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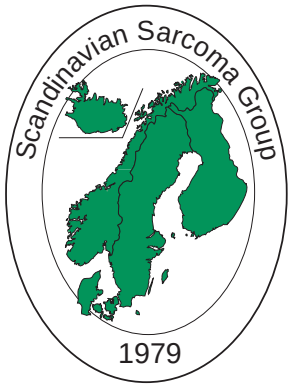

Abstracts

L1 Imatinib in non-GIST solid tumors

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L2 EURAMOS-1, A randomized European/American Osteosarcoma Study

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Background: Broad international collaboration is essential for randomized trials in rare diseases such as osteosarcoma and thus 4 multinational study groups (COG, COSS, EOI, SSG) agreed to collaborate in the European and American osteosarcoma study group, EURAMOS. The EURAMOS-1 study was opened for accrual in April 2005.

Patients and methods: Major eligibility criteria are resectable osteosarcoma and age ≤40 years. The primary aim of the study is to determine whether altering postoperative therapy based on histological response benefit patients. This report is based on the January 2011 accrual report.

Results: As of January 2011 2106 patients have been enrolled (1095 COG, 487 COSS, 413 EOI, 111 SSG) from 328 centers in 21 countries (mean 6 pts/center) and 1192 patients are randomized. The SSG patients are recruited from 12 centers in S (n=6), N (n=3), D (n=2) and F (n=1) (mean 9 pts/center). 90% of the SSG patients are included in a quality-of-life sub-study. No toxic death is reported among SSG patients. As for the whole study population 53% of the SSG patients are good histological responders.

Interpretation: The inclusion rate is on target but the accrual period will be extended from planned 4 to 6 years (stop mid 2011) to reach the target number of patients randomized. The large number of institutions involved in EURAMOS-1 needs to be taken into account when planning future international osteosarcoma trials.

L3 Update of EUROBOSS; A prospective European study for high-grade bone sarcoma in patients older than 40 years

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Background: Bone sarcoma in patients above 40 years is very rare. In 2002, three European sarcoma study groups; Scandinavian Sarcoma Group, Italian Sarcoma Group and Cooperative Osteosarcoma Study Group joined to launch EUROBOSS, the first international prospective study for this patient cohort.

Methods: Eligible are patients aged 41–65 years with osteosarcoma and other pleomorphic or spindle cell high-grade sarcomas of bone. Patients with chondrosarcoma and small round cell tumors are ineligible. Patients receive neo-adjuvant or adjuvant chemotherapy with a combination of doxorubicin, cisplatinum and ifosfamide. Poor responders are salvaged with addition of methotrexate (8 g/m^2).

Results: By Feb 2011 298 patients (COSS 125, ISG 119, SSG 54) including 68 (23%) with metastases at diagnosis are recruited. The most common subgroups are osteosarcoma (n=144), dedifferentiated chondrosarcoma (n=37) and MFH (n=30). 50% of the patients have experienced delay in chemotherapy administration and 31% a dose reduction and 1 toxic death is recorded (sepsis). 54 SSG patients are recruited from 5 centers in Sweden and Norway. For SSG, 15 patients are in CR 1, 9–75 months from diagnosis and 21 patients are dead of disease.

Interpretation: The planned intensive chemotherapy is feasible with 1 toxic death reported. To better analyze specific aspects and characteristics on histologic subtypes and subgroups the study will continue to end 2012 or to start of the planned EURAMOS-2 study.

L4 Euramos II – Ewing sarcoma

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L5 Chondrosarcoma: Skip Metastases

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Purpose: Investigate the incidence, clinico-pathological characteristics and clinical impact of skip metastases (mets) in chondrosarcoma.

Materials/Methods: Review clinical, radiographic and pathology materials of 700 chondrosarcomas. Skip mets defined as: foci of chondrosarcoma occurring within the medullary cavity, away from the primary tumor and separated from the primary by either normal bone (i.e. intramedullary skip mets), or a joint (i.e. trans-articular skip mets).

Results: 4 patients (pts) with chondrosarcoma skip mets were identified: ages 33–77 years, 3 males. All involved the femur. The primary lesions were classified as grade 3 conventional chondrosarcoma (2), or dedifferentiated chondrosarcoma (2). All were intra-medullary skip mets. 3 pts had a single skip mets; one had multiple skip mets within a single bone. 2 pts died of disease; both had local relapse and lung mets. 2 pts are disease-free at 3 and 5 years. The possibility of skip mets was suspected preoperatively in only 1 case; MRI observation.

Interpretation: Although rare, skip mets occur in chondrosarcoma and appear to be associated with high-grade primary tumors, their presence does not portend a uniformly poor prognosis. But, their recognition is important to assure complete tumor extirpation at the time of definitive chondrosarcoma surgery. MRI appears to be the most sensitive test for skip mets assessment. Of interest, the incidence of skip mets in chondrosarcoma is the same order of magnitude as that reported in osteosarcoma.

L6 ABC can easily be treated with polidocanol

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Purpose: To present our experience and results of percutaneus sclerotherapy of aneurysmal bone cysts (ABC).

Patients: All 26 patients from Jan 2007 to Sept 2010, where radiology and cytology were consistent with ABC, were treated with repeated injections of 30 mg/mL polidocanol. The mean age was 14 (3–27) years. There were 17 lesions in the long bones, 3 in the pelvic bones, 2 in the sacrum, 3 in the foot, and 1 in a finger. The sclerotherapy was performed under fluoroscopic or CT guidance and under local or general anesthesia. Each injection consisted of 2–4 mg polidocanol per kg body weight. 3 injections with an interval of 4 weeks was the most common schedule. Radiological assessment was performed regularly after the last injection. More than 3 injections were given if the lesion did not heal.

Results: All except 1 patient was successfully treated after mean 3 (1–11) injections. 1 patient with an ABC and pathologic fracture in a finger needed 11 injections. 1 patient had 3 injections (proximal ulna) without signs of healing, and was operated. The only side effect was in 3 patients who experienced local inflammatory reaction after the sclerotherapy.

Interpretation: Our results are in concordance with published data from India, showing that percutaneus sclerotherapy with polidocanol is a safe alternative to surgery for the treatment of ABC. It is especially valuable in the pelvis and sacrum where surgery is associated with considerable morbidity.

L7 Integrative analysis of genome-wide genetic and epigenetic changes in human osteosarcomas

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Background and purpose: Genetic and epigenetic alterations are frequently seen in cancer, and are responsible for the deregulation of differentiation and proliferation programs. Using different microarray technologies, we have analyzed genetic and epigenetic changes genome-wide in the well-characterised EuroBoNeT panel of 19 human osteosarcoma cell lines. By integrating different levels of genome-wide information, we can identify genes and transcriptional networks deregulated in osteosarcomas.

Methods: We have analyzed the panel of 19 osteosarcoma cell lines, as well as 4 normal bone samples and 2 primary osteoblast cultures. DNA copy number changes have been mapped at high resolution using the Affymetrix Genome-Wide Human SNP Array 6.0, methylation of more than 27,500 CpG sites have been analyzed using the Illumina Infinium Methylation27 BeadChip, whereas global gene expression patterns have been obtained using the Illumina HumanWG-6 Expression BeadChip. Data integration is performed using R scripts, and pathway and network analyses are done using GeneGO.

Results: We have identified a number of recurrent regions of DNA copy number changes in the osteosarcoma cell lines, and a comparison between the cell lines, normal bone and osteoblast cultures revealed a number of genes with altered expression and DNA promoter methylation. Integration of the different types of genome-wide data revealed a number of recurrently altered genes involved in important biological functions.

Interpretation: Important alterations identified will be validated and further investigated in the EuroBoNeT panel of osteosarcoma patient samples. The EuroBoNeT osteosarcoma cell line panel will serve as a well-characterized genetic and epigenetic model system for basic and preclinical studies.

L8 Risk factors among the European postmarketing adult osteosarcoma – Surveillance study cases

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Background and purpose: An ongoing postmarketing drug surveillance study to identify potential risk factors in a population-based series of adult osteosarcoma cases through the Scandinavian Sarcoma Group (SSG) registry and the Finnish national cancer registry is underway. We present an update as of September 2010 of the preliminary data from this study, which was earlier described in Acta Orthopaedica 2009 (Suppl 3334); 80:67-74.

Methods: Incident cases of histologically confirmed primary osteosarcoma diagnosed from Jan 2004 to the present in adults aged 40 years and older are identified through the SSG registry and the Finnish national cancer registry. Demographic characteristics; treatment history; and exposure to possible risk factors, including radiation, infection, or trauma at the site of tumor are abstracted from the medical records.

Results: 67 of 89 osteosarcoma cases identified as of Sept 2010 have been abstracted. The proportion of cases exposed to possible risk factors for osteosarcoma was 25% for radiation and 12% for injury or infection at site of tumor. Sites of radiation and osteosarcoma tumor matched for 15/17 radiation cases. Among these, mean time between radiation and diagnosis was 13 (2–36) years.

Conclusion: Data from this ongoing surveillance study, as well as a companion study conducted in the United States, add to the knowledge about adult patients with osteosarcoma and complement information from the literature describing the distribution of possible risk factors.

