GIST, melanoma and sarcoma

NEW DIAGNOSTIC TECHNIQUES IN EARLY DIAGNOSIS OF MELANOMA IN SITU

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The incidence of malignant melanoma is increasing every year. Revealing melanoma in situ on time is increasing good prognosis of these patients. To evaluate the role of digital-epiluminescence microscopy (DELM), in the differential diagnosis of cutaneous pigmented lesions and to improve the early diagnosis of melanoma in situ, 3834 pigmented lesions from 3927 consecutive patients were evaluated using digital-epiluminescence microscopy; in the period of three years (2000-2003), in a prospective study at the Dept. of Surgical Oncology of the Belgrade UMC “Beznajka Kosa”. After clinical examination and skin-surface microscopy of the pigmented skin lesions, suspicious skin lesions, undergone to further surgical procedures of removing skin lesions, with ‘ex tempore’ biopsy. From the total number of 3927 patients, we were suspicious about the malignancy of the pigmented skin lesion in about 147 patients. 147 patients underwent to surgical treatment, from which all of 144 patients (97.6%) had pigmented skin lesion diagnosed by ‘ex tempore’ biopsy during surgical management as a malignant pigmented skin tumor (malignant melanoma). From the total number of patients with suspicious pigmented skin tumors (147 patients) on 97.6% patients diagnosis made by DELM was the same as diagnosis got from ‘ex tempore’ biopsy, which means that this procedure is highly accurate, especially if we know that all 15 patients with melanoma in situ verified with ‘ex tempore’ biopsy, was diagnosed prior with DELM, what is 100% accuracy.

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NEOADJUVANT CHEMO-RADIATION THERAPY OF MELANOMA PATIENTS WITH REGIONAL LYMPHGENOUS METASTASES

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Purpose: To assess the efficacy of intensive neoadjuvant chemo-radiation therapy for melanoma patients (pts) with regional metastases.

Methods and materials: 226 pts were enrolled in this study for the last 10 years (79 males and 147 females). Group 1 (n=122) underwent surgical treatment only: wide local excision (WLE) of primary lesions and therapeutic regional lymphadenectomy. The treatment scheduler for another 104 pts (Group 2) consists of intensive neoadjuvant X-ray or gamma irradiation of skin melanoma (60-75 Gy) and metastatic regional lymph nodes (40-45 Gy); the cycle of chemotherapy (DTC, gplatin and Vincristine) was done simultaneously with radiation therapy. Such preoperative chemo-radiation treatment lasts for 5-8 days. Upon completion of neoadjuvant chemo-radiotherapy the size of primary skin melanoma shrinks by 20-30% in average. The same type of surgery like in pts from Group 1 was performed in Group 2. In postoperative period these pts received additional 4-6 cycles of chemotherapy, and after that biotherapy by INF-x27G for year.

Results: Survival analysis estimates by using the Kaplan-Meier method and the log-rank test. The 5-year overall (OS) and disease-free (DFS) survival rates were 28.7% and 23.0% in pts of Group 1, and 43.3% and 37.9% in pts of Group 2 respectively. Median survivals were 28 months (Group 1) and 49 months (Group 2; p<0.008 if the OS rates were estimated), and 24 months (Group 1) and 39 month (Group 2; p=0.017) respectively when the DFS was estimated.

Conclusion: The results of this study confirm the efficacy of neoadjuvant chemo-radiation therapy for pts with regional lymph node metastases. The neoadjuvant treatment gives the possibility to increase on 14.3% patients’ 5-year OS/DFS.

