SSG Working Group Meeting

November 30, 2020

Teams

Minutes from the Oncology Group

The meeting was web-based on the Teams platform due to the corona pandemic. The coordination of the meeting was done from Lund by Eva-Mari Olofsson and Jacob Engellau. Representation was good with a total of 30 members present from the SSG-centers in **Sweden** in Lund, Gothenburg, Örebro, Stockholm, Uppsala, and Umeå, In **Norway** from Oslo, Bergen and Trondheim, From **Iceland** in Reykjavik, **Denmark** in Copenhagen and Aarhus and **Finland** from Turku.

1. Jacob Engellau (Lund) opened the meeting with guidelines for the digital format to ensure an optimal meeting in a digital form. English had been agreed to be the spoken language.

2. Kjetil Boye (Oslo), chairman for the Medical Oncology group. The SSG-bylaws state that the chairmen for the working groups are to be (re)elected every 5 years. However, due to the current limitations caused by the corona pandemic, Kjetil has agreed to stay on as chairman for the Medical Oncology group until we have an opportunity to meet in physical form. In Iceland, Olöf Bjarnadottir, previously in Lund but now returned to Reykjavik, has become responsible for soft-tissue and bone sarcomas, and was welcomed into the SSG-community.

3. Akmal Safwat (Aarhus), chairman for the SSG, introduced the issue of the planned SSG congress in Tampere April 21-23, 2021. Due to the corona pandemic, the meeting will not be held as planned, and different options for a solution and alternative was discussed. In principle, two alternatives were seen as possible solutions.

    1. Postponing the congress 1 year to April 2022, maintaining the location in Tampere, the planned program and invited speakers. The working group meeting in December, 2021 will then be held as usual, perhaps again web-based depending on the pandemic circumstances.
    2. Postpone the congress to October 6-8, 2021, attempting to maintain the program with the invited speakers, if they are available also then. The working group meeting December 2021 would then be shifted to January, 2022.

Overall, there were arguments supporting both options, although option 1 had the strongest support. A decision will be forthcoming following discussions with the organizing committee in Tampere and the next SSG Board-meeting, after which Akmal will give notice to the SSG.

4. New Ewing sarcoma protocols – Kjetil Boye. Not much has happened since the last working group meeting. Deliberations within and between the two European protocols not-yet launched continue. The protocols are not yet fixed and have over time become less divergent.

    1. **EE20XX**, a United Kingdom initiative with Bernadette Branding as principal PI. The EE20XX has no funding for the protocol yet. The protocol is based on Standard chemotherapy but with three randomizations addressing a benefit of;
    R1: adding a TKI to the standard chemotherapy regimen.
    R2: randomizing between standard radiotherapy, or a dose-escalation, and,
    R3: randomizing between no maintenance therapy, or adding a maintenance treatment following the end of standard post-operative treatment.

2. **iEuroEwing**, a continuation of the Euro Ewing group, with Uta Dirksen in Essen as PI. The iEuroEwing protocol has funding arranged. Also this protocol has standard chemotherapy as its core, and in the previous version the investigational aspects addressed a possible benefit in two alterations. A revised protocol has not been circulated yet.
   R1: a randomization between adding ponatinib to standard chemotherapy, and,
   R2: randomizing between adding Temozolamid-Irinothecan (TemIri) to standard chemotherapy.

In the discussions that followed, the importance of a common commitment from both pediatric-and-adult tumor groups in the Nordic countries was stressed. Also, the importance of a secured funding for the per-protocol treatment and follow-up was underlined. The time-to-definitive local treatment was discussed. The benefit of adding TemIri is under question which may make this a less attractive option. For historical reasons, and established working relationships the Danish SSG-centers have decided to follow the UK initiative and the pediatric oncologists in Sweden are leaning towards the iEuroEwing protocol. But, as of the protocols are yet finalized, the SSG-Oncology group did not settle for any of the options at the meeting. There is to be a EEC (European Ewing Consortium) meeting in January 2021, after which more details may then be presented.

