courses of chemotherapy have been administered to 35 pts. After the first course 18/35 pts developed leukopenia grade 4 and 7 pts had non fatal febrile episodes necessitating antibiotic therapy. These 18 pts received additional 54 courses of chemotherapy followed by G-CSF. Although 24 episodes of leukopenia grade 4 were noticed, only one patient developed a febrile infection. 17/35 pts continued treatment after the first course without support of G-CSF. Four of them developed leukopenia grade 4 after the second and third course, respectively, so that only 13 pts received all cycles of chemotherapy without G-CSF. None of several clinical parameters, such as pts' sex and age, performance status, localization of metastases or WBC before treatment could predict the probability of development of leukopenia grade 4. So far, response rates are: CR 6%, PR 24%, SD 38%, and PD 32%. *Conclusion:* The above described regimen is a hematotoxic combination. However, it can be given to about 30% of adult pts with metastatic STS without support of G-CSF. With regard to the high cost of G-CSF we believe that it is justified to administer the first course of this chemotherapy without support of G-CSF. However, under these conditions, the immediate initiation of antibiotic treatment in cases of fever must be guaranteed.

867 PUBLICATION

SUPERFICIAL SOFT TISSUE SARCOMAS OF THE ADULTS

L. Cany, E. Stöckle, J.M. Coindre, A. Ravaud, G. Kantor, N.B. Bui
Institut Bergonié, 180, rue de Saint-Genès, 330746 Bordeaux Cedex, France

A series of 105 consecutive patients with superficial soft tissue sarcomas was analysed to assess the evolution of these tumors. There were 56 men and 49 women, aged 16 to 80 years (median: 56.4 years). Tumor localizations were 59 limbs (56.2%) and 41 non-limbs. The median tumor size was 3 cm (range 1 to 15 cm). Histological types were mainly malignant fibrous histiocyto-fibromas (n = 39 / 36.8%), leiomyosarcomas (n = 20 / 18.9%), dermatofibrosarcomas protuberous (n = 8 / 7.5%). According to the FNCLCC grading, tumor grade was: grade 3 = 24, grade 2 = 54, grade 1 = 28.

With a median follow-up of 112 months (range 19 to 321 months), the 5-year overall and disease-free survival were 75% and 46%. In monofactorial analysis, tumor grade is the only predictive factor for overall survival (grade 1 vs grade 2: $P = 0.02$; grade 2 vs grade 3: $P = 0.0002$), and for metastasis-free survival (grade 1 vs grade 2: $P = 0.05$; grade 2 vs grade 3: $P = 0.0006$). For grade 2 tumors, metastases occurred only after a deep, local recurrence. Age, tumor size, tumor localizations were not statistically significant. For the local relapse-free survival, tumor size (<5 vs $\geqslant 5$ cm) was the only predictive factor ($P = 0.0006$).

868 PUBLICATION

IMPACT OF LOCAL RECURRENCES IN SOFT TISSUE SARCOMA SURGERY

J. Høie, Ø.P. Solheim, A.E. Stenwig
Norwegian Radium Hospital, 0310 Oslo, Norway

Primary surgery in soft tissue sarcomas may be a dilemma between saving functions, abstain of mutilation and the potential of local recurrence. *Material:* 394 consecutive patients treated before 1990 have been analyzed.

Results: 100 patients presented with 150 recurrences; 79 patients with one recurrence only. In these 79, distant spread were seen concomitant with the local recurrence in 27, another 25 patients are free of disease following treatment of their recurrence, in 15 wide primary excisions were impracticable, and 6 patients were above their 80-ties. In 6 patients only, more extensive primary surgery should be advocated. In 7 patients with 4 to 8 episodes of recurrence, 2 died of distant disease, 1 of the local disease and 4 are free of disease. *Conclusion:* impact of local recurrence is moderate and may be accepted in lieu of mutilating surgery.

869 PUBLICATION

SUCCESSFUL AGGRESSIVE CHEMOTHERAPY IN PATIENTS WITH CHONDROSARCOMA: A REPORT OF FOUR CASES

P. Reichardt[1], S. Lentzsch[1], P. Hohenberger[2], B. Dörken[1]
[1]*Free University of Berlin, University Medical Center Rudolf Virchow, Robert-Rössle-Hospital, Department of Medical Oncology*
[2]*Department of Surgery, D-13122 Berlin, Germany*

Chondrosarcoma (CS) is uniformly reported to be resistant to any chemotherapy. A possible exception may be mesenchymal CS where occasional responses can be seen. Still the literature is scarce.