NEOADJUVANT CHEMO-RADIATION THERAPY OF MELANOMA PATIENTS WITH REGIONAL LYMPHGENOUS METASTASES

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Introduction: Imatinib mesylate induces an objective response in the majority of patients with advanced, unresectable GIST. An analysis of early (median of 25 months) follow-up data from a phase II trial of imatinib found that halting further tumor progression, with or without regression, was associated with significantly improved survival (P<0.002). The objective of this study was to explore the correlation between response to imatinib and long-term survival using the 52 months follow-up data from the phase II trial. In this trial, a total of 147 patients with advanced GIST were randomly assigned to 400 mg or 600 mg daily of imatinib. After a median follow-up of 32 months, 2 patients (1%) achieved complete response (CR), 98 (67%) partial response (PR), 23 (16%) experienced prolonged stable disease (SD). Progressive disease (PD) continued in 17 patients (12%), and 7 (5%) had unknown or unacceptable response. At 48 month follow-up, the estimated survival was 9% for PD, 64% for SD, and 82% for CR combined. Multivariate Cox regression was used to adjust for baseline differences in clinical variables that may have contributed to outcomes. Patients with larger tumors (>40 cm2) and with above-normal serum albumin levels (<3.48 g/dL) had worse prognosis of survival (p<0.05). Univariate Cox regression demonstrated no statistically significant difference in the risk of mortality between SD and CR/PR, while these both differed significantly from PD. Multivariate Cox regression model showed that compared to PD, adjusted relative risks of mortality were 0.08 (95% CI: 0.04-0.18) for CR/PR and 0.12 (95% CI: 0.04-0.33) for SD. Stable disease can confer symptomatic benefit but more importantly survival benefit. Treatment with imatinib results in
Introduction: Sunitinib malate (SU11248; SUTENT®) is an oral, multitargeted RTK inhibitor of KIT, PDGFR, VEGFR, RET, and FLT3, recently approved by the US FDA for the treatment of GIST after disease progression on or intolerance to imatinib mesylate (IM) therapy and of advanced RCC. The purpose of this trial was to assess the efficacy and safety of sunitinib compared with placebo in pts with IM-resistant or -intolerant GIST.

Methods: Pts in this double-blind, placebo-controlled trial received sunitinib at 50 mg/day on a 4/2 schedule (4 weeks on treatment, followed by 2 weeks off). The primary endpoint was time to tumor progression (TTP); secondary measures included overall survival (OS), objective response rate, pain relief response rate (PRR), who had no change in the presence of disease, and overall survival (OS).

Results: Median TTP was >4-fold as long with sunitinib as with placebo at an interim analysis (27.3+ vs 6.6 months, P=0.001), and the trial was unblinded, allowing placebo pts to cross over to sunitinib. Sunitinib was associated with a 51% reduction in relative risk of death compared with placebo (HR, 0.49; P=0.007), although median OS was not reached at analysis (update to be presented). Of 207 evaluable sunitinib pts, 14 (7%) had achieved a partial response (PR) and 36 (17%) stable disease (SD) for 222 wks, compared with 0% and 2%, respectively, of 105 placebo pts. Of 59 pts on placebo who crossed over, 10% had achieved PR and 7% were progression free for ≤22 wks. Of 9 sunitinib pts identified as IM-intolerant, 4 achieved PR, compared with 0 of 4 such placebo pts. The overall PRR for sunitinib was favorable compared with placebo (17.4% vs 9.5%, respectively; HR, 0.68; P=0.064), as well as for 174 pts who reported pain/analgic use at baseline (31.0% vs 17.2%, P=0.052). Median time to pain progression has not been reached but initial data favors sunitinib (HR, 0.67; P=0.1165). Health status was similar between treatment arms. The most common all-cause AEs with sunitinib were fatigue, diarrhea, abdominal pain, nausea, and anorexia, all mainly grade 1/2 severity.

Conclusions: Sunitinib treatment is associated with significant efficacy and acceptable tolerability in pts with IM-resistant or -intolerant GIST.
and been treated for a median of 84 days (range, 1–406). 38% of pts had dose interruptions, 15% had dose reductions, and 12% discontinued treatment due to adverse events (AEs). The most common all-cause AEs were fatigue (43%), diarrhea (37%), nausea (30%), vomiting (25%), and abdominal pain (23%), which were mainly grade 1/2 events. The most common grade 3/4 AEs were fatigue (46%), anemia (6%), abdominal pain (5%), hand-foot syndrome (4%), hypertension (4%), neutropenia (4%), and thrombocytopenia (3%). Grade 4 AEs were rare. Of 152 pts for whom preliminary efficacy data are available, of whom 123 had remained on therapy, having received 3 treatment cycles (median; range, 2–7), 14% have demonstrated a partial response and 63% stable disease. One patient achieved a complete response. Updated data will be presented.

