**9410** POSTER

**Anti-apoptotic Effect of Decoy Receptor 3 in Human Malignant Fibrous Histiocytoma Cells**

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**Background:** Decoy receptor 3 (DcR3) is a soluble secreted protein which belongs to TNF receptor superfamily, and inhibits Fas/Fas ligand (FasL) apoptotic pathway by binding to FasL competitively with Fas. Previous studies have reported that overexpression of DcR3 is detected in various human malignancies, and that DcR3 plays an important role on tumour progression. We previously reported that DcR3 overexpression was observed in human osteosarcoma and malignant fibrous histiocyoma (MFH) cells, however, the role of DcR3 in musculoskeletal tumours has not been studied. The purpose of this study was to evaluate the effect of DcR3 inhibition in Fas/FasL apoptotic pathway in human MFH cells.
**Methods:** TNMY1, human MFH cell line that expresses the high level of DcR3, was used in this study. TNMY1 cells were transfected with either DcR3-siRNA or control siRNA. After siRNA transfection, each cell was cultured in medium with or without FasL, and cell proliferation assay was performed at 0, 24 and 48 hours of incubation. Also, cell lysate was collected from each transfected cell which was treated with or without FasL, and we performed immunoblot analysis to evaluate the expression of DcR3, Fas and apoptosis-related proteins, such as Caspases and PARP.
**Results:** DcR3-siRNA transfection sufficiently suppressed DcR3 expression in TNMY1 cells compared with control cells without affecting Fas expression. FasL treatment significantly decreased cell proliferation in DcR3-siRNA transfected cells compared with control cells after 24 and 48 hours of incubation. Apoptosis-related proteins, cleaved Caspase-3 and cleaved PARP, were detected in cells which were treated with FasL after DcR3-siRNA transfection, however both proteins were not observed in control cells.
**Conclusions:** Previous studies revealed that DcR3 blocks Fas/FasL apoptotic pathway by binding to FasL competitively with Fas, and that overexpression of DcR3 is associated with tumour progression in various human malignancies. However, the role of DcR3 in musculoskeletal tumours is still unknown. In this study, we demonstrated that FasL treatment with DcR3 inhibition caused a svnergistic cytotoxic effect and induced apoptosis in human MFH cells. These results suggest that DcR3 may have an anti-apoptotic effect via inhibiting Fas/FasL apoptosis pathway in human MFH, and that DcR3 may be a potent therapeutic target for human malignant musculoskeletal tumours.

**9411** POSTER

**Coexistence of GISTs With Other Malignancies − More Than a Simple Coincidence?**

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**Introduction:** Over the last decade, several changes occurred in the diagnostics, treatment and understanding of pathogenesis in gastrointestinal stromal tumours (GISTs). However, their coexistence with other malignancies of different origin remains a challenging situation during the clinical treatment course.
**Methods:** Patients diagnosed for GIST in our centre were identified retrospectively. A subgroup, associated with other types of malignancies, was selected and the clinical, pathological (macroscopic, microscopic, and immunohistochemical) features and the clinical follow-up were statistically analysed.
**Results:** Thirty four (24 male, 10 female) of 85 GIST patients (40%) were associated with other malignancies (n = 38) in the period 2000–2009. The mean age was 69.7 years (range 56−86). GIST-associated malignancies were: stomach (n = 7), rectal (n = 5), oesophageal (n = 4), pancreatic (n = 4), colon (n = 3), papilla (n = 2) and oro-/hypopharyngeal (n = 2) adenocarcinoma, as well as plasmacytoma (n = 2), melanoma (n = 2), prostate (n = 2) and urothelium adenocarcinoma (n = 1), hepatocellular carcinoma (n = 1), neuroendocrine tumour (n = 1), thyroid cancer (n = 1) and non-Hodgkin lymphoma (n = 1). The majority of GISTs occurred in the stomach (65%) and small intestine (29%), with rare occurrence in the rectum (3%) or esophagus (3%). In the majority of cases (82.5%), GISTs were asymptomatic and were accidentally found during diagnostic or therapeutic procedures for associated malignancies. Open surgery was performed in 32 cases, laparoscopic surgery or endoscopic therapy in 2 cases. GIST's size ranged from 0.1 to 9 cm (mean size: 2.2 cm) and all of them had a low (<5/50HPFs) or absent mitotic activity. CD117 was expressed in 82.5% and CD34 in 70.5%. Twenty nine tumours (85.3%) were classified as very-low- or low-risk tumours. Imatinib mesylate was administered in 2 patients. During follow-up (range 3–117 months, mean: 33.7 months), 2 patients suffered from local recurrence (n = 1) or distant metastases (n = 1) of GISTs. Postoperative mortality was 5.8%. Eight patients (23.5%) died of associated malignancies, one patient for other reasons.
**Discussion:** The coexistence of GISTs with other malignancies should draw the attention of clinicians towards these accidentally findings. Little is known about the possible common origin of GISTs and associated malignancies. The prognosis in this combination of tumours is usually not determined by the GISTs. Therefore treatment algorithms should be focused on the prognostic relevant malignancy.

