

# The 36<sup>th</sup> Meeting of the Scandinavian Sarcoma Group

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## Abstracts

## **L1 Identification of new targets and combinations in the treatment of rhabdomyosarcoma and Ewing's sarcoma.**

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We have documented a crucial role for IGFIR signaling in several paediatric sarcomas. These studies, along with the development of fully human IGFIR antibodies led to clinical testing of these blocking antibodies in rhabdomyosarcoma, Ewing's sarcoma, and osteosarcoma, along with a variety of other sarcomas. In general these single agent Phase studies showed objective responses rates below 20%. Furthermore, responding patients typically had relatively short-lived duration of response.

Our preclinical models using rhabdomyosarcoma xenografts treated with IGFIR antibodies predicted short duration responses that mimicked the clinical observations. We have begun to dissect the mechanisms of acquired resistance in our preclinical models. We found that Akt is rapidly re-activated in the setting of persistent IGFIR down-regulation, and this can be somewhat abrogated by mTOR inhibition. Furthermore, in both rhabdomyosarcoma and Ewing's sarcoma, the Src-family kinase (SFK), YES, is rapidly activated upon IGFIR blockade, suggesting a bypass resistance mechanism, and combination SFK inhibitors plus IGFIR blockade leads to more durable responses in both rhabdomyosarcoma and Ewing's sarcoma xenografts.

A typical example of a cancer-specific translocation driven tumor is the EWS-ETS (typically EWS-FLI-1) fusion oncoprotein seen in the overwhelming majority of Ewing's sarcomas. This fusion transcription factor leads to aberrant transcriptional activation or repression of a battery of genes, but the critical downstream targets necessary for tumorigenesis remain elusive. While transcription factors are in general felt to be non-druggable, several groups including ours have begun to screen for inhibitors of the activity of the EWS-FLI-1 mutant transcription factor, and I will discuss our identification of mithramycin as a candidate EWS-FLI-1 inhibitor. In addition, PARP inhibitors have been shown to target mutant ETS transcription factors and I will discuss our data demonstrating PARPi effects of EWS-FLI-1 transcriptional activity and proposed clinical trials of PARPi in Ewing's sarcomas.

## **L2a Surgery or not in Ewing's sarcoma of the spine, sacrum and pelvis. A Scandinavian sarcoma group experience**

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**Purpose:** The importance of surgical treatment for Ewing's sarcoma (ES) of the spine, sacrum and pelvis remains a highly contested issue in bone sarcoma. We investigated local control rate and survival in relation to treatment.

**Methods:** Patients with ES of the spine, sacrum, and pelvis, diagnosed between 1986 and 2009, were identified through the Scandinavian Sarcoma Group registry. Data regarding local treatment (surgery and/or radiotherapy), local recurrence, and overall survival were analyzed and compared between the 3 locations of tumors.

**Results:** 123 patients with ES in the spine (24), pelvic bones (74 patients), or the sacrum (25 patients) were identified. For patients with ES localized to the spine or pelvis, 2/3 underwent surgery, some with additional radiotherapy. In comparison only 1/10 of patients with an ES in sacrum underwent surgery. Local tumor recurrence was detected in 1/5 spine tumors but only 1/20 sacral or pelvic tumors. All patients with local recurrence eventually died in metastatic disease. Overall survival was 60% in patients with ES in spine or sacrum, but only 30% in patients with pelvic tumors.

**Interpretation:** The choice of local treatment of ES in spine or pelvis was not related to outcome (local recurrence rate and overall survival) in this cohort. This provides further proof that surgical treatment does not significantly affect outcome of ES in these sites. Radiotherapy alone appears to be sufficient as local treatment for ES of the sacrum. Our data is suggestive of the reigning dogma of local treatment in Ewing's sarcoma, i.e. local excision is indicated, preferably with at least marginal margin, if it can be performed without significant loss of function.

## L2b Surgery or radiotherapy for Ewing's sarcoma

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**Background:** Ewing's sarcoma (ES) is highly responsive to external beam radiation therapy (EBRT) and often occurs in bones not easily resected. Hence, radiotherapy is an integral part of multimodal treatment and is used in approximately 60% of ES patients. The radiation doses needed to sterilize microscopic and macroscopic ES are in the 40 and 50 Gy levels, respectively. Hence, normal tissue tolerances of most adjacent normal organs can be respected. EBRT is used postoperatively in close or positive resection margins and following poor tumor response to neo-adjuvant chemotherapy. EBRT as definitive local treatment is typically used instead of surgery when tumors cannot be radically removed or where surgery results in serious morbidity. In ES an often discussed, but still not proven hypothesis, is that EBRT is equally effective as surgery regarding local tumor control with equivalent overall survival when given sequentially together with an effective multi-drug chemotherapy regimen

**Methods:** Review of the literature and clinical examples of definitive EBRT from our Institutions will be presented. Attempts will be made to gain updated information from the SSG Central Register on the numbers and outcomes of ES patients given EBRT as the sole local treatment modality.

**Results and interpretation:** The high local recurrence rate in SSG IV (19%) resulted in change for EBRT in the subsequent SSG IX and ISG/SSG-3 protocols. That included earlier timing of EBRT as 1.5 Gy given twice daily given sequentially with chemotherapy, allowing lower overall treatment time with higher dose-intensity of chemotherapy. The true benefit of twice daily EBRT has not been adequately studied, and most centres advocate one fraction per day of 1.8 – 2,0 Gy. A recent publication reports the use of proton therapy for paediatric ES where several patients not having surgery for their primary tumor but with excellent local tumor control (Rombi et al. 2012). Of unsettled concern might be the risk of a pathological fracture; post radiotherapy, when ES is within a weight-bearing bone and the ever present concern giving EBRT to children.

### **L3 Reconstructive surgery in pelvic sarcomas**

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For the preoperative surgical planning of pelvic sarcomas the exact knowledge of the anatomy is necessary. Most of the tumors are very large. We have to correlate the measurements in the CT and MRI with respect to tumor size and tumor location which we will find during surgery. The old MSTS classification of pelvic tumors is not exact enough. Therefore a new classification will be presented. In pelvic tumor surgery we will have 40% major complications, due to the lack of soft tissue coverage, necessary resection of muscles and large dead spaces. Many patients need radiotherapy as well chemotherapy postoperatively. After tumor resection there is either no necessity to reconstruct the bone defect or for reconstruction we can use the resected and extracorporeal irradiated tumor bone, massive allografts, tumor prostheses and biologic reconstructions. The results of the different methods will be discussed. Overall if we look at the relatively bad prognosis of pelvic sarcomas and the known high complication rate during and after surgery we always have to ask ourselves do we have the manpower for an extended internal wide tumor resection as well for an extended external hemipelvectomy.

## **L4 Scandinavian sarcoma group (SSG) - Bone sarcoma trials**

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EURAMOS-1 was closed June 2011 and the results from the good-responders arm were presented at this year ASCO meeting. With current follow up, EFS for MAP+IFN was not superior to MAP alone. However, one quarter of the patients did not start Interferon, half of those who started terminated therapy early and follow-up continues. The results from the poor-responders arm will be available in 2014. SSG is participating in the EURAMOS strategy group and hopefully their work will lead to a new collaborative study. The good-responders arm (MAP without Interferon) is the current standard treatment utilized by SSG and most other in EURAMOS.

EUROBOSS (bone sarcomas 40-65 y) will close 2014. About 400 patients are included. If surgical complete remission is obtained the prognosis is fairly good with a 5-year overall survival of 70% and event-free survival of 49%.

SSG (at least some centers) will participate in EURELOS, a register study with the aim of collecting detailed treatment and outcome data for recurring osteosarcoma. Necessary applications will be completed soon.

A pilot project with Modufolin (an active metabolite to leucovorine), with a potential improvement of rescue after high dose Methotrexate in osteosarcoma will be started at the Skåne University Hospital, Lund, in due time. Other SSG centers will be involved later.

Ewing's sarcoma (ES): As standard treatment SSG uses the ISGSSG-III protocol for localized ES and the IV protocol as standard for metastatic ES (for selected patients). [www.ssg-org.net](http://www.ssg-org.net). The Swedish paediatricians however, have recently joined the new version of the Euro-Ewing's protocol. SSG is member of the Euro-Ewing's consortium by whom an EU application (FP7) for various studies in Ewing's sarcoma has been an important issue this year.

## **L5 Treatment of rhabdomyosarcoma (RMS) and Ewing's sarcoma (ES)**

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Much progress has been made in treating localized rhabdomyosarcoma and Ewing's sarcoma. However, treatment of metastatic disease for both these tumors remains problematic. In general, treatment involves multi-disciplinary care teams and involves local control with surgery or radiation therapy, as well as systemic chemotherapy. In this presentation, I will discuss current approaches to treatment of both of these tumors, and end with a discussion of newer therapeutic approaches aimed to improve outcomes, particularly in advanced stage disease.

### **RMS**

There are 2 major histological subtypes of RMS, including embryonal (ERMS) and alveolar (ARMS). Currently in the US, these tumors are now stratified according to risk group. Specifically, embryonal tumors are considered low risk if they are Stage I tumors using the TMN system or Stage 3 tumors that are surgically resected. In the US, these tumors are currently treated with 3 cycles of VAC chemotherapy, followed by local control, followed by an additional 4 cycles of VA if they are very low risk, or 12 cycles of VA if they are low risk. Current 5-Yr FFS is between 87-90% for these groups of patients. Intermediate risk patients have embryonal Stage II or III tumors that are not surgically resectable, or any Stage I, II, or III alveolar tumors. These patients are currently randomized between 14 cycles of VAC, with XRT commencing at week 4 of treatment, or 5 cycles of VAC followed by 9 cycles of alternating VAC/VI therapy. Currently these patients have a 5-YR FFS of 65-73%. High risk patients are any patients with either embryonal or alveolar histology that present with metastatic disease. Currently these patients are treated with a backbone of VDC/IE with a randomization to receive either intermittent Irinotecan/Tem, vs Irinotecan/IGFIR Ab, or Irinotecan/Tem/IGFIR Ab. Currently high risk RMS patients have a 5-YR FFS of less than 30%. Specific issues such as second look surgery and salvage treatment for recurrence will also be discussed.

### **ES**

Greater than 85% of Ewing's sarcoma patients are characterized by the hallmark chromosomal translocation t(11;22). The single most important

risk stratification is the presence or absence of metastatic disease. Approximately 25% of patients will present with overt metastatic disease (lung, bone and bone marrow) and overall survival in these patients is less than 30%. Additional high risk factors include large, axial tumors, and older age. Current recommendations for treatment in the US includes VAdriaC alternating with I/E every 2 weeks for 6 cycles, followed by local control with an additional 8 cycles of alternating VAdriaC/IE given q 2 weeks for 16 weeks. This regimen was compared to every 3 week therapy and the 4-YR EFS was 76% for the every 2 week therapy 65 % 4-YR EFS for the q 3 week schedule. It is important to point out this was only advantageous for patients less than 18 yo without metastatic disease. Treatment approaches for patients with metastatic disease will be discussed. It should also be noted that in Europe, the current approach is slightly different, with the backbone therapy being VIDE (no CTX). Other specific issues such as XRT vs surgery, the role of HD chemotherapy with autologous stem cell rescue, and the current 3 arms of the EuroEwing's 99 study will be discussed.