Conclusions: Consistent with prior phase I-III data, sunitinib is associated with acceptable tolerability and promising efficacy in pts with IM-resistant or -intolerant GIST.

CLINICAL BENEFIT OF CONTINUOUS DAILY DOsing OF SUNITINIB IN PATIENTS (PTS) WITH ADVANCED GASTROINTESTINAL STROMAL TUMOR (GIST)

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Introduction: Sunitinib malate (SU12486, SUTENT®) is an oral multitranslated RTK inhibitor of KIT, PDGFR, VEGFR, RET, and FLT3, recently approved by the US FDA for the treatment of GIST after disease progression on or intolerance to imatinib mesylate (IM) therapy and of advanced renal cell carcinoma. Sunitinib, at 50 mg/day on a 4/2 schedule (4 wks on treatment followed by 2 wks off), has shown significant efficacy and acceptable tolerability in prior phase I/II and III trials of advanced GIST. The purpose of this study was to assess the clinical benefit of continuous daily dosing of sunitinib in such pts.

Methods: In this ongoing, multicenter, phase II trial, pts receive continuous once-daily dosing of sunitinib at a starting dose of 37.5 mg in the morning or evening (prior to sleep). Subsequent doses are titrated based on individual tolerability. Treatment will be continued for up to 1 year, unless disease progression or significant AEs occur. The primary endpoint is the clinical benefit rate, defined as the percent of pts with confirmed complete response, partial response (PR), or stable disease (SD) for 224 weeks based on RECIST.

Results: Initial data are available for 35 of 61 enrolled pts, of whom 33 have received continuous sunitinib at 37.5 mg/day for >16 wks (12 pts), >12 wks (12), >8 wks (2), and >4 wks (7). Dose was reduced in only 1 pt (hand-foot syndrome), and 2 pts discontinued (withdrew consent, death due to GIST progression). The most common all-cause AEs were hand-foot syndrome, stomatitis, fatigue, weakness, diarrhea, and gastrointestinal reflux, of which most were grade 1 severity. Reported grade 3 events were hypertension (2 pts), fatigue (2), hypokalaemia (2), and non-febrile neutropenia (2). Of 19 pts for whom efficacy data are available and who have received 28 weeks of treatment, 2 had unconfirmed PRs, 2 had disease progression, and 15 demonstrated SD.

Conclusions: At this stage of analysis, the clinical benefit of continuous daily dosing of sunitinib in pts with IM-resistant or -intolerant GIST may be similar to that observed with intermittent dosing. These findings suggest that continuous dosing may be a feasible treatment alternative and possibly provide further improvement in pt outcomes.

HISTOPATHOLOGICAL AND CLINICAL EVALUATION OF PATIENTS DIAGNOSED AS GASTROINTESTINAL STROMAL TUMORS

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Introduction: Gastrointestinal stromal tumors (GIST) located in gastrointestinal tract (rarely in abdominal and retroperitoneal regions) are derived from mesenchymal/stromal cells and express the KIT receptor (stem cell factor receptor, CD 117). Although 5% of them are KIT receptor (-), they can be easily diagnosed by their typical morphology. They are most common mesenchymal tumors of gastrointestinal tract.

Method: In this analysis; we evaluate 38 patients immunohistochemically and clinically for 1) CD117 positive 2) KIT positive 3) macroscopical and microscopical features have prognostic values and must be explained in pathological reports.

Discussion: GISTs can just be diagnosed immunohistochemically. Presence of KIT is one of the major diagnostic factors. Besides immunohistochemical parameters, macroscopical and microscopical features have prognostic values and must be clearly explained in pathological reports.

GASTROINTESTINAL STROMAL TUMOR (GIST): OUR EXPERIENCE IN THE MANAGEMENT OF 32 PATIENTS

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Background: Gastrointestinal stromal tumors (GISTs) represents 0.1-3% of gastrointestinal neoplasms; most cases occur in people 40 to 80 years old, and more common in men than in women. More than half of all GIST pts show locally advanced, recurrent, or metastatic disease (mainly to liver or peritoneum).