**9412** POSTER

**Brain Metastasis in Sarcoma − Presentation, Treatment Strategies and Survival in This Rare Clinical Setting**

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**Background:** Brain metastasis (mets) is rare in sarcoma. Risk factors, optimal management strategies and therapeutic outcomes of such metastases are not well studied. We aimed to evaluate the incidence, clinical characteristics and treatment outcomes of parenchymal brain mets in patients (pts) with sarcoma.
**Methods:** Single center retrospective analysis. Overall survival was calculated from diagnosis of brain metastasis to time of death.
**Results:** Thirteen pts (1.7%) with complete electronic medical records were identified from our sarcoma database. Median age was 55 yrs (range, 21−71 yrs), 8 were males. Histology of the primary sarcoma was undifferentiated pleomorphic sarcoma (6 pts), uterine leiomyosarcoma (2 pts), epithelioid sarcoma, embryonal rhabdomyosarcoma, alveolar soft part sarcoma, Ewing's sarcoma and osteosarcoma (1 pt each). Synchronous brain mets were identified in 3 (23%) pts while 77% subsequently developed brain mets at a median of 19 months (mths) (range 6−90 mths) after initial diagnosis. Five (38%) pts had solitary brain metastasis while 62% developed multiple lesions. Four (31%) pts underwent aggressive therapy for brain mets, defined as either surgical resection (1 pt) or multimodality treatment (1 pt had chemotherapy plus whole brain radiotherapy [WBRT]; 2 pts had surgical resection plus WBRT). The remaining 9 pts received conservative treatment with WBRT alone (7 pts), chemotherapy alone or best supportive care (1 pt each). Median overall survival (OS) for the entire cohort was 4.0 mths (95% CI 1.3−6.7). Median OS for pts who underwent aggressive therapy vs conservative approach was 4.0 mths vs 3.6 mths respectively (p = 0.234). Of note, in 10 pts who died, 90% had progressive systemic disease which contributed significantly to mortality. There was no clear association between histological subtype of sarcoma and median OS due to small sample size.
**Conclusion:** Brain mets in sarcoma is rare, usually co-exists with significant systemic disease and is associated with a grave prognosis. In our study, there was no significant difference in OS between pts treated with an aggressive vs conservative approach. Progressive systemic disease was a main cause of death. Achieving better systemic disease control may be important in influencing outcome in pts with sarcomatous brain mets. Better risk stratification and selection of patients who may benefit from aggressive/multi-modality treatment is needed.

**9413** POSTER

**Primary Localized Gastrointestinal Stromal Tumours (GIST) of the Duodenum − a French Sarcoma Group (FSG) Retrospective Review of 84 Patients (pts)**

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**Background:** Duodenal GIST represents only 3−5% of all GISTs. Clinicopathologic data are mainly derived from small series. We conducted a retrospective analysis of duodenal GISTs over the past 17 years.
**Methods:** Pts with localized duodenal GISTs were identified in two ways: a group of 75 pts reported via survey from 20 FSG centers, and a group of 9 pts enrolled in the BFR14 trial.

