SECTION 3

PERSPECTIVES IN THE CHEMOTHERAPY AND BIOLOGICAL THERAPY OF BONE AND SOFT TISSUE SARCOMAS

ORAL PRESENTATIONS

ID 214

Is it possible to evaluate the risk before and during preoperative chemotherapy in osteosarcoma?

G.N. Machak[1], B.I. Dolgushin[1], N.V. Kochergina[1], A.D. Ryjkov[1], M.D. Aliev[1], A.V. Kuznetsova[2], O.V. Senko[2]
[1] N.N. Blokhin Russian Cancer Research Center, Moscow, Russian Federation
[2] Computer Center of Russian Academy of Sciences, Russian Federation

Introduction: Tumor necrosis rate is the standard criteria for risk assessment in osteosarcoma patients, included in neoadjuvant protocols. In order to evaluate the risk at early stages, we have investigated several tumor and treatment related characteristics, which were assessed at diagnosis and during induction chemotherapy.
Material and Methods: The database included 593 osteosarcoma patients. Between 1979 and 1986 preoperative treatment comprised one 72-hour IA infusion of DOX 90 mg/m^2 and radiotherapy 40 Gy. From 1986 to 1999, preoperative chemotherapy consisted of 3-5 monthly cycles of IA DOX 90 mg/m^2 or CDDP 120 mg/m^2. In the last protocol, induction consisted of 3-4 cycles of DOX and CDDP in similar doses. After local treatment, response adapted adjuvant chemotherapy was administrated. The clinical, radiographic, angiographic, perfusion, scintigraphic and biochemical characteristics were monitored during induction. Cox regression and SWS method were used in multivariate analysis.
Results: At presentation, stage IIIB, tumor volume >150 ml, growth rate >80 ml/mos. and elevated ALP level were predictive for higher progression risk in univariate and multivariate analysis. Overall and disease-free survival were significantly related to early tumor response, characterized by disappearance of clinical symptoms, tumor volume less than 300 ml, tumor regression, radiographic bone healing, decreasing of tumor vascularity, low level of tumor perfusion, low ^{99}Tc uptake or decreasing of its level and normalization of ALP activity. The degree of tumor regression, the radiographic and biochemical responses after 2 cycles entered in the multivariate prognostic model, which allowed to predict the course of disease at this stage of treatment. The same criteria were predictive after completion of preoperative chemotherapy.
Conclusions: The use of modern imaging methods allows predicting the course of disease in osteosarcoma before and during induction chemotherapy. It permits to make appropriate therapeutic decisions before definitive surgery. The impact of risk and response adapted treatments on the local effectiveness, limb-salvage rate and survival has to be evaluated in prospective trials.

ID 220

Treatment results for patients with high-risk Ewing's sarcoma family tumor (HR ES)

N.M. Ivanova, A.V. Shvarova, A.Z. Dzampaev, I. Dolgopolov, I. Glekov, G.L. Mentkevitch
N.N. Blokhin Russian Cancer Research Center, Moscow, Russian Federation

Introduction: The purpose of the current research is to study treatment results for patients with high-risk ES\PNET.
Material and Methods: From January 1995 to January 2006 103 pts (45 male, 58 female) with disseminated (28), poor prognosis (75) ES (72) or PNET (31) were included in research. Induction chemotherapy (CT) consisted of vincristine 1,5 mg/m^2/d, days 1,8,15, adriamycin 37,5 mg/m^2/d, days 1,2 as a 24-h infusion, cyclophosphamide 2,1 gr/m^2/d, days 1,2 (1, 3, 5 cycles), and ifosfamide 2,4 gr/m^2/d, days 1 through 5, VP-16 100 mg/m^2/d, days 1 through 5 (2, 4 cycles). All patients achieved PR after 2 CT courses with 82% (52-98%) decrease in tumor volume. All patients underwent through a complex treatment in the following volume: polychemotherapy, X-ray therapy in summary focal dose 36-57 Gy on necessity large pole X-raing of the lungs in summary focal dose 12 Gy and surgical interference of organs saving character. 50 pts received HD CT with support of peripheral blood stem cells, harvested after second course of polychemotherapy in the condition of full sanation of the marrow.

