their second metastatic relapse. Primary end point is the DFS at 12 months compared to a historical group of patients.
Results: To date, we have enrolled 17 patients: 8 patients were enrolled in the Viscum arm and 9 patients in the Etoposide arm, 8 female and 9 male, median age 35 years (11−65), median follow up 19 months (1−42). Median DFS is currently 17.5 months (5−42) for the Viscum album arm and 4 months (1−12) for the Etoposide arm. Viscum patients had a lower toxicity compared to patients treated with Etoposide. An interim analysis will be done once we have 20 treated study patients (10 for each arm).
Conclusions: Viscum album showed promising results as adjuvant treatment in prolonging DFS after a second relapse. It seems to have the same advantages compared to other immunostimulants (IFN, MTP-PE) at lower costs. A larger multi-center trial would be desirable to determine efficacy of Viscum therapy in osteosarcoma patients compared to other immunostimulants currently approved in osteosarcoma treatment like Mifamurtide.

9428 POSTER

Pharmacokinetics and Pharmacodynamics of Liposomal Mifamurtide in Patients With Osteosarcoma

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Background: Liposomal mifamurtide (muramyl tripeptide-phosphatidyl ethanolamine; L-MTP-PE, MEPACT®) is an immunomodulator indicated for osteosarcoma (OS) treatment in combination with post-operative multi-agent chemotherapy. Here we report the results of a pharmacokinetic (PK) and pharmacodynamic (PD) substudy in a primarily pediatric and adolescent high-grade OS population in an ongoing compassionate use study (MTP-OS-403; EudraCT 2009–017204−89).
Materials and Methods: Patients with relapsed or metastatic OS received L-MTP-PE at 2 mg/m^2 via intravenous infusion over 30 or 60 mins twice-weekly for 12 weeks then weekly for 24 weeks. Blood samples were collected for up to 72 hours following the first infusion. Serum MTP-PE concentrations were measured by LC-MS/MS; TNF-α and IL-6 levels were by sandwich immunoassay. PK/PD data were analyzed by noncompartmental analysis using WinNonlin.
Results: Data from 28 patients were included in the PK (17/11 had 30-/60-min infusions) and 27 in the PD (13/14 had 30-/60-min infusions) analyses. The median (range) age was 15 (6−39)/15 (6−42) years and body surface area (BSA) was 1.58 (0.77–2.31)/1.55 (0.77–2.24) m^2; 61%/56% were male. Following an initial rapid decline in MTP-PE serum concentrations during the first 30 mins after infusion cessation, MTP-PE serum concentrations declined in a log-linear manner over 2−6 hours post-dose with a mean (%CV) terminal half-life of 2.04 hours (22%). BSA-normalized geometric mean (%CV) clearance was 1,250 mL/min/m^2 (43%) and steady-state volume of distribution was 262 L/m^2 (45%). Serum IL-6 levels peaked at 4 hours (regardless of infusion duration) and TNF-α peaked at 2 hours in the 30-min and 4 hours in the 60-min group, returning to baseline ~24 hours post dose. No readily apparent relationships were observed between age and BSA-normalized MTP-PE clearance or effects on serum IL-6 and TNF-α.
Conclusions: The PK properties of L-MTP-PE observed in this study in a largely pediatric and adolescent OS population are similar to those previously reported in healthy adults (Venkatakrishnan et al. ENA 2010, abstract 661). Importantly, there were no readily apparent effects of age on BSA-normalized MTP-PE clearance and the immunomodulatory PD effects. These results support the use of L-MTP-PE at the current recommended dose of 2 mg/m^2 across the age range relevant to its indication in the treatment of OS. Evaluation of safety and efficacy is ongoing.

