

NCRI Sarcoma Clinical Studies Group

The Group has continued to work well throughout 2005/6. The main events for the Group have been the long awaited opening of the EURAMOS trial for osteosarcoma and the agreement to fund VORTEX, a radiotherapy volume trial for extremity sarcomas. During the year the group was peer reviewed and as a direct result of that, the group held a 2-day "away day" to discuss the future strategy of the Group.

Membership

Membership of the group: Mr A Abudu and Dr B Seddon joined the group during the course of the year. A number of members of the group including the chairman were rotated/reselected in the summer of 2006. 5 Members left the Group and Mr Rob Pollock, Mr A Abudu, Dr David Hughes and Dr Lucinda Billingham were appointed as new members. As a result the CSG now comprises of 4 medical oncologists, 2 clinical oncologists, 1 pathologist, 4 surgeons 1 statistician and 2 paediatric oncologist. We have 2 very active consumer representatives. Mr Grimer was reappointed as chair for a further 3 years in June 2006.

Portfolio and accrual

The current open studies are:

EURAMOS – a randomised trial of chemotherapy in operable osteosarcoma. This will be the largest trial of osteosarcoma ever attempted in the world and is a huge collaboration between Europe and North America. The trial is now open for recruitment and accrual is going according to plan in the UK.

EUROEWING – a randomised trial for patients with Ewing's sarcoma. Accrual is going largely according to plan and the plans for future trials are being drawn up.

EORTC 62012 – a trial of chemotherapy in advanced soft tissue sarcoma. Accrual is going as planned.

EORTC 62911 – a trial of radiotherapy in inoperable fibromatosis.

In 2005/6 just over 5% of all patients with sarcomas were entered into trials – with the opening of EURAMOS And VORTEX this should increase to 20%+ over the next year .

In terms of trials in set up; VORTEX – is a trial comparing volumes of radiotherapy in patients following resection of high grade soft tissue sarcomas. A biobank has been funded as part of this study and will be based in Christie's Hospital in Manchester. There is a large quality of life element to this study, which should potentially accrue up to 50% of all patients with soft tissue sarcomas patients in the UK once it is up and running.

New papers of the analysis of B006 (the previous osteosarcoma study) and EICESS 92 (the previous Ewing's study) have both been submitted for publication. The EICESS study showed a significant difference in survival between patients treated in Germany and in the UK and as result of this, the Group are planning to have a workshop investigating potential reasons for this, which is thought to be largely due to differences in local management of the primary tumour.

The Group have discussed several future studies. A trial of chemotherapy in patients with synovial sarcoma has been compiled in conjunction with paediatric oncologists as many patients with synovial sarcoma are in the paediatric/adolescent age group.

There remains controversy as to the optimum follow up for patients with sarcomas and the Group have carried out an analysis of current practice in the UK. This has been the source of an article submitted for publication. There is wide variance in follow up but there is some difficulty in constructing a randomised trial. We hope to do some modelling to propose an optimum follow up strategy with patients with sarcomas. There is continuing interest in trials for GIST and new studies are planned. The Group is planning to submit an application for funding to do a phase 2 study of oestrogen resector blocker drugs in advanced chondrosarcoma. The Group are planning to collaborate with the Italians in carrying out a phase 2 study of drug treatment of advanced chordoma.

Strategy

As a result of the away day, attention was focused on the trials which we realistically believe that we can produce in the next three years and other measures, which can be taken to improve outcomes for patients with sarcomas. We note that the NICE guidance has recently been produced which confirms the importance of early diagnosis and prompt referral to a treatment centre for patients with sarcoma. The group strongly believes that centralisation of care will lead to increased entry into clinical trials and thus, having a portfolio of studies suitable for most patients with a sarcoma is to be desired. Studies which the group are going to be working on over the next few months include:

- A phase 2 study of Sunitinib in patients with angiosarcoma, a phase 3 study of Gemcitabene/Docetaxel v Doxorubicin in patients with advance soft tissue sarcomas.
- PET scanning as a staging tool will be investigated.
- The group is going to form a translational sub group so that key workers on translational research can be linked to the sarcoma GST.
- In conjunction with the Complementary Therapy CSDG, we would be working to look at the role of acupuncture in post amputation pain.
- We hope to develop trials of proteomics as predictors of outcome in soft tissue sarcomas.