We report 4 patients treated with aggressive chemotherapy consisting of ifosfamide 2.5 g/m^2/day days 1 to 5, epirubicin 45 mg/m^2/day days 2 and 3 and Filgrastim 5 μg/kg/day s.c. days 6 to 15.

The first pt., a 35 ys. old female with a local recurrence and multiple lung metastases of a mesenchymal CS showed a CR of all detectable tumor manifestations after 6 cycles and is disease free for 14+ month. The second pt., a 28 ys. old male with multiple lung mets. of a CS is in continuous complete remission for 3+ month. Two additional patients with multiple lung mets. of a CS showed a stable disease for 13 and 3 months respectively after completion of 4 cycles. Both patients were put on oral chemotherapy with trofosfamide and are still under treatment.

We conclude that in selected cases of CS aggressive treatment should be considered, especially in younger patients.

870 PUBLICATION

DESMOID TUMORS (AGGRESSIVE FIBROMATOSIS): RETROSPECTIVE STUDY

O. Sousa, L. Carvalho, I. Silva, M. Bento, E. Vieira
Department of Radiation Oncology, Instituto Português de Oncologia 4200 Porto, Portugal

Although benign, desmoid tumors are locally aggressive neoplasms which infiltrate adjacent tissues, resulting in a high incidence of local recurrence after conservative resection. Between 1982 and 1993, 10 female and 5 male patients with histologically confirmed desmoid tumors were referred to Instituto Português de Oncologia—Porto. Age ranged from 12 to 47 years, with 2 newborn patients. Sites of disease included head and neck (n = 5), shoulder girdle (n = 3), chest wall (n = 2), abdomen (n = 2), extremities (n = 2) and back (n = 1). Patients were treated with surgery alone (n = 3) or surgery plus radiation (n = 12). Ten patients underwent radiation therapy for uncertain, positive margins or subtotal resection and 2 received planned postoperative radiation (microscopically negative margins), the majority being treated to a tumor dose of 40–70 Gy. With a medium follow up of 4.5 years, 14/15 patients are without evidence of disease and one died with progressive multicentric disease. In the irradiated group, 2 patients with infield recurrence and another with marginal recurrence were successfully treated with surgery. In summary, we believe that moderate doses of radiation can improve local control rates minimal long-term effects.

871 PUBLICATION

LOW EFFICACY OF 1 HOUR INFUSION-HIGH DOSE IFOSFAMIDE (IFO) IN PREVIOUSLY PRETREATED SARCOMA

M. Tubiana-Hulin, F. Cvitkovic, F. Lokiec, L. Bozec, A. Goupil, M. Janvier, F. Turpin, J. Rouëssé
Centre René-Huguenin, Saint-Cloud, France

Following Antman's report (Sem Onc 1990; 17: 7–15) underlining a better efficacy for fractionnated bolus Ifo infusion modality than the 24 h continuous infusion, as treatment in relapsing sarcoma patients, in October 93 we began a phase II study of high dose (HD) Ifo at 4 g/m^2/d on 3 consecutive days (12 g/m^2/cycle) given over 1 hour/d with Mesna (doses $\times$ 1.5) every four weeks until progression. Twelve patients (pts) were entered, their characteristics as follows: median age 40 ys (18–62); sex 5 M/7 W; PS $\leqslant$ 1 12/12 pts; histologic types: bone sarcoma (sarc) 3 (2 osteosarc, 1 fibrosarc), soft tissue sarc 9 (synovialosarc 3, liposarc 2, other types 4). Ten pts had metastatic disease and 2 a locally advanced inoperable sarcoma. All pts were pretreated with chemotherapy, (1 regimen, (rg) 6 pts, 2 reg, 6 pts), the MAID regimen in 7 of them. Four/9 pts treated previously with intermediate dose of Ifo 9 g/m^2/cy (IDIFO) had responded to it.