L9 SSX, a new player in the epigenetic regulation of mesenchymal stem cell differentiation and cancer

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Our main interest is in identifying the genes and pathways associated with sarcoma genesis and progression and with the biology of normal mesenchymal cells. In particular, our study focuses on the SSX family of genes which are aberrantly expressed in several tumor types and, apart from germ and mesenchymal stem cells are not expressed in normal cells. Through whole cell assays, and protein-protein interaction and transcriptome analysis we investigate how these genes promotes tumor growth and their normal role in mesenchymal stem cell regulation. The ultimate goal of our work is to clarify the pathways and targets affected by SSX in both healthy and cancerous cells and to use this knowledge as the solid foundation on which to theorise future therapeutic strategies to improve the prognosis that comes with sarcoma.

SSX: Synovial Sarcoma X chromosome

SSX in tumor cells

To elucidate the oncogenic properties of SSX in cancer we use a melanoma cell line, DFW established in our lab that contains a conditional siRNA system which inhibits SSX expression. We also use a similar but transient siRNA transfection of an osteosarcoma cell line, SAOS-2, chosen for its known high SSX expression.

We have shown

- SSX expression is cell cycle dependent
- SSX expression peaks at the G1/S phase and its loss inhibits entry into S phase
- Tumour cells lacking SSX do not proliferate, but maintain a viable state
- SSX induces a mesenchymal phenotype characterised by MMP2 expression and increased invasive capacity in DFW melanoma cells
- SSX promotes β-Catenin transactivation which is associated with β-Catenin phosphorylation at Tyrosine residues
- Using qPCR arrays we have highlighted a number of genes associated with epithelial to mesenchymal transition that are affected by inhibition of SSX expression in SAOS-2 cells

SSX is a therapeutic target

- SSX inhibition reduces resulting tumour size
- SSX inhibition reduces proliferation in tumours, shown by loss of Ki-67 detection
- SSX has been shown to elicit an immune response in vitro

SSX in Mesenchymal Stem cells

SSX is expressed in foetal mesenchymal stem cells (MSCs). In these cells, SSX and MMP expression is associated with cell invasion through matrigel layers. Using siRNA, we have shown inhibition of SSX expression in MSCs reduces their migration and invasive capacity by a factor of 2. We have shown that differentiation of MSCs into osteoblasts or adipocytes correlates with a down-regulation of SSX and MMP expression.

SSX interacting proteins suggest a function for SSX in epigenetic control of transcription.

Using MS we identified proteins that complex with SSX. These include: β-Catenin, Histones H2, H3 and H4 and an S100 protein. We have already confirmed some of these findings by western blot.

SSX has also been shown to co-localise with the PcG protein Bmi-1 giving further weight to a function associated with epigenetic control.

L10 Postradiation angiosarcoma after breast cancer; high recurrence rate and poor survival despite free surgical margins

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Background and purpose: Breast irradiation is a part of breast conserving treatment (BCT) for breast cancer. Postradiation angiosarcoma of the breast wall is a rare and severe long-term complication to BCT. Patients often have localized, but multifocal disease confined to the breast at presentation. Surgery is the only potential curative treatment. We characterized a population based cohort of postradiation angiosarcomas from two tertiary hospitals in order to get insight in this disease and define the surgical treatment and outcome.

Patients and methods: 36 patients, median age 67 (53–89) years, with a history of radiation for breast cancer and a histologically proven angiosarcoma were identified since 1995. Of these 36 patients, 30 underwent surgery and were included in this study. Disease-free survival (DFS) and overall survival (OS) were calculated according to Kaplan Meier.

Results: The total radiation dose to the breast/thoracic wall ranged from 45–70 Gy. The median time for the development of angiosarcoma was 7 (4–25) years. In 23 cases an ablation was performed, in 3 cases a local resection because of previous mastectomy and in 4 cases a local resection without previous mastectomy. 3 patients underwent resection of all irradiated tissue during the 2nd operation, which can be seen as a specific margin, and were excluded from further analysis. In 15 of 27 cases microscopical complete excision (free margin) could be obtained after the 1st operation, and in another 4 cases after the 2nd operation. Of these 19 patients with free margins, 11 patients developed, after a median follow-up of 6 (3-86) months after the 1st operation, a local recurrence, 4 patients developed a distant metastasis and local recurrence and 2 only distant metastases. The median follow-up for these 19 patients was 27 (3-88) months, and the median DFS and OS were 16 (1–86) and 27 (3–88) months, respectively.

Interpretation: Despite free margins, more than half of the patients developed a local recurrence, followed by dismal prognosis and median overall survival of just over 2 years. More insight in the tumor biology of this rare sarcoma is required for the development of novel therapeutic strategies.

L11 Preoperative chemotherapy in patients undergoing pulmonary resection for metastatic soft tissue sarcoma

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Background and purpose: Approximately 50% of patients with soft tissue sarcoma develop metastasis, primarily to the lungs. Although complete surgical removal may lead to long term survival optimizing treatment in the metastatic situation is warranted. Hence preoperative chemotherapy was included for selected patients.

Methods and results: 110 patients with soft tissue sarcoma who underwent complete pulmonary metastasectomy at our institution from 1980 to 2007 were included in this retrospective study. 68 (62%) received preoperative chemotherapy. Time to first metastasis was shorter in the preoperative chemotherapy cohort than in the surgery only cohort (median 15 vs. 35 months, p=0.002), and the number of metastases was higher. The median post-metastasis sarcoma specific survival (DSS) was 28 months with preoperative chemotherapy and 49 months with surgery alone (p=0.23), and time to progression (TTP) was significantly lower (median 12 vs. 20 months, p=0.042). 7% of patients in the preoperative chemotherapy cohort had good histological response and. These showed had improved DSS compared with poor responders (p=0.0438) and with surgery alone (p=0.0986). Radiological response criteria also displayed improved DSS and TTP for patients with partial response compared with progressive disease (median 44 vs. 18 months, p=0.014 and 16 vs. 8 months, p=0.012, respectively).

Interpretation: Although conclusions are difficult to draw from this highly selected cohort, our study indicates no overall benefits in outcome for patients undergoing preoperative chemotherapy prior to pulmonary metastasectomy. Patients with good histological or radiological response, though, might profit in outcome.

L12 Lung metastases in osteosarcoma. Diagnostic challenges

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Lung is the most frequent location of osteosarcoma metastases, and were the main cause of death before the chemotherapy era. Their discovery may change the therapeutic protocol, at the onset of the disease, before the local surgery after neoadjuvant chemotherapy, and in the follow-up. Unfortunately there is no sensitive and specific imaging technique, and we must decide knowing well the advantages, but also limitations of each imaging technique.

Pulmonary nodules are the usual pattern of lung metastases. They may be ossified, and calcifications are not a diagnostic factor (versus granulation nodules). But other images, rarer, must also be recognized. The metastasis may be a solitary large ossified lung mass, ossified hilar lymph nodes, an esophagomediastinal fistula, lymphangitic carcinomatosis, pulmonary artery tumor emboli, a solitary large pleural deposit along the major fissure, multiple pleural deposits, diffuse pleural calcification, pneumothorax, diaphragmatic deposits, an isolated chest wall deposit without lung involvement, or a bulla with thin walls.

Radiographs are much less efficient (half of the lesions are not detected) than CT which is the reference technique, even if surgery with palpation detects around 20% more nodules. PET has a limited spatial resolution (5 mm), but PET-CT combines both modalities and advantages.

If sensibility of CT is quite good, its specificity is poor. Detected nodules are actually metastases in half of the patients. If 1 nodule only is detected, its probability of being a metastasis is around 30%. The follow-up CT just before the local surgery does not solve the problem: both metastases and granulation nodules may increase, be stable or decrease.

Conclusion: CT positive predictive value is limited, but as surgery is the only way to cure metastatic patients, CT will still be used as the reference technique until a more specific approach can be found.

L13 Lung metastases in osteosarcoma - oncological challenges - experience from the COSS registry and results of a survey

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Introduction: COSS, the interdisciplinary Cooperative German-Austrian-Swiss Osteosarcoma group, founded in 1977, has since registered over 3500 bone sarcoma patients from over 200 institutions. Registry data has helped to define prognostic factors in syn -and metachronous osteosarcoma lung metastases (OLM). However their implication on the practical management of OLM continues to pose a challenge. In order to distinguish areas of consensus and controversy for diagnostic and therapeutic decisions in OLM we performed a survey amongst selected experts in the field.

Methods: A postal survey on the management of pulmonary metastases in osteosarcoma was sent to 17 representatives from international study groups and selected institutions.

Results: Tje response rate was 94% andj showed uniform approaches in areas like imaging methods used for initial staging and use of manual exploration with thoracotomy. It demonstrated, diverse practices regarding exploration of the unaffected site in unilateral pulmonary disease, and approach to lesions disappearing under chemotherapy. Furthermore, agreement on the size of a lesion considered to distinguish between benign and metastatic origin varied.

Discussion: Based on the survey and the current literature detection methods and principles of multimodal therapy will be discussed.

