be discussed for certain unusual diseases with characteristic anatomic presentations. Angiosarcoma of the scalp, a disease with unique technical challenges due to its extensive nature in proximity to the brain, and locally extensive dermatofibrosarcoma protuberans often need special radiotherapy approaches. In addition certain diseases are more likely to develop lymph node metastasis and the radiotherapy approach to these and patients with established lymph node will be discussed. Rhabdomyosarcoma is often exquisitely sensitive to chemotherapy and radiotherapy and may have extensive lymph node involvement and primary disease. Protocols that exploit the interaction between systemic treatments will also be highlighted. Potential molecular opportunities will be also discussed. For example, beta-catenin is a potent regulator of the WnT pathway involved in wound healing and fibromatosis patients have globally elevated beta-catenin levels that may confer a wound healing by protecting against the adverse effects of pre-operative radiotherapy. The mdm2 gene (an E3 ubiquitin ligase that targets p53 for proteasomal degradation) is amplified and over-expressed in 1/3 of STS. In vitro and in vivo pre-clinical models have demonstrated the effectiveness of the combination of radiation and proteasomal inhibitors in a broad range of histologic sub-types and it is possible that this may augment radiotherapy in STS with suitable expression profiles.

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Medical management of soft tissue sarcomas

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Soft tissue sarcomas (STS) are known to be relatively insensitive to chemotherapy and single agent doxorubicin remains the treatment of choice for many subtypes, even after decades of searching for improved therapy. Combination chemotherapy with doxorubicin plus ifosfamide is commonly used but there is little or no evidence in favour of the combination for palliation of advanced disease, in contrast to adjuvant or neoadjuvant therapy indications and this question remains the subject of a multinational randomised trial (EORTC).
Individual subtypes are now identified that appear to respond favourably to a variety of other chemotherapy agents: angiosarcoma – taxanes; leiomyosarcoma – gemcitabine + docetaxel; leiomyosarcoma & liposarcoma – ET-743 (trabectidin). As yet the molecular basis for this apparent selectivity is unknown.
Gastrointestinal stromal tumour (GIST), which is driven by activating mutations in *KIT*, or less commonly *PDGFRA*, is of course amenable to therapy with the receptor tyrosine kinase inhibitor imatinib (Glivec). The majority of patients experience partial response or disease stabilisation with relatively little serious toxicity, accompanied by marked symptomatic improvement and prolonged survival. Tumours with the most common exon 11 *KIT* mutation are most sensitive to imatinib and the responses are more durable than in the case of exon 9 mutant tumours. It is now known that treatment needs to be continuous, that a higher dose of the drug is beneficial in the treatment of exon 9 mutant tumours and that resistance will develop after a number of years, necessitating exploration of treatment with alternative tyrosine kinase inhibitors, e.g. SU11248, AMG706. Research is ongoing into the role of imatinib as adjuvant therapy for completely resected tumours.
The success of imatinib in treating (GIST) has raised expectations that other sarcomas will become treatable by the new generation of molecularly targeted therapies. Although inhibitors of EGFR are being investigated in synovial sarcoma and malignant peripheral nerve sheath tumour there are few other striking examples, other than dermatofibrosarcoma protuberans (DFSP), which is activated by a translocation that results in overexpression of PDGFB. Imatinib is effective here via inhibition of PDGFR. It is hoped that further investigations into the molecular biology of STS will lead to a similar improvement in the treatment of other diseases.

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Surgery adapted to lab data – the way to a tailored approach