Results: 35 cycles (cy) were administered, median number of cy/pt = 2 (1–6). All pts were evaluable for response. The only PR (8 weeks duration) was a previous complete responder to IDIFO. Of the 3 minor responders observed (median duration 3 months), one had previously responded to IDIFO. Seven pts had disease progression and there was one stabilisation. Toxicity/cy included: 7 febrile neutropenia episodes during the 1st cy, 2 of them despite G-CSF prophylaxis; all following cycles were administered with G-CSF; 1 grade 3 and 1 grade 2 thrombopenia, 1 grade 3 renal insufficiency, 1 grade 2 haemorrhagic cystitis. CNS toxicity related to treatment was seen in 1 cy (1 transient confusion). There was no dose modification, and no toxic death occurred. All treatment discontinuations were caused by progressive disease, or patient refusal (1 pt).

Conclusion: Our experience with HDIFO (12 g/m^2/cycle) contrasts with other reports showing a good efficacy of HDIFO in refractory sarcomas (Brain ASCO 95 A1641). Our series consists of pts pretreated

with IDIFO (9 g/m^2/cycle) and our administration modality (1 hour instead of C.I.V.) may account for the 50% decrease of AUC and half life between the 1st and 3rd treatment days observed in our pharmacokinetic study (Lokiec *et al.* ASCO 95).

872 PUBLICATION

EMBRYONAL RHABDOMYOSARCOMA (ERMS) IN ADULTS: RESULTS OF TREATMENT

M. Valladares, J.J. Reina, J.C. Valenzuela, M. Noguer, M. Bolanos, P. López, M. Ruiz, P. Pastor, J.A. Moreno
H.U. "Virgen del Rocio", 41013 Sevilla, Spain

Many studies suggest that adults patients (p) who develop a so-called pediatric cancer have a worse prognosis than do children. We have reviewed 7 adult p with ERMS, that we treated between Dec 1975–March 1991. Diagnostic was done by surgical biopsy in all cases. Age range was 16–42 years, mean 26.6. All p were males. All p underwent surgery. The distribution (G, IRS-1) was: GI three p (42.8%), GII one p (14.3%), GIII two p (28.6%), GIV one p (14.3%). Primary sites were genitourinary tract in 5 p, 71.4%, parameningeal, in maxillary-ethmoid sinus, 1 p, 14.3%, and chest wall, 1 p (14.3%). Radiation therapy was delivered in 5 p, with a dose range of 40–55 Gy; volume ranged from tumor bed to inverted Y. All p received chemotherapy. CYVADIC was given to two p. The others programs were VAC, vincristine plus doxorubicin (D) and cyclophosphamide, ifosfamide (I) and etoposide, I plus dactinomycin plus D. The p with parameningeal site received intrathecal methotrexate. Six p (85.7%) suffered progressive disease. Time to progression was 4.5 ± 2.16 months (median and SD). Metastatic sites involved lung (2 p), lung and bone (2 p), meninges (1 p) and lung, liver, soft tissues and brain (1 p). The actuarial 3-year survival (Kaplan-Meier) was 16.7%. Median survival was 9 months. Only 1 p was alive and disease-free after 38 months of follow-up. This report suggests that adults with embryonal rhabdomyosarcoma have a worse prognosis than children. Further improvements in our knowledge of biology of RMS and new therapeutic strategies are needed.

Palliative treatment

873 ORAL

KADIAN™/KAPANOL™—A ONCE DAILY MORPHINE FORMULATION

A.F. Broomhead[1], R.O. Kerr[2], W.J. Tester[3], R.L. Bowles[1], C. Maccarrone[4], G.P. Hodsman[4]
[1]FH Faulding & Co Ltd, Adelaide, Australia
[2]Central Texas Oncology Associates, Austin, TX, U.S.A.
[3]Medical Ontology Hematology Associates, Philadelphia, PA, U.S.A.
[4]Glaxo Australia Pty Ltd, Melbourne, Australia