L14 Lung metastases in osteosarcoma: single institution based experience

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Background: Resection of pulmonary metastases improves outcome in osteosarcoma (OS) patients and factors influencing survival are important in clinical decision making.

Patients and Methods: 88 consecutive OS patients at LUMC under the age of 40 with pulmonary metastases, all with detailed clinical data, were included.

Results: 56 of 88 patients were treated by metastasectomy. Resectability was the main prognostic factor. In patients with primary non-metastatic OS a longer relapse-free interval was associated with better survival. Independent risk factors for worse survival were male sex, higher number of metastases and nonnecrotic metastases. Also after repeated metastasectomies, a subset of patients could be cured.

Interpretation: This single center cohort of patients with detailed clinical data enabled us to identify important risk factors for overall survival in OS patients with pulmonary metastases. Using a less detailed but much larger dataset of the European Osteosarcoma Intergroup (EOI) with 564 OS recurrences, the relationship between early-recurrence and poor survival was confirmed and good histological response to preoperative chemotherapy was related to better postrelapse survival. Currently our center participates in a phase II study investigating isolated lung perfusion with melphalan during metastasectomy procedures. Prospective studies investigating the added value of systemic therapy to pulmonary metastasectomy at recurrence are needed, preferably including new agents.

L15 Surgical challenges

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L16 Current status and consensus of treatment of abdominal sarcomas

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Retroperitoneal sarcomas (RPS) and the more rare abdominal sarcoma subtypes (except of GIST) comprise 10–15% of all sarcomas in adults. The most common histological subtypes are liposarcomas (LPS) and leiomyosarcomas (LMS). Histological subtype is important in LPS as well and dedifferentiated (WD/DD) LPS are succinct entities with pathognomonic molecular features (mdm2 amplification).

There is consensus that initial treatment at less-experienced centers with ‘shelling-out’ procedures results in unfavorable outcome. Even in experienced hands, the anatomic site of RPS often implies proximity and invasion of contiguous structures and organs making R0 resection difficult to achieve. Predictive factors for local recurrence-free survival is high grade, DD-LPS, resection margins status, surgery performed in referral centers and adding of radiation therapy (RT). Retrospective studies demonstrate that compartmental-oriented (a priori multivisceral) resection improves outcome.

When adding RT, preoperative RT is preferable to postoperative RT as treatment planning is oriented to clearly defined tumor structures, and the tumor may displace radiosensitive structures outside the treatment field. Postoperative RT is often limited by the fact that the small bowel occupies the former tumor bed and prevents effective RT. Studies have demonstrated that even preoperative chemo-radiation up to a total dose of 50.4 Gy is feasible and does not adversely affect subsequent surgical resection. Additional RT seems to improve local control in retrospective studies. However, there is no proof that preop. RT also adds to compartment-oriented resection in experienced hands. Its potential advantage must be weighted against potential side-effects. This needs a formal phase III randomized study to evaluate the risk/benefit ratio with the control arm being surgery alone.

L17 Selection of patients diagnosed with GIST for adjuvant therapy

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Background and purpose: Adjuvant therapy of patients diagnosed with operable GIST with imatinib improved recurrence-free survival in a randomized trial (DeMatteo RP et al. Lancet 2009; 373:1097–1104). Since more than 50% of patients with operable GIST are cured by surgery alone, identification of patients who most likely benefit from systemic adjuvant therapy is an important research question.

Methods: The relevant literature and the currently available risk stratification schemes were reviewed. Ongoing research on the topic is discussed.

Results: Several currently available risk stratification schemes function reasonably well in selection of the patients for adjuvant therapy. These include the proposed Consensus classification, the Armed Forces Institute of Pathology (AFIP) classification, the modified Consensus classification and the Gold nomogram. Good prognostic performance of the Consensus classification has been verified in several GIST series, and recently also the performance of the modified Consensus classification. Global pooled analysis of indi-vidual patient data from population-based series provides novel aspects for risk stratifi-cation. Mitotic count, the primary tumor size, tumor site and tumor rupture carry impor-tant prognostic information and are useful for risk stratification, but in the future the im-portance of gene mutations and other tumor molecular features will likely be increas-ingly used for estimation of the risk of GIST recurrence.

Interpretation: The currently available risk stratification methods are useful in selection of GIST patients for adjuvant therapy.

L18 Efficient referral of soft tissue sarcomas – do simple referral guidelines and an open access lump clinic result in redundant referrals?

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Background and purpose: Soft tissue tumors suspicious of soft tissue sarcoma (STS) should be referred to a sarcoma centre for diagnosis and treatment. The Scandinavian Sarcoma Group's referral guidelines are simple (superficial tumors ≥5 cm, all deep-seated). In the southern Swedish health care region (1.5 mill inhabitants) these guidelines are combined with an open-access lump clinic with no requirements of prereferral investigations or level of referring institution. This has resulted in referral of nearly all STS to our sarcoma centre before surgery but also a lot of tumors which after investigation turned out to be benign. We here present a retrospective study describing all soft tissue tumors examined at our centre during 1 year in order to determine the ratio between malignant/benign tumours referred.

Methods: All patients with soft tissue lumps visiting our out-patient clinic for the first time during 2004 were identified (n=246). Data regarding cytological and imaging investigations were collected as well as final diagnosis and further management.

Results: Preliminary data from 225/246 patients show that 15% had a STS, 7% had other malignancies and the remaining had benign diagnoses. 40% of all patients with a benign diagnosis were operated at the sarcoma centre (eg deep lipomas [30%], neurilemmomas [5%]) and 16% were referred to a local hospital for treatment. 42% were not treated once the benign diagnosis was made.

Interpretation: Simple referral guidelines combined with an open-access lump clinic is efficient for centralization of STS treatment. We consider the number of benign tumors referred manageable and, moreover, many of the benign tumors are best treated by oncologic surgeons.

L19 Simple guidelines and short Pathways for efficient referral of patients with soft tissue sarcoma

A Study of 100 consecutive patients with tumors of the extremities or the trunk wall

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Background and purpose: Optimal management of patients with soft tissue sarcoma (STS) requires multidisciplinary treatment at a sarcoma centre. However, recognition and diagnosis of STS is difficult, often delayed and many patients are poorly treated. We have an open-access lump clinic and have developed simple referral guidelines (all superficial tumors ≥5 cm and all deep-seated tumors should be referred; no investigations needed).

Methods: We characterized referral pathways and lead times in a population-based series of 100 consecutive patients with STS in extremities or the trunk wall diagnosed in the southern Swedish health care region served by our sarcoma centre.

Results: A general practitioner was primarily contacted by 3/4 of the patients. The majority was referred to a local hospital. One third of all patients were directly referred to our sarcoma centre. Patients directly referred had a shorter time to evaluation by a sarcoma specialist. 97 of the 100 STS patients were referred and importantly all 58 deep-seated and 28/42 superficial STS were referred before surgery.

Interpretation: We conclude that simple referral guidelines, implementation among general practitioners and an open access lump clinic at our sarcoma centre has resulted in a favorable referral pattern. Moreover, since direct referral from general practitioners shortens time to evaluation by a sarcoma specialist we suggest that referral guidelines should be kept simple, spread to general practitioners and that sarcoma centres should provide open access lump clinics.

L20 Soft tissue sarcoma of the extremity and trunk wall – nationwide and population-based study from Finland 1998-2001

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Background and purpose: We defined an optimal treatment protocol for soft tissue sarcoma (STS) and then retrospectively reviewed all STS patients with primary extremity and trunk wall tumor diagnosed in Finland 1998–2001. Comparison to the optimal treatment protocol was then performed.

Methods: All patients (n=219) with primary STS of the extremity or trunk wall diagnosed 1998–2001 were retrieved from the records of Finnish Cancer Registry. Histologic review was also performed.

Results: Histologic specimens of 200/219 patients were available for review. 5 lesions were changed into benign lesions or grade 1 liposarcoma. Otherwise reviewed diagnoses wouldn't have changed treatment. 6% of patients weren't referred to a tertiary sarcoma center. 44% of patients had no histologic diagnosis preoperatively and that very strongly predicted more than 1 operation. 27% of patients had a wide final margin but only two thirds of the patients with less than wide margin received radiation therapy. The estimated sarcoma-specific survival rate and local control at 5 years was 68% and 77%, respectively, for the whole study population.

Interpretation: Due to rarity, STS can be difficult to diagnose. Our nation-wide study shows that even after a whoops procedure patients may have good local control and survival if referred to a specialized sarcoma center and further therapy planned and given by a multimodality team. Because of the small number of cases annually in Finland, STS treatment should be centralized to fewer hospitals than the 5 present sarcoma groups; 1 in each university hospital.

L21 Refined diagnosis and prognosis in soft tissue sarcoma

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This work aimed at evaluating relevant prognostic issues in soft tissue sarcomas (STS), from diagnosis (study I), to validation (study II) and identification (studies III and IV) of new prognostic markers.

In **study I**, we applied 32K BAC arrays and gene expression profiling to extremity STS, 18 pleomorphic leiomyosarcomas and 31 undifferentiated pleomorphhic sarcomas, with the aim of identifying molecular subtype signatures. Both the gains/losses and gene expression signatures revealed striking similarities between the two tumor types, which were indistinguishable using unsupervised hierarchical cluster analysis and significance analysis for microarrays, thus suggesting a shared lineage of these STS subtypes.

