Minutes from SSG Working group meeting Nov 28-30th, 2010 Copenhagen

Bone Sarcoma Studies

OSTEOSARCOMA

EURAMOS-1

By Oct 2010, 2005 patients (ñptsò) have been registered, and 1151 pts are randomized. The number of pts registered is according to plan, but less than expected is randomized (~57 % vs. 90 %). From SSG 103 pts (5%) have been registered. The Trial steering committee has decided to continue the study through April/May 2011 to reach 1260 randomized pts. So far 13 SUSARs have been reported, of which 9 are related to MTX administration. More cardiotoxicity are reported in the MAPIfn arm compared with to the other arms. Underreporting in the control arm or longer reporting period in the test arm are possible explanations. The reported toxicity including treatment related death is not higher than expected.

Next study: All participating inter-groups recognize EURAMOS as an important structure for future randomized trial in osteosarcoma, and thus support continued collaboration. A new protocol, EURAMOS-2 however, is not ready to start. A three armed design study to evaluate whether the addition of muramyl-tripeptide to standard chemotherapy with MAP improves EFS and OS would be a very important issue, but funding of MTP by Takeda (producing MTP) for this study design will not be offered. MTP was approved in Europe by EMEA 2009 for use by localized osteosarcoma patients younger than 30 years.

Previous trials have failed to define a clear advantage for MTP in osteosarcoma. There is consensus among the international bone sarcoma groups, including SSG, to not add MDP to standard chemotherapy in OS. No decisions regarding next studies have been taken, and the discussions will continue among the international groups.

Probably no new protocol will be available when the EURAMOS-1 closes during spring.
Until the next study is ready to start, SSG has decided that standard chemotherapy for osteosarcoma in Scandinavia should be: MAP, the short arm in EURAMOS-1, to both good and poor histological responders, and by localized or metastatic disease.

Sigbjørn Smeland reported that he would not assume any new responsibilities as part of SSG trials, but will fulfill his obligations in ongoing projects such as EUROBOSS (2001), EURAMOS-1 (2002), ISG SSG IV (2000) and LIVESTRONG (2008). Many thanks to Sigbjørn for his strong drive, and important contribution in putting SSG on the map regarding international collaboration on bone sarcoma trials. K.Sundby Hall will replace Sigbjørn in international committees and participate in the protocol writing group for EURAMOS-2. Additionally, Kirsten Sundby Hall, Mikael Eriksson and Catherine Rechnitzer will participate on behalf of SSG in overseeing the Euramos strategy group. The purpose of the group is to conceive new studies and be responsible for core strategic policy of the overarching EUROMOS group.
There will also be a translation biology study closely connected to EURAMOS-2, and Ola Myklebost is representing SSG. Study-specific investigations and storage of specimen are the main goals.

EUROBOSS

Collaboration between ISG, COSS and SSG. The protocol covers a heterogeneity regarding histologic subtypes and stage of high-grade bone sarcomas in pts older than 40y. EUROBOSS is the biggest prospective trial in this category of patients. In contrast to younger patients 30 % have experienced dose reduction and a high incidence of neurotoxicity is reported. Good survival results are reported in high-

grade, MFH and osteosarcoma, with localized disease (OS: 47 % 3y EFS in 56 pts) and dismal outcomes in metastatic patients even after radical metastasectomy (no pts disease-free at 3y). The study will be ongoing until 12/2012, if not replaced by EURAMOS-2 at an earlier date.

EWINGS SARCOMA

The results of ISG/SSG III have recently been published in Annals of Oncology Nov 8, 2010. The most important conclusion is that high-dose chemotherapy with stem cell support improves survival in pts with a poor response to induction chemotherapy. ISG/SSG IV (metastatic disease) with 100 pts recruited was closed, Oct. 2009. In an abstract at CTOS meeting Nov 2010, Ferrari et al. showed a 4-years over-all survival rate of 65% for those who received HDCT. Some data are lacking from the SSG patients, and the relevant centers are requested to send their data as soon as possible to the SSG-secretariat, Lund. S. Ferrari is preparing the results for publication.

SSG has no ongoing trials for Ewing sarcoma. SSG has been invited by ISG to participate in their new protocols for localized and metastatic Ewing. The bone sarcoma group and SSG Board have earlier this year discussed the protocols and have found no strong advocates for participation. The opinion of SSG is that the results of ISGSSG III study (the old protocol) are so good that this protocol is considered standard chemotherapy for localized Ewing sarcoma.. The results of high-dose therapy in advanced Ewing sarcoma are still uncertain, and we are anxiously awaiting the final results of ISGSSG IV.

EWING 2008 (a continuation of EURO-E.W.I.N.G. 99) is recruiting slower that anticipated, totally 85 patients. Most active groups are GPOH (Germany, Austria) and COG (recruits to R2pulm). Discussions with COG are ongoing regarding a prospective study on preoperative treatment in EWING 2008, given as a compressed regimen (18 weeks) randomizing between VIDE x 6 and VDC/IE x 9. SSG will closely follow this discussion.

SSG treatment recommendations for Ewing sarcoma: Previously SSG has recommended ISG/SSG III as standard therapy in localized disease based on the convincing results of the ISG/SSG III study. For metastatic disease the role of HDCT is not confirmed and the SSG recommendation for standard therapy is for **any** metastatic disease:

1. ISGSSG III Good responder arm (without HDCT)

or

2. Control arm (R2) in Ewing 2008; 6 courses of VIDE followed by 8 courses of VAI

Oslo 09.12.2010
Kirsten Sundby Hall
Sigbjørn Smeland