## **L6 Surgical treatment in paediatric bone sarcomas (including special surgical techniques for growing bones)**

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Limb-salvage surgery has progressively enlarged its indication in paediatric patients with musculo-skeletal sarcomas and reconstructive techniques specifically addressed to children are now available. Due to the significant incidence of bone sarcomas in the lower limb the resected segments often include one femur or tibia growth plate and the consequent loss significantly affects the final outcome because of the predictable limb discrepancy at the end of growth.

The goal of reconstructing the skeletal continuity of femurs or tibias in children to obtain, after skeletal maturity, a functional gait without leg discrepancies is pursued in two different ways:

- a) biological reconstruction using bone allografts or autografts. These techniques represent the first choice in diaphyseal reconstruction but have enlarged their use also in intercalary resections with iuxta-articular osteotomies. The problem of the longitudinal growth loss may be addressed by several procedures as minimal overlengthening of the primary implant, dynamic epiphyseal fixations, contralateral knee epiphysiodesis or late bone lengthening procedures.
- b) artificial mega implants using modular or custom-made prostheses: The use of megaprotheses in children has increased significantly after the development of internal lengthening mechanisms that may gradually compensate for the inevitable limb length discrepancy.

Due to the small numbers in each centre, all new surgical procedures in children must be considered as experimental “on progress” products and must be monitored by the scientific societies and by the different institutions.

## L7 Radiotherapy of paediatric sarcoma

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Approximately 100 paediatric/adolescent patients receive radiation therapy yearly in Sweden. They are mainly treated according to international treatment protocols. Radiotherapy of these patients in Sweden is centralised to 6 university hospitals.

Of these 100 patients approximately 15 are sarcoma patients. They are treated with a combination of surgery, chemotherapy and radiotherapy, mainly according to protocols. This means that the intention and radiation dose is set, but since the localization of the sarcoma varies, the radiotherapy also varies. The localization of the tumor, the surrounding tissues and not least the patient's age are factors that have to be taken into account when planning the treatment.

Radiotherapy is not only aiding in the cure of sarcoma, but can also induce side effects that the children will have to deal with for the rest of their lives. It is therefore of great importance that the treatment volume is kept as small as possible without jeopardizing the chance of cure. With modern treatment techniques this is possible to a high degree. A treatment of a 14-year-old girl with a Ewing's sarcoma of the mandibular is shown in Figure 1. The treatment is planned to spare organs at risk (spinal cord, mouth, eye) as much as possible. Figure 2 shows an example of a 6-year-old child with embryonal rhabdomyosarcoma, a large volume treated with rotational radiotherapy to spare liver and kidneys.

The radiotherapy process and different treatment techniques will be discussed in the presentation.

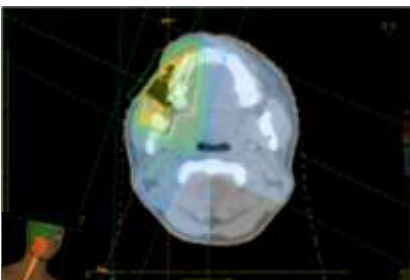


Figure 1. Girl with Ewing's sarcoma.

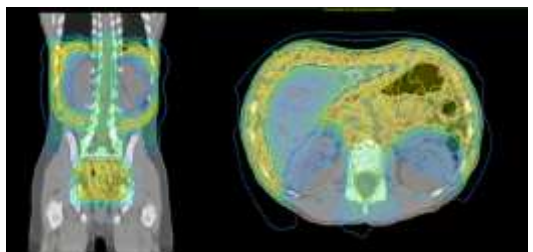


Figure 2. Boy with RMS.

## **L8 Proton radiation of paediatric sarcomas**

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**Background and purpose:** Sarcoma treatment in children is often a challenge, high doses to the tumor and as low doses as possible to surrounding normal tissue. Proton therapy has advantages compared to photon therapy due to a more optimal dose distribution and should be useful in children, in order to reduce side effects. The access to proton therapy is increasing worldwide and many centers give priority to children.

**Methods:** Presentation of proton radiation of paediatric sarcomas in general and at The Svedberg Lab (TSL) in Uppsala. Since 2007, we have treated 12 children with rhabdomyosarkomas and 6 children with other sarcomas at TSL with proton therapy.

**Results and interpretation:** Proton radiation of sarcomas is promising with superior dose distribution compared to photon treatment resulting in less late side effect.

## **L9 Soft tissue sarcomas in adults and children; therapeutic differences and similarities**

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**Background:** Soft tissue sarcomas (STS) form a set of different mesenchymal extraskeletal malignant tumors that may occur at any age, but the incidence of the different subtypes differs in paediatric and in adult age. As a result, when paediatric and medical oncologists talk about STS they might mean different things. Whether the biology and clinical behavior of a given histotype is the same in patients of different ages remains to be seen. Moreover, different therapeutic approaches are sometimes adopted by paediatric and adult oncologists treating the same tumor (as regards the use of chemotherapy, for instance), and different overall outcomes have been reported in paediatric and adult series.

**Methods:** Synovial sarcoma and rhabdomyosarcoma are two high-grade STS subtypes that occur in adolescents and young adults. Literature series have been reviewed and discussed, with a particular focus on the differences in treatment approaches and outcomes crosswise the ages.

**Results:** Despite of a lack of consensus on the role of chemotherapy in synovial sarcoma, clinical protocols in paediatric and adult groups have tended to converge towards a common strategy in the last years. A different access to clinical trials and to referral centers still remains a potential problem. Adults with rhabdomyosarcoma fare better if they are treated like paediatric patients, but this would happen in a minority of cases.

**Interpretation:** Despite cultural and logistic problems, new forms of fruitful cooperation between paediatric and medical oncologists dealing with STS are necessary.

## **L10 A paediatric cancer registry in southern Sweden for clinical follow up and research on late complications in long term survivors after childhood cancer: BORISS**

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**Background:** During the last 40 years long-term survival after childhood cancer has increased dramatically from 20-30% to 80% in high income countries. However, the treatment (surgery, radiotherapy, chemotherapy) causes some kind of late side effects in more than two thirds of the survivors, in one quarter of whom serious or even life threatening.

**The database:** A Late Effect Clinic started in Lund in 1987 to meet the need for follow-up after childhood cancer. To correlate side effects to the given treatment all treatment data have systematically been collected into a database, BORISS, which contains all individuals < 18 years of age diagnosed with cancer in the Southern Health Care Region of Sweden (population 1.8 million) since 1970. This population based registry comprises detailed information on the cancer disease and treatment: details of surgery, dose and fractionation of radiotherapy and target organs, and cumulative doses of all chemotherapeutic agents given. The register contains 2.476 individuals of whom 1.761 are alive (June 2012).

### **Applications based on BORISS**

**Clinical:** to give individuals visiting the Late Effect Clinic solid advice on late effects including a written summary of their treatment to understand the risk of late complications and to use when they visit other health care institutions.

### **Research projects:**

**Reproductive function in male** childhood cancer survivors. Dissertation 2010. Patrik Romerius.

**Female fertility** after childhood cancer. Ongoing project in cooperation with the reproductive clinic in Malmö. Helena Mörse.

**Endocrine effects** after treatment for childhood leukemia. Dissertation 2010. Cecilia Follin.

**Impairment of hearing** after childhood cancer treatment. Dissertation planned 2013. Einar-Jon Einarsson.

**Socio-economic outcome** after childhood leukemia treatment. Dissertation planned 2014. Anna Sällfors-Holmqvist.

**Cardiologic late effects** after childhood cancer treatment. Project led by the paediatric cardiologists and oncologists. Olof Broberg.

**Neuro-psychological follow-up after paediatric brain tumor in southern Sweden – a registry study.** Dissertation planned 2015. Ingrid Tonning-Olsson.

## **L11 Trabectedin – Standard use and novel results**

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Soft tissue sarcomas are a heterogeneous group of tumors arising predominantly from the embryonic mesoderm. They account for about 1% of all adult malignancies, with an incidence close to 6/100000/year in most countries worldwide. The prognosis of patients with advanced metastatic soft tissue sarcoma remains poor with a disease-free survival at 5 years less than 10%. Despite improvements in local tumor control due to surgery and radiotherapy, distant metastasis and death remain a significant problem in 50% of patients. Only few chemotherapeutic agents have been identified to be active with reported response rates for doxorubicin and ifosfamide single agent or combination from 10-15% as single agent to 20-25% for combination treatments. Trabectedine given at a dose of 1.5mg/m<sup>2</sup> as CI over 24h every 21 days has been demonstrated to improve time to progression in patient with advanced sarcoma progressing after doxorubicin and ifosfamide. In most prospective and retrospective studies reported so far including from 300 to 1800 patients, the median PFS is in the range of 3.6 months with a median overall survival of 12-16 months in advanced STS patients. Long term progression free survival up to 10 years has been reported in few patients in marked contrast with other reported agents in the sarcoma literature. Molecular characteristics of sarcoma strongly influence response to trabectedine with high tumor control rates in patients with myxoid LPS with the specific t (12, 16) translocation, both in advanced and neoadjuvant phase. Combination treatment with doxorubicin is feasible and provided high tumor control rates in early studies; these combinations are currently tested in randomized studies. Recent studies with long term outcome pointed out to the favorable outcome of patients receiving prolonged treatment beyond 6 courses as compared to those interrupting the treatment after 6 courses without progression. A randomized trial testing the value of maintenance treatment with trabectedine has been completed recently (T DIS trial). Finally, trabectedine has recently been shown to exert antitumor activity acting on non tumoral stromal cells, in particular of the macrophage lineage. These different studies will be presented.

## **L12 Novel biomarkers in sarcoma**

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Sarcoma is the collective term for a group of malignancies presently comprising more than 50 specific subtypes. Each of these histopathologic entities displays more or less characteristic morphologic and immunohistochemical features, and is associated with a certain risk of locally aggressive growth and distant spreading. Thus, the correct classification of a newly diagnosed lesion is important for optimal management of sarcoma patients. However, the rareness of sarcomas, their sometimes overlapping histopathologic features, and the existence of a variety of benign tumors that may mimic sarcomas, makes the diagnostics difficult. Furthermore, even among patients with phenotypically identical sarcomas the outcome may vary considerably, and for only a few sarcoma types are curative drugs presently available. The finding of specific biomarkers - such as gene fusions, mutations, and amplifications - has already contributed to improved subclassification of sarcomas and, in a few cases, paved the way for new treatment strategies. During the last decade, a large number of new insights into mechanisms behind sarcoma development, examples of which will be presented, have been obtained. Bearing in mind the ever increasing possibilities to probe tumor genomes and transcriptomes, it is not far-fetched to expect that future classification of sarcomas will be based on expected responsiveness to targeted therapies rather than on phenotype alone.