In **study II**, whole-tumor sections from 239 STS were reviewed for size, vascular invasion, necrosis, and growth pattern. All factors provided independent prognostic information with HR of 2.2–2.6 for development of metastases in multivariate analysis. When combined into a prognostic model, referred to as SING (size, invasion, necrosis, growth), high risk of metastasis was predicted with a sensitivity of 74% and a specificity of 85%. SING compared favorably with other used systems.

In **study III**, Ezrin expression was evaluated by immunohistochemistry on tissue microarrays from a mixed series of 256 STS. Increased ezrin expression predicted development of metastasis (HR=1.8, p=0.007) and local recurrence (HR=1.8, p=0.02) and was strongly correlated to necrosis and growth pattern. Ezrin is therefore a potential marker for identification of high-risk sarcoma patients.

In **study IV**, we assessed the prognostic value and clinical applicability of five proliferation markers: KI-67 antigen, Top2a, p21, p27Kip1 and S-phase fraction in a mixed series of 196 STS of the extremities and the trunk wall. High S-phase fraction and high expression of Ki-67 and Top2a significantly correlated to risk for metastasis with HRs of 1.9–4.4. Classification and regression tree analysis showed that KI-67 antigen, Top2a and S-phase contributed to identify subgroups of patients with different risk for metastasis. This explorative analysis suggests that proliferation markers could have a role in STS prognostication.

L22 Risk factors of soft tissue sarcoma – a population based case control study covering all cases in the south of Sweden 1988-2009

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Background and purpose: There are no consensus of risk factor of soft tissue sarcoma, one reason may be sarcomas are rare. The present study of possible risk factors is the largest to date.

Patients and methods: All 870 STS cases (extremity and trunk wall) in the Southern Swedish health care region (1.5 mill inhabitants) between 1988 and 2009 were collected along with community controls matched for sex and age. A questionnaire on life style, treatments and chemical exposures was sent to all participants. Relative risks were calculated for each factor.

Results: Increased risks were observed for participants with a first degree relative with STS, 95% CI (1.0–26), exposure to radiation therapy, 2.8 (1.8–4.3) and having received any blood transfusions in connection to an operation or otherwise, 1.8 (1.4–2.4). Decreased risks were observed for those with short stature and weight at puberty, 0.6 (0.4–0.7) and 0.8 (0.6–1.0). Minor increases were observed for exposure to herbicides 1.1 (0.7–1.8) and pesticides 1.1 (0.7–1.7), but not for obesity, 1.0 (1.0–1.0).

Interpretation: Genetic susceptibility appeared to be important. Increased risk with blood transfusions indicate a possible presence of oncoviruses among blood donors. Short stature and low weight at puberty appeared to have a protective effect. A link to herbicides and pesticides was not corroborated.

L23 5-year results from a Scandinavian Sarcoma Group (SSG XIII) on adjuvant chemotherapy combined with accelerated radiotherapy in high-risk soft tissue sarcoma of the extremities and trunk wall

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Purpose: To evaluate adjuvant chemotherapy (CT) and interpolated, accelerated radiotherapy (RT) to adult patients with high-risk soft tissue sarcoma (STS) in the extremities or trunk wall[1].

Methods: High-risk STS was defined as high-grade morphology including at least 2 of the following criteria: tumor size >8 cm; micro-vascular invasion; or tumor necrosis. 6 cycles of doxorubicin and ifosfamide were prescribed to all patients. RT to 36 Gy was interposed between the second and third cycle of CT after marginal margin regardless of tumor depth, or following wide margin in deep-seated tumors. A boost of 9 Gy was delivered between the third and fourth CT cycle in case of intralesional margin.

Results: In 119 eligible patients the 5-year estimates of local recurrence rate (LRR), metastasis-free survival (MFS) and overall survival (OS) were 12%, 59% and 68%, respectively. The group (n=60) receiving RT to 36 Gy had a LRR of 10%; conversely, the LRR was 29% in the group (n=16) given 45 Gy. The presence of vascular invasion and low CT dose-intensity had a negative impact on MFS and also on OS. Toxicity was moderate regarding both CT and RT.

Interpretation: Accelerated RT interdigitated with CT in high-risk STS yielded good local and distant disease control with acceptable treatment-related morbidity. Vascular invasion was a potent prognostic factor for MFS and OS. The importance of CT was stressed by the effect on survival

of CT dose-intensity. A higher split-course RT dose following intralesional surgery was not sufficient to compensate for the poorer surgical margin.

1. Five-Year Results From a Scandinavian Sarcoma Group Study (SSG XIII) of Adjuvant Chemotherapy Combined With Accelerated Radiotherapy in High-Risk Soft Tissue Sarcoma of Extremities and Trunk Wall. Jebsen NL, Bruland OS, Eriksson M, Engellau J, Turesson I, Folin A, Trovik CS, Hall KS. Int J Radiat Oncol Biol Phys. 2010 Oct 8. [Epub ahead of print]

L24 SSG XX: A Scandinavian Sarcoma Group treatment protocol for adult patients with high-risk soft tissue sarcoma of the extremities and trunk wall – an update

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In 2007 the Scandinavian Sarcoma Group (SSG) initiated a new adjuvant protocol, SSG XX, based on SSG XIII and improved knowledge of prognostic factors. In SSG XX patients with high-grade soft tissue sarcomas (STS) having either vascular invasion or the presence of at least 2 of the risk factors: size >8 cm, necrosis, or infiltrative growth, are included. 6 cycles of doxorubicin 60 mg/m^2 and ifosfamide 6 g/m^2 are given postoperatively (A) with interpolation of hyperfractionated/accelerated radiotherapy. 2 daily fractions of 1.8 Gy are given postoperatively between cycle 3 and 4 for 10 consecutive days (36 Gy) to patients with marginal margins for subcutaneous or deep tumors and with wide margins for deep tumors. For intralesional margins 1.8 Gy x 2 for 12,5 days (45 Gy) are given. No radiotherapy is given for subcutaneous tumors when wide margins are obtained. A preoperative treatment arm (B) is available for patients who carries an obvious risk for intralesional surgery. They receive 6 cycles of chemotherapy with radiotherapy (36 Gy) administered between cycle 2 and 3.

150 patients are planned to be recruited is and are expected to be reached in 2012. At present 93 patients have been included in arm A and 8 patients in arm B. The protocol has proved practically feasible with mild toxicity. Update experiences will be presented.

L25 Ki-67 antigen and soft tissue sarcomas: new look at an old marker

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Background and purpose: With neo-adjuvant treatment options available, the need for prognostic markers to define high risk patients for metastasis before surgery is increasing. We evaluated proliferation measures in a large series of high grade STS with correlation to prognosis.

Methods: 203 high-grade primary STS of the extremities and the trunk wall representing the 3 most common subtypes; malignant fibrous histiocytoma (n=97), leiomyosarcoma (n=65) and liposarcoma (n=41) were selected for the study. Immunohistochemistry determined expression of Ki-67, Top2a, p21 and p27. S-phase fraction was quantified using flow cytometry. Metastasis-free survival (MFS) was used as end-point for all analyses, and MFS rates were calculated according to the Kaplan-Meier method. Interactions between clinical variables and their impact on metastasis was evaluated using CART analysis.

Results: In univariate analysis high Ki-67 expression (HR=4.5), high Top2a expression (HR=2.2) and high S-phase fraction (HR=1.8) were significantly correlated with risk for metastasis. P21 and p27 can not significantly predict risk for metastasis.

In multivariate analysis Ki-67 expression remained significant after adjustment for size, for vascular invasion and for necrosis, but not with grade and for SIN (Size, Vascular Invasion, Necrosis). In CART analysis, vascular invasion was the strongest risk factor. In the subgroup without vascular invasion, Ki-67 expression was the strongest prognostic factor.

Interpretation: Ki-67 was the strongest prognostic factor in the preoperative setting, thereby allowing better identification of patients who would benefit from neo adjuvant treatments.

L26 Reactivation of the p53 tumor suppressor function as therapeutic strategy for soft tissue sarcomas

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Background and purpose: Inactivation of the p53 tumor suppressor function is an oncogenic event in nearly all cancers. In the absence of inactivating gene mutations, p53 function can be abrogated in some tumors by other mechanisms that impact the fate of p53 or repress its transcriptional activity. Mutations in the p53 gene are relatively uncommon in soft tissue sarcomas (STS) and more recently it has became evident that the function of p53 is abrogated in some STS subtypes, suggesting that a disfunctional p53 is responsible for a refractory response to chemotherapeutic drugs.

We recently reported that in synovial sarcomas, the chimeric oncoprotein SS18-SSX, promotes the ubiquitination and degradation of p53. This was associated with stabilized protein levels of the p53 regulator HDM2 induced by the SS18/SSX. Consequently, we hypothesize that drugs that reactivate the function of wild type53 could have therapeutic potential for these tumors.