Results: 5-year disease-free survival was 75,6±5,2%, 5-year disease-free survival without HD CT was 76,1±6,9%, 5-year disease-free survival with HD CT was 59,3±7,2%.

ID 43

Oncological outcomes following treatment of soft tissue sarcomas of the hand and wrist

A. Pradhan, Y. Cheung, R. Grimer, O. Al-Muderis, M. Thomas
Royal Orthopaedic Hospital, Birmingham, United Kingdom; Royal Marsden Hospital, London, United Kingdom

Introduction: Soft tissue sarcomas (STS) in the hand are rare tumours treated by surgical excision often combined with radiotherapy. Anatomic constraints make it difficult to achieve wide margins due to limited expendable soft tissue. Sacrifice of important structures to allow adequate margins can result in significant functional loss. Controversy still exists on whether limb-sparing surgery or amputation provides the best overall treatment in this location. This study compares oncological outcomes following treatment of hand and wrist soft tissue sarcomas from two regional centres of the UK.
Material and Methods: 64 patients with new primary, non-metastatic, STS in the hand and wrist diagnosed between 1990 and 2001 were identified from the centres' local databases. Further clinical details were extrapolated from patient clinical notes.
Results: There were 44 male and 20 female patients, with ages ranging from 11 to 92 years (median age 44 years). The three most common diagnoses were synovial sarcoma, clear cell sarcoma and epithelioid sarcoma. 17 patients had amputations and the rest limb salvage. The period of follow up ranged from 3 to 180 months. The overall survival was 79% at 5 years and was related to the grade and size of the tumour. There was a 25% risk of local recurrence almost all arising in patients with limb salvage. These patients had no worse a prognosis than those having amputations primarily.
Conclusions: This large series of hand and wrist STS has shown that survival is not affected by radical surgery or adjuvant treatment however local control can be compromised with limb sparing surgery. Inductive two-drug chemotherapy improves 2-year EFS from 35% to 68%. Limb salvage surgery didn't decrease EFS vs. amputation.

ID 207

Taurolidine: A novel anti-neoplastic agent induces apoptosis of osteosarcoma cell lines

B. Fuchs, D. Walters
Balgrist University Hospital, Zurich, Switzerland

Introduction: Osteosarcoma (OS) is an aggressive bone malignancy that primarily affects children and adolescents. Presently, treatment of osteosarcoma involves surgical resection and multi-agent neo-adjuvant chemotherapy. The addition of neo-adjuvant chemotherapy to surgical resection has increased OS patient 5 year survival rates by over 50% compared to surgery alone. However, the increase in survival has reached a plateau despite the use of the most active chemotherapeutic agents. Furthermore, current chemotherapeutic agents, which include cisplatin, methotrexate and doxorubicin, are all associated with high toxicity and numerous side effects. Consequently, the discovery of novel treatments for osteosarcoma is essential. Taurolidine, the active agent of Taurolin, is a broad spectrum antibiotic that has been used clinically to reduce post-operative infections for over 15 years. Recently, Taurolidine has also been shown to have in vitro and in vivo anti-neoplastic properties against a variety of cancers including glioblastoma and malignant melanoma.
Material and Methods: We examined the effect of taurolidine on osteosarcoma cell lines, U2OS, SaOS and sublines (LM3, LM5, LM7), MG-63 and sublines (M6, M8) and HU-09 and sublines (L13, M112), using cytotoxicity, apoptosis and migration assays.
Results: Although these cell lines possess different genetic defects and/or different metastatic potential, Taurolidine treatment inhibited the growth of M and inducedall osteosarcoma cell lines tested with an IC50 range of 35-50 apoptosis in a dose-dependent manner. Taurolidine-induced apoptosis has previously been reported to be caspase-dependent. Of note, pre-treatment of osteosarcoma cells with Z-VAD-fmk, a general caspase inhibitor, prevented Taurolidine-induced apoptosis.
Conclusions: We conclude that Taurolidine induces apoptosis of OS cell lines in a caspase-dependent manner and that Taurolidine may have potential as a novel OS chemotherapeutic agent.