## L13 GIST – The break through

*H. Joensuu*

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Treatment of few other types of cancer has improved as rapidly as that of gastrointestinal stromal tumor (GIST). At the end of the last millenium surgery was the only effective treatment, whereas now there are several highly effective agents available for advanced GIST, and efficacy and safety of adjuvant treatment has been demonstrated. Imatinib is currently the standard agent for the first-line treatment of advanced GIST. Imatinib is also the standard agent in the adjuvant setting, and is usually administered for 3 years when the estimated risk recurrence is considered high after surgery alone. Sunitinib has efficacy in the patient population with advanced GIST who progress on imatinib or who do not tolerate imatinib, and regorafenib has substantial activity in a patient population who have progressed on both imatinib and sunitinib. Important further advances have been made in the field of molecular pathology since the discovery of *KIT* and *PDGFRA* mutations, such as identification of frequent succinate dehydrogenase gene mutations in wild-type GISTs. Improvements have been achieved also in stratification of the risk of recurrence after surgery, follow-up of GIST patients, and in palliative care. More than 10 novel agents are being evaluated in clinical trials in the advanced setting, and a few new randomized trials to test novel treatment approaches are about to start. The treatment of GIST patients has thus fully transformed. Patients diagnosed with GIST now usually face several years of life with good quality even when metastases are detected at the time of the diagnosis.

## **L14 Novel systemic treatments in sarcoma**

*I. Judson*

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Sarcomas are frequently characterised by specific defining genetic events, such as chromosomal translocations, activating mutations, chromosomal amplification etc. The identification of activating mutations in *KIT* led to the use of the tyrosine kinase inhibitor (TKI) imatinib for GIST. We have since seen the same drug successfully used for 2 translocation-related diseases: DFSP and tenosynovial giant cell tumor. Loss of *TSC1 / 2* in PEComa upregulates the mTOR pathway and inhibition with sirolimus can be effective. However, responses may be relatively shortlived and the challenge is to identify and overcome the mechanisms of resistance. Well-differentiated /de-differentiated liposarcoma (DDLPS) is characterised by amplification of chromosome 12q13-15 resulting in upregulation of CDK4 and MDM2, simultaneously promoting cell cycle and inhibiting apoptosis. It has been demonstrated that inhibitors of MDM2 could be useful in DDLPS. The development of inhibitors of IGF1-R raised expectations that these agents would be useful against Ewing's sarcoma, in which disease the EWS-FLI1 fusion protein upregulates the IGF signalling pathway. Responses were observed, but they were generally shortlived and objective responses were few. Research continues to identify mechanisms of susceptibility and resistance. Paradoxically, the biggest recent success of targeted therapy has been with the anti-angiogenic agent pazopanib. The PALETTE trial confirmed the activity observed in phase II and the drug is now licensed for treatment of chemotherapy refractory soft tissue sarcomas. Why should sarcomas respond to monotherapy with a multi-targeted TKI? Another mystery yet to be unravelled.

## **L15 Current developments in osteosarcoma**

*S. Bielack*

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Chemotherapy, mostly including high-dose methotrexate, doxorubicin, and cisplatin, combined with surgery, has been osteosarcoma standard for decades. Tumor response to preoperative chemotherapy is an eminent prognostic factor. Potential biologic correlates to prognosis are under investigation.

Recent years have witnessed a shift away from amputation towards limb-salvage. Expandable endoprostheses allow limb-salvage even prior to skeletal maturity.

The question whether additions to standard chemotherapy improve outcomes is controversial. While some believe liposomal muramyl-tripeptide improves prognosis, critics argue that the randomized trial investigating the agent left many questions. The EURAMOS consortium investigated maintenance with pegylated interferon alpha-2b (ifn) in good responders to upfront chemotherapy. The primary outcome analysis of EFS resulted in a hazard ratio of 0.82 in favor of ifn, but the confidence interval included 1. This does not support adding ifn to standard chemotherapy. Interpretation is complicated by considerable portions of patients not starting or not completing ifn (ASCO 2013, abstr LBA10504)). Results of the poor responder randomization of high-dose-ifosfamide/etoposide in poor responders are pending.

Phase-2 trials investigating inhaled lipid cisplatin and sorafenib suggest that these merit further investigation, while inhaled GM-CSF proved ineffective. COSS, ISG, and SSG cooperate in the prospective European RELapsed Osteosarcoma registry EURELOS. First analyses confirm observations from retrospective series and suggest that recurrences detected by imaging may have more favorable outcomes than those detected by symptoms. Work-Package 7 of the ENCCA-Network, combines investigators working on tumor biology with clinical trialists and is dedicated to fostering translational research activities in bone sarcomas.

## **L16 Pathophysiology and biomarkers in giant cell tumor**

*T. Böhling*

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Giant cell tumor (GCT) is a locally aggressive bone tumor with high recurrence rate and occasional metastatic potential. Histologically GCT is composed of mononuclear stromal cells (the true neoplastic cells) and multinucleated giant cells as well as mononuclear histiocytic cells. By ordinary histology it is not possible to determine which tumors are more aggressive, and thus a better understanding of the biology of these tumors is needed to get predictive tools and to develop the treatment. Currently the clinically most important biological phenomenon identified in GCT is the production of RANK-ligand by the stromal cells, which activate the giant cells, and subsequently osteolysis.

GCT have been studied by numerous methods in the search for prognostic markers, including cytogenetics, microRNA expression profiling as well as protein expression studies. By cytogenetics several recurrent findings have been found, including clonal telomeric associations, however, these do not correlate to the clinical outcome. The miRNA expression profile of GCT show differences in metastatic and non-metastatic tumors, including the expression of *miR-136*. On protein level several potential prognostic markers have been identified, including the expression of NFIB, glutathione peroxidase 1 and matrix metalloproteinases.

Our understanding of the pathophysiology of GCT has increased rapidly. However, we cannot yet recognize those tumors with more aggressive and especially metastatic potential. Some promising markers have been identified, but their use has to be tested in larger clinical settings.

## **L17 Giant cell tumors - Surgery**

*A. Kivioja*

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Giant cell tumors exist in bones and soft tissues with different ways of behavior. Although some medications are under development, the main treatment is surgical. This presentation is about giant cell tumors of bone. Wide resections generally lead to less recurrence but more disability. The preferred method of treatment of GCT is surgery in which the tumor cavity is evacuated and filled with cement. The technique of evacuating the cavity and especially what adjuvants should be used has been studied with only few randomized studies. High-speed burring is generally considered an important step in the evacuation. In some anatomical sites resection would be the first option as the functional impairment is low, e.g. the proximal fibula. Tumors of the distal radius are said to behave aggressively and it has been recommended to use distal radius resection instead of intralesional surgery. The cavity wall has been treated in different studies with phenol, liquid nitrogen, hydrogen peroxide, water and so on. Generally the cavity has been filled either with bone or preferably with cement. There are also studies suggesting not to fill the cavity at all. The follow-up scheme should include local radiographs and in specific cases also chest radiographs to detect eventual lung metastases. The treatment of pulmonary metastases is variable, mostly surgery is considered for those cases where there is progression. Differential diagnosis when considering surgical options should include ABC and brown tumors. In recurrences and in cases with pathologic fractures before treatment the main approach is still intralesional.

## **L18 Radiotherapy in giant cell tumor of bone**

*C. Blomqvist*

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Giant cell tumor of bone (GCT) is a neoplasm occurring predominantly in young adults. The mean age of onset in a recent large study from SSG was 35, and most patients were between 20 and 40<sup>1</sup>. The metaphyses of long bones is the most common site followed by the axial skeleton. Morphologically the tumor is characterized by sparse mononuclear tumor cells and osteoclast-like giant cells. Recently, the growth factor RANK-ligand has been reported to be crucial in the pathogenesis of this disease<sup>2</sup>. Although histologically benign GCT may occasionally metastasize to the lungs.

Adequate surgery with wide surgical margins or marginal/intralesional surgery with cementation is the treatment of choice and ensures local control in most patients<sup>1</sup>. In patients with local recurrence or lesions not suitable for non-mutilating surgery other treatment options include medical treatment with antiosteoclastic agents and radiotherapy.

Local control can be achieved by radiotherapy in 80-85% of cases not suitable for surgery<sup>3-6</sup>. Early reports, however, indicated that radiotherapy of GCT might be associated with an unacceptable risk of malignant transformation<sup>3</sup>. Several recent studies have indicated that these risks may be considerably lower with modern radiotherapy<sup>4-6</sup>. Nevertheless, the risk of secondary cancer has to be taken into account and carefully weighted against the benefits of radiotherapy. After treatment the patient should preferably be followed for the remaining lifetime due to the risk of radiation induced tumor and lung metastases

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## **L19 Safety and efficacy of Denosumab for giant cell tumor of bone**

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**Background:** Giant cell tumor of bone (GCTB) is a rare, usually benign, but locally aggressive, destructive tumor. Surgery is the mainstay of treatment, and there are no standard or approved medical treatments for GCTB-tumors not amenable for surgery, or for the rare cases of disseminated, benign GCTB.

The stromal cells in GCTB are believed to be the neoplastic component, and through high expression of RANK-ligand (RANKL) recruit and stimulate the formation of the destructive osteoclastic giant cell component expressing RANK receptors. Denosumab is a fully human antibody against the RANKL and through this mechanism block the tumor-driving RANKL-RANK signalling pathway in GCTB.

**Methods:** The 20062004-trial for GCTB is ongoing and data regarding safety and efficacy will be presented based on an interim analysis of 282 patients.

**Results:** Denosumab was safe, with generally mild side effects. Patients required calcium and vitamin-D supplementation, and the rate of osteonecrosis of the jaw was 1%. In surgically unsalvageable patients, clinical benefit without disease progression was seen in 96%. For patients with surgically salvageable tumors, surgery was deferred in 74% of patients, and in patients who underwent surgery 16/26 had less expensive surgery than originally planned.

**Interpretation:** Denosumab is safe and efficient in benign GCTB and should be considered for recurrent, locally advanced or disseminated GCTB.



## **L20 Multinational collaboration: A long-term surveillance program for osteosarcoma and potential exposure to Teriparatide**

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**Background and purpose:** A postmarketing safety program is ongoing to assess a possible association between teriparatide treatment and osteosarcoma in humans, a concern arising from toxicology studies. The program includes a 10-year retrospective surveillance study in 5 Nordic countries (since 2004), a 15-year retrospective case-series surveillance study in the United States (US) (since 2003), and a 12-year prospective patient registry in the US (since 2009). Interim results are provided.

**Methods:** Incident adult cases of primary osteosarcoma are identified in the Nordic countries through the SSG network and in the US through cancer treatment centers and population-based cancer registries. Demographics and risk factors are ascertained by medical records in the Europe and by telephone interview in the US. In the patient registry, patients may enroll when prescribed the medication; outcomes are assessed through annual linkage with US cancer registries.

**Results:** By March 31, 2013, data had been retrospectively collected on 91 osteosarcoma cases from Denmark, Finland, Norway, and Sweden and interviews had been completed for 690 cases in the US. In addition, the third annual linkage had been completed with 26,810 patients from the prospective patient registry and 1,641 osteosarcoma cases from 38 participating state cancer registries, covering 86% of the US population aged 18 years and older. No cases of teriparatide exposure preceding a case of osteosarcoma have been observed in these studies.

**Interpretation:** Currently, the 3 studies do not support a causal association between teriparatide treatment and osteosarcoma in humans.