Methods and results: We investigated the effect of nutlin-3 (Roche), a small chemical compound that inhibits the p53-HDM2 interaction. As expected, nutlin-3 disrupted the p53-HDM2 interaction, stabilizing p53 levels and reconstituting its transcriptional function. The reactivation of p53 induced by nutlin-3, reverted the refractory response of these tumors to differenty genotoxic drugs, like doxorubicin and actinomycin D.

We have now evaluated the activity of a newly discovered, small molecule deacetylace inhibitor and p53 activator tenovin 6, in experimental models of synovial sarcoma and rhabdomyosarcoma. In synovial sarcomas or rhabdomyosarcomas with a wild type p53 gene, tenovin-6, restored p53 levels, increased the levels of p21 and inhibited tumor cell proliferation.

At difference to the effect of nutlin 3, this response was not directly associated with the expression of the SS18/SSX fusion protein, but functions associated to the de-acetylating function of sirtuins. The mechanism of action is presently being investigated.

Interpretation: Our results indicate that the chemical reactivation of p53 in combination with low doses chemotherapeutic drugs is a potential therapeutic strategy for soft tissue sarcomas with wild type p53.

L27 Retroperitoneal sarcoma (RPS). A retrospective study in two Scandinavian sarcoma centers

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Purpose: Analysis of characteristics and prognostic factors in a retrospective cohort of patients with RPS treated at two Scandinavian sarcoma centers: Bergen, Norway, and Lund, Sweden, with focus on the effect of adjuvant radiotherapy (RT) on local control and survival.

Methods: Characteristics of patients and tumors were recorded. Cox regression was used to analyse prognostic factors for local control, metastases and overall survival.

Results: The study included 142 patients: 70 from Norway diagnosed 1988–2009 and 72 from Sweden diagnosed 1998–2009. The proportion of high-grade tumours was 78%. Liposarcoma (39%) and leiomyosarcoma (33%) were the most frequent histotypes. The rate of patients undergoing primary surgery at a sarcoma centre increased from 79% before 2003 to 86% after 2003. Among 101 patients that underwent surgery with curative intention, 5-year local recurrence free survival, metastasis free survival and overall survival were 55%, 54% and 56%, respectively. Large tumour size and positive margin were significant prognostic factors for local recurrence. Local control was significantly better in the 45 patients who received adjuvant RT (HR=0.3, p=0.004). High malignancy grade was the only significant risk factor for metastases (HR=3.5, p=0.02). High age was a negative prognostic factor for overall survival. The use of adjuvant RT was associated with an improved overall survival (HR=0.4, p=0.01).

Interpretation: Both 5-year local control rates and overall survival were better in the group receiving adjuvant RT, and were also comparable to results from other studies despite the high proportion of high-grade tumours in our material.

L28 Sexuality and body image among teenagers with sarcoma

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Background and purpose: Today we know that teenagers treated for bone sarcoma are coping well. They get educated, they work and have a good quality of life equal to the general population. However, we know little about their body image and sexual health, except for statements from the clinical practice of health care professionals, and the patients preferences in the context. Front line care providers often do not have the time or training to focus on these quality of life issues, and on the other side the private nature of the topic can prevent teenagers from pursuing help.

Methods: Searching the data bases Medline, Embase, PsycInfo and Cinahl gave few hits concerning the 4 key words sarcoma/teenagers/sexuality/ body image. Sexuality when separating Kaposis sarcoma gave 1 hit. Body image gave 6 hits, all of them with little or no relevance to this topic.

The Norwegian Radium Hospital has organized 1-day courses for teenagers who have been treated for sarcoma. In our institution we have looked at their evaluation of the course.

Results: This presentation will give some few results from the few findings from databases, and data collected from our patient coursers.

Interpretation: Data base searches gave surprisingly few findings. Further research is needed. First step is to start talking about body image and sexuality with teenagers treated for sarcoma. This presentation hopefully will encourage you to talk about sexuality and body image with your adolescent patients.

L29 Cryopreservation of ovary tissue, a possibility for sarcoma patients?

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L30 To lose a child to cancer – 449 Swedish parents' experiences

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In 2001 we performed a nationwide study of parents having lost a child to cancer 4–9 years earlier in Sweden; 449 of 561 (80%) bereaved parents participated. Non-bereaved parents were also invited in the study; 457 of 659 (69%) participated. The aim was to assess bereaved parents' long-term psychological morbidity and to identify modifiable health care related factors affecting psychological morbidity in bereaved parents. Parents who lost a child to cancer were found to be at increased risk of anxiety and depression for 4–6 years following the loss. Parents reported that the child suffered from severe symptoms prior to death. Unrelieved pain in the child was found to affect the parents still 4 to 9 years following the loss. Parents who received information about their child's poor prognosis were more likely to care for their child at home until death. In addition, parents who were aware of their child's imminent death suffered less psychologically in the long term, especially fathers. Parental support from health care professionals during the child's illness and following the loss facilitates the grief process. Yet, support from family, friends and others, many years after the loss were found to be even more important.

L31 Rehabilitation (orthopedic surgeon and physiotherapist collaborate) Growing prosthesis in children

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L32 Hope and despair. Philosophy of life, expectations and optimism in cancer patients and their spouses

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Background and purpose: To explore philosophy of life, expectations and optimism in patients and spouses in two different cancer situations, and to determine whether these aspects had relevance for psychological distress and quality of life.

Methods: The first situation was being newly diagnosed with advanced cancer. Data on philosophy of life, optimism and psychological distress were gathered at one occasion. The second situation was having completed curative cancer treatment. Data on expectations for the recovery period, optimism, psychological distress and quality of life were gathered at three occasions.

Results: Being optimistic was of most clear importance for psychological distress in the patients and spouses studied in both situations. Being newly diagnosed with an advanced cancer mainly provoked negative mental changes, which often included existential questions related to higher levels of psychological distress. Spouses often had more difficulties than patients, handling the situation. Patients' expectations for the recovering situation were often not met, however, this generally had little importance for psychological distress or quality of life, instead positive mental changes were helpful if the recovering period was tough.

Interpretation: In the early stage of the palliative phase, the whole situation of both patients and their spouses, including existential questions, could be penetrated. When a patient has completed curative cancer treatment the recovery progress needs to be evaluated and if the period is perceived as tough, the patient should be offered professional help.

L33 Omvårdnad av patienter med lungmetastaser

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L34 Physical therapy for sarcoma patients in palliative care

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In this presentation I will describe the approach of the physiotherapist who works with sarcoma patients in palliative care. As a basis of our practice in this field we follow "The national guidelines for physical therapy in palliative care", written by Haukeland University hospital, the department of physical therapy, Haraldsplass Diaconal Hospital and the Specialist Centre for Palliative Healthcare for the West of Norway.

Treatment in palliative care is more focused on symptoms than on the diagnosis itself. WHO defines palliation as a system of support to help the patient to live as actively as possible until death occurs. The goal of palliative rehabilitation is described as limiting the consistencies of the development of advanced disease. A multidisciplinary approach is needed and the physiotherapist often has an active role.

The goal of physical therapy in palliative care is to optimize quality of life. Aspects of this would be to maintain function or to slow down the negative development of progressive loss of function; prevention of complications caused by immobilization, prevention and relief of pain and other symptoms and promotion of physical and psychological well-being.

In the presentation I will describe some general principles for the physiotherapist working with palliative patients and some of the most current physical therapy approaches we use to attain the main goal. I will illuminate these approaches with examples from my clinical practice with sarcoma patients.

L35 Influence on the health of the partner affected by tumour disease in the wife or husband

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Background: The partner is often the most important person in providing support for a person with cancer. However, the partner might also be affected by him/her self. We used population based register data to compare different aspects of health among partners before and after the cancer diagnosis.

Methods: We analyzed health care use, diagnoses, and health care costs among partners (N=11 076) and sick leave among partners of working age (N=1923).

Results: Health care use and health care costs for partners increased in the years following the cancer diagnosis of the person with cancer, mainly for inpatient care. The number of diagnoses increased significantly among partners in the whole sample (RR 1.24; 95% CI, 1.21 to 1.24), with the largest increase in psychiatric diagnoses (RR 2.02; 95% CI, 1.73–2.37). Costs of health care increased most for younger male partners (age 25 to 64 years). Sick leave among partners increased around the time of the cancer diagnosis for the person with cancer. Partners of persons with lung cancer had the highest number of sick days and of sick leave episodes with the highest standardised sick day ratio (SSR) compared to the general population (SSR 1.76; 95% CI 1.24–2.40).

Interpretation: Living as a partner of a person with cancer may lead to a decreased health. Supporting the partner through the illness trajectory will benefit both the partner and the person with cancer. The results indicate that apart from the individual perspective, there are also economical incentives for including the partner in supportive cancer care.

L36 Första året på Nordens första barnhospice

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L37 Sjukgymnastisk rehabilitering efter benamputation för sarkom

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Sjukgymnastik vid benprotesanpassning vid sarkom är i högsta grad individuell. Protesanpassningen kräver en lyhörd sjukgymnast och behandlingen kan pendla mellan intensiv träning och ingen träning alls.

Protesanpassning bör planeras utefter onkologisk behandling samt patientens motivation och ork. Detta innebär bland annat att en patient som inte har ork att prova en benprotes under onkologisk behandling ska ges tillfälle att avvakta med protesrehabilitering.