ID 205

Immunogene therapy with GM-CSF/B7-1 in the treatment of fibrosarcoma

J.P. Cashman, J.O. Larkin, G. Casey, M.C. Whelan, C. Collins, M. Tangney, G.C. O'Sullivan
Cork Cancer Research Centre, Mercy University Hospital, Cork, Ireland

Introduction: Gene therapy induced expression of immunostimulatory molecules at tumour cell level may evoke antitumour immune mechanisms by recruiting and enhancing viability of antigen processing cells and specific tumouricidal lymphocytes. The anti tumour efficacy of a plasmid coding for Granulocyte Macrophage Colony Stimulating Factor (GM-CSF) and B7-1 costimulatory immune molecule, delivered into growing murine fibrosarcoma by electroporation was investigated.
Material and Methods: JBS fibrosarcomas were induced subcutaneously in Balb/C mice and were randomised at 80 mm^3 to control and treatment groups. One day prior to treatment, the portal circulation was seeded with tumour cells. Gene delivery was assessed by in vivo imaging, cytokine measurement and anti-tumour cytotoxicity (in vitro and in vivo). Responses were determined by liver examination.
Results: Anti-tumour responses were found only in those treated by GM-CSF/B7-1 electroporation, with complete tumour regression in greater than 60%, and significant slowing of growth in remaining animals. Complete responders, when rechallenged, failed to develop tumours with the same tumour cell type but developed tumours with an alternative tumour cell type (CT-26). In vitro cytotoxicity was increased and a modified Winn Assay showed effective adoptive transfer of tumour specific immunity. When

tumours were surgically excised following immunogne therapy, these animals were rechallenged with a tumourogenic dose of JBS, to mimic minimal residual disease. It was found that 100% of these animals resisted rechallenge, indicating the potential for this therapy to used in a neo-adjuvant setting. Using a liver metastatic model, effective cure of distal metastases was achieved following treatment of the primary subcutaneous tumour.
Conclusions: We conclude that immunogene-therapy of a murine fibrosarcoma model, by electroporation with GM-CSF/B7-1 plasmid induces effective local and systemic antitumoural immune responses which are durable. This treatment strategy could be applicable in the clinical setting for effective elimination of both primary tumours and associated metastatic disease.

ID 68
Predictive value of 8 candidate genes on osteosarcoma therapy outcome
J. Fellenberg, A. Zahlten-Hinguranage, G. Delling, L. Bernd
Department of Experimental Orthopedics, Orthopedic Hospital, University of Heidelberg, Germany
Department of Orthopedic Surgery, University Hospital, Hamburg, Germany

Introduction: Osteosarcoma ist the most common primary tumor of the bone, typically affecting the long tubular bones of children and adolescents. The introduction of adjuvant and neoadjuvant chemotherapy markedly improved the outcome with long term relapse free survival rates ranging from 55 to 75%. However, the remainder of patients poorly respond to chemotherapy with an increased risk of relapse and the development of metastasis. Histologic response to chemotherapy is currently the strongest prognostic factor in high-grade osteosarcoma, but it can only be assessed after several weeks of therapy. Thus, detection of chemosensitivity at the time of diagnosis would be of great clinical importance. The aim of this study was the evaluation of the predictive value of 8 drug-regulated genes by the correlation of gene expression data with clinical parameters.
Material and Methods: Paraffin sections from 35 osteosarcoma biopsies were analyzed (18 good responder and 17 poor responder). The response to preoperative chemotherapy was assessed histologically according to the six-grade scale of Salzer-Kuntschik. Tumor cells were isolated by Laser-Microdissection followed by gene expression analysis using quantitative real-time PCR.
Results: Out of the 8 genes analyzed, the expression of rhoA, impdh2 and pro1959 was significantly elevated in tumors that poorly respond to chemotherapy (2.1-, 2.3- and 6.0-fold, respectively) ($p=0.017$, $p=0.019$ and $p=0.012$). A significant negative correlation of gene expression and disease-free survival could be detected for prohibitin, ferritin light-chain and pro2000, respectively.
Conclusions: This study suggests a possible role of rhoA, impdh2 and pro1859 as prognostic marker for the early detection of chemoresistance in osteosarcomas. In addition, the correlation of prohibitin, ferritin light-chain and pro2000 gene expression with the disease-free survival may indicate a more aggressive malignancy. Together, these candidate markers may be of clinical importance, in order to stratify patients at diagnosis into low and high-risk groups improving the outcome of high-risk patients and minimizing the toxicity of therapy for low-risk patients by means of a risk adapted therapy.