Methods: From January 2001 to March 2006 we observed 32 pts with GISTs; all were CD117+. The main characteristics of these pts were: median age 61 yr; sex: F/M (19/13); primary tumor localization: stomach 17 (53%), small intestine 8 (25%), colon-rectum 2 (6%), retroperitoneum 4 (13%), liver 1 (3%); first symptoms: epigastric pain 5 (16%); abdominal pain 5 (16%); hematemesis 2 (6%); palpable abdominal mass 1 (3%); defecation disorders 2 (6%); melena 3 (9%); rectal bleeding 1 (3%); ascites 1 (3%).

Results: Radical surgical resection was performed in 27 patients (84%) and 2 pts received a debulking surgery. No postoperative mortality or major complications were observed; 3 pts showed an advanced disease. Seven (22%) pts (classified in the high-risk class) developed recurrence, local or at distance, and the median time to relapse was 7.5 months (range 2–11). One pt with advanced disease died before any treatment and 11 pts received Imatinib (I), at the standard dose (400 mg/d), starting to the date of diagnosis of advanced disease (4 pts) or metastatic relapse (7 pts) and then until development of intolerance or PD. Main toxicities of I included: neutropenia G3 (4%), skin rash (4%), peritoneal edema (4%). We achieved 3 PR (lasing 12+), 2+ and 40 mos), 6 SD and 2 PD. With a median follow-up of 20.5 mos, all but three pts (dead for PD) were alive; the overall survival rate was 91% and the median overall survival was 18 mos (range 1–52).

Conclusion: Surgical resection remains the only effective treatment for GISTs. Histological and immunohistochemical examinations remain essential for a definitive diagnosis and to assess the risk of aggressive behaviour. However, in pts with advanced or relapsed disease treatment with I is effective with an high disease control rate. A multidisciplinary management including medical oncologists, surgeons, radiologists and pathologists is recommended.

EFFICACY AND SAFETY OF ADJUVANT POST-SURGICAL THERAPY WITH IMATINIB IN PATIENTS WITH HIGH RISK OF RELAPSEING GASTROINTESTINAL STROMAL TUMOR

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Background: Gastrointestinal Stromal Tumor (GIST) is the most common mesenchymal tumor of the gastrointestinal tract and surgical resection is the only curative treatment, but even after complete resection, GISTs have a high rate of recurrence and disease-related mortality. New options became available with the application of imatinib. The primary objective of the study was to evaluate the efficacy and safety of adjuvant post-surgical therapy with imatinib in GIST patients who had high risk to relapse.

Methods: This was a prospective, open-label, multi-center trial. All patients qualified to receive a debulking surgery. No postoperative mortality or major complications were observed; 3 pts showed an advanced disease. Seven (22%) pts (classified in the high-risk class) developed recurrence, local or at distance, and the median time to relapse was 7.5 months (range 2–11). One pt with advanced disease died before any treatment and 11 pts received Imatinib (I), at the standard dose (400 mg/d), starting to the date of diagnosis of advanced disease (4 pts) or metastatic relapse (7 pts) and then until development of intolerance or PD. Main toxicities of I included: neutropenia G3 (4%), skin rash (4%), peritoneal edema (4%). We achieved 3 PR (lasing 12+), 2+ and 40 mos), 6 SD and 2 PD. With a median follow-up of 20.5 mos, all but three pts (dead for PD) were alive; the overall survival rate was 91% and the median overall survival was 18 mos (range 1–52).

Conclusion: Surgical resection remains the only effective treatment for GISTs. Histological and immunohistochemical examinations remain essential for a definitive diagnosis and to assess the risk of aggressive behaviour. However, in pts with advanced or relapsed disease treatment with I is effective with an high disease control rate. A multidisciplinary management including medical oncologists, surgeons, radiologists and pathologists is recommended.
received imatinib (400 mg, once a day) for at least 12 months. Primary endpoint was relapse or metastasis rates at 1 year and 3 years. There were totally 57 patients (34 men, 23 women) enrolled in the imatinib treatment and until this interim analysis (Dec 15th 2005), 13 patients have completed at least 12 months of imatinib treatment. The average age at the time of diagnosis was 50.6 years old. The primary tumor site was stomach in 50.9%, small intestine in 38.6%. A total 92.9% of patients had tumors at the size of no less than 5 cm and 73.7% of patients had a mitosis count over 6/50HPF. The majority of patients had positive CD34 (82.9%) and negative SMA, S-100 and Desmin results respectively.