Sjukgymnastisk information gällande protesrehabilitering och amputation (fantomsensationer mm) bör vara tydlig men bör ej ges innan patienten och anhöriga är mottagliga. Det kan däremot vara av vinst för patienten att tidigt med hjälp av sjukgymnast välja ut en avspänningsteknik som hon/han kan lära sig att behärska. Patienten ska likaså få hjälp av sjukgymnasten med att etablera kontakt med stumpen/ amputationsstället.

Första protesen borde vara en positiv compliance under onkologisk behandling och behöver inte uppfylla någon annan funktion.

L38 Lydiagården – centrum för cancerrehabilitering

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Lydiagården har sedan 1992 bedrivit psykosocial cancerrehabilitering. Lydiagårdens rehabiliteringsmodell erbjuder psykosocial rehabilitering under 5 dygn till patienter som har avslutat sin primära cancerbehandling och inte har kvarvarande tumör (aktiva veckor) och dels till patienter med kvarvarande tumörsjukdom (kroniska veckor) samt till närstående. Syftet med rehabiliteringen är att öka individens förmåga att handskas med sin sjukdom och livssituation med ökad livskvalitet för att snabbare komma tillbaka till vardags- och eventuellt till yrkeslivet.

Rehabiliteringsprogrammet innehåller både enskilda och gemensamma moment. De olika delarna är information och undervisning, fysisk aktivitet, samtal, kulturell och kreativ verksamhet.

I rehabiliteringsteamet ingår onkologläkare, sjuksköterskor, sjukgymnast, kurator samt själavårdare och konsulter.

Under åren 1992–2010 har 6 186 patienter och 1 691 närstående genomgått Lydiagårdens rehabiliteringsprogram. 80% är kvinnor, vanligast med bröstcancer som erbjuds specifika rehabiliteringsveckor. Män med prostatacancer är underrepresenterade. Trots detta genomfördes 2 rehabiliteringsveckor för 21 män med prostatacancer.

Utvärdering av rehabiliteringsvistelsen sker kontinuerligt med en enkät. Denna har under alla år varit positiv. Under 2010 visade den att 93% var nöjda eller mycket nöjda med undervisningsdelen, 95% angav att deras förväntningar hade uppfyllts och angående den totala upplevelsen var 98 % nöjda eller mycket nöjda. Mätning av ångest och depression med HAD sker vid rehabiliteringens början och slut. Denna visar att ångestnivån minskade hos såväl patienter som närstående.

Utveckling av verksamheten sker kontinuerligt. Under år 2007 och 2010 genomfördes “familjeveckor” där en av föräldrarna hade kronisk cancersjukdom. Utvärderingarna från denna var mycket positiva från såväl föräldrarna som barnen.

L39 Kropp og kreft

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L40 Undertrycks behandling av svårläktasår – praktisk erfarenhet

C. Bernhardsson, M. Lundsten
Ortoped mott Norrlands Universitetssjukhus, Umeå, Sverige

L41 Vacuumbehandling/NPWT-kliniska riktlinjer

S. Green
Mølnycke Health Care

L42 Prevention/treatment of mucositis after Methotrexate

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Background and purpose: Many sarcoma patients have serious problems with mucositis due to chemotherapy, osteosarcoma patients treated with high-dose methotrexate). Standard treatment is mouth rinsing with Leucovorin. In addition many of them use Düsseldorf mixture. Despite this, most of them experience serious problems with sore and dry mouth during the treatment.

We investigated whether Caphosol mouthwash addes to Leucovorin mouth wash was of value.

Method: The patient receives a diary with various questions that they have to fill out every day they use Caphosol. For example they have to say how many times they use Caphosol per day.

The leader of the project has her own form she has to fill out on the background of both the patient diary, and her own examination of the patients mouth etc. The project will end when 5 patients has used Caphosol throughout their entire treatment period of 9–12 months.

Results and interpretation: At the moment there is one patient participating in the project. She seems to have a good effect of Caphosol and says “I won’t dare to not use it!” When the project closes we have hopefully been able to find a tool to prevent and treat dryness of mouth and oral mucositis.

L43 Prevention and assessment of chemotherapy-induced nausea and vomiting in children and adolescents with cancer

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Background and purpose: Young age is a known risk factor for chemotherapy-induced nausea and vomiting (CINV; symptoms with most negative impact on the childs quality of life during their treatment. CINV could have potentially serious consequences such as dehydration, acute renal failure, electrolytic imbalances as well as malnutrition and weight loss. Few evidence-based data are available to guide clinicians in the treatment of children and there is a shortage of satisfactory tools for self-assessment.

The aim of this project is to try to adapt the current emesis standards for adults for CINV to children to prevent the effect of emetogenic chemotherapy and to evaluate the tolerability and efficacy. The purpose is also to find a valid self-assessment tool.

Methods: We are evaluating the tolerability and efficacy of a treatment consisting of a long acting 5HT3-antagonist, corticosteroid and a NK1 antagonist. The children register their CINV themselves in a diary, designed by the Swedish Emesis Registry (SER), from the start of chemotherapy to 10 days post therapy. For small children we are using a modified Wong-Baker scale with four faces representing no nausea, mild, moderate and severe CINV. Episodes of vomiting and nausea as well as overall wellbeing are recorded. Some patients prefer interviews instead of a diary.

Results and interpretation: A new long acting 5HT3-antagonist has been tested and shown to have a much better effect on CINV and has been well tolerated. Our modified Wong-Baker scale has been a useful tool to assess CINV in children.

L44 Starts strong – Lasts long

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L45 Kan manuell myofasciell behandling anvendes til pasienter med sarkom? Teori

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L46 Kan manuell myofasciell behandling anvendes til pasienter med sarkom? Praksis

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P1 Outcome for non-operated patients with metastatic spinal cord compression

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Purpose: Assess survival and neurological function among cancer patients whom we decided not to operate for spinal cord compression.

Patients: Data was prospectively collected for 112 cancer patients referred 2002–10 for spinal metastases. Patients without radiological proof of compression of neurological structures were not included. Neurological function was assessed according to Frankel: A-C non-walkers and D-E walkers. The Tokuhashi score was applied to assess global function and prognosis. Prostate (41%), breast (12%), and lung cancer (11%) were the commonest primary lesions. The compression was located in the thoracic spine in 78 %.

Results: The median survival was only 2.5 months. The Tokuhashi score was highly predictive for survival. Half of the patients with Tokuhashi score ≤4 were dead within 1 month and almost none survived 6 months. In the group with Tokuhashi scores ≥5 all survived 1 month and median survival was 15 months. Among walkers who survived 12 months 95% retained their walking ability. 10 patients (15%) were later operated for neurological worsening 2 weeks -4 years after initial presentation. 8 of 10 regained or retained walking ability after surgery and all survived 3 months after surgery.

Interpretation: Most patients with poor neurological function and extensive cancer disease will not benefit from spinal surgery. Patients with good function can safely be treated non-surgically as only few will progress to significant neurological deficit and can then be operated.

P2 Multifocal osteosarcoma. A case report

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Background: Multifocal osteosarcoma is a rare condition with poor prognosis. It is defined as occurrence of osteosarcoma at 2 or more sites without pulmonary metastasis. It may be synchronous (more than 1 lesion at presentation) or metachronous (new tumor developing after initial treatment).

Case report: A 15 year old boy, was diagnosed with multifocal osteosarcoma of synchronous type. At referral he had pain in his right knee. Radiographs revealed a tumor mass in the proximal fibula. Bone scan showed occurrence at multiple sites including tibia, femur, fibula, humerus bilaterally, several ribs and ilium. Pulmonary metastasis was not detected on CT. Open biopsy of the proximal fibula showed osteosarcoma. Cytogenetical tests showed no P53 mutation. The patient underwent chemotherapy according to EURAMOS protocol. No surgery was performed. After 3 months of chemotherapy tumor volume increase was observed in some sites. A new tumor was observed in the left fibula. To determine the viability of the tumor and to decide further treatment new biopsies from both fibulae showed viable tumor and tumor necrosis about 80%. Chemotherapy was then continued (MAPIE arm). MRT exam 11 months after diagnosis showed that some tumors had decreased in size, no change in most tumors and minimal increase in some. The patient remains clinically well 12 months after diagnosis and has no pulmonary metastasis.

Discussion: In general multiple osteosarcoma has a poor prognosis and patients die within 5–16 months. Treatment according to the EURAMOS protocol seems favorable in our patient. Further treatment (interferon) will be decided according to the results of a new biopsy.

P3 A case illustrating some diagnostic, oncological and surgical challenges in the management of osteosarcoma lung metastases

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A 41-year-old woman with 10 months of knee pain due to a 18 x 10 x 8 cm bone tumor in the distal femur, was admitted to the Norwegian Radium Hospital in April 2007. Biopsy revealed a highly malignant osteosarcoma with osteoblastic and teleangiectatic differentiation. Tumor enclosed nerves and vessels, hence she was amputated. At diagnosis a 16 x 12 mm lung lesion was detected by CT. The patient was included in the Euroboss I protocol.