ID 245
The perspectives in combined treatment of soft tissue sarcomas
B. Bokhyan, N. Mekhtieva, E. Stepanova, D. Kolokolov, D. Burov
N.N. Blokhin Russian Cancer Research Center, Moscow, Russian Federation

There is no common opinion on advantages of different approaches in the treatment of soft tissue sarcomas. Heterogeneity of clinical groups makes the comparison of the results difficult because of rarity of such tumors and using different methods. Searching the new treatment methods in soft tissue sarcomas is still going on. Studying tumor markers is a new a direction in disease outcome prediction and selection of individual chemotherapy. The number of characteristics which pretend to be of prognostic value is increasing constantly. Tumor location, size, depth, histological type, grade, surgical margins, distant metastases, local recurrence are usually used by us as prognostic factors. In order to improve the outcome prediction and individualization of treatment new factors were studied. They were Bcl-2, p53, MDM2, Ki-67, pRB, FAS, p27, MMP2, MMP9, TIMP2, bFGF, VEGF, Skp2. In this study we made an attempt to analyze their prognostic value and contribution to individualization of soft tissue sarcoma treatment.

POSTER SESSION

ID 238
Chondrosarcoma in children – chemotherapy and/or only surgery?
A. Szymborska, W. Wozniak
Institute of Mother and Child, Department of Oncological Surgery, Warsaw, Poland

Introduction: Authors present own experiences in treatment of chondrosarcoma in children. In the courses of 13 years, i.e. from 1992 to 2005 in Clinic 44 pts. with diagnosed chondrosarcoma have been treated. In majority of cases there were primary bone tumors with stage of G2, G3.
Material and Methods: 44 patients has been hospitalized, of age 6 to 21 years. 27 girls and 27 boys. In 38 pts. it was a localized form. Evolution of type and histological grade of tumors malignancy enable to choice the proper therapy methods, including the extend of operative treatment, introduction of chemotherapy. 31 limb-sparing operations have been done, multilative were carried out in 9 pts. Chemotherapy has been diagnosed. Additionally in 5 pts. radiotherapy was used.
Results: Good functional score we observed in 30 pts. Local recurrences were in 4 cases. In 6 pts. the metastasis foci in lungs have been found. In the discussed group of pts. alive 37 pts., two pts. is out of observed group.
Conclusions: In majority of cases there were tumors of low and medium stage of histopatological malignancy (G1, G2) more often giving local recurrences than distal metastases.

ID 194

Combined treatment of pediatric osteosarcoma: twenty-year experience

N.M. Ivanova, A.Z. Dzampaev, A.S. Petrosjan, Y.N. Soloviev, A.V. Shvarova, R.M. Kaiumov, Y.U. Pashkov, L.V. Valentei, A.V. Igoshin, M.D. Aliev
N.N. Blokhin Russian Cancer Research Center, Moscow, Russian Federation