Results: Until the cut-off date of interim analysis, there was no evidence of tumor relapse or metastasis in all patients and no death was reported either. The average duration of follow-up was 208.3 days. Twenty patients (43.5% of the safety population) experienced 54 adverse events (AEs) and 18 patients (40% of the safety population) had AEs related to the imatinib treatment based on the decision of investigators. AEs included edema (26.6%), gastrointestinal reaction (15.9%), skin hypopigmentation (15.3%) and leucopenia (8.9%) in sequence. No serious AE was found in this study.

Conclusions: Imatinib is a promising adjuvant post-surgical therapy in patients with high risk of relapsing GISTs. Based on this study, a randomized controlled trial will be necessary.

513P IMATINIB MESYLATE RESPONSE IN GASTROINTESTINAL STROMAL TUMORS: EXPERIENCE OF CERRAHPSA MEDICAL FACULTY

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Objective: We aimed to evaluate the patients with Gastrointestinal Stromal Tumor (GIST) which is refractory to radio- and chemotherapy and their responses to imatinib mesylate.

Material and methods: 27 patients with GIST were retrospectively evaluated in aspects of clinical and morphological properties.

Results: Median age and male/female ratio were 58.4(12-83) years and 19/8, respectively. Primary tumor localisations were as small bowel (n=13), stomach (n=9), omentum-peritoneum (n=2), and colonic site (n=2). On the other hand, primary focus could not be detected in 5 patients. Average tumor size was 13 cm(1.7–39 cm). C-KIT was positive in all cases. Leading initial complaints were abdominal ache (n=14), abdominal mass (n=5), weight loss (n=5), constipation (n=4), gastrointestinal bleeding (n=4), sublees (n=2), polyporias (n=1), and cholestatic icterus (n=1). The most common metastatic sites were as liver (%65) and omentum-peritoneum (%65). Besides, pleural effusion in two cases, subcutaneous metastatic nodules in one case, and bone metastases in one case were obtained. In 15/26 patients who were undergone to wide resection, recurrence were detected median 23.7 months (2–63 months) later. In the remaining nine patients, median disease-free survival was 11.5 months (3–36 months).

None of these patients were followed-up without any treatment. Four patients have taken adjuvant imatinib mesylate in 400mg/day dose because they were in high risk group. Remaining two of 26 patients were lost to follow-up. Imatinib mesylate in 400mg/day dose were given in 12 patients who had metastatic disease. Dose increased to 600 mg/day in cases of progression and to 800 mg/day in those had an insufficient response to initial drug treatment. The average median time on drug was 17.6 months. In these patients, median time to progression was 13.6 months. None of patients ceased the treatment because of side effects. Time to progression in patients the drug was ceased at the end of one year ranged between 3-6 months. Conclusion: Imatinib mesylate is a highly effective, safe and well-tolerated treatment strategy in GISTs. It should be used continuously till the progression.

513P ONE INSTITUTIONAL EXPERIENCE WITH IMATINIB MESYLATE IN THE TREATMENT OF GASTROINTESTINAL STROMAL TUMORS

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Background: Although imatinib mesylate is highly effective for the treatment of metastatic gastrointestinal stromal tumors (GISTs), more than 30% of the tumors acquire secondary resistance within 2 years after imatinib treatment. To prevent or remove the resistant clones, residual tumors after imatinib treatment might be resected. We investigated clinical significance of surgical resection of GIST lesions after imatinib treatment.

Methods: Between June 2001 and June 2005, 80 patients with metastatic or unresectable GISTs were treated with imatinib at Asan Medical Center, Seoul, Korea. Of these, clinical data of 27 patients who underwent surgical resection of residual or progressing tumors were reviewed.