From April to November 2007 she received 9 cycles of cisplatin, doxorubicin and ifosfamide, the last 4 with 25% reduced dosage due to thrombocytopenia.

In September 2007 complete remission of the lung lesion was observed, leaving surgical intervention unwarranted, thus chemotherapy was completed. Follow-up included CT scans bimonthly, revealing lesion reoccurrence by March 2008. Right-sided thoracotomy was performed, and 5 small lung lesions were resected with a lung laser. No viable cancer cells were detected, only fibrous tissue indicating total tumor regress after chemotherapy. Re-thoracotomy was performed March 2009, and 3 more metastases were removed.

During the next 9 months she received and tolerated well, gemcitabine 600 mg/m^2 every forthnight plus muramyl tripeptide (MTP) 2 mg/m^2 twice weekly for 3 months and once weekly for 6 months. 3 months later a 3 mm suspicious lesion appeared in the right lung, increasing to 4 mm by November 2010.

This case demonstrates some treatment challenges for osteosarcoma patients with metastatic lung metastases. A multi-disciplinary sarcoma team should be responsible for treatment plan. More studies are warranted regarding the role of MTP in the treatment of osteosarcoma.

P4 Awareness day for sarcomas

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Background: Frustration over meeting many patients with recently discovered sarcoma with a symptoms since long time and metastasis at the time of diagnosis. Lack of knowledge about sarcoma among GPs and other Healthcare Professionals. Honoring sarcoma survivors and their relatives organize a preliminary meeting for a Patient Association.

Purpose: Increased attention on sarcomas for health care personal and if possible decrease time from appointment with GP to diagnosis and start of treatment. Organize a possibility for sarcoma patient to meet, learn from and support each other.

Methods: Awareness day for health care professionals with lessons about: what sarcoma is, how to detect, how to refer to a sarcoma center and treatment for sarcomas. Gathering for sarcoma survivors and their relatives with entertainment and food and beverage.

Results: 264 GPs, physiotherapists, nurses and other health care professionals participated at the conference of Sarcoma Awareness. 250 sarcoma survivors and their relatives joined the evening event.

Interpretation: The response from the attendants shows that there is a need for information about sarcomas for health care professionals. Former patients have responded that they need a fellowship to support and help each other.

P5 Molecular cytogenetic characterization of a t(1;5)(q43;q33) in a mesenchymal chondrosarcoma

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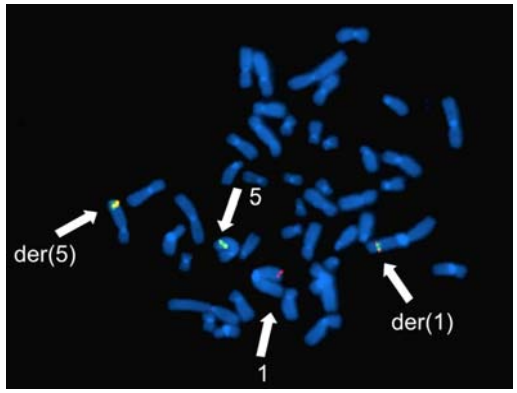
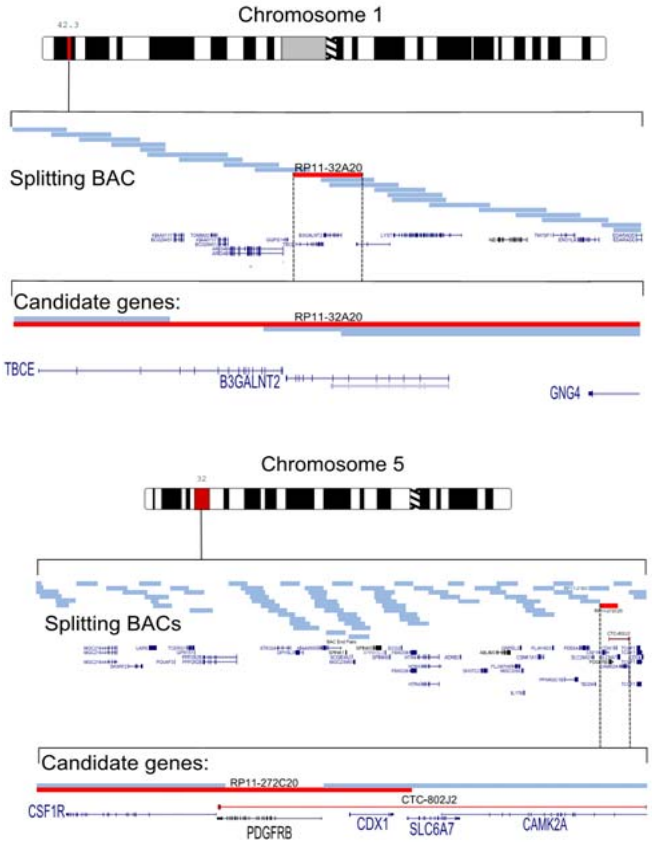
Introduction: Mesenchymal chondrosarcomas are rare sarcomas with a characteristic histological appearance. Nearly nothing is known about the pathogenetic events underlying them. No fusion genes or recurrent translocations have been described in these tumors. Patient and methods: A 65-year-old woman was diagnosed with a tumor in the pelvis. The tumor was resected, showing a small-celled chondroid tumor consistent with the diagnosis extraskeletal mesenchymal chondrosarcoma. Cytogenetic analysis was performed and further FISH analyses were done with a panel of Bacterial Artificial Chromosome (BAC) clones to identify the breakpoints.

Results: In all cells a t(1;5)(q43;q33) was found as the sole cytogenetic abnormality. A normal karyotype in peripheral blood leukocytes ruled out the possibility of a constitutional aberration. Hybridization with BAC RP11-32A20 mapping to chromosome band 1q42 gave 3 signals while hybridization with BAC CTC-802J2 mapping to 5q32 also showed a split signal.

Interpretation: The splitting BACs in 5q32 are overlapping the platelet-derived growth factor receptor beta (PDGFRB) gene, a known fusion partner in cancer. The splitting probe in 1q42 has no obvious candidate fusion partner. Further studies using more detailed molecular techniques will elucidate which genes are involved, and will hopefully be presented.





P6 Mesenchymal cancer stem cell of sarcoma and the role of EGFR and its ligands

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Background: Tumorogenic transformation of soft tissue sarcoma (STS) may origin in a small subset of mesenchymal cancer stem cells (CSC). CSC has been isolated in brain tumors and their resistance to conventional therapies has been confirmed. Understanding the mechanisms of this transformation may influence the treatment of STS because these patients often experience treatment failure. It is well known that the EGFR is overexpressed in STS but the role for the EGFR system in mesenchymal CSC is unknown.

Material and methods: A human CSC model with a progenitor non-tumorogenic clone TERT4 and a tumorogenic clone TERT20 were investigated for the expression of the 4 receptors (HER1-4) and 7 activating ligands (AR, HB, EPI, Beta, Met, NRG1A and NRG1B) by using PCR. The activity of the EGFR was investigated using specific antibodies and visualized by Western blot.

Results: TERT4 and TERT20 had approximately the same level of expression of EGFR whereas the level of HER-2 was significantly lower in TERT 20. The ligands AR, HB, EPI and BETA had a significantly higher level of expression in TERT20 than in TERT4. The EGFR activity of the TERT20 cell linie was high and could be inhibited by the EGFR specific agent elotinib resulting in reduced cell proliferation.

Interpretation: It is the expression of ligands rather then the level of EGFR which is important in mesenchymal CSC transformation. By blocking the EGFR receptor it may by possible to influence the tumorogenesis, however clinical STS tissue must also be investigated.

P7 Two fatal cases following total lung irradiation for metastatic bone sarcoma

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We present 2 female patients, both 18 years old, who died shortly after total lung irradiation. Both received a conventional fractionation: 1.5 Gy x 13 – total dose 19.5 Gy.

Patient 1 had a metastatic osteoblastic osteosarcoma; primary tumor in her proximal tibia surrounding the nerve-/vascular bundle and numerous bilateral lung lesions and treated according to EURAMOS-1. MTX lung toxicity developed. She was found ineligible for lung surgery. Hence, femur amputation was not considered justified. She then received external beam radiotherapy, both to the primary tumor and as total lung irradiation. 153Sm-EDTMP was administered before lung irradiation to boost the dose. Shortly after completion she experienced couching and moderate dyspnea. Antibiotic treatment was initiated. A rapid progress of diffuse pneumonic infiltrates and dyspnea developed. CT revealed extensive ground-glass opacities, progressing to involve the total lung parenchyma.

Patient 2 presented with a large Ewing's sarcoma in the right pelvic region and multiple bilateral lung lesions. She was treated with chemotherapy according to the ISG/SSG III, operated with marginal resection, and received radiotherapy to the right pelvic region. Towards the end of radiation she developed acute abdomen and upon surgery radiation induced changes in the small intestine was demonstrated. 4 months later total lung radiation was given. Towards the end of this treatment, pulmonary infections occurred. Antibiotics were given but dyspnea developed leading to ARDS.

Both patients were treated in intensive care units, by high-dose steroids, and antibiotics and kept on respirator for 2 and 3 weeks. Both died due to pulmonary failure.