Introduction: we review our experience of combined treatment of pediatric osteosarcoma.
Material and Methods: From 1980 to 2003 one hundred and thirty eight patients (median age 10,8 years) with osteosarcoma(OS) were treated in our institute.135 patients underwent surgery. 129 patients had limb salvage surgery. All patients retrospectively divided into two groups according to scheme of chemotherapy: basis group and group of control. Forty two patients (38 with localized OS and 4 (9,5%) with metastatic OS) of control group were treated with monochemotherapy (cisplatin or doxorubicin) and surgery. Ninety six patients (87 with localized OS and 9 (9,3%) with metastatic OS) of basis group were treated according to the following scheme: primary two-drag chemotherapy (cisplatin plus doxorubicin), surgery and maintenance alternating chemotherapy (ifosfamide and etoposide were added).
Results: The efficacy of preoperative chemotherapy was 30% in the control group. Complete response (CR) was registered in 7,5% of patient and partial response (PR) — in 22,5%. Nine percent of patients of basis group achieved CR, 48 % patients of basis group had PR. The summary efficacy of two-drug regimen in basis group was 57%.Two-year event-free survival (EFS) of patients of control group was 35%.2-year EFS of patients of basis group was 68%.
Conclusion: Inductive two drug chemotherapy improves 2-year EFS from 35% to 68%. Limb salvage surgery did not decrease EFS versus amputation.

ID 218

Pediatric malignant tumors of the rib: results of multimodality

N.M. Ivanova, A.V. Igoshin, A.Z. Dzampaev, A.V. Shvarova, I.V.Glekov
N.N. Blokhin Russian Cancer Research Center, Moscow, Russian Federation

Introduction: We sought to establish the outcome and optimal therapeutic sequence for patients with primary malignant tumors of ribs.
Material and Methods: a retrospective analysis of institutional experience between 1976 and 2005 was performed. Seventy nine patients with primary malignant tumors of ribs were identified. The age is ranged from 3 to 16 years. 47 patients were male, 37 - female. 74 patients had a Ewing sarcoma (ES), three patients - osteosarcoma (OS) and two - chondrosarcoma (CS). Localized disease was diagnosed in 60 patients with ES and 2 with CS. Other patients had metastatic disease. 92% of patients with ES were included in high risk group (tumor volume over 100 ml or/ and metastatic disease at presentation). 47 patients (64%) underwent surgery. Since 1998 the treatment of patients with ES included intensive chemotherapy (adapted to risk group) with 5-drug regimen (vincristin, adriamicin, cyclophosphamide, ifosfamide and etoposide) and local control (surgery and radiation therapy in 100 % cases). 21 patients (28%) were treated in this new study. 7 of these had metastatic disease and underwent megatherapy with peripheral blood stem cells transplantation. 53 patients with ES were included in control group.
Results: In the new protocol 5-year event-free survival (EFS) of patients was 72%. In the control group EFS at 5 years was 28%.
Conclusions: Surgery is absolutely necessary in the treatment of malignant tumors of ribs. New treatment protocol with intensive risk-adapted chemotherapy increase 5-year event-free survival from 28% to 72%.

ID 221

Overcoming of hematological toxicity by small doses of PBSC in high-risk pediatric ST sarcomas

A.V. Shvarova, N.M. Ivanova, G.L. Mentkevich, R. Ravshanova
N.N. Blokhin Russian Cancer Research Center, Moscow, Russian Federation

Introduction: The purpose of the current research is to study toxicity of the intensive polychemotherapy including 8 courses on the following scheme: Etoposide + Cyclophosphamide + Carboplatin.
Material and Methods: The methods starting from 1999 until present time in the Research Institution of Pediatric Oncology in the Russian Cancer Center. 36 patients in the age from 2 to 14 years old (17 males and 19 females) with soft tissue sarcomas of high risk group including rhabdomyosarcomas (19) and synovial sarcomas (17) underwent through a complex treatment in the following volume: polychemotherapy, X-ray therapy on initial tumor in summary focal dose 45-50 Gr on necessity large pole X-raing of the lungs in summary focal dose 12 Gr and surgical interference of organs saving character. On the stage of consolidating all the patients were made reinfusion of subtransplantational doses of autological stem cells of peripheral blood.
Results: When holding consolidating therapy with hematopoietic support of PBSC the number of heavy leukopenia stayed on the level of 94,0%, thrombocytopenia on the level of 79,1%, but the length of the neutropenic fever decreased from 5,56±1,59 days to 3,42±0,45 days. When holding chemotherapy course, following after X-ray therapy, the support by PBSC might reduce the severity of thrombocytopenia and decrease the frequency of development of organotoxic complications. 2-year event-free survival was 52%, overall 2-year survival — 53,5%.