9429 POSTER

MGMT Promoter Methylation in Soft Tissue Sarcoma

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Background: Gene silencing of MGMT (O6-methylguanine-DNA methyltransferase) by promoter methylation increases the efficacy of combined therapy of alkylating chemotherapeutic and radiation. The purpose of this study was to assess the frequency of MGMT promoter methylation in soft tissue sarcoma to identify patients eligible for alkylating agent chemotherapy with concurrent radiotherapy.
Material and Methods: Paraffin tumour blocks of 61 patients with different STS subtypes were evaluated. The methylation status of the MGMT promoter was assessed by methylation-specific polymerase-chain-reaction analysis. Furthermore immunehistochemistry was applied to verify expression of MGMT.
Results: MGMT promoter methylation was detected in 12/61 patients (19%, 4/17 liposarcoma, 3/11 MFH, 1/8 leiomyosarcoma, 0/8 myxofibrosarcoma, 1/8 MPNST and 3/9 synovial sarcoma). There was no correlation of MGMT promoter methylation with age, gender, tumour grade, size or site.
Conclusion: Generally, MGMT-promoter methylation is not a frequent event in soft tissue sarcoma. A general recommendation to use alkylating agents combined with irradiation in soft tissue sarcoma cannot be justified. However, there might be subtypes like synovial sarcoma better prone for radiosensitizing with alkylating agents based on MGMT promoter methylation results. Further research in this area is clearly warranted.

9430 POSTER

Assessing Tumour Diameter Versus Tumour Volume as a Prognostic Value at Diagnosis in Rhabdomyosarcoma

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Objective: The purpose of this study is to determine whether measuring tumour volume is more prognostic than tumour maximum diameter at the time of diagnosis and local control for pediatric rhabdomyosarcoma patients.
Patients and Methods: Medical records of one hundred and nine patients who were diagnosed with rhabdomyosarcoma from July 2007 till July 2010 were reviewed retrospectively. Eighty-seven cases were found to be non metastatic. And, for the sixty-two patients with measurable disease, patient demographics, including age, sex, pathologic report as well as surgical grouping were obtained. Tumour diameter was assessed radiologically at diagnosis, at time of local control and at end of treatment. The initial CT, MRI, or both, were obtained for all patients (n = 62) and were reviewed by the study radiologist. Also, we estimated the association between patients' characteristics and the risk of failure or death using cox proportional hazards regression models.
Results: The tumour diameter ranged from 1.8 to 18 cm with a mean of 6.7 cm and a tumour volume ranging from 1.62 to 1099.7 cm^3 with a mean volume of 139.7 cm^3. No significant correlation was found between tumour diameter or tumour volume with sex, age or histological subtype. Both initial tumour diameter and tumour volume did not have a significant effect on overall survival but both had a significant effect on failure free survival.
Conclusion: Both tumour diameter and tumour volume changes significantly affects failure free survival and both act as a good prognostic factor to detect treatment response.

9431 POSTER

Whole-body-PET/MRI a New Way of Imaging in Soft Tissue Sarcomas

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Background: Simultaneous positron emission tomography (PET) and magnetic resonance imaging (MRI) is a new imaging technique combining metabolic and cross-sectional diagnostic imaging. Up to now the only available clinical data are drawn from feasibility studies in small series of head and neck cancers and intracranial tumours. So far there exist no data of PET/MRI for evaluating soft tissue sarcomas (sts). MRI is the recommended imaging method in most types of sarcomas. PET is of emerging importance for the management of patients with sts. The combination of MRI with metabolic PET imaging could provide an interesting approach for imaging in sts.
Methods: We report the first two patients examined with an Ingenuity PET/MRI system (Philips Healthcare). It combines a 3 Tesla MRI scanner and a PET scanner with time-of-flight technology. MRI and PET data are acquired sequentially in analogy to PET/CT. All patients were examined before start and after two cycles of chemotherapy. The first patient