**Results:** Pts were: 44 females, 40 males, with a median age of 57 years (30−84), and median ECOG 0 (0−3). Abdominal pain, anemia, and GI bleeding were the most common symptoms. Tumours (T) were mainly located on D2 (31%), or D3/D4 (33%), with a median size of 6 cm (1.5−30). All pts had resection of the primary T. Surgical procedures were: local resection (LR) -[segmental duodenectomy (n = 24), wedge local resection (n = 27), local excision (n = 5)], and duodenopancreatectomy (DP, n = 13). Resections were R0/R1 in 69 pts (82%). T characteristics included: KIT+ (n = 74), CD34 + (n = 43), mitoses/50 HPF $\leqslant$ 5 (n = 51), or >5 (n = 20), Miettinen low-risk (n = 24), and high-risk (n = 19), necrosis (n = 25), spindle cell (n = 62), Mutations were documented in 24/28 cases, usually in KIT exon 11 (n = 22). 8 pts received neoadjuvant imatinib (IM) therapy resulting in 4 PR, 3 SD, 1 PD. 12 pts received adjuvant IM therapy. With a median FU of 36 months (4–250), 74 pts (88%) are alive. Twenty-eight (33%) pts relapsed: 5 localized, and 25 metastatic. The 4-year OS and EFS rates were 89.5% and 64.6% respectively. The 6-year OS and EFS rates were 89.5% and 32.4%. Univariate analysis showed that: age and ECOG PS have an impact on OS ($p = 0.003$, $p < 0.001$), necrosis, spindle-cell type, T size, mitoses/50 HPF, and Miettinen risk are predictive of relapse ($p < 0.001$). In multivariate analysis tumour size and mitoses/ 50 HPF only were predictive of relapse ($p < 0.001$).
**Conclusions:** Pts with completely resected primary duodenal GIST seem to have favourable prognosis. LR rather than DP should be pursued if possible to preserve optimal pancreas function. Neoadjuvant IM may potentially allow more locally advanced GISTs pts to undergo LR.

**9414** POSTER

### A Retrospective Analysis of Presentation and Outcome in Ewing's Sarcoma − a Single Institute Experience

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**Aims:** To analyse the clinical characteristics of patients of Ewing's sarcoma and to evaluate the survival & prognostic factors influencing treatment outcome with multimodality treatment.
**Material and Methods:** In this retrospective analysis, a total of 81 patients of ewing's sarcoma were studied from January 2003 to March 2010. All the patients were analyzed for presenting features, sites of involvement, treatment recieved and distant metastasis. Kaplan meyer test was applied for survival function. Analysis of failure was done in 39 patients with various risk factors such as age, bulky disease, extaosseous sites and soft tissue involvement.
**Results:** With median follow up of 30 months, this study showed that with initial modality therapy, the complete response rate was 53.08% and distant metastasis was seen in 38.27% in which the lung was the most common site (54%). The median survival as showed in the study was 24.5 months. This study highlighted that patients having central lesions or bulky disease (>100 cc) or extraosseous presentation or soft tissue invovement have poor disease free survival as compared to the contrary.
**Conclusion:** Most significant prognostic factors affecting disease outcome in Ewing's sarcoma are the bulk of disease and site of involvement at presentation. Extraosseous Ewing's sarcoma adversely affects disease free survival and aggressive treatment should be considered in these patients for better disease control and survival.