ID 140

Complementary treatment for chemotherapy-induced nausea and vomiting

M. Bergum, G.S. Haugen
The Norwegian Radium Hospital, Oslo, Norway

It is a well known fact that nausea and vomiting are the most frequent, and often experienced as the worst side effects from chemotherapy-treatment. These adverse side effects can in

large scale alter a patient's quality of life, and worsen cancer-related problems such as cachexia and fatigue. It is therefore very important to achieve satisfactory relief from nausea and vomiting. The department of Physiotherapy at the Norwegian Radium Hospital has during the last few years introduced electrotherapy i.e. transcutaneous electrical nerve stimulation (TENS) as a complementary treatment for preventing and minimizing nausea and vomiting due to chemotheraphy drugs. Patients of all ages and sexes treated for high-graded sarcoma have been offered this treatment if they have not achieved satisfactory relief from antiemetic medication. The patients have been very interested in the use of TENS and some report a subjective feeling of getting less nauseated. Most important is the feeling of control and management. Studies comparing TENS and acupuncture have shown that the latter is expected to be even more effective on nausea and vomiting than TENS. As a result of this we have just prepared a protocol on a pilotproject where we plan to use acupuncture against chemotherapy-induced nausea and vomiting. The preliminary results will be presented at the conference. We would also like to present the patients' and our experience with these complementary treatments.

ID 216

Neoadjuvant chemotherapy protocol without high-dose methotrexate in osteosarcoma

G.N. Machak, V.A. Sokolovsky, E.E. Kovalevsky, M.D. Aliev
N.N. Blokhin Russian Cancer Research Center,
Moscow, Russian Federation

Introduction: The purpose of this study was to evaluate the local response and long-term results in osteosarcoma patients, treated with neoadjuvant chemotherapy without high-dose methotrexate.
Material and Methods: From December 1999 to December 2005, 101 patients were included in this study. Most of them had IIB extremity osteosarcoma. Induction chemotherapy consisted of 3-4 cycles of DOX 90 mg/m^2 and CDDP 120 mg/m^2 IV or IA. Surgery was performed at week 20. Adjuvant chemotherapy in good responders comprised the drugs used preoperatively. In poor histological responders, IFO 9 g/m^2 and VP-16 500 mg/m^2 were added to DOX and CDDP.
Results: Limb-salvage rate was 91%. Fifty-four of 82 patients (66%) had > 90% of tumor necrosis. Overall survival (OS) and disease-free survival (DFS) at 5 years was 48±9%, and 45±8%, respectively. The response to induction chemotherapy was related to initial ALP level. The rate of good responders was 94% (16/17) in patients with normal marker level versus 48% (30/63) in patients with elevated ALP level, $p = 0.0006$. The following factors were predictive for outcome in univariate analysis: stage ($p = 0.007$), ALP level ($p = 0.015$), tumor necrosis ($p = 0.006$), and completeness of adjuvant chemotherapy ($p = 0.0006$). Stage and initial ALP level retained their significance in Cox regression. In IIB osteosarcoma the predicted 3-year OS was 91% in patients with normal ALP level, and 74% in alternative group. In IIIB osteosarcoma with elevated ALP level the probability to survive 3 yrs was only 28%. DFS was also related to initial ALP level. The predicted 3-year DFS in patients with normal ALP level was 74% compared with only 24% in patients with elevated ALP level.
Conclusions: We conclude that this protocol is effective in terms of limb-salvage rate and percent of good histological responders. The most impressive long-term results can be expected in IIB osteosarcoma with normal ALP level at presentation.