## **L21 Improvements in the diagnostic process of sarcomas. Effects of a national implemented cancer pathway**

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**Background and purpose:** Delay in cancer diagnosis and treatment is a universal challenge. We describe the effect of a political attempt to accelerate the diagnostic and treatment process with implementation of cancer pathways in a large sarcoma centre.

**Methods:** The National Health Board has in collaboration with the medical specialty societies standardized the diagnostic processes and defined a "cancer pathway" for each cancer form with specific time limits for the diagnostic period until treatment start. The inclusion criteria for suspicion of a soft tissue sarcoma or a bone sarcoma was a MR-scanning of the tumor with suspicion of malignancy and at least one of the following symptoms: Soft tissue tumor > 5 cm, soft tissue tumor on or below the fascia, fast growing soft tissue tumor, palpable bone tumor or deep persisting bone pains. In the sarcoma centre we reviewed the data of all the 1126 referred patients from 2 years before and 2 years after the implementation of the cancer pathway. For each patient we calculated the mile stones, time intervals and registered the size of the tumor at referral.

**Results:** Median soft tissue tumor size at referral was reduced from 7.0 to 4.9 cm Median time from referral to start of treatment was reduced from 28 to 18 working days for soft tissue tumors and from 31 to 14 days for bone tumors.

**Interpretation** A political initiated cancer pathway for sarcoma significantly accelerated the diagnostic process.

## **L22 Bone sarcomas in the Scandinavian sarcoma group central register - 25-years' experience**

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**Purpose:** To give a descriptive presentation of bone sarcomas in the Scandinavian Sarcoma Group Central Register through 3 time periods 1986–1990, 1991–2000 and 2001–2010 and to present the overall survival for the main diagnostic subgroups.

**Methods:** Patients from Norway and Sweden were included. The patients were checked with national population registers and with the SSG international treatment protocols. Survival was updated in April 2013.

**Results:** 892 Norwegian and 1440 Swedish patients with primary malignant bone tumors were reported. Only 4 of 12 participating centers reported more than 10 new cases per year. 33% of the patients had chondrosarcoma, 29% osteosarcoma, 14% Ewing's sarcoma, 7% chordoma and 17% had other types of sarcoma. The distribution of histological diagnoses, age and localization of the primary tumors were similar in Norway and Sweden. A slight increase in non-extremity localized tumors was observed (38%, 41% and 45%). There was a difference in malignancy grading between the 2 countries. An increase of patients with metastases at diagnosis was noted during the last decade. Overall survival in Ewing's sarcoma has improved but not in osteosarcoma.

**Interpretation:** The SSG register is based on reports by the clinicians and is not linked to the National Cancer registers. Incomplete registration has to be considered. Increased rate of metastases at diagnosis may be explained by improved radiological diagnostics. However, no improvement in survival for patients with non-metastatic osteosarcoma was seen. Improved survival in Ewing's sarcoma may be explained by more frequent use of high-dose chemotherapy.

## **L23 Postirradiation sarcoma following treatment of breast cancer: a nationwide, population-based analysis**

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**Background and purpose:** Postirradiation sarcomas (PISs) are sarcomas arising from irradiated tissue after a latent period. The long latent period and rarity of postirradiation sarcomas make studies challenging. The incidence of invasive breast cancer has increased continuously. A more conservative surgical treatment approach with increasing use of radiation therapy is preferred in early stage disease. Therefore, the late adverse effects of radiation therapy are also increasing. The poorer sarcoma-related survival in patients with PIS compared to sporadic sarcomas in a single-institution study including all anatomical locations was mainly due to unfavorable factors overrepresented among PIS patients. In addition, the limited possibility to offer adjuvant therapy may have contributed. Using nationwide, population-based data from the Finnish Cancer Registry, our goal was to identify patients with PIS following treatment for breast cancer and to report the given treatment and outcome of these patients. The sarcomas are to be histologically re-examined.

**Patients and methods:** There were 103 patients reported to Finnish Cancer Registry with breast cancer and then subsequent sarcoma localized superior to the diaphragm diagnosed in 1987 or later. Excluding sarcomas in the distal upper limb, head and neck, contralateral breast, and sarcomas diagnosed simultaneously with the breast cancer left 88 patients for further analyses.

**Results:** At this point we have collected patient records for further examination. All patients are female. The median age at the time of breast cancer was 57 (38-76) years. The interval between breast cancer and sarcoma was 10 (1-25 years). The final results will be given at the meeting.

## **L24 Patterns of local recurrence and dose fractionation of adjuvant radiotherapy in 462 patients with soft tissue sarcoma of extremity and trunk wall. A Scandinavian sarcoma group study**

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**Background and purpose:** To study the impact of dose fractionation of adjuvant radiotherapy (RT) on local recurrence (LR), and the relation of LRs to the radiation fields.

**Methods:** LR-rates were analysed in 462 adult soft tissue sarcoma (STS) patients who from 1998 to 2009 underwent surgical excision and adjuvant RT at five Scandinavian sarcoma centres. Medical records were reviewed for dose fractionation parameters, and to determine the location of the LR relative to the radiation portals.

**Results:** 55/462 patients developed a LR (12%). Negative prognostic factors included intralesional surgical margin (hazard ratio (HR): 8, 95% CI: 3-20), high malignancy grade (HR: 6, CI: 1.3-26), age at diagnosis (HR per 10 years: 1.3, CI: 1.03-1.6) and malignant peripheral nerve sheath tumor (MPNST) histological subtype (HR: 7, CI: 2.5-17). RT dose was tailored to margin status. No correlation between RT dose and LR rate was found in multiple Cox regression analysis. Two thirds of LR's occurred within the primary RT volume.

**Interpretation:** No significant dose-response effect of adjuvant RT was demonstrated. Interestingly, patients given 45 Gy accelerated RT (1.8 Gy

twice daily/2.5 weeks) interposed with chemotherapy had the best local outcome. A total dose of 50 Gy/25 fractions seemed adequate following wide margin surgery. The risk of LR was associated with histopathological subtype, which should be included in the treatment algorithm of adjuvant RT in STS.

## **L25 Radiation associated angiosarcoma after breast cancer improved survival by excision of all irradiated soft tissue of the thoracic wall?**

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**Background and purpose:** Radiation-associated secondary angiosarcoma (sAS) is a rare complication after breast cancer treatment. The prognosis is dismal. Surgery is difficult and recurrences are common also after wide surgical margins. We here present a small series of patients where extensive surgery has been performed.

**Methods:** 5 women with sAS after treatment of breast cancer (primary sAS in 3, local recurrence of sAS in 2) were operated with excision of all irradiated skin and extra-thoracic soft tissue. Reconstructions were performed with combined vascularized flaps and split-thickness skin grafts.

**Results:** Surgical margins were wide in 2/3 of cases treated for primary tumors. These 2 patients are both alive without disease at 5 years follow-up (FU). The third patient had distant metastasis diagnosed 1 month after surgery and died 6 months later. The 2 patients treated for local recurrences were both operated with wide surgical margins. One had lymph-node metastasis after 9 months. She was operated and received adjuvant treatment and is without disease at 4.5 years FU. The other patient was treated for a new local recurrence 2.5 years later but is free of disease at 5.5 years FU. All wounds healed primarily but in some cases complementary reconstructive surgery was performed due to unfavourable cosmetic results.

**Interpretation:** Our results indicate that resection of all irradiated skin and extra-thoracic soft tissue in sAS after breast cancer may result in long-term survival.

## L26 New soft tissue tumors entities

*M. Miettinen*

NCI, Bethesda, Maryland

This presentation highlights a selection of recently described tumor entities emphasizing those that are clinically more important. Low-grade fibromyxoid sarcoma can be challenging to recognize as a malignancy. It is a very low-grade tumor, but nevertheless can metastasize and also progress into a higher grade tumor that may contain areas similar to osteosarcoma. Although most present with an intramuscular soft tissue mass, some are diagnosed with pulmonary metastases of an occult soft tissue tumor later detected in thigh or retroperitoneum. Course of disease can be very slow with metastases appearing after long delay, and some patients live years even with pulmonary metastases. The tumor contains a distinctive CREB3L2-FUS (or rarely CREB3L1-FUS) fusion translocation, and therefore FUS break-apart probe is a practical means in its diagnosis. Immunohistochemically typical is MUC4 expression rarely seen other soft tissue tumors except synovial sarcoma. Sclerosing epithelioid fibrosarcoma, originally reported as a high-grade fibrosarcoma variant, seems to be largely merging with low-grade fibromyxoid sarcoma probably representing its progression form. Epithelioid sarcoma-like hemangioendothelioma (also known as pseudomyogenic hemangioendothelioma) is a low-grade, vascular tumor composed of spindled or epithelioid cells with no tendency for vasoformation, yet endothelial markers should as CD31 and ERG are readily demonstrated. It can form multiple masses and in some cases have metastatic bone involvement. Prognosis is generally good, although some patients have developed distant metastases and died of disease. PEComa refers to perivascular epithelioid cell tumors that can be understood as renal angiomyolipoma analogs. Outside kidney they have a predilection to uterus and pelvic organs but may also occur in peripheral soft tissues; pulmonary lymphangiomyomatosis is also a form of PEComa. These tumors are diagnosed by their immunohistochemical smooth muscle-like differentiation combined with the presence of melanocytic determinants, HMB45, and MelanA (but not generally S100 protein thus separating them from melanoma). Clinically most are benign but there are malignant variants, among them some tumors composed of epithelioid cells (such as epithelioid angiomyolipoma). Oncologically PEComa is of interest as it harbors activated MTOR signaling pathway, which can be potentially targeted with MTOR inhibitors. Among gastrointestinal stromal tumors, succinate dehydrogenase deficient GISTs forms a new sub-entity with a

strong clinical correlation and characteristic multinodular epithelioid morphology. They typically occur in children and young adults and instead of KIT/PDGFRA mutations they are driven by SDH-deficiency similar to the one known in a subset of paragangliomas. This activates HIF pseudohypoxia and insulin-like growth factor 1-receptor signaling. SDH-deficient GISTs are notorious for unpredictable behavior. Some patients develop liver metastases but unlike ordinary GIST patients, they can survive for a long time nevertheless. Long-term follow-up studies indicate 15% tumor-related mortality. Immunohistochemical detection of SDHB is a diagnostic test, and some patients have SDH-subunit germline mutations, while in some cases epigenetic silencing may be the pathogenesis.

## **L27 Cancer related fatigue – what do we know and how do we help our patients?**

*R. Gjessing*

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Department of clinical service, Oslo Norway

Fatigue is the most common symptom of cancer. Cancer patients often tell about tiredness weeks and months before they got their cancer diagnosis. Fatigue is also a sideeffect during cancer treatment. Patients tell that their fatigue was expected during treatment, but they were not prepared of the fatigue after their chemotherapy or radiotherapy. Fatigue is a physical and a mental dimension. The physical dimension described by the patients of lack of energy and fatigue that does not go away with sleep or rest. Mental fatigue is described as problems with concentration, memory problems and slip of the tongue. Fatigue has a major impact on the daily lives of patients. Fatigue affects work, social life, sexual function and self-esteem. Research shows that fitness training in customized quantity is important for improving fatigue. It is important that patients do not sleep too much during the day, but rather take short breaks. It is also important that health professionals prepare patients for fatigue and those patients feel that we listen to their stories about how these serious late effects experienced.