presented with a primarily unresectable pleomorphic sarcoma of the abdomen starting chemotherapy in neoadjuvant intention. The second patient presented with a progressive multifocal myxoid liposarcoma of the pelvis after previous combination chemotherapy.
Results: Simultaneous PET/MRI shows a high contrast imaging without artefacts.in all patients. After 2 cycles of neoadjuvant chemotherapy the 1st patient showed no shrinkage in tumour volume while the FDG uptake (SUV) decreases up to 58%. Therefore treatment was continued. In staging prior to start chemotherapy in the 2nd patient, there were two lesions detectable in MRI with no or only minimal FDG-uptake. The complete and follow up data will reported at presentation.
Conclusion: To our knowledge we report the first two patients with sts examined with whole-body-PET/MRI. The combination of simultaneous PET and MRI is feasible also in sarcoma patients and can provide additional information in diagnosis and treatment of sts. For treatment monitoring with repeated PET/MRI the lower radition exposure is a major advantage. Focusing on regions of interest can result in shorter MR sequences and save imaging time. Further studies should evaluate PET/MRI as imaging method in staging and treatment evaluation in sts.

9432 POSTER

Age, Location and Histology in Soft Tissue Sarcomas − Single Institutional Review

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Background: Soft tissue sarcomas (STS) are rare tumours. The heterogeneity in location, histopathology and clinical behavior determine major difficulties in the medical management in terms of diagnosis and therapeutic approach. The aim of this study was to evaluate the demographic features of our population, considering age at presentation, anatomical location and histological subtypes.
Methods: From a prospective database of STS of 1435 patients (pts), we reviewed the medical records of pts treated at our institution from 1994 to 2010. Pts were divided by age (15−30 years (y), 31−50, 51−70 and ⩾71), location (upper limb, lower limb, head and neck, trunk, visceral, retroperitoneum, pelvis, others) and histological subtypes.
Results: 1016 pts were eligible for analysis. Median age was 51 years (15−95); 521 were women (51%). The most frequent histologies were, leiomyosarcoma (13%), GIST (13%), liposarcoma (LPS − 12%), malignant fibrous histiocytoma (MFH − 10%). 40% of the population was between 51−70 y. In the age group between 15−30 y, rhabdomyosarcoma was the most common histology (14%), between 31−50, leiomyosarcoma (15%) and GIST in the others. The most common primary locations were the lower limb 238 pts (23%), pelvis (uterus included) 17% and retroperitoneum 12%. Lower limbs and pelvic primary locations were more frequent in males and females, respectively. Frequency of histologic subtypes by location: leiomyosarcoma in pelvis (46%), MFH and LPS in lower limbs (44% and 38% respectively) and 60% of GIST were located in the stomach.
Conclusions: Data obtained in a large cohort of pts in a single institution across 16 years of experience introduced GIST as the second most frequent histologic subtype. Pelvic location was another remarkable feature due to the inclusion of uterus sarcoma. This data is consistent with recent series that analyzed histology and location of STS.

9433 POSTER

Metastatic Epithelioid Hemangioendothelioma Improved During Pregnancy − Hormonal Interaction?

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Epithelioid hemangioendothelioma (EH) is a rare malignant vascular neoplasm of endothelial origin and unpredictable clinical course and prognosis. It may present in several sites, most commonly liver and lungs. No standard therapeutic strategies are available, surgical resection is the treatment of choice whenever possible. Although it is a chemoresistant disease, in the presence of metastatic nonresectable disease, several antineoplastic agents have been proposed.
We describe a case of a young woman with hepatic EH (HEH) metastatic to the peritoneum and lungs. DCA presented with abdominal pain, large ascites, nausea and vomit, September 2005; stage IV, HEH diagnosis was established and chemotherapy was started.
Patient received 6 cycles of epirrubicin, ifosfamide and etoposide with no response, and treatment was modified to low dose interferon, which showed stable disease for 18 months. July 2008 patient was diagnosed pregnant, which she decided to keep. Interferon was immediately stopped − mid first trimester. She had a full term pregnancy and natural delivery. Ascites vanished during pregnancy and liver and lung lesions kept stable by recist criteria (slighted reduced), compatible with disease response. She showed no signs of disease progression during lactation period, which was prolonged until the baby reached 24 months (February 2010). At this point she started showing signs of asymptomatic, slow disease progression, she is currently under observation. Immunohistochemistry was performed: CD34 positive, factor VIII positive, AE1/AE3 negative, estrogen receptor negative, progesterone receptor negative.
Literature is scarce regarding metastatic EH systemic treatment. There are case reports and small series using interferon and thalidomide, most with no response or stable disease. We found no relation on hormonal modifications or pregnancy and EH on literature. To our knowledge there are no case reports of full term pregnancy in EH patients, and neither of disease response related to pregnancy and/or lactation.