Although oral morphine remains the opioid of choice for the management of moderate to severe cancer pain, controlled-release morphine formulations have only enabled dosing every 8 to 12 hours. Kadian™/Kapanol™ (K) is novel polymer-coated morphine sulfate pellets (20, 50, 100 mg) in a capsule designed for 12 to 24 hourly dosing. This randomized, double-blind, double-dummy, parallel group study compared the efficacy and safety of K q12h or q24h to MS Conlin® tablets (MSC) q12h. Eligible patients with cancer pain were titrated to adequate analgesia with a stable dose of immediate-release morphine sulfate (IRMS) over a 3 to 14 day lead-in, then randomized to one of the three treatments for 7 ± 1 days. Rescue medication was IRMS tablets. Primary measures of efficacy on the final day were time to first rescue medication and total dose of rescue as a % of total daily dose (TDD) of morphine (%IRMS). Secondary measures were: daily—visual analogue scale (VAS) of pain intensity, quality of sleep, and incidence of morphine-related side effects; final day—VAS and verbal rating scale (VRS) of pain intensity, VRS of pain control, and patient global assessment of pain control and investigator global assessment of efficacy. 152 patients completed final day assessments at 28 centres in the U.S.A.. Mean age was 61 yrs and TDD of morphine was 138 mg. 54 patients were treated with K q24h, 45 with K q12h, 53 with MSC. The number requiring rescue on the final day was K q24h 46%, K q12h 51%, MSC 55%. Time to first rescue was K q24h 6.8 h, K q12h 7.5 h, MSC 6.3 h. %IRMS was K q24h 39.2, K q12h 29.2, MSC 42.9. There were no significant differences for all measures. Patient global assessment (good or very good) significantly favoured K q24h over MSC (K q24h 89%, K q12h 76%, MSC 68%, $P = 0.018$). There were no significant differences for other secondary measures. Kadian™/Kapanol™ q24h and q12h had efficacy and safety similar to MSC q12h but had the added advantage of 12 to 24 hourly administration with a trend to less rescue medication use. Patient global assessment significantly favoured Kapanol™/Kadian™.

874 ORAL

TTS-FENTANYL VS ORAL MORPHINE IN CANCER PAIN

S. Ahmedzai, D.J. Brooks, TTS-fentanyl Trial Group
Palliative Medicine Section, Sheffield University, S10 2JF, U.K.

This was a multicentre, open, randomised, cross-over study of transdermal fentanyl (FEN) and sustained release oral morphine (MOR) to compare health related quality of life (QoL). Patients receiving oral morphine for cancer pain from 44 U.K. palliative care centres were randomised to receive 15 days FEN followed by 15 days MOR or vice versa; 202 patients entered the study and 110 completed it (mean age 61.5, 44.5% female). Immediate release oral morphine was available at any time for breakthrough pain. Cross-over comparisons were available from 127 patients. Pain levels were similar in both groups ($P = 0.296$) but during the FEN phase patients experienced significantly less constipation ($P < 0.001$) and nausea ($P = 0.04$). The proportion of patients reporting 'quite a bit' or 'much' constipation was 34.8% in the MOR phase and 15.0% in the FEN phase, figures for nausea were 20.3% and 14.9% respectively; 60% (73/122) of patients preferred FEN ($P = 0.037$, binomial test), 14 (10%) did not distinguish between treatments. Further symptoms and scales from the EORTC QLQ-C30 QoL questionnaire and patient daily diary data on pain, sleep and sedation will be presented.

875 ORAL

ORAL METHADONE FOR THE TREATMENT OF CANCER PAIN

F. De Conno, L. Groff, E. Zecca, C. Brunelli, C. Ripamonti
Palliative Care Division, National Cancer Institute, Milan, Italy

Methadone is an opioid analgesic drug still little used in cancer pain therapy. In a prospective study 162 advanced cancer patients with pain were treated with oral methadone. The aims of the study were: to assess the analgesic activity of methadone over time, the dosages of drug required for maintaining analgesia and side effects. Pain intensity before (TO) and during treatment (0–90 days) was evaluated by the Integrated Score (range 0–240), side effects (insomnia, drowsiness, confusion, xerostomia, nausea, vomiting, constipation and breathing difficulty) were evaluated through a Likert type scale with four points (no, a little, a lot, very much). Pain relief was calculated in respect to TO at 7–15–30–45–60–90 days. The results of the study show a significant mean reduction of pain of 25 points in the Score in respect to TO which was maintained all through the assessment period. The average of the mean daily dosages (calculated as mean doses at each evaluation time) used for pain control was 14 mg for 1st week of treatment and was gradually increased to 23 mg/day during the last week. Only a slight increase in drowsiness was observed. We believe that oral methadone should be considered as a valid alternative to oral morphine in cancer pain treatment due to its analgesic efficacy, tolerability and its low cost.