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Despite the recent advances of developing a molecular profile of sarcomas or to detect the decisive mutation for sarcoma progression, surgery is the mainstay of treatment of primary, non-metastatic sarcomas.
However, the era of identifying molecular targets also yields important results for surgical decision making.
Dermatofibrosarcoma protuberans (DFSP) represents a disease often recurring locally due to inadequate margins of safety and being not suitable for radiotherapy. The detection of PDGFRa ligands that can be blocked with imatinib leads the way to successful treatment of formerly irresectable cases.
In **GIST**, mutation analysis of tumors responding to imatinib therapy is the decisive element to decide on resectional treatment in responding patients. Depending on the mutation present, patients with long-lasting responses to be expected can be separated from those with presumably only short term tumor control. In patients with multifocal progression parallel to tumor sites with long-lasting response, mutation analysis guide the way whether a radical surgical approach needs to be pursued or whether different drugs (other types of tyrosine kinase inhibitors) should be used for continuing treatment.
The establishing of a molecular profile of **sarcoma subtypes** (e.g. **synovial sarcoma** and EGFR expression, **angiosarcoma** and integrin expression, **liposarcoma** and expression of PPRy ligands or certain fusion proteins) show the way to a tailored approach. There is also little scope for further improvement in survival with surgical treatment of **chondrosarcoma**. Inhibition of PTHLH signalling or bcl-2 antisense therapy could be future options for tumor control. Locally advanced or recurrent tumors not amenable to surgery with adequate clear margins may be controlled with extensive surgical and multimodality procedures. Hopefully in the future, progression arrest could also be achieved by individualized targeted therapy.
Diagnosis of sarcoma is no longer histological and immunohistological alone with accurate subgroup classification but provides important information for subsequent treatment decisions. Thus, a molecular staging of sarcomas should accompany TNM/AJCC staging in the future.

Scientific Symposium
Non-myeloablative transplantation in solid tumours

136 Abstract not received

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Complications of therapy, supportive care

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The graft versus leukemia (GVL) effect has been shown to be a major component of the anti-leukemic efficacy of allo stem cell transplantation (ASCT). In patients suffering from refractory solid malignancies, only anecdotal evidence of a "graft-versus-tumor" (GVT) effect had been reported thus far. Since the initial report suggesting some clinical and biological clues supporting a GVT effect, at least in breast cancer, the overall experience of ASCT in patients with solid tumors (ST) remained scarce. In 2001, 6413 ASCT were reported to the European Group for Blood and Marrow Transplantation (EBMT) registry, but only 149 (2%) were performed in patients with ST. On the other hand, the benefit of immunotherapeutic approaches for selected ST is now widely documented in a non-allogeneic setting, indicating that some immune effectors are able to induce tumor regression. In the allogeneic setting, the importance of minor HLA antigen mismatch was shown to be an important determinant of immune tumor control. Based on the initial case reports, we started in 1996 to investigate the potential of ASCT in patients with advanced metastatic ST. Our main objective was to investigate the feasibility of ASCT defined as a procedure being acceptable for both patients and the medical oncology community. Our initial experience combined with that of others confirmed that standard dose myeloablative ASCT is associated with a GVT effect, but also a prohibitive transplant related toxicity rate. The introduction of reduced intensity preparative regimens that could mediate a potent GVT effect in patients with hematological malignancies offered an attractive tool for investigation in patients with ST. Based on these encouraging results, we investigated ASCT for ST with an anti-thymocyte globulin (ATG)-based reduced intensity conditioning regimen (RIC). Fifty seven patients, of whom 39 had a progressive disease (PD) at time of ASCT, received a RIC ASCT combining fludarabine, anti-thymocyte globulin (ATG) and busulfan. Patients were analyzed in terms of engraftment, transplant related mortality (TRM), disease response and outcome. In this setting, RIC was associated with rapid engraftment and low overall TRM (9%; 95%CI: 1–16). The cumulative incidence of objective responses (OR) reached 14% (95%CI: 6–30) with this being significantly higher in patients without PD [44% (95%CI: 21–67) vs. 0; $P < 0.0001$] at time of ASCT. Achievement of OR translated into a significantly better overall survival (OS). In multivariate analysis, OS was significantly influenced by disease status at time of ASCT (odds ratio, 4.88; $P < 0.001$) and chronic GVHD occurrence (odds ratio, 2.86; $P < 0.01$). Overall, these results showed that OR can occur after RIC ASCT for resistant ST with a relatively low TRM and potential benefit especially in patients with slowly progressive disease. Further studies are warranted in patients with less advanced ST.