ID 197

The primary treatment results by using of high doses of methotrexate for the children with osteosarcoma

N. Ivanova, K. Savlaev, A. Dzampaev, A. Shvarova, A. Petrosjan, A. Ivanov, K. Koshechkin, V. Baykova, M. Aliev
N.N. Blokhin Russian Cancer Research Center,
Moscow, Russian Federation

Introduction: the purpose of the current research is to study toxicity of the intensive cemotherapy including high doses of methotrexate and to increase the survival of children with osteosarcoma.
Material and Methods: the methods starting from 2003 until present time in the Research Institution of Pediatric Oncology in the Russian Cancer Center. 22 patients in the age from 5 to 16 years (13 males and 9 females) with osteosarcoma (localised disease - 12 patients, 10 - metastatic disease) underwent through a complex treatment in the following volume: polychemotherapy consisted of adriamicin, drugs of platinum, ifosfamide and etoposide, and also high doses of methotrexate — 12 mg/m^2 per infusion. Surgical interference was priority of organs saving character. The maximum doze of methotrexate was 20 g per infusion, 40 g was summary dose per cours.
Results: all patients achieved partial response with decrease in tumor volume. 16 patients are alive without disease now, 4 were died of progressive disease and 2 patients are alive now with progressive disease.
Conclusions: the modern chemotherapy with using high dose methotrexate improve survival patients with osteosarcoma.

ID 217

Intravenous versus intra-arterial chemotherapy in osteosarcoma of the extremities

G.N. Machak, Yu.N. Soloviev, V.A. Sokolovsky, M.D. Aliev
N.N. Blokhin Russian Cancer Research Center,
Moscow, Russian Federation

Introduction: The aim of this study was to compare the local response and long-term results in osteosarcoma patients treated with intravenous and intra-arterial preoperative chemotherapy.
Material and Methods: Chemotherapy consisted of 3-4 monthly cycles of DOX 90mg/m^2 as 96-hour CI and CDDP 120 mg/m^2 as 4-hour IA infusion (arm A) or 2-hour IV infusion (arm B). Surgery was performed at week 20. The histological response was evaluated according to Huvos score.
Results: The rate of good responders (grade III-IV by Huvos) was 81% (35/45) and 49% (19/39) in arms A and B, respectively, $p = 0.002$. Complete tumor necrosis occurred in 23% of arm A patients and in 8% of arm B patients, $p = 0.05$. At minimal follow-up time 12 mos, 33% (3/9) of patients from arm B developed local recurrence after limb-salvage surgery compared with only 6% (1/16) of patients from arm A, $p = 0.076$. For the moment, we have no evidence that the CDDP administration way could influence the overall and metastases-free survival.

Conclusions: In this two-drug induction chemotherapy regimen, the intra-arterial administration of CDDP was more advantageous in terms of tumor necrosis rate and local control, especially after limb-salvage surgery. The impact on the long-term results has to be analyzed after a longer follow-up period.

ID 281

Chemotherapy efficacy in patients with bone sarcomas and soft-tissue sarcomas

A.Yu. Fedotov, L.M. Kogonia, Yu.Ya. Belyakov, E. Chelnokova, I.M. Grishina
Cancer Clinic No.2, Moscow, Russia; Clinic No. 84, Moscow, Russia

A total of 43 patients (pts) aged 23 to 59 years received treatment for sarcoma during 2003 through 2005 including 31 cases with osteogenic sarcoma, 8 cases with soft-tissue sarcomas and 4 cases with bone chondrosarcoma. The treatment was given on an outpatient basis and included combination chemotherapy by CAP or CVDIC schedules. All the pts underwent specific treatment as surgery (40%), chemoradiotherapy (15%) or multi-modality approach. All pts had advanced disease with large tumors or recurrence, lung metastases, 7 pts presented with marked pain (used narcotic analgetics). Therapy was repeated at a 3 — 4 week interval. Adverse effects of chemotherapy included nausea and vomiting (45%), hemopoiesis suppression of various degree (74.5%), nephrotoxicity (12%), alopecia (83.5%), stomatitis (23%). Assessment of efficacy was performed after every two polychemotherapy cycles. Amelioration of pain syndrome was detected already after the first cycles, 5 (13.5%) pts presented with sustained analgesia through all cycles. Response was achieved in 11 (25.6%) cases including complete response in 6 (>50%) and partial response in 5 (<50%) cases; 9 (20.9%) pts had stable disease and 23 (53.5%) had disease progression. Response to chemotherapy lasted for 4 to 8 months on the average. In conclusion, second-line chemotherapy increases efficacy of multi-modality treatment and improves quality of life in cases with bone and soft-tissue sarcomas.