## L28 Network focused care and young people with cancer

P. Riis Olsen, *Clinical Nurse Specialist, MSN, PhD.*

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**Background:** Several research findings identify social network and support systems as important aspects in the rehabilitation and coping processes of teenagers and young adults (TYAs) with cancer and their parents. At the oncology youth unit, Aarhus University Hospital in Denmark, the first of its kind in the country, nurses have developed a systematic intervention programme in caring for TYAs with cancer and their significant others (parents and on rare occasions a partner). Nursing activities are directed towards interactions intending to help the TYAs and their significant others in maintaining contact with a supportive social network.

**Method:** A grounded theory study explored this nursing practice.

**Results:** *Creating a space for teenagers' and young adults' normal growth and development* was identified as the mutual basic social process. Nurses, TYAs and significant others tried through actions and interaction to resolve problems related to TYAs' developmental needs and risk of social isolation due to the cancer trajectory.

Two parallel but interacting patterns of behaviour pushed this process forward:

1) Nurses engaged in various **Bridging** processes by strategies of '*Tuning in*', '*Framing the situation*', '*Navigating towards the goal*' and '*Connecting people*'.

2) TYAs and significant others activated resources that aimed at **Keeping their world together** by '*Embracing the program*' and '*Building strength*'. Based on the empirical findings in this study **the concept Network Focused Nursing** has been developed.

## **L29 Exercise oncology - A strategy for improving cancer patients well-being during and after treatment.**

*K. Bloomquist*

The University Hospitals Centre for Health Research (UCSF), Copenhagen, Denmark

**Background:** Originally a randomized controlled trial, ‘Body and Cancer’ has been offered as an exercise intervention simultaneously with patients receiving chemotherapy in the Copenhagen area since 2007. This 6 week, 9 hour weekly, supervised multimodal exercise intervention consists of high and low intensity components and has been administered to over 1400 participants to date, with over 21 cancer diagnoses represented.

**Purpose:** To present the ‘Body and Cancer’ program, findings and experiences against the backdrop of the growing evidence base in exercise oncology. Furthermore, experiences from local survivor based exercise associations will be presented.

**Results:** ‘Body and Cancer’ has been shown to reduce fatigue, improve vitality, aerobic capacity, muscular strength as well as physical and functional activity and emotional wellbeing. These findings are in agreement with other exercise intervention studies. Most of these studies were conducted either during or following adjuvant therapy in women with breast cancer.

**Interpretation:** There is relatively strong evidence and considerable rationale for promoting exercise to cancer patients during and after treatment. It is a well-tolerated and safe adjunct therapy that has a positive effect on treatment related side-effects along with health related gains related to exercise. However, as most studies have been conducted in women with breast cancer a gap in knowledge exists. Future studies are warranted in order to tailor exercise prescription to the specific needs of survivors with other cancer diagnosis.

## **L30 Reconstructive surgery in soft tissue sarcoma**

*E. Tukiainen*

Helsinki University Central Hospital, Finland

## **L31 Scandinavian sarcoma group (SSG) - Soft tissue sarcoma trials**

*M. Eriksson*

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SSG has a tradition of performing adjuvant studies in soft tissue sarcoma. Based on our earlier experiences from the trial SSG XIII we are presently running the trial SSG XX at 10 sites in Sweden and Norway since 2007. This trial is a non-randomized study exploring chemoradio therapy in selected patients with soft tissue sarcomas in extremities or trunk wall and a high risk of recurrence according to experiences from our SSG registry. By June 24, 2013, 141 patients have been included in Group A which consists of patients with primary surgery. Furthermore, we have 16 patients registered in Group B; patients with an obvious risk of intralesional margins at primary surgery who therefore were given pre-operative chemoradio therapy. The way of selecting patients for adjuvant therapy and the use of interfoliated shortened radiotherapy between chemotherapy cycles are the two most specific features of the trial. 158 patients have to be registered in group A, and the expectation is that the study is fully recruited in early 2014. No new adjuvant study is planned to follow this one, and the matter of potential recommendations as to adjuvant therapy post trial will be discussed.

GIST is the single most common type of soft tissue sarcoma, and after the publication of the SSG XVIII/AIO adjuvant trial, showing that 3 years of adjuvant imatinib in high risk patients was superior to 1 year, we are presently planning the start of a new adjuvant trial, SSG XXII. This trial will compare the new standard of 3 years with a total length of 5 years of therapy by randomizing patients that have fulfilled the standard treatment of 3 years to two additional years or no more adjuvant therapy.

SSG XXI, "PAGIST", is a non-randomized trial in third line treatment for advanced GIST who has failed both imatinib and sunitinib. The drug of investigation is a new generation tyrosin kinase inhibitor, pazopanib, which is already approved for patients with other types of soft tissue sarcoma failing chemotherapy. This is the first SSG trial with the participation from all 5 Nordic countries, and furthermore, 3 German centers have also joined the trial. By June 24, 32 of the planned number of 72 patients have been enrolled in the trial.

An update of the described projects will be given at the presentation.

## **L32 Rehabilitation including social and physical activity and education in children and teenagers with cancer (RESPECT)**

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**Background and purpose:** In Denmark, 200 children under the age of 18 are annually diagnosed with cancer. During treatment, children have reduced contact with their normal school environment, leisure activities and friends. Long-term survivors describe compromised age-appropriate social relationships, difficulties with resuming physical activities and educational achievement. We tested a multi-modal rehabilitation program aimed to preserve the educational, physical and everyday life of the child during treatment.

**Material:** The study includes a national cohort of newly diagnosed children with cancer (6– 18 years). Intervention group (n=120): Children diagnosed at Rigshospitalet in the period 2013-2015. Control group (n=120): Children diagnosed at the University Hospitals in Odense, Aarhus and Aalborg in the period 2013-2015. Outcome data are also compared with: a) Danish children with cancer treated throughout 2012; b) sibling closest in age; c) the intervention group patient's classmates.

**Methods:** Validated questionnaires, semi-structured qualitative interviews, physical performance.

### **Intervention program:**

- Education of the child, the child's classmates, teachers and parents on his/her cancer disease.
- Appointment of two classmates as "ambassadors" .
- Continued education that parallels/copies the educational curriculum from the child's regular school.
- An individualized physical training program combining supervised and non-supervised training 3-5 times per week.
- Bi-weekly joined days at the hospital with the ambassadors.

**Results:** This is an ongoing study. The feasibility study shows that the intervention program is well accepted by the children and parents. No severe adverse events have been documented.

**Interpretation:** It is feasible to include health “ambassadors” to support children during cancer treatment.

### **L33 Children with sarcomas – Nursing challenges: How can we as nurses assist families to optimal cope with children who has sarcoma?**

*P. Kettler*

Section for Paediatric Haematology and Oncology, Womens and childrens division, Rikshospitalet, OUS, Oslo, Norway.

**Background and purpose:** It is very demanding for the patients and for the whole family when a child is diagnosed with sarcoma. Each of them will likely experience a wide variety of emotions and behaviors which may vary greatly from family member to family member. It is important to understand that just as each person is unique, so too is the way each individual behaves during difficult times. Families find different ways to express thoughts and feelings and it is important that they can experience stability and control by creating room for the family to do their everyday tasks, and hobbies they like to do individually and together. Families need to feel security and stability, they want to be treated as individuals, and this is the start for us nurses to gain the confidence and trust of patients and families. This presentation explores sources of relevant information and experience in how nurses best assist both patient and families.

**Methods:** Study of literature. Use of own experience and experiences of colleagues. Consultations and assistance from patient services.

**Conclusion:** The child and the family need to be respected for how they cope with the situation .

The nurse can provide continuous information to the family about the illness, the treatment and the outcomes.

The nurse should take time to listen to how the family feels and how they want to cope.

The nurse should create an atmosphere of security, prepare the patient well. Patient should be encouraged to participate in their treatment.

The nurse should divert the patient during painful procedures.

The nurse can provide the child opportunity to play.

The nurse should encourage the parents to participate in parent meetings and to take good care of themselves (physical training etc.).

The nurse should encourage the parents to focus on the childs strengths.

The nurse should encourage the family to accept support from social network.

### **L34 Low level laser therapy in the treatment of oral mucositis in a paediatric haemato – oncology and stem cell transplantation unit**

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**Background and purpose:** Despite the implementation of evidence based mouthcare guidelines, oral mucositis (OM) remains a frequently encountered and painful complication of chemotherapy. There is an increasing evidence that low level laser irradiation can reduce the severity and duration of mucositis. We assessed the effectiveness, quantitatively and qualitatively, of low level laser therapy (LLLT) for the treatment of chemotherapy induced OM in paediatric patients.

**Methods:** When mucositis occurred, patients were treated using AlGaAs diode laser every 2 days until complete healing of the mucositis. Patients were evaluated for pain severity by the visual analogue scale or the faces pain scale before and immediately after LLLT. OM grades (WHO-criteria) as well as functional impairment were evaluated. Both nurses and dentists were trained to assess OM and to administer LLLT in an identical way.

**Results:** From May 2009 till December 2012, 142 children (of a total of 415 patients), mostly with diagnosis of leukemia, lymphoma, osteosarcoma or Ewing's sarcoma, treated with chemotherapy and suffering from chemotherapy-induced mucositis, were treated with LLLT. Of these 142 patients, 49 had undergone a hematopoietic stem cell transplantation. Age ranged from 0 to 17 years.

During 343 mucositis episodes, 986 treatments with LLLT were done and 3909 lesions were treated.

Distribution of mucositis grade was : grade 1 (n=1614), grade 2 (n=1497), grade 3 (n=535), grade 4 (n=113) and unknown (n= 150). Cheeks (n=1000), tongue (n=796), lips (n=661), gums (n=376) and pallatum (n=326) were the most frequent sites affected.

Mean 4 to 5 treatments were necessary to heal mucositis and to obtain overall pain relief. For 318 lesions there was no pain reported. For 2205 lesions there was an immediate pain relief or the pain remained the same. In 1386 cases pain scores were missing due to noncooperation or young age of the patients or invalid scores.

**Interpretation:** LLLT, in addition to standard oral care can reduce pain. 4 low level laser treatments per mucositis episode seem to be a realistic approach. Further research and controlled randomized trials are necessary to confirm the efficacy of LLLT and to develop more general guidelines.



### **L35 Organizing patient interests in the Nordic countries – patients helping patients**

*F. Dyne Homb*

Oslo

In the Nordic countries there are only 2 sarcoma patient organizations; Sarkomer in Norway and Finnish GIST Patient Network. Representing rare cancer is important; a few strong voices are better than many small ones! Many sarcoma patients are alone with a disease that is hard to cope with alone. There is therefore important to create a Nordic sarcoma voluntary community where former sarcoma patients can help new sarcoma patients with advice and support. A patient organization can do many things and my statement is that patient organization can contribute to the sarcoma communities in the Nordic countries and in Europe. I will show in my presentation that the possibilities for such organizations are many.