**9415** POSTER

### Sporadic Desmoid Tumours of the Chest; Long Term Follow-up of Twenty-eight Multimodally Treated Patients

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**Background:** Desmoids of the chest are extreme rare borderline tumours. Radical surgical resection is considered to be the primary treatment. Achieving negative margins is often a challenge. Cases with positive surgical margins are associated with high risk of local recurrence.
**Patients and Methods:** A retrospective multicenter review was undertaken of twenty-eight patients who underwent surgery for sporadically appearing desmoids of the chest between 1988 and 2008. Clinico-pathological data were investigated in detail. Authors have statistically analyzed the relationships between gender, age, tumour size, radicality of the first surgery, impact of the pharmacologic treatment, estrogen receptor positivity, and the development of local recurrences after a median follow-up period of 104 months.
**Results:** Primary surgery was radical in fourteen patients (50%). Mean pathologic diameter was 72.14 mm. Wide surgical excision was performed in twenty-seven primary cases, out of which ten cases (37%) were full-, and seventeen cases (63%) partial-thickness chest wall resections. Synthetic mesh stabilisation was used in nine cases and soft tissue coverage in six patients. Morbidity rate was 25%. Recurrencies were found in 63% of the cases, with a mean time of 30.5 months to first recurrencies. Our investigation confirmed that microscopically free surgical margin of the first tumour resection significantly affected local tumour control.
**Conclusions:** Because the radicality of the first surgical resection is of essential importance for long time local control of chest desmoids, accurate preoperative diagnostics and well planned aggressive surgical resection of the primary tumour is recommended. Due to the low incidence of desmoids, multicentric randomized investigations would be mandatory to establish evidence based protocol for desmoid tumours.

**9416** POSTER

### Limb-sparing Surgery and Radiotherapy for Soft Tissue Sarcomas of the Extremities

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**Background:** Standard treatment for soft tissue sarcomas (STS) of the extremities is limb-sparing surgery followed by adjuvant radiotherapy (RT) in case of close surgical margins and/or adverse prognostic factors. Purpose was to evaluate local control, survival, RT related side effects and functional outcomes after limb-sparing surgery followed by RT for STS.
**Material and Methods:** All patients treated for STS in the Leiden University Medical Center between 1995 and 2010 were included; 338 patients were treated, of whom 121 had STS of an extremity, treated with limb-sparing surgery and RT with curative intent. Radiotherapy was delivered preoperative in one patient (50 Gy), or postoperative: 114 patients 60 Gy, 6 patients 66 Gy. Few patients (11%) received chemotherapy. Data on survival and recurrences were retrieved from the hospital oncological database, whereas data on early and late toxicity were collected retrospectively from patients notes. Statistical analysis was done using long-rank tests, Kaplan–Meier method and Cox regression analysis.
**Results:** Median follow-up was 93 months. Actuarial local recurrence rates at 5 and 10 years were 9.1% and 11.7%. The only significant factor for local failure was high tumour grade. Distant metastases rates at 5 and 10 years were 31% and 36.8%. Five- and 10-year overall survival rates were 69% and 54%, and disease-free survival rates 59.5% and 43%, respectively. Acute radiation related toxicities occurred in 91% of the patients: 37% grade 1, 35% grade 2, 17% grade 3 and 2% grade 4. Late toxicity was reported in 72%: 51% grade 1, 19% grade 2 and 2.5% grade 3. Conservation of function was good, with 23% having some degree of decreased range of joint motion, which was mostly mild: 19% grade 1, 3.3% grade 2 and 1% grade 3. Mild limb edema was recorded in 26%.
**Conclusions:** Limb-sparing surgery with adjuvant radiotherapy for patients with STS provides excellent local control and high survival rates with acceptable toxicity and good functional outcome.

**9417** POSTER

### Reirradiation and Hyperthermia for Radiation-associated Sarcoma

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**Background:** Radiation-Associated Sarcoma (RAS) is a rare entity with a poor prognosis. As a result of a rising prevalence of breast cancer and a higher percentage of patients treated with irradiation as part of multidisciplinary treatment, an increase of incidence of RAS of the breast and chest wall is to be expected. We evaluated the role of reirradiation and hyperthermia in the treatment of RAS in the thoracic region.
**Material and Methods:** Between 1979 and 2009, 16 patients with RAS in the thoracic region were treated in the Academic Medical Centre and the Institute Verbeeten with reirradiation and hyperthermia. In 13 cases this treatment was given for irresectable disease and three times after resection as adjuvant treatment.