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High Dose Doxorubicin–Ifosfamide (HDDI) Combination Therapy for Soft Tissue Sarcomas (STS)

F. Arganaraz[1], M. Chacón[1], J. Kaplan[2], R. Chacón[1]. [1]*Alexander Fleming Institute, Medical Oncology, Buenos Aires,* [2]*Alexander Fleming Institute, Surgical Oncology, Buenos Aires, Argentina*

Background: Doxorubicin (D) and ifosfamide (I) are the most effective drugs used in STS. The value of dose intensive regimens both in localized and advanced disease is unclear. The aim of this study was to evaluate safety and efficacy (RECIST) of HDDI in terms of objective Response Rates (RR), Time to Progression (TTP) and Overall Survival (OS). Independent factors for OS were also analyzed.
Methods: Retrospective analysis of medical records from our STS database of 1287 patients (pts) from January 2000 to May 2008. We selected pts treated in the neoadjuvant, adjuvant and advanced settings. Chemotherapy regimen used was: D 75 mg/m^2 in 72 hs continuous infusion (c.i.); I 10 g/m^2 (5 doses of 2 g/m^2); MESNA and G-CSF every 21 days. Kaplan Meyer method was used for survival; log rank test and cox proportional regression for univariate and multivariate analysis.
Results: 73 pts were treated, 29 females, 44 males. Median (Md) age: 41 years (15−67). Most frequent histologic subtypes: leiomyosarcoma 19%, malignant fibrous histiocytoma 16%, liposarcoma 15%. 59 pts were advanced (81%); 9 neoadyuvant; 5 adyuvant. Md metastatic sites: 1 (1−4). PS 0−1: 97%. Md of cycles: 4 (1−12). Md follow up: 59 months (2−96). Overall RR 51%, Complete Response (CR) 15%, Partial Response (PR) 36%, Clinical Benefit 81% (CB). Md TTP 7 months (IC95% 6−11), Md OS 21 months (IC95% 16−31). R0 surgery after HDDI (27 pts) was the only significant factor for OS in multivariate analysis. Febril Neutropenia: 40 pts (65%). 2 related deaths (1 for sepsis/1 secondary leukemia).
Conclusion: The combination of HDDI is an effective therapy in terms of response rates. The management of toxicity must involve a multidisciplinary team. This regimen should be considered as an option for first line therapy in patients with STS.

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The Prognostic Value of Genetic Variations of VEGF-a and VEGFR2 Genes in GIST Patients Treated With Sunitinib

P. Rutkowski[1], I. Lugowska[1], M. Brzeskwiniewicz[2], K. Wasilewski[2], E. Mierzejewska[3], K. Szamotulska[3], A. Klimczak[1], E. Bylina[1], J. Limon[2]. [1]*Maria Sklodowska-Curie Memorial Cancer Centre, Department of Soft Tissue/Bone Sarcoma and Melanoma, Warsaw, Poland;* [2]*Medical University of Gdansk, Department of Biology and Genetics, Gdansk, Poland;* [3]*Institute of Mother and Child, Department of Epidemiology, Warsaw, Poland*

The present study investigated the influence of the single nucleotide polymorphisms (SNPs) in vascular endothelial growth factor A (VEGF-A)gene: −2578C/A, −460 T/C, +936C/T and +405 G/C and VEGF Receptor 2 (KDR)gene: 1416T/A and rs 1531298 on prognosis and sunitinib-related toxicity in patients with gastrointestinal stromal tumour.
Methods: Blood samples were collected from 37 patients with locally advanced or metastatic GIST, treated with sunitinib due to imatinib resistance. The SNPs of the genomic DNA were analysed by PCR and their relationship with disease progression and incidence of adverse events grade >2 according to Common Toxicity Criteria were studied.
Results: In VEGFA gene, the C-allele in the −460 T/C and the T-allele in the +936 C/T polymorphism were associated with significantly higher risk of hypothyroidism (OR: 10,1; P = 0.041 and OR: 10.5; P = 0.015, respectively). No impact of SNPs on arterial hypertension, hand-foot-syndrome and diarrhea was observed. The genotype +405CC was related to lower probability of disease progression (OR: 0.17; P = 0.049). The analysed polymorphisms in VEGFR2 gene were not correlated with any of the outcomes studied.
Conclusions: The results indicate that the three polymorphisms of VEGFA gene have a functional influence on disease progression and sunitinib-related toxicity in GIST patients, plausibly through changed VEGF-A protein level. The possible clinical implications of these findings need further investigation.