### **L36 Prostheses – what's new?**

*G. Prestbakmo,*

Oslo

### **L37 Special prostheses to sarcoma patients**

*B. Hedegaard, M. Sølvesten, D. Øyen Ougaard*

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We present the special prostheses used in the sarcoma group at Aarhus University Hospital. We want to tell about a new offer in Denmark, on the basis of an example of a sarcoma patient, who earlier had a traditional prosthesis and now has osseointegrated prosthesis. The presentation is not based on a scientific study, but on working experiences within sarcoma patients. So far 20 patients have gone through surgery, including sarcoma patients and trauma patients. Because osseointegration is new in Denmark, we have not yet seen the long-term results.

## **L38 When to use a tumor prosthesis**

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There is no consensus on when to use endoprosthetic reconstructions after bone resection for primary bone tumors. Consequently there are wide variations between sarcoma groups and even between surgeons within a sarcoma group. The most important considerations involve the location of the tumor, the age of the patient, and the number of epiphyses that have to be sacrificed.

As a general tendency there will be less attractive endoprosthetic solutions the younger the patient is, and for those above 50 years of age, most will prefer an endoprosthetic solution, regardless of tumor locations as long as it is proximal to the elbows or knees. Some patients prefer biological reconstructions, even if more function are lost initially, if there is a high risk of complications after prosthetic reconstruction or prosthetic reconstruction necessitates frequent follow-ups or admissions to the hospital for service operations.

Biological reconstructions may be attractive to patients with a high level of activity, and more concerned about durable function than about cosmetics. Most surgeons will be more concerned about soft tissue coverage over an endoprosthesis than over a biological reconstruction that can be varied to adapt to the available soft tissue. Biological reconstructions and amputations may not be acceptable in all cultures.

Tumor endoprostheses can be used in all situations when there is loss of bone tissue, like after failed joint reconstructions for arthritis/arthrosis, after trauma and occasionally for reconstruction of bone destroyed by metastases.

## **L39 Rehabilitation after amputation in upper extremity**

*E. Thomsen Rasmussen, P. Leicht, S. Jensen*

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**Background and purpose:** A malignant tumor may require limb amputation. Amputations concerning the upper extremity occur at any level. Rehabilitation after amputation may include training in the use of an artificial arm. This presentation illustrates prosthetic rehabilitation opportunities for patients with upper extremity amputation caused by sarcoma.

**Methods:** The rehabilitation team with surgeon, orthotist and occupational therapist decide in close interprofessional cooperation what kind prosthesis could be suitable for the patient. The choice is between functional prosthetics, myoelectric, I-limb, Bionic-, and passive cosmetic prosthetics. The aim of providing any prosthetics is to offer the patient the best technical solution to compensate for the loss of function and to provide the best psychological well-being. Training in the use of the artificial limb is done by occupational therapist. Occupational therapy intervention provides opportunity for patients to optimize their ability to manage their activities of daily living and to develop or maintain skills necessary to participate in all aspects of their daily life.

**Results:** Most patients who agree to receive an artificial arm are successfully rehabilitated.

**Interpretation:** Close interprofessional cooperation in the rehabilitation team and close cooperation with the patient is important to achieve the best results of the rehabilitation.

## **L40 Working as a sarcoma nurse in a plastic surgery ward**

*K. Olenius, L. Kanerva, T. Oja, E. Haaranieni*  
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**Background:** A sarcoma team was created at Meilahti Hospital in Helsinki in 1987, and a nurse has been officially included in the sarcoma meetings since 2005. The meetings take place weekly. The sarcoma team participants are generally the sarcoma nurses, a radiologist, a pathologist, an oncologist and a surgeon. Ward 3 of Töölö Hospital has 2 sarcoma nurses whose job is to participate in the meetings and, in accordance with the instructions they receive there, to work with patients and direct them to further care. Ward 3 of Töölö Hospital provides plastic surgery care. In 2012, surgery was performed on a total of 1,862 patients (an average of 150 patients per month), 76 of whom were sarcoma patients (an average of 6 patients per month).

**Aim:** The aim of the sarcoma team is to ensure a consistent, multidisciplinary approach to care. The team is responsible for diagnosing sarcomas and providing access to appropriate treatment. Patients receive efficient, high-quality care. After surgical intervention, centralised follow-up care and monitoring are carried out at the appropriate locations according to the sarcoma team's instructions. Patients receive personalised and up-to-date information about their treatment.

**Conclusions:** Nurses are in charge of making sure that patients receive the treatment and follow-up care they need. A sarcoma nurse carries a great deal of responsibility and plays a critical role in clinical pathway implementation for sarcoma patients.

## **L41 Nutrifriend 1100 in cancer –”Protector of good and killer of evil”?**

*T. K. Nystrøm*  
Smartfish, Oslo

## **L42 Rehabilitation of sarcoma patients**

*H. Gustafsson*  
Töölö Hospital, Plastic Surgery Ward, Helsinki, Finland

Töölö Hospital is a part of Helsinki University Hospital. Ward 3 of Töölö Hospital provides plastic surgery care. In 2012, surgery was performed on a total of 1,862 patients (an average of 150 patients per month), 76 of whom were sarcoma patients (an average of 6 patients per month).

The physiotherapist is an important part of the team together with surgeons, nurses and other professionals treating sarcoma patients. Physiotherapy starts immediately after the operation and continues through the whole healing process both in polyclinics and in the patient’s home town. Physiotherapy consists of movement exercises, guidance and teaching how to use mobility aids. The aim of physiotherapy is to provide patient-centered care and trying to restore and maintain the patient’s mobility.

The presentation shows 2 cases of how the rehabilitation proceeds.

## **L43 Activity week - challenge yourself**

*K. Heiberg Rasch, M, Evertsen*

Vestfold Hospitals Trust, Clinic for Physical & Rehabilitation Medicine  
Kysthospitalet (Coast Hospital), Stavern, Norway.

“Activity week” is a provision offered to those who have undergone treatment for sarcoma. It was introduced in the summer of 2012 and we initially admitted seven participants, all of whom had previously stayed at the hospital on one or more occasions.

The main purpose of “Activity week” is to enable these patients to meet others in the same, or similar situations; to give them a forum where they can discuss and share their experiences with each other. Furthermore, with the help and guidance of a multi-disciplinary team consisting of doctors, psychologist, nurses, healthcare assistants, physiotherapists, occupational therapists and sports therapist. The participants are encouraged to challenge their own limitations and boundaries through trying out new or resuming former activities.

There are two “Activity weeks” planned for summer 2013.

## **P1 Progress update for the postmarketing adult osteosarcoma surveillance study in five Nordic countries**

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**Background and purpose:** A 10-year postmarketing drug surveillance study was initiated in 2004 to assess a possible association between teriparatide treatment and osteosarcoma in humans, a concern arising from toxicology studies. The primary objective is to identify incident cases of adult osteosarcoma and determine if any had a prior history of teriparatide treatment and also to identify potential risk factors. Cases are identified by regional and national cancer registries in Denmark, Finland, Iceland, Norway, and Sweden through collaboration with the Scandinavian Sarcoma Group (SSG) registry; data collection activities are concluding this year.

**Methods:** Incident cases of histologically confirmed primary osteosarcoma diagnosed from January 2004 through December 2013 in adults aged 40+ years are identified through the SSG registry network. Following patient consent, demographic characteristics; treatment history; and exposure to possible risk factors, including radiation, infection, or trauma at the site of tumor are abstracted from medical records.

**Results:** Of 115 osteosarcoma cases identified by March 31, 2013, 91 have been abstracted; 40 in Sweden, 31 in Finland, and 10 each in Norway and Denmark. Possible pre-existing risk factors for osteosarcoma were radiation (22%) and injury or infection at tumor site (12%). Sites of radiation and tumor matched for 85% of radiation cases; time between radiation and diagnosis ranged from 2 to 36 years (mean 13.5 years; median, 9 years). None of the cases abstracted had been exposed to teriparatide prior to diagnosis of osteosarcoma.

**Interpretation:** This surveillance study adds information about the long-term safety profile of Forsteo and adult patients with osteosarcoma.

## **P2 Epidemiology and treatment results in a nationwide unselected cohort of osteosarcoma**

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**Background:** About 15 people are diagnosed with osteosarcoma (OS) each year in Norway. The treatment is based on intensive chemotherapy together with surgery, and the long-term survival rate is currently 65 percent.

Still we have particularly limited knowledge about patients with “non-classical OS”, i.e. age above 40 years, metastasis at the time of diagnosis or primary OS in the axial skeleton; about 45 % of all patients. Thus, the aim is to achieve a complete overview of all OS patients diagnosed in Norway from 1975 until today with clinical data during treatment and follow-up. We aim to obtain complete information on epidemiologic, demographic and geographic variables, and connect these to the type of OS, completed treatment and outcome.

**Methods:** The cohort is based on all cases reported as OS to the Cancer Registry for all subgroups, complemented with data from the four regional institutions involved in sarcoma management. Only histologically verified OS is included, in line with the current WHO Classification. All questionable histological reports, in addition to all low grade and extraskelatal OS, are histologically re-evaluated. We have also evaluated all spindle cell sarcoma arising in bone (SCS).

**Preliminary results:** About 520 OS and about 110 SCS are included in the study so far, from a gross cohort of 720 patients. Low grade OS appears to account for a larger part of all OS than earlier presented, and telangiectatic and small cell OS seemingly comprise a smaller percentage. The frequency of OS seems to be independent of geographic native district. Males are more frequently affected in line with previous studies.



### **P3 Integrative genome analyses of ring chromosomes in sarcoma reveal a multitude of amplified and overexpressed genes that promote proliferation or inhibit apoptosis**

*K. H. Nord<sup>1</sup>, G. Macchia<sup>2</sup>, J. Tayebwa<sup>1</sup>, J. Nilsson<sup>1</sup>, F. Vult von Steyern<sup>3</sup>, O. Brosjö<sup>4</sup>, N. Mandahl<sup>1</sup>, F. Mertens<sup>1</sup>*

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**Background and purpose:** Specific subtypes of sarcoma commonly carry amplified genetic material in the form of ring chromosomes. These structures accumulate and amplify material from many different parts of the genome. However, their exact content remains poorly understood for most sarcoma subtypes. The purpose of the present study was to characterize the content of ring chromosomes and extract potential driver oncogenes.

**Methods:** Various histological subtypes of predominantly high grade soft tissue sarcomas with ring chromosomes were investigated using cytogenetic, SNP array, FISH, and global gene expression analyses. Recurrently amplified and overexpressed genes were identified using the statistical algorithm JISTIC combined with the Mann-Whitney *U* test.

**Results:** Ring chromosomes in sarcomas amplify and overexpress more than one hundred potential driver oncogenes. Many of them are already known to induce cell growth, promote proliferation and inhibit apoptosis, and several of them are potential drug targets. The most commonly amplified gene was *MDM2*, and tumors with high copy numbers of this gene generally showed co-amplification and overexpression of multiple genes on chromosomes 1, 6 and 12. Tumors without *MDM2* amplification showed less recurrent amplicons and frequent loss of *CDKN2A* and *RBI*.

