.3%) the previous year. The high level of recruitment is due in a large part due to our ongoing genome wide association project which has recruited successfully in the last year. There still remains scope to improve randomised trial recruitment and this remains a key aim of the Group.

Table 1: Testis CSG portfolio

Acronym	Title	Status	UK PI
Accelerated BEP	Accelerated BEP chemotherapy for intermediate and high risk metastatic germ cell tumour.	Open	Dr Michael Williams
BEP Continuous Infusional Bleomycin - TE3	A randomised phase III toxicity study of day 2,8,15 Short (30 Minute) versus day 1,2,3 long (72 Hours) infusion bleomycin for patients with IGCCCG good prognosis germ cell tumours	Open	Dr Jonathan Shamash
Familial TGCT	Identification and molecular analyses of families with susceptibility to Testicular Germ Cell Tumour Cancer	Open	Dr Robert Huddart
Gem-TIP	Phase I/II multicentre trial of salvage chemotherapy with Gem-TIP for relapsed germ cell cancer	Open	Dr Ben Mead
Long Term Effects of Chemo on Bone*	An investigation of the long term effect of chemotherapy on bone, particularly focusing on the incidence of osteoporosis in such patients	Closed - in follow-up	Professor Robert Coleman
SIGNIFICANT*	A randomised prospective double-blind, placebo controlled trial of prophylactic oral levofloxacin following chemotherapy for lymphoma and solid tumours.	Closed - follow-up complete	

TE08	A randomised trial of two CT scans Versus five CT scans in the surveillance of patients with stage I teratoma of the testis	Closed - in follow-up	
TE21/EORTC 30983	Randomised phase II/III study of taxol-BEP versus BEP in patients with intermediate prognosis germ cell cancer.	Open	Dr M Sokal
TE22	A study of 18-FDG PET in the prediction of relapse in patients with a clinical stage I non-seminomatous germ cell tumour	Closed - in follow-up	Dr Robert Huddart
TE23	Randomised phase II trial of intensive induction chemotherapy (CBOP/BEP) and standard BEP chemotherapy in poor prognosis male germ cell tumours	Open	Dr Robert Huddart
TER2	Risk of testis cancer in the families of patients with bilateral testicular germ cell malignancy	Closed - in follow-up	Dr Stephen Harland
The Late CT Study	Assessment of the utility of CT follow up in the long term follow up of patients with metastatic non seminomatous germ cell tumour	Open	Dr Robert Huddart
The UK Genetics of Testicular Cancer Study	Identification of testicular germ cell tumour susceptibility genes	Open	Dr Robert Huddart
TIP	A phase II study of paclitaxel, cisplatin and ifosfamide as induction therapy in the treatment of patients relapsing after BEP (bleomycin, etoposide, cisplatin) chemotherapy for patients with metastatic germ cell tumours.	Closed - follow-up complete	Professor Malcolm Mason
TRISST	Trial of imaging and schedule in seminoma testis	in Set-up	Dr Jonathan Joffe

Trials in development

Two studies are currently in set up. The main clinical study is a study of a single cycle of BEP chemotherapy in stage I high risk NSGCT, the 111 study. This study is currently going through ethical and pharmacological review and should open later this year. The other successfully funded study is a translational study looking at prognostic factors in stage I NSGCT [funded by MRC]. This study will follow up on putative prognostic factors identified in a study at the Institute of Cancer Research using clino-pathological material from previous NCR1 studies in stage I NSGCT. A similar translational study in metastatic NSGCT using patients in a number of previous studies is being worked up for funding.

The QoL/Survivorship Subgroup is preparing 2 studies due to seek funding over the next 6 months. One study (TRYMS) that is being developed by Professors Ross' team in Sheffield is in collaboration with ourselves and the Lymphoma CSG will look to at the benefits of hormone replacement therapy in men with low/borderline low testosterone levels. The second protocol (TICKIT) led by Dr Jeff White and his team will address the issue of reported risk of cardiovascular disease in men treated by BEP chemotherapy. This novel study will look at changes in vascular markers and coronary calcification in

this population as a tool to identify at risk individuals to be targeted for secondary prevention.

On the treatment side a study to see if the addition of carboplatin to radiotherapy improves outcomes compared to standard therapy in stage IIA/B seminoma remains in discussion.