5. DOREMY, Nina Jebsen (Bergen) presented the results from the now closed study on myxoid liposarcomas (mLPS). The study stems from The Nederlands Cancer Institute (NKI), with Rick Haas as principal investigator. Sweden and Norway participated, but only Norway contributed with patients. The question addressed was whether a lower pre-operative RT-dose of 36 Gray in 18 fractions is equally effective as the standard of 50 gray in 25 fractions with a primary end-point of pathological response of >50% necrosis, secondary endpoints being frequency of post-operative complications, local control, acute- and late toxicity, and overall survival.
   The results have very recently also been published:

   Dose Reduction of Preoperative Radiotherapy in Myxoid Liposarcoma: A Nonrandomized Controlled Trial. *Jules Lansu et al. JAMA Oncol. 2020 Nov 12.*

   The results are compelling, with 100% local control at a median f-u of 3 years, little toxicity, and post-operative complications and support a change in the SSG recommendations. For myxoid liposarcomas, these would henceforth be as follows:

   1. RT to 36 Gy/18 f for mLPS if pre-operative RT is indicated.
   2. Primarily for moderate-to-high grade tumors, and deep-seated location.
   3. There is a risk of inadequate surgical margins irrespective of tumor grade.
   4. If resection of a local recurrence would result in mutilation/amputation/significant functional sequelae.

   More results will be published when the f-u is longer, but with the low incidence of acute and late radiotoxicity, and the impressive local control rate at 3 years, there seems to be a strong case for pre-operative radiotherapy in mLPS.

6. Clarification of SSG treatment policy for:

    1. Denosumab in GCTB, Jacob Engellau raised the need for compiling our experiences of the use of denosumab in GCTB now some 12 years since it was first introduced. Lately, several publications have come in which both treatment strategies, and potential pit-falls are addressed. Notably are:

        i. **Current concepts in the treatment of giant cell tumor of bone**.
        Van der Leiden L. et al.
        Current Opinion in Oncology, 2020, 32(4):332-338
        ii. **Denosumab in giant cell tumor of bone in the pelvis and sacrum. Long-term treatment or bone resection.**
        Sambri A., et al.
        Journal of Orthopaedic Sciences. 2020, 25: 513-519.
        iii. **Denosumab in giant cell tumor of bone: Current status and pitfalls.**
        Li H., et al.
        Frontiers in Oncology. October 2, 2020

    There is a need to clarify denosumab in the context of the neo-adjuvant, adjuvant and definitive setting. Also, how to manage non-adequate responders. More detailed as:

- Selection of patients for neo-adjuvant denosumab
- Length of neo-adjuvant denosumab befor surgery
- Evaluation of response
- Inadequate responders-when to re-biopsy
- Malignant transformation, what is the SSG experience?
- Long-term treatment. How long is long-term? Dosage and f-u?
- A topic for the next SSG Congress?

    The discussion did not reach a conclusion, but Jacob Engellau offered to do a literature search and suggest recommendations for a later meeting to decide on. Difficult cases were also discussed.

    2. New medical treatment strategies for STS/BS – Kjetil Boye gave the current background from published results of studies on checkpoint inhibitors. The treatment practices in different centers are not harmonized, and some centers have implemented new targeted drugs and immunotherapy, some centers to a lesser degree. To summarize, the topic may be referred in the following SSG policy proposal:

- Undifferentiated pleomorphic sarcomas (UPS)
    - ✓ PD-1 inhibitors have a demonstrated efficacy as monotherapy
    - ✓ No evidence for an increased effect of combinations
- Alveolar Soft Part Sarcoma (ASPS)
    - ✓ There is evidence for the efficacy of PD-1 inhibition, or PD-L1 inhibition
    - ✓ Support for PD-1/PD-L1 inhibition in combination with axitinib
- Angiosarcoma (AS)
    - ✓ Support for PD-1 inhibition as monotherapy for AS in head & neck and scalp
    - ✓ Unclear of the efficacy in other AS; other regions and RT-induced.
- A need for the SSG to cooperate with European studies in other subtypes.

    Kjetil Boye will take the responsibility for preparing a draft for SSG recommendations on checkpoint inhibitors in sarcoma and circulate it to the group.

7. Plenum discussion: Changes in activities in clinical sarcoma trials during the covid-19 pandemic. Nina Jebsen introduced the discussion by giving a background of the changes in provisions for clinical trials in general, and for early clinical trials (phase 1) in particular. Worldwide, the pandemic has resulted in a shift of resources from clinical trial units to core hospital care. This ha led to an increased interest from pharmaceutical companies to conduct early clinical trials in the Nordic countries. Nina is involved in NORDIC NECT (Nordic Network for Early Clinical Trials), a collaborative effort in the Nordic countries to make this region more attractive for early clinical trials.
   A center-by-center survey was carried out in the meeting of the consequences we have experienced during the current pandemic at respective center. No conclusive results, but the importance of closer collaborative efforts was evident. As an organization, the SSG currently lacks a format for facilitating such collaborations between representatives at the respective SSG-centers, and clinical trial units in the larger centers.

8. No other topics were broached

9. The meeting was summarized by Kjetil Boye. The minutes to be compiled by Jacob Engellau and, following review by Kjetil, sent out to the members in the SSG Oncology group.

10. The meeting was closed