In retrospect, the MTX lung toxicity and the GI-toxicity following radiotherapy for the primary tumor might be signs of increased individual radiotoxicity.

P8 Effect of a multimodal high intensity exercise intervention in cancer patients undergoing chemotherapy: randomized controlled trial

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Purpose: To assess the effect of a multimodal group exercise intervention as an adjunct to conventional care on fatigue, physical capacity, general wellbeing, physical activity and quality of life in patients with cancer who were undergoing adjuvant chemotherapy or treatment for advanced disease.

Materials and Methods: 269 patients with cancer (73 men, 196 women), mean age 47 years, representing 21 diagnoses participated in a 9-h weekly training program for 6 weeks. The intervention consisted of supervised exercise comprising high intensity cardiovascular and resistance training, relaxation and body awareness training and massage in addition to conventional care. Main outcome measures included EORTC, QLC-30, MOS, SF-36, Leisure Time Physical Activity Questionnaire, muscular strength (1RM), and maximum oxygen consumption (Vo2max).

Results: Adjusted for baseline score, disease, and demographic covariates, the intervention group showed improvement at six weeks for the primary outcome, fatigue of -6.6 points, p=0.02. Significant effects were seen on vitality, physical functioning, role physical, role emotional, and mental health scores as well as mean differences between groups for Vo2max, and for muscular strength. No significant effect was seen on global health status /quality of life.

Interpretation: A supervised multimodal exercise intervention including high and low intensity components could safely be used in patients with various cancers who were receiving adjuvant chemotherapy or treatment for advanced disease. The intervention reduced fatigue and improved vitality, aerobic capacity, muscular strength, and functional activity and emotional wellbeing, but not quality of life.

P9 Education and coping course for people treated for sarcoma

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Background: Patients with sarcoma undergo a long multimodal treatment. Many of our patients struggle with side effects after treatment has been completed. We have seen a need for these patients to receive information relating to the long term side effects, as well as getting together with others in the same situation.

Purpose: To give the participants a possibility to meet and talk with others in the same situation, as well as to increase their knowledge about long-term side effects and enhance their ability to cope.

Methods: 4 night classes with different topics, including sexuality, fatigue, changed body image, physical activity and coping strategies. These seminars were split between lectures and group discussions for the participants.

Results: There were 17 participants but some did not attended all classes. The evaluation form that was handed out to the participants showed that most of them gained value from the course and indicated that they would have liked to continue with a follow up course.

Interpretation: Sarcoma patients who have completed their treatment will benefit from meeting other people in the same situation as well as getting increased knowledge about long-term side effects. This can be achieved by offering them an education and coping course.

P10 Prognostic impact of hypoxic markers in soft tissue sarcoma

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Purpose: We aimed to explore the prognostic impact of the hypoxia induced factors (HIFαs) 1–2, the metabolic HIF-regulated glucose transporter GLUT-1 and carbonic anhydrase IX (CAIX) in non-gastrointestinal stromal tumor soft tissue sarcomas (non-GIST STS).

Methods: Duplicate cores with viable tumor tissue from 206 patients with non-GIST STS were obtained and tissue microarrays were constructed. Immunohistochemistry (IHC) was used to evaluate expression of hypoxic markers.

Results: In univariable analyses, GLUT-1 ($p<0.001$) and HIF-2α ($p=0.03$) expression correlated with a poor disease-specific survival (DSS). In the multivariate analysis, however, only high expression of GLUT-1 (HR 1.7, 95% CI: 1.1–2.7) was a significant independent prognostic indicator of poor DSS.

Interpretation: GLUT-1 is a significant independent negative prognostic factor in non-GIST STS.

P11 Biological function of the metastasis-promoting protein S100A4 in osteosarcoma

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Background and purpose: S100A4 is a small, Ca2+-binding protein belonging to the S100 protein family. It is localized in the nucleus, cytoplasm and the extracellular space, and its overexpression promotes metastasis in several tumor types. We have previously shown that downregulation of S100A4 expression in human osteosarcoma cells inhibits secondary growth in experimental metastasis models in rats. The present study was initiated to investigate the biological mechanisms by which extracellular S100A4 may promote metastasis in osteosarcoma.

Material and methods: The human osteosarcoma cell lines OHS, II–11b, KPDX, Saos-2, U2OS, HOS, MG63, OSA and OS25 were used. cDNA expression microarray was used for identification of S100A4 target genes, and mRNA expression was validated by RT-PCR. Protein expression was measured by ELISA and immunoblotting, and kinase activity profiling was performed using the PamGene technology.

Results: We have identified a set of 136 S100A4 target genes, and S100A4-induced expression of the targets osteopontin, ephrin-A1 and optineurin was validated. S100A4-stimulated expression of these genes was dependent on activation of the NF-κB pathway, and the signal transduction mechanisms responsible for S100A4-mediated NF-κB activation have been extensively characterized. Moreover, using kinase activity profiling, 32 kinase substrates were significantly regulated by S100A4 treatment, including the cell surface receptors EGFR and PDGRF.

Conclusions: We have identified and characterized genes and signal transduction mechanisms regulated by the metastasis-associated protein S100A4 in human osteosarcoma. These findings contribute to the understanding of the complex molecular mechanisms of osteosarcoma metastasis. We conclude that S100A4 signaling or S100A4 target genes may represent promising targets for specific anti-metastatic therapies in the future.

P12 Exposure to possible osteosarcoma risk factors in a US postmarketing osteosarcoma surveillance study

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Background: An ongoing multiyear population-based surveillance study provides the opportunity to characterize the demographic profile plus environmental and treatment exposures in osteosarcoma patients aged 40 years and older.

Methods: Incident cases of primary osteosarcoma are identified through participating cancer registries in the US. Once patients are identified and consent is obtained, demographic and risk factor information is collected by telephone interview.

Results: As of Sept 2010, 449 cases of osteosarcoma diagnosed between Jan 2003 and Dec 2008 were interviewed. Among all cases identified, mean age was 62 years, 49% were female, and 80% were white. Osteosarcoma NOS (68%) and chondroblastic osteosarcoma (12%) were the most common morphologic types; leg bones (29%) were the most common tumor site. Reported prevalence of possible risk factors was 19% for history of radiation treatment, 20% for prior trauma or infection at site of cancer, and 6% for history of Paget's disease. Among those reporting a history of radiation treatment, 75% (65 of 87) reported prior radiation treatment at or near the primary tumor site.

Conclusions: Data from this ongoing surveillance study and the companion European component add to the knowledge about adult patients with osteosarcoma and complement information from the literature describing the distribution of possible risk factors.

P 13 Multiple occurrence of dermatofibrosarcoma protuberans, an effect of immunosuppression?

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Background: Dermatofibrosarcoma protuberans (DFSP) is a slow growing tumor and the diagnosis is often delayed for months to years. DFSP commonly extends far beyond the clinical margins; which probably accounts for the high recurrence rate with inadequate surgical margins. Wide excision of 3 cm or more including the fascia, is recommended.

Case report: A 73 year old women was diagnosed with DFSP both in the right groin and the left knee region. The patient had had immunosuppressive treatment after a liver transplantation in 1984 because of primary biliary cirrhosis. Renal failure (supposedly as an effect of the immunosuppressive treatment) led to kidney transplantation in 1991. 2007 the patient noticed a blue/red skin manifestation in the right groin. Biopsy then and also a year later showed dermatofibroma/blue nevus. The tumor area increased, and a red-to-violaceous plaque was also found on the left knee. Biopsy performed 2010 showed DFSP at both locations.

Discussion: This patient might have developed DFSP simultaneously at two sites because of the immunosuppressive therapy. Multiple occurrence of other malignancies in conjunction with immunosuppression have been described previously.

P14 Distinct microRNA expression profiles in imatinib mesylate sensitive and resistant gastrointestinal stromal tumor cells

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Background and purpose: Gastrointestinal stromal tumors (GIST) are the most common sarcoma in the gastrointestinal tract, mostly results from mutations of the receptor tyrosine kinases *KIT* or *PDGFRA*. The development of imatinib mesylate (IM), a tyrosine kinase inhibitor that targets both KIT and PDGFRA, improved the outcome of patients. Despite that, approximately 20% of patients were found to have primary resistance to IM, and most responding patients develop secondary resistance and progress within 2 years. In this study, we aim to investigate the role of microRNAs in drug resistance of GIST.

Material and methods: Using a microarray approach, we examined global microRNA expression in a series of 12 IM-sensitive and 6 IM-resistant GIST samples. 118 microRNAs were significantly overexpressed and 17 were underexpressed in the IM-resistant group, compared to the sensitive group.

Interpretation: To determine the significance of the findings, we are evaluating some of the selected microRNAs in a larger series of clinical samples using TaqMan assay. To uncover the role of microRNA-mediated gene regulation in IM-resistant GIST, we are addressing if these candidate microRNAs confer IM resistance phenotype and elucidate the underlying mechanisms using experimental systems. Our findings may advance the understanding of the role of microRNA regulation in acquisition of drug resistance in GIST, which may ultimately lead to improved treatment of GIST.