EMSOS - SPECIAL SESSION:

INTERNATIONAL PROJECTS (TRIALS, COLLABORATION)

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Prognosis and therapeutic targets in the Ewing family of tumors - sixth framework program - 1st year

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Introduction: The project through collaborative studies will define prognostic markers and new therapeutic targets in the Ewing's sarcoma family of tumours (ESFT) to provide rigorous scientific justifications for the development of clinical trials for this rare disease, which is manifested for the most part in children.
Material and Methods: The main objective of this project is to evaluate the prognostic relevance of selected markers (EWS/FLI-1, secondary genetic alterations, CD99, IGF-IR, NOVH, erbB-2 and TTF1) and the effectiveness of therapeutic approaches targeting some of these molecules.
Results: During this first year we have obtained some clear answers with respect to prognostic and therapeutic relevance of erbB-2, CD99 and IGF-IR. In addition the genetic profile of experimental models with differential metastatic ability have identified some new prognostic molecular markers that appear to have statistical significance (Gal3BP, Hint1, calnexin).
Conclusions: Cytogenetic profile of cell lines and tumor samples identified some novel small deletions and amplifications. Two tissue arrays have been constructed and are now available for the analysis of some new other genes. Finally the project is taking steps in the construction of new therapeutic tools, such as antisense oligos against EWS/FLI1 in new, more effective vectors and chimerized antibody against CD99.

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Successful multinational implementation of the European and American Osteosarcoma Study EURAMOS-1 within the European Science Foundation's ECT-EUROCORES scheme

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Four multinational groups (COG, COSS, EOI, SSG) representing 14 countries (A, B, CAN, CH, D, DK, FIN, H, IS, N,

NL, SE, UK, USA) collaborate in EURAMOS-1. After successfully overcoming a multitude of organizational, financial and regulatory hurdles, all four collaborating groups initiated recruitment during 2005. The issue of sponsorship represented a major challenge, which was finally solved by finding an institution willing to act as central European sponsor (MRC London), which in turn delegated responsibilities to national institutions on a per-country basis. As of December 31st, a total of 74 patients from 43 institutions in eight participating countries were registered into the trial (D=39 patients / 26 institutions, S=4/3, N=7/2, UK=14/6, CH=4/2, NL=1/1, B=1/2, USA=3/2). More centres are becoming accredited to participate in each of these countries. The trial is now also open for recruitment in CDN, DK, and FIN, and it is expected that A and H will soon follow. Further countries expressed their interest to join. An Intergroup Safety Desk has been established and an elaborate system for SAE reporting to a multitude of competent authorities and ethics committees has been successfully implemented. Quality of life assessments taking into account age and language specific requirements have also been initiated. In addition to running the clinical trial, EURAMOS cooperates with the osteosarcoma work package of the European Network to Promote Research into Uncommon Cancers in Adults and Children: Pathology, Biology and Genetics of Bone Tumours (EuroBoNeT) in order to advance the understanding of osteosarcoma biology.
In summary, after overcoming a multitude of challenges, EURAMOS-1 is now actively recruiting patients in 11 countries on two continents.

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EUROpean Bone Over 40 Sarcoma Study (EURO-B.O.S.S)
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Introduction: EUROBOSS is a multicentre prospective study for patients older than 40 years with highly malignant sarcoma of bone: Osteosarcoma, Fibrosarcoma, Malignant Fibrous Histiocytoma (MFH), Leiomyosarcoma, Dedifferentiated Chondrosarcoma. The present EUROBOSS protocol is based on the experience of the participating intergroups in the treatment of spindle cell bone sarcomas and their past and present osteosarcoma protocols.
Material and Methods: The study is a first step of a process to establish the standard chemotherapy treatment with the aim to improve outcome for patients with these rare tumours. In this regard, the study aims to determine the feasibility of intensive chemotherapy in this age group, and/or separate efficacy analyses according to the different histologic categories and whether the number of patients recruited by the cooperating groups permits future randomised studies. Primary aim is to evaluate clinical outcome and chemotherapy-related toxicity in patients 41-65 years old with high-grade bone sarcoma treated with a three-drug chemotherapy regimen containing adriamycin (ADM), cisplatin (CDP) and ifosfamide (IFO), and the addition of methotrexate (MTX) to poor histologic responders.
Results: At January 2006, 90 patients were enrolled. The median age was 52 years (41-65), 54% were male and 46% female. Femur (44%), Tibia (19%), Pelvis (10%) and Humerus (8%) were the most frequent site of disease. 18% of patients were metastatic at presentation. Primary high grade osteosarcoma (41%), high grade spindle cell sarcoma (28%), dedifferentiated chondrosarcoma (18%) were the most frequently reported histologic diagnosis, but also MFH (4 pts), leiomyosarcoma (3 pts), small cell osteosarcoma (1 pt), fibrosarcoma (1 pt), radioinduced sarcoma (1 pt), dedifferentiated parosteal osteosarcoma (1 pt) were reported.
Conclusions: The study is ongoing oad open to collaboration with other Groups or Institutions, after agreement of all participating groups.

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Dedifferentiated Chondrosarcoma – results of a European wide study
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Introduction: Dedifferentiated chondrosarcoma is a rare but highly malignant manifestation that can occasionally arise in patients with cartilage tumours. There remains uncertainty as to the best treatment for this condition and in particular whether chemotherapy may have a role in improving prognosis.
Material and Methods: Members of EMSOS were invited to contribute data on patients, tumours, treatment and outcomes of patients with dedifferentiated chondrosarcoma.
Results: 8 centres contributed data on 306 patients from 6 countries. The mean age was 57 (range 15 to 89) and the most common site was the femur (46%) followed by the pelvis (29%). 25% of patients presented with a pathological fracture and the most common high grade component identified was MFH. 23% had metastases at diagnosis and these patients had a median survival of 5 months. 30% of patients received chemotherapy with 47% under 60 having chemotherapy compared with 10% over 60. One third of this group had neoadjuvant chemotherapy and the rest had adjuvant treatment. 88% had surgery with limb salvage in 80% of this group. The overall survival was 38% at 2 years and 24% at 5 years but in patients without metastases at diagnosis these figures were 43% and 26% respectively. Poor prognostic factors for survival were: Metastases at diagnosis, amputation or no operation, local recurrence, age over 60 and pathological fracture at presentation. We were unable to identify any group in whom chemotherapy appeared to have a survival benefit.
Conclusions: Dedifferentiated chondrosarcoma carries a dismal prognosis. Although 30% of patients received chemotherapy in this study we were not able to prove that it improved survival. Early diagnosis and complete surgical excision still offer the best prognosis for this condition.