**Interpretation:** The present data suggest that there are two fundamentally different subgroups of ring chromosomes: one associated with *MDM2* amplification and one showing a much more heterogeneous amplification pattern. Ring chromosomes of the latter type may represent a secondary genetic event and are commonly found in tumors with complete loss of either *CDKN2A* or *RBI*.

## **P4 Bone and soft tissue sarcomas in the knee region – relation to routine MR knee imaging**

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<sup>1</sup>Dept of Radiology, <sup>2</sup>Dept. of Orthopaedics, The Norwegian Radium Hospital, Oslo University Hospital, Oslo, Norway

**Background and purpose:** The knee region is a common site for MRI due to pain or injuries. We wanted to find out how many sarcomas in the knee region treated at The Norwegian Radium Hospital over a 2-year period could have been recognized as a possible malignant tumor on a routine knee joint MRI.

**Methods:** From the NRH sarcoma database 2009-2010 all patients with bone or soft-tissue sarcomas in the knee region were identified. Available images were retrospectively reviewed to decide if parts of or the whole tumor would have been visible on a knee MR centered on the joint with a defined 20 cm field of view (on routine knee MR FOV is often as small as 14 cm). The presenting symptoms were noted.

**Results:** There were 20 bone sarcomas in the knee region: 13 osteosarcomas, 3 chondrosarcomas and 4 other sarcomas (2 MFH, 1 synovial sarcoma of bone and 1 leiomyosarcoma). 19 of 20 patients had pain as their main symptom and reason for imaging. All patients were referred to the sarcoma center untouched.

There were 11 soft-tissue sarcomas, none primary intraarticular: 7 myxofibrosarcoma / MFH, 2 synovial sarcomas, 1 angiosarcoma, and 1 Kaposi sarcoma. 8 patients presented with a lump, 1 with pain and 2 with skin changes. 6 patients had had intralesional surgery for presumed benign lesions.

**Interpretation:** Even if benign bone lesions and soft tissue masses are frequently seen around the knee on routine MR, differential diagnosis versus sarcoma should be considered in symptomatic patients.

## **P5 Fusion of the *ZC3H7B* and *BCOR* genes in endometrial stromal sarcomas carrying an X; 22-translocation**

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**Background:** Endometrial stromal sarcomas (ESS) are genetically heterogeneous uterine tumors in which a *JAZF1-SUZ12* as well as *PHF1* rearrangements have been described. We looked for the putative fusion gene brought about by the X; 22-translocation that occur in a subset of ESS.

**Methods:** We investigated two ESS carrying a der (22) t(X; 22) (p11; q13) by means of high-throughput paired-end RNA-sequencing, PCR, Sanger sequencing, and FISH to find the fusion gene.

**Results:** Whole transcriptome sequencing of one of the tumors identified a *ZC3H7-BCOR* chimeric transcript. Reverse Transcriptase-PCR confirmed the presence of a *ZC3H7-BCOR* chimeric transcript in both ESS carrying a der(22)t(X;22). In both ESS exon 10 of *ZC3H7B* (from 22q13; accession number NM\_017590 version 4) was fused to exon 8 of *BCOR* (from Xp11; accession number NM\_001123385 version 1). *BCOR-ZC3H7B* cDNA fragments were amplified in only one case suggesting that *ZC3H7B-BCOR*, on the der(22)t(X;22), is the pathogenetically important fusion gene.

**Interpretation:** The *ZC3H7B-BCOR* fusion gene characterizes a subset of ESS characterized cytogenetically by a X;22-translocation. The putative *ZC3H7B-BCOR* protein would contain the tetratricopeptide repeats and LD motif from *ZC3H7B* and the AF9 binding site (1093-1233aa), the 3 ankyrin repeats (1410-1509 aa), and the NSPC1 binding site of *BCOR*. Although the presence of these motifs suggests various functions of the chimeric protein, it is possible that its most important role may be in epigenetic regulation. Whether or not the (patho)genetic subsets of ESS distinguished by the presence of *JAZF1-SUZ12*, *PHF1* rearrangements, and *ZC3H7B-BCOR* correspond to any phenotypic, let alone clinically important, differences, remains unknown.

## **P6 Whole-transcriptome sequencing identifies novel *IRF2BP2-CDX1* fusion gene brought about by translocation t(1;5)(q42;q32) in mesenchymal chondrosarcoma**

*F. Micci*<sup>1,2\*</sup>, *I. Panagopoulos*<sup>1,2</sup>, *K. B. Nyquist*<sup>1,2,3</sup>, *J. Thorsen*<sup>1,2</sup>, *L. Gorunova*<sup>1,2</sup>, *B. Bjerkehagen*<sup>4</sup>, *S. Heim*<sup>1,2,3</sup>

<sup>1</sup>Section for Cancer Cytogenetics, Institute for Medical Informatics, The Norwegian Radium Hospital, Oslo University Hospital, Oslo, Norway; <sup>2</sup>Centre for Cancer Biomedicine, University of Oslo, Oslo, Norway; <sup>3</sup>Faculty of Medicine, University of Oslo, Oslo, Norway; <sup>4</sup>Department of Pathology, The Norwegian Radium Hospital, Oslo University Hospital, Oslo, Norway.

**Background:** Mesenchymal chondrosarcomas (MCs) account for 3–10% of primary chondrosarcomas. The cytogenetic literature includes only ten such tumors with karyotypic information and no specific aberrations have been identified. Using a purely molecular genetic approach a *HEY1-NCOA2* fusion gene was recently detected in 10 of 15 investigated MCs (Wang et al., 2012). The fusion probably arises through intrachromosomal rearrangement of chromosome arm 8q. We report a new case of MC showing a t(1;5)(q42;q32) as the sole karyotypic aberration.

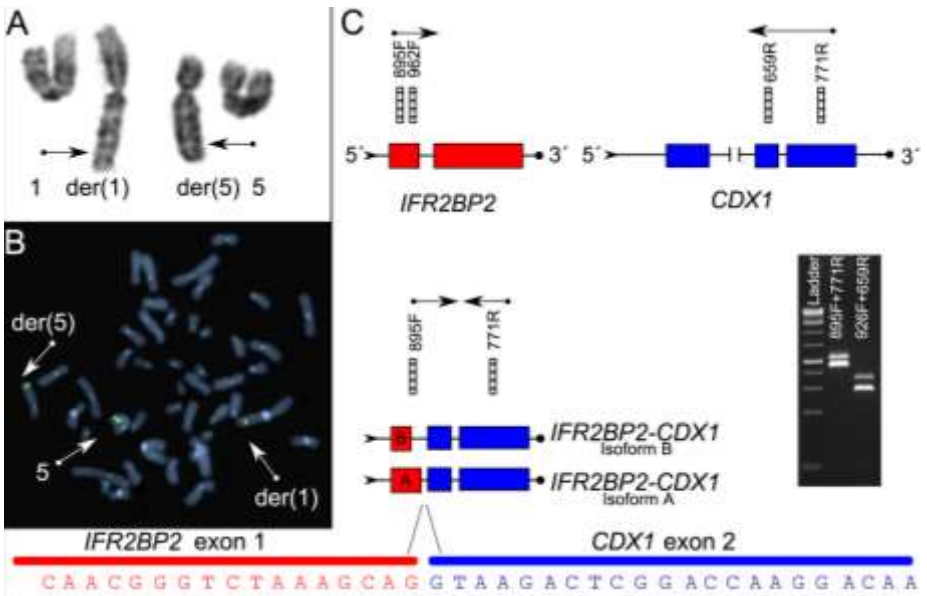
**Methods and results:** Using FISH and whole transcriptome sequencing analysis we found a novel fusion between the interferon regulatory factor 2 binding protein 2 gene (*IRF2BP2*) and the caudal type homeobox 1 gene (*CDX1*) arising from the 1;5-translocation. The *IRF2BP2-CDX1* has not formerly been described in human neoplasia. In our hospital's archives 3 more cases of MC were found, and we examined them looking for the supposedly more common *HEY1-NCOA2* fusion, finding it in all three tumors but not in the case showing t(1;5) and *IRF2BP2-CDX1* gene fusion.

**Interpretation:** The biological implications of the predicted fusion protein IRF2BP2-CDX1 can only be speculated upon, but as both fusion partners are involved in transcriptional regulation, a protein disturbing DNA transcription is likely. The *IRF2BP2-CDX1* fusion is thus suggested to take part in MC tumorigenesis and/or progression. Furthermore, the identification of a new fusion gene demonstrates that genetic heterogeneity exists in mesenchymal chondrosarcoma.

### **Reference:**

Wang L, Motoi T, Khanin R, Olshen A, Mertens F, et al. (2012) Identification of a novel, recurrent HEY1-NCOA2 fusion in mesenchymal chondrosarcoma based on a genome-wide screen of exon-level expression data. *Genes Chromosomes Cancer* 51: 127-139.

**Figure legend:** Cytogenetic and molecular details of the *IRF2BP2-CDX1* fusion gene. (A) Partial karyotype showing the aberrant chromosomes 1 and 5 together with their normal homologs. Arrows point to the breakpoint positions. (B) DAPI-stained metaphase harboring the t(1;5). Upon hybridization with probe CTC-802J2 mapping to 5q32, three fluorescent signals were detected (on the normal chromosome 5, the derivative chromosome 5, and the derivative chromosome 1) indicating a breakpoint within the genomic area covered by that BAC. (C) In the upper panel, the structure of the wild type *IRF2BP2* and *CDX1* genes is shown in grey and black, respectively. Bars indicate positions of primers yielding products by cDNA PCR. In the lower panel, the two identified fusion gene transcripts are illustrated. By sequencing the fusion was found to consist of *IRF2BP2* exon 1 (isoform A or B) fused to exon 2 of *CDX1*. The base sequence shown originates from isoform A. A gel blot demonstrating the two PCR products is shown in the right panel. The primer combinations used are specified.



