SSG Working group meeting Dec 2-4, 2012, Malmø

Report from the Oncology subcommittee

Bone and soft tissue sarcoma (K. Sundby Hall, Mikael Eriksson)

BONE SARCOMAS

EURAMOS-1

The protocol was closed June 30, 2011. In total 2260 patients have been included and 1309 randomised. From SSG, 119 patients were included. It is expected that the results of the good response arm will be available March 2013, while those from the poor response arm will be available late 2013. Until a new protocol is ready, the good response arm (without interferon) is the preferred method of treatment utilized by SSG and most other EURAMOS partners. However, there have been no decisive developments regarding the plans for a new protocol, **EURAMOS-2.** Similarly, two drugs have been thoroughly discussed for testing as add on to adjuvant chemotherapy:

1. Mifamurtide, which Takeda has refused to support as part of a new Euramos-2 protocol. While Mifamurtide has been approved in many European countries, there is still an international concensus across the largest osteosarcoma groups and the National Institute of Health that additional investigation is needed before this expensive drug can be recommended for routine use.

2. Zoledronic acid (Z): After the negative response from the COG scientific committee to test Z in a randomized study with chemotherapy, the Euramos collaborative group has no plans to proceed with this drug. However, the concept of randomized addition of Z to chemotherapy is investigated by the French sarcoma group, and other groups are welcome to participate in this work. The French has omitted anthracyclines in the osteosarcoma treatment, but they plan an amendment to the protocol, allowing any standard chemotherapy, e.g. MAP. This approach could have been utilized by SSG in its treatment of patients. However, agreement was reached within the oncology group to await the results of Euramos-1 before entering into a formal collaboration with the French.

KSH, ME and Catherine Rechnitzer are actively participating in the “Euramos strategy group”, with participants from the four groups cooperating in Euramos-1 and some other European groups (Spain, Italy, France). They are conducting regular telephone conferences and meetings in connection with ASCO and CTOS to keep each other updated of on-going projects, hopefully leading to a new collaborative study in the future.

(Later in the Euramos-1 newsletter for Dec 2012 it was reported that the results of the good-response arm will be available late 2013 and for the poor-response arm not before 2015).

EUROBOSS (bone sarcomas 40-65 y)

Closure of the protocol is postponed to Dec 2014. In total, 366 patients are included, among them 230 patients without metastases at diagnoses. SSG has recruited 60 patients, COSS 159 and ISG 147. Dr. Miriam Wilhelm, a young doctor at the COSS office, showed in an abstract (at a haematology/oncology congress in Stuttgart Oct 2012) that by surgical complete remission, five years total survival is 70% and event free survival is 49%. About 30% of patients will need a dose reduction due to toxicity.

MODUFOLIN

The Swedish company Isofol has developed an active metabolite to leucovorin (Modufolin), with a potential improvement for the rescue after high dose Methotrexate in osteosarcoma, and wish to involve SSG centers for a pilot project. Many oncologists argued for the need for more pharmacokinetic studies. Discussions with the firm will continue.

EURELOS

Eurelos is a collaboration with COSS and ISG, with the aim of collecting data of different treatment results for recurring osteosarcoma. The oncology group has agreed to participate, but necessary applications has not been completed, and the organizational details surrounding SSG participation have not yet been fully agreed upon. KSH and ME will push this process forward.

EWING SARCOMA

The protocol ISG/SSG III is still used as standard treatment for localized disease in SSG (except the Swedish pediatricians). The data was published in early 2011 in Annals of Oncology. The data from ISG/SSG IV (metastatic Ewing) was published in Annals of Oncology 23;2970-2076, 2012. SSG had recruited 20 patients and ISG 82 patients. The median follow-up for survivors was 62 months (range 24–124). The 5-year EFS probability was 0.43 and the 5-year OS probability was 0.52. The most important prognostic factors for poor prognosis were (i) a poor histological or radiological response at the primary tumor site and (ii) an incomplete remission of lung metastases after primary chemotherapy.

The oncology group agreed that these results should influence SSG`s

treatment strategy in the future. The protocol ISG/SSG IV, including HD-BuMel and total lung irradiation, should be used as standard treatment for metastatic Ewings sarcoma for selected patients, provided the following were observed after primary chemotherapy: 1. a good response at the site of primary tumor 2. complete remission of lung metastases. This treatment strategy will be defined as standard treatment on www.ssg-org.net

The Swedish pediatricians have recently formerly joined the new version of the Euro-E.W.I.N.G.-protocol. SSG is participating in a significant ongoing European EU application process for various studies in Ewing`s sarcoma. The studies on new drugs would probably be of most interest for SSG. KSH will, together with Lars Hjorth, participate in a meeting regarding these opportunities later in December 2012.

Stefano Ferrari has, on behalf of the Italian sarcoma group, proposed a follow-up study with collection of data on ISG/SSG III and IV patients. Several variables which have not previously been collected are needed. SSG centres that have recruited patients into these protocols will be contacted from the SSG office. The oncology group agreed to participate in this follow-up study, not only for the purpose of conducting follow-up of the patients, but also for maintaining the collaboration with ISG. KSH and Kjetil Boye will be the driving forces.

LONG TIME MORBIDITY AND SSG`S GUIDELINES FOR FOLLOW-UP

The proposed written information for patients and their primary care doctors will be put on www.ssg-org.net . The form can serve as template and be modified by the oncologist according to the various needs for information.

SOFT TISSUE SARCOMA

SSG XX

The adjuvant trial for soft tissue sarcomas in extremities and trunk wall is running without any major problems. In total, 143 patients (of 158 planned) have been registered in the study. Pathological review has been performed for 80 patients so far. The main analysis will be performed 2 years after inclusion of the last patient, hopefully culminating in a publication by 2015. The publication will be part of the doctoral thesis by Marie Ahlstrøm, Lund.

NEW ADJUVANT PROTOCOL

SSG is invited by the Italian sarcoma group to join its new adjuvant protocol, comparing standard neo-adjuvant chemotherapy in STS with histiotype-based therapy. This treatment could possibly be an alternative when SSG XX is fully enrolled. The opinions of the oncologists were somewhat divided, and many were sceptical of participation.

NEW PROTOCOL FOR FIBROMATOSIS

For many years a phase II trial on the use of Multiferon in fibromatosis (desmoid tumors) has been discussed within SSG. These discussions have motivated the involvement of an Oslo-based CRO company, Smerud Medical Research International AS, and an application for EU funding. The application, Eurostar, has been submitted, and a decision is expected later this month. Pending the decision, SSG will consider cooperating with Smerud and the Swedish company SOBI, which owns and produces Multiferon. Jan Peter Poulsen at Radiumhospitalet, will function as the primary investigator. Further work with a protocol is necessary with participation by radiologist, pathologist and orthopedic surgeon.

RECRUITMENT OF ONCOLOGISTS- WHAT ARE THE PROBLEMS?

During the discussion, it became evident that there is not only shortage of medical oncologists in the sarcoma fields, but also pathologists and radiologists. The discussion concluded with the following: On behalf of the SSG board, ME, JE and KSH will write a letter to the 6 RCCs in Sweden and express SSG`s great concern of the situation, and that the leaders of the RCCs must give preference to education of sarcoma specialists and increase the number of positions for sarcoma doctors. In Norway SSG`s concerns will be included in the national guidelines for treatment of sarcoma (a revision of the guidelines is planned in 2013).

CHAIRMAN, SUBCOMMITTEE : ONCOLOGY-RADIOTHERAPY

Nina Jebsen replaces Øyvind Bruland, Jacob Engellau(JE) continues.