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Combination Chemotherapy With Gemcitabine and Docetaxel in the Treatment of Metastatic Soft Tissue Sarcomas − a Single Institution Experience

V. Conde-Herrero[1], C.S. González-Rivas[1], J. Soberino[1], V.E. Castellón-Rubio[1], A. González-Vicente[1], B. González-Astorga[1], R. Luque-Caro[1], J. Valdivia-Bautista[1], J.A. Ortega[1], J.R. Delgado-Pérez[1]. [1]*"Virgen de las Nieves", Medical Oncology, Granada, Spain*

Background: Soft tissue sarcomas (STS) constitute a heterogeneous family of solid tumours of the mesenchymal cell origin and accounting for approximately 1% of all cancer diagnoses. Metastatic STS (mSTS) remains an incurable disease, except resectable lung metastases or localized metastatic disease.
Multidisciplinary treatment is the standard of care of primary lesions and limited metastatic disease. Chemotherapy (ChT) is the main option treatment for unresectable mSTS.
Gemcitabine (Gmb) and Docetaxel (Dtx) combination is an active treatment in mSTS especially in leiomyosarcoma (LMS) subtype.
Material and Methods: We review 13 cases of mSTS, who received Gmb 675 mg/m^2 intravenously (IV) over 60−90 minutes on days 1 and 8 plus Dtx 60−75 mg/m^2 IV on day 8 +/− Filgastrim or Pegfilgastrim support every 3 weeks between January 2005 and February 2011 in our hospital. Tumour response in 2 patients (pts) is pending evaluated. Pts did not receive in any case more than 8 cycles.
Median age was 58 years (37−80). 4 pts were men and 9 women. 8 pts (61%) presented advanced LMS. 1 patient (pt) presented an Angiosarcoma. 1 pt a Pleomorphic malignant fibrous histiocytoma. 1 pt a Myxoid liposarcoma. 1 pt a Small round cells monofasic synovial sarcoma. 1 pt a low grade Malignant fibrous hystiocitoma. The median of previous ChT lines was 0 (0−4). Gmb/Dtx combination was the first line in 7 pts.
Results: From 11 pts evaluable for response, 2 pts (18%) obtained partial response (PR) and 2 pts (18%) stable disease (SD). 7 pts (64%) presented progression disease (PD). The global response rate (RR) was 18%, the clinical benefit (CB) (RR+ SD) was 36%, and the median progression free survival (PFS) was 121 days (60–184). 1 pt remains with PR since the end of treatment 18 months ago. 2 pts with lung metastases obtained SD with Gmb/Dtx treatment and they were operated of lung metastases in two times.
Toxicities grade 3−4: aenemia: 1 pts (8%); febrile neutropenia: 2 pts (15%); neutropenia: 2 pts (15%); thrombocytopenia: 3 pts (23%); diarrhea: 3 pts (23%); Alopecia: 9 pts (69%). No patient stopped ChT by toxicity. There were no toxic deaths.
Conclusion: In our experience, Gmb/Dtx combination is an active ChT regimen in mSTS. The toxicity profile is good and the toxicities are manageable. Gmb/Dtx is a good alternative of treatment in mSTS in first line, especially in LMS, or after progression to Doxorubicin and/or Ifosfamide ChT regimens in other subtypes of STS.

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Viscum Album Fermentatum Pini Versus Oral Etoposide as Adjuvant Treatment in Osteosarcoma Patients After Second Relapse

A. Longhi[1], E. Mariani[2], J.J. Kuehn[3]. [1]*Ist. Oncologico della Svizzera Italiana, Ospedale Regionale, Bellinzona, Switzerland;* [2]*Ist. Ortopedico Rizzoli, Musculoskeletal Oncology Department, Bologna, Italy;* [3]*Onkologische Klinik, Lukasklinik, Arlesheim, Switzerland*

Background: Osteosarcoma is a highly malignant bone tumour affecting mainly adolescents. With the recommended neoadjuvant chemotherapy it can be cured in approximately 60% of cases. Few experimental target drugs are currently available through phases I and II trials for relapsed and inoperable patients. We know from historical controls that the risk to relapse increases after the second relapse. Relapse-free survival then decreases to <20% after 12 months. Although no final proof of evidence for oral Etoposide is available, it is often used in clinical practice due to reported good results in advanced childhood cancer with response rates of 15%. Oral Etoposide is well tolerated, easy to administer and affordable. Interferon or MTP-PE (muramyl tripeptide phosphatidyl ethanolamine; Mepact®) have also been used as adjuvant treatment with encouraging results in advanced osteosarcoma (improved disease-free survival [DFS] of 7%) but these treatments are significantly more expensive and less well tolerated.
Material and Methods: Viscum album fermentatum Pini (Viscum) is a highly popular herbal medicinal product across central Europe with immunomodulatory activity. Encouraged by the preliminary findings of a pilot study that showed a prolonged DFS of more than 12 months in four out of five with Viscum album treated osteosarcoma patients after their second relapse, we started a two-arm randomized study comparing Viscum album fermentatum Pini s.c. to oral Etoposide in patients free from disease after