## **P7 Do we need plastic surgeons to cover soft tissue defects after pelvic sarcoma resections?**

*T-T. Pakarinen<sup>1</sup>, J. Nieminen<sup>2</sup>, P. Suomalainen<sup>1</sup>, H. Kuokkanen<sup>1</sup>, T. Lont<sup>2</sup>, M. Laitinen<sup>1</sup>*

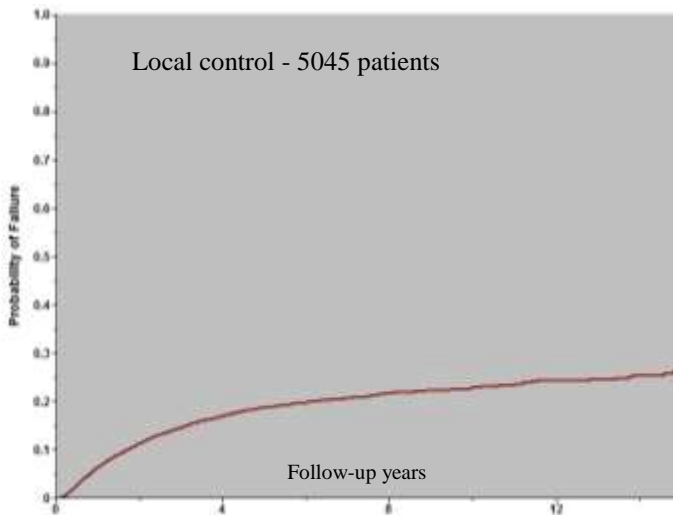
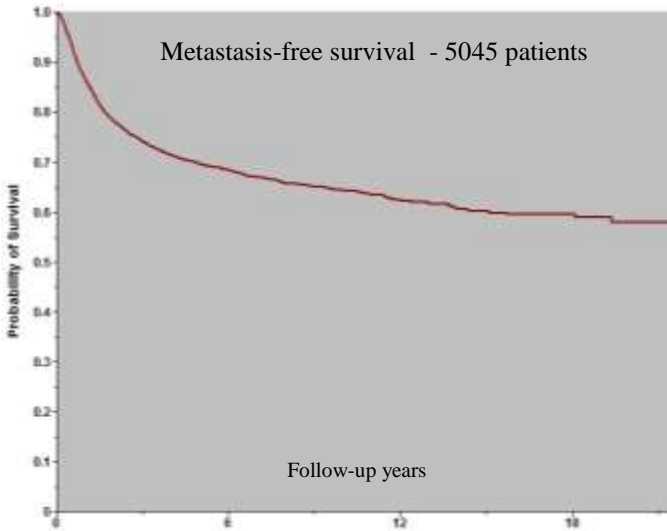
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**Background:** Pelvic sarcomas frequently requires extensive non-anatomic bone and soft tissue resections to achieve adequate margins. Reconstruction of bone and soft tissue defects is demanding and is prone to complications. We report single centre results of a treatment philosophy of pelvic sarcoma reconstructions. Our treatment protocol includes liberal use of local or free flaps to cover soft tissue defects and eliminate dead space with adequately vascularized tissue. Resection and reconstructions are often performed in two separate operations (2-staged treatment strategy) where resection and hardware reconstruction is followed by appropriate soft tissue reconstruction.

**Patients:** 2008-2013 26 pelvic sarcoma patients (21 bone and 5 soft tissue sarcomas) required resection of pelvic bone(s) and a retrospective analysis of this patient cohort was conducted.

**Results:** There were 17 males and the mean age was 52 (19-76) years. The mean follow-up time was 21 (1-68) months. Local pedicular or free flap coverage was used in 18 patients (Group Plast+) and 2-staged treatment strategy was used in 8 patients. The 30-day deep infection rate was 12% (Plast+ 6%, Plast- 25%) and during the entire follow-up time the infection occurred in 38% (Plast+ 28%, Plast- 63%). 4 external hemipelvectomies were performed (2 as planned primary operation and 2 after severe deep infection).

**Conclusions:** Surgery of pelvic sarcomas is prone to complications and should be employed in centres with adequate experience and annual caseload. A continuous co-operation with orthopedic oncologists and plastic surgeons seems to decrease postoperative infectious complications.



## **P8 Persistent wound drainage after tumor resection and endoprosthetic reconstruction of the proximal femur**

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**Background:** Persistent wound drainage is associated with an increased incidence of periprosthetic infection and occurs in about 4% of conventional total hip arthroplasties. Similar data is not available for endoprosthetic reconstruction of the proximal femur after tumor resection, where reported infection rates are substantially higher.

**Methods:** To establish the duration of postoperative surgical wound drainage, duration of administration of antibiotics and the date of discharge, we performed a retrospective review of all adult patients who underwent endoprosthetic reconstruction of the proximal femur after tumor resection for primary or metastatic bone tumors in our department during the last year.

**Results:** Of 42 patients operated in 2012, complete data were available in 41. 19 patients had prolonged wound drainage (7 days or longer), with accordingly prolonged hospital stay and antibiotic administration. Mean duration of post-operative wound drainage was 8 (2 – 45) days, mean duration of administration of post-operative antibiotics was 8 (1 – 45) days and mean hospital stay was 9 (3 – 45) days.

**Interpretation:** We found a surprisingly high prevalence of prolonged drainage from the surgical site after endoprosthetic reconstruction of the hip in tumor patients, probably reflecting multiple factors: the extent of the procedure, prolonged surgical time, significant perioperative blood loss, associated comorbidities and the burden of primary disease and its treatment.



## **P9 Sunitinib in metastatic solitary fibrous tumor**

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Solitary fibrous tumor (SFT) is a rare type of soft tissue tumor with unpredictable clinical course and local and distant recurrence rates of about 15-20%. The role of drug treatment in advanced SFT is not known. We report two patients treated with sunitinib for metastatic SFT.

The first patient was a 45-year-old male with locally advanced retroperitoneal SFT of the pelvis with 2 lung metastases 30 months after primary resection. 3 months after metastasectomy multiple lymph node metastases and new pulmonary metastases were detected. Based on data of effect of anti-angiogenic therapy in SFT, treatment with sunitinib was initiated. The patient received 4 courses of sunitinib 50 mg/d, 4/6 week regime with stable disease as the best response. He did not respond to chemotherapy as second line and died 4.5 years after diagnosis. The second patient was a 70-year-old male with locally advanced pleural SFT. He recurred with pulmonary metastases few months after primary resection. Sunitinib was initiated after confirmed growth of metastases. The selected schedule was continuous treatment 37.5 mg/day, but dose reduction was necessary due to grade 3 side effects. The patient has stable disease with tolerable side effects under ongoing therapy with 25 mg/day 7 months after start of treatment.

Conclusion: Sunitinib is feasible in management of metastatic SFT with disease stabilization as best response.

## **P10 Radiotherapy and medical treatment of desmoid tumors in Finnish patients**

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**Background and purpose:** Desmoid tumors are rare soft tissue tumors which can recur even after radical surgery but they do not metastasize. Our aim was to examine the outcome of radiotherapy and systemic treatment of desmoids in a single-institution series.

**Methods:** Data included 48 patients with histologically confirmed desmoid tumors retrieved from pathology reports and treated with surgery, radiotherapy, and/or systemic therapy in Helsinki University Central Hospital between 1987 and 2012. Radiologic images for response evaluation were reviewed. Treatment responses were assessed according to RECIST criteria 1.1. Radiation treatment planning images were merged with diagnostic radiologic images of local failures to investigate the dose distribution.

**Results:** Definitive radiotherapy was evaluated for 21 tumors. The objective response rate was 9/21 with no progressive disease response. For the tumors reaching partial or complete response, median time to response was 11 (4 -28) months. After postoperative radiotherapy 6/19 patients were diagnosed with a local recurrence. All these local recurrences occurred after intralesional resection. The median time to recurrence was 19 (9 -72) months. Various systemic therapy approaches were assessed in 17 cases with variable responses.

**Interpretation:** Radiotherapy is a valuable option for treating desmoid tumors. Achieving a response may take from months to years. After intralesional surgery and postoperative radiotherapy, the risk of local failure is still considerable. Final results will be presented at the meeting.

## **P11 Multiple occurrence of dermatofibrosarcoma protuberans, an effect of immunosuppression?**

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Departments of Plastic Surgery, Radiology and Pathology , Kuopio University Hospital, Finland , University of Eastern Finland, (A.I. Virtanen Institute for Molecular Sciences Department of Biotechnology and Molecular Medicine), Department of Plastic Surgery, Akademiska Sjukhuset, Uppsala, Sweden

**Background:** Angiogenesis, crucial for tumor progression, is a process regulated in the tissue micro-environment and one of the best *in vivo* methods available to study it is microdialysis. The endothelial cell specific growth factor family, (vascular endothelial growth factor) VEGF is essential for growth of new capillaries as well as it plays a part in lymphatic system in disseminating tumor cells.

**Methods:** Microdialysis was used to sample VEGFs in tumors and adjacent normal appearing tissue in STS patients preoperatively. VEGFs were also measured in serum and analyzed by using ELISA, and RNA analysis was performed for sarcoma samples.

**Results and interpretation:** Material consisted of 10 patients: mean age 74 (54- 86) years, female: male 7:3. Histology was: 6 MFH, 1 myxofibrosarcoma, 1 extraskelatal chondrosarcoma, 1 synovial sarcoma and 1 liposarcoma. Interestingly VEGF-A was found almost in every patients' tumor microlysate but in the control site the amount of VEGF-A was significantly lower/lacking. Only 2 patients had measureable amount of placental growth factor (PIGF). Surprisingly, we could not detect remarkable amounts of other VEGFs or soluble receptors either in test or control samples. The serum samples taken from healthy donors showed a little bit higher amounts of VEGFs compared to serum samples taken from the sarcoma patient.



## **P12 The real life data of trabectedin as maintenance therapy in patients with advanced soft tissue sarcoma. The Swedish experience from Karolinska university hospital**

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**Background:** The long-term outcome of patients with advanced soft tissue sarcoma treated with trabectedin outside clinical trials and the utility of maintenance treatment has only been rarely reported.

**Methods:** Between 2007 and 2013, patients with advanced soft tissue sarcoma failing doxorubicin could be treated with trabectedin at Karolinska University Hospital using the standard 3-weekly regimen. Data from 20 patients were collected and analyzed.

**Results:** Trabectedin was given in second, third, fourth, fifth and sixth line in metastatic phase in 4, 9, 5, 1 and 1 of patients. 4 patients are still alive. The median TTD (Time to Death) was 9 (1-29) months. The median TTP (Time to Progression) and OS (overall Survival) were 4 (1-34) months and 16 (2-36) months. The median number of courses was 6 (1-38). Best response achieved were partial response (PR, n=4, 20 %) and stable disease (SD, n=14, 70 %). Only 2 of the patients had progressive disease (PD). 3 patients had to be hospitalized for treatment-related side effects. There was a need to reduce the dose of trabectedin among all patients, with doses decreased 25% (n=14), 35% (n=5) or 50 % (N=1). 8 of the patients needed G-CSF support.

**Interpretation:** In this Swedish data set, trabectedin yielded similar or better PFS and OS compared to the registration study, even though all patients were treated with dose reductions.

## **P13 How do cancer survivors experience and cope with the sequelae of primary bone cancer and its treatment?**

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**Background:** The principle aim of this project is to study how women and men, having received treatment for bone sarcoma involving the lower extremities and pelvis, experience and cope with the consequences related to the diagnosis and its treatment. The study focuses on practical, social, emotional and cultural challenges cancer survivors face after having completed their curative treatment and expected to be recovered and function in the society.

- 1 How do 25 previous patients experience and cope with functional impairments in their daily life.
- 2 How do they cope returning to work and resuming social life and leisure activities after treatment?
- 3 How does functional impairment and bodily deviations affect their identity and self-esteem?

**Purpose:** Most of these patients are young adults, and they have undergone extensive treatment. Such a study of individuals treated for bone sarcomas will provide new knowledge and expand our understanding of cultural, psychosocial and existential aspects of daily living. This may enhance understanding about these concepts, which in the next step might improve cancer care and quality of life among these cancer survivors.

**Methods:** In this qualitative and phenomenological (Interpretative Phenomenological Analysis) study, both perspectives and methodological approaches are founded on subjective experiences based on the informant's life-world described in semi-structured interviews. The study is anchored within a humanistic science research tradition.

**Preliminary results:** 17 of 25 interviews have so far been completed. Preliminary results reveal among other findings: An impressive coping and low degree of anxiety. Also major functional impairments having changed their daily life; especially leisure- and sport activities.