9434 POSTER

Localized Colorectal (CLR) Gastrointestinal Stromal Tumour (GIST) − Clinical Characteristics, Patterns of Relapse and Clinical Outcomes of This Uncommon GIST Primary Site

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Background: Colon and rectum are uncommon primary sites for GIST. Risk stratification models in clinical use do not address colonic GIST and primary surgical management of rectal GIST is often complicated by anatomical factors precluding sphincter-preserving complete excision. We studied the clinical presentation and treatment outcomes of patients (pts) with CLR GIST and compared this with GIST of other primary sites.
Material and Methods: Single center retrospective study. Eighteen consecutive pts (9%) with CLR GIST from 2002–2010 with complete medical records were identified from our database.
Results: Median age of pts was 59 yrs, 11 were males, 5 and 13 had colon and rectal GIST respectively; 16 were non-metastatic at presentation. Thirteen pts underwent surgical excision, 5 had biopsy only (1 metastatic disease, 1 incidental finding, 2 declined surgery and 1 initially diagnosed as stromal tumour of uncertain malignant potential). Of 12 pts (3 colon, 9 rectal) with localized GIST who underwent surgical resection, local R0 and R1 resection margins were achieved in 67% and 33% respectively. Of 9 pts operated for localized rectal GIST, 3 had abdomino-perineal resection and 2 experienced inadvertent tumour spillage. 25% and 75% of pts had tumours >2−<5 cm and >5−<10 cm respectively; 17% and 83% had 0−5 mitoses and >10 mitoses per 50HPF respectively. Only 2 pts received adjuvant imatinib (IM). At a median follow-up of 50 months, 7 of these 12 pts (1 colon and 6 rectal) relapsed. All pts with relapsed rectal GIST failed locally and 50% had additional metastatic sites of involvement at time of 1st failure. Estimated median relapse free survival (RFS) of pts with resected localized CLR GIST was 55 mths. Although median tumour size of CLR GIST was significantly smaller than those of gastric and small bowel origin ($p = 0.021$), this did not translate to a difference in RFS ($p = 0.683$). Other clinical predictors of GIST relapses, including number of mitoses and adjuvant IM use, was not significantly different ($p = 0.083$ and $p = 0.393$ respectively) between CLR GIST and gastric/small bowel GIST.
Conclusions: This study highlights the unique challenges in the management of CLR GIST, in particular rectal GIST. Although smaller in size at presentation, it is associated with high surgical morbidity and local relapses. Strategies to enhance local control and reduce surgical morbidity including use of neoadjuvant/adjuvant IM should be further explored in this cohort of GIST pts.

9435 POSTER

A New Promising Strategy in Chondrosarcoma − Quaternary Ammonium as Vector of Radioisotopes and Cytotoxics Toward Cartilage Proteoglycans

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Background: Currently, cartilage tumours remain ongoing therapeutic challenges due to their chondrogenic extracellular matrix (ECM) that potentially hampers drug delivery. Neither chemotherapy nor radiotherapy is effective against chondrosarcoma (CHS). Ourstrategy consists in using the quaternary ammonium function, that exhibits a high affinity for