The Group has an ambitious agenda for the next three years. Confirmation during the course of the year that two clinical trial units would receive funding to support the sarcoma group has been most welcome. The CTUs in Birmingham and UCL have received funds to assist the work of the CSG and we will continue with them to develop clinical trials for patients with sarcoma.

Sarcoma Cancer Group Portfolio

Acronym	Title	PI(s)	Status
Adjuvant Glivec in GIST (EORTC 62024)	Intermediate and high risk localized, completely resected, gastrointestinal stromal tumors (GIST) expressing KIT receptor: a controlled randomized trial on adjuvant Imatinib mesylate (Glivec) versus no further therapy after complete surgery.	Prof Penella Woll Dr Paolo G. Casali	Open
BO06	A Randomised Trial of pre-operative and post-operative		in follow-up

	doxorubicin plus cisplatin at standard dose or increased dose intensity with Granulocyte Colony-Stimulating Factor (G-CSF) in Operable Osteosarcoma		
EORTC 62012	Randomised trial of single agent doxorubicin versus doxorubicin plus ifosfamide in the first line treatment of advanced or metastatic soft tissue sarcoma.	Prof Ian Robert Judson	Open
EORTC 62931	Randomized phase III trial of adjuvant chemotherapy with high-dose doxorubicin, ifosfamide and lenograstim in high grade soft tissue sarcoma.	Prof Penella Woll	In follow-up
EORTC 62991	Phase II pilot of moderate radiotherapy for inoperable aggressive fibromatosis	Dr Martin Robinson	Open
ET 2000 03 (EURO-E.W.I.N.G. 99)	European Ewing Tumour Working Initiatives of National Groups: Ewing Tumour Studies 1999	Prof Ian Robert Judson Dr Ian Lewis	Open
EURAMOS 1	A randomized trial of the European and American Osteosarcoma study Group to optimize treatment strategies for resectable osteosarcoma based on histological response to pre-operative chemotherapy	Dr Sigbjørn Smeland Dr Neyssa Marina Dr Stefan Bielack	Open
Gemcitabine and Docetaxel in leiomyosarcoma	A phase II trial to assess the activity of Gemcitabine and Docetaxel as first line chemotherapy treatment in patients with unresectable leiomyosarcoma	Dr Beatrice Seddon	Open
SC20	A phase III international randomised trial of single vs. multiple fractions of re-irradiation of painful bone metastases.	Ms Orla Cummins	Open
VORTEX	Randomised trial of volume of post-operative radiotherapy given to adult patients with eXtremity soft tissue sarcoma	Dr Martin Robinson	in Set-up

Mr Rob Grimer, Chair

Appendix 1: Key strengths and issues from the Interim Progress Review, September 2005

Strengths:

- The good working linkage between the CSG and the EORTC Group.

The Group needs to consider:

- The link with the EORTC Sarcoma Group and how best the CSG can establish a clear role for itself and develop its own trials
- Developing sufficient critical mass
- Addressing issues of poor attendance at Group meetings
- Appointing additional pathologists, radiologists and translational scientists and individuals from key sarcoma centres not currently represented
- Opening up membership to young enthusiastic academics to champion particular trials or to find new drugs and develop new trials
- The establishment of a phase II subgroup
- The extent to which the CSG and the Bone Sarcoma group remain distinct
- Developing a broader range of studies e.g. QoL, psychosocial, early diagnosis, follow up, epidemiology and phase II studies
- Developing studies in radiotherapy for osteosarcoma with marginal excisions, radiofrequency ablation and cryotherapy trials and studies of the significance of measures of co-morbidity in survival
- Meeting with new agent development expertise to consider which phase II studies to prioritise
- Developing translational studies where possible
- Linking with a sister CSG with a strong tradition of translational studies and identifying a mentor for a named individual within the Group charged with leading on the development of translational studies
- The next adjuvant trials in soft tissue sarcoma, osteosarcoma and Ewings sarcoma
- An overnight or away day to plan strategy