Meetings

The Group discussed its portfolio and work at the British Uro-oncology group in September 2009. The Group was also pleased to participate in the 1st joint NCRI Urological meeting in January. This meeting was well attended and allowed the 4 Urological CSGs to share their strategies and discuss cross cutting themes with a significant proportion of the Urological community. The group would welcome the opportunity to participate in further meetings in future years.

Collaborations

The Group is pleased to have developed links with the Teenage and Young Adult CSG and will continue to seek common ground with other CSG's on cross cutting themes in general and on QoL/Survivorship in particular. We are actively seeking international collaborations on our stage I trials. Discussions with the NCIC of Canada in particular are at an advanced stage. Members have also collaborated/are collaborating with European colleagues in a number of pan European initiatives (e.g. in the role of PET scanning in seminoma)

3-year strategy

Our overall strategy is to pursue research in the following domains as agreed in our Group's progress reviews:

- Understanding the biological basis of testis cancer with a strong emphasis on the translational research as a component of clinical trials.
- Improved surveillance and diagnostic imaging in order to detect and manage disease relapse earlier.
- Improving outcome of poor prognosis groups.
- Examination of the issues of long-term toxicity following treatment, including how to best manage this aspect and develop new treatment strategies to minimise these risks without jeopardising improved outcomes.

Over the next 3 years we will continue to develop ideas, with particular emphasis on translational and survivorship protocols (points 1 and 4) which are less well represented in our portfolio. We would look to have at least 1 of the new survivorship protocol and our translational study in stage I NSGCT during 2009 and develop additional protocols during 2010. On the therapeutic side we would expect to complete 3-4 of our therapeutic trials over the next 18 months (TE3, TE23 and accelerated BEP, Gem TIP) with a view to developing the next generation of such studies. Our main focus on the therapeutic side however will be to promote, support and see to conclusion our new stage 1 trials (TRISST, 111 study).

Priorities for next year

The Groups priorities for next year are to:

- Successfully launch the 111 studies and our translational study in Stage 1 NSGCT.

- Complete development of the 2 protocols addressing survivorship issue.
- Complete recruitment to TE23, TE3 and accelerated BEP
- Expand recruitment into TRISST and develop the protocol as an intergroup study with NCIC.

Dr Robert Huddart, Chair

Appendix 1

NCRI Testis CSG 2008/09 Publications and abstracts report

Huddart RA. Survival from testicular cancer in England and Wales up to 2001. *Br J Cancer* 2008;99 Suppl 1:S83-5.

Linger R, Dudakia D, Huddart R, Tucker K, Friedlander M, Phillips KA, et al. Analysis of the DND1 gene in men with sporadic and familial testicular germ cell tumors. *Genes Chromosomes Cancer* 2008;47(3):247-52.

Mai PL, Friedlander M, Tucker K, Phillips KA, Hogg D, Jewett MA, et al. The International Testicular Cancer Linkage Consortium: A clinicopathologic descriptive analysis of 461 familial malignant testicular germ cell tumor kindred. *Urol Oncol* 2009.

Mai PL, Chen BE, Tucker K, Friedlander M, Phillips KA, Hogg D, et al. Younger age-at-diagnosis for familial malignant testicular germ cell tumor. *Fam Cancer* 2009.

Rapley EA, Turnbull C, Al Olama AA, Dermitzakis ET, Linger R, Huddart RA, et al. A genome-wide association study of testicular germ cell tumor. *Nat Genet* 2009;41(7):807-10.

ASCO Abstracts 2008

R. T. Oliver, G. M. Mead, P. J. Fogarty, S. P. Stenning, for the MRC TE19 and EORTC 30982 trial collaborators. Radiotherapy versus Carboplatin for stage I seminoma: updated analysis of the MRC/EORTC randomised trial (ISRCTN27163214), *Proceedings of ASCO 2008, abstract #1. [oral-plenary]*

G. Mead, S. D. Fossa, R. T. Oliver, P. J. Fogarty, P. Pollock, S. P. Stenning, for the MRC and EORTC trial collaborators. Relapse patterns in 2466 stage 1 seminoma patients (pts) entered into Medical Research Council randomised trials. *Proceedings of ASCO 2008, abstract #5020 [oral]*

ASCO abstract 2009

S.J Harland, R. Welch, R. Huddart, S. Stenning, P. Pollock, R. Gabe On the necessity for postchemotherapy surgery for residual abdominal masses in metastatic germ cell tumours (NSGCT) of testis Proc of ASCO 2009 *JClin Oncol suppl 27 No 15S p255s [Poster]*