Results: Of a total of 27 patients, after a median 19 months (range, 2 to 45 months) of imatinib treatment, surgical treatment was performed to remove residual tumors (RT) in 17 patients, and progressive disease (PD) in 10 patients. Complete resection was possible in 13 patients with RT and in 3 with PD. Number of resected tumors ranged from 1 to 11. Clinical courses of the patients were much different according to the disease status at the time of surgery; with a median follow-up of 14 months (range, 1–59) after surgery, the median progression-free survival was not reached in RT group, but only 5 months (95% confidence interval (CI), 4–7) in PD group (P < 0.0032).

Especially, 5 out of 6 patients with general progression or new solid lesion showed rapid progression median 5.5 months after surgery, while only one out of 4 patients with focal progression showed disease progression after surgery. The median overall survival was not reached in RT group, and 13 months (95% CI, 5–21) in PD group (P = 0.0188).

Conclusion: These data suggest that patients with residual or focal progressive disease may get benefits from aggressive surgical resection combined with imatinib treatment.
survival at 12 months was 30% for patients with high serum levels of YKL-40 and 100% in the case of patients with normal serum levels (P=0.07).

Conclusions: Our results confirm better sensitivity for YKL-40 than for the other known melanoma markers (MIA, S-100, LDH). Despite the short median follow up time, there is a trend favoring overall survival in patients with normal YKL-40 levels.

THE TYROSINE KINASE RECEPTOR, EPHA2, IS OVEREXPRESSED, BUT NOT ASSOCIATED WITH N-RAS OR B-RAF MUTATION IN METASTATIC MELANOMA LESIONS

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Background: EphA2 is a tyrosine kinase receptor in the ephrin family and function as an oncprotein, and has been shown to be associated with poor clinical outcome in several cancer types. We examined whether EphA2 is overexpressed in metastatic melanoma lesions and whether its expression is associated with N-Ras (exon 3) or B-Raf (exon 15) mutations in these lesions, which are commonly observed in melanoma.

Methods: The tumor samples were collected from 26 patients with metastatic melanoma, and immunohistochemical analysis of EphA2 was performed on formalin-fixed, paraffin-embedded archival tissues. PCR and DNA sequencing was performed using either snap frozen tumor samples or formalin-fixed, paraffin-embedded tissues. Frequency tables and Fisher’s Exact test were used to determine if there was an association between overexpression of EphA2 and N-Ras or B-Raf mutation, and between overexpression of EphA2 and B-Raf mutation.

Results: Of 26 patient tumor samples, 15 (58%) had expression of EphA2 in more than 5% of the melanoma cells counted, and 11 (42%) had minimal or no expression. Of 24 patient samples analyzed, 3 (12%) had N-Ras mutation, and 11 (42%) had minimal or no expression of EphA2. Of 24 patient samples analyzed, 3 (12%) had N-Ras mutation, and 11 (42%) had minimal or no expression of EphA2 and B-Raf mutation. Of 24 patient samples analyzed, 3 (12%) had N-Ras mutation, and 11 (42%) had minimal or no expression of EphA2 and B-Raf mutation. Of 24 patient samples analyzed, 3 (12%) had N-Ras mutation, and 11 (42%) had minimal or no expression of EphA2 and B-Raf mutation. Of 24 patient samples analyzed, 3 (12%) had N-Ras mutation, and 11 (42%) had minimal or no expression of EphA2 and B-Raf mutation. Of 24 patient samples analyzed, 3 (12%) had N-Ras mutation, and 11 (42%) had minimal or no expression of EphA2 and B-Raf mutation. Of 24 patient samples analyzed, 3 (12%) had N-Ras mutation, and 11 (42%) had minimal or no expression of EphA2 and B-Raf mutation.

Conclusion: EphA2 is overexpressed in 58% of the tumor samples of patients with metastatic melanoma, but there is no association with either N-Ras or B-Raf mutations. However, it will be important to study if EphA2 overexpression is associated with clinical outcome in patients with melanoma.
Nine patients had stage I disease, 15 had stage II and 8 had stage IV disease. Surgical presentation. Eighteen (53%) patients were classified as osteoblastic osteosarcoma. Results: Twenty two (65%) of the patients were male and 12 (35%) were female. Between January 1995 and April 2006 at Hacettepe University, Faculty of Medicine, outcomes of the extremity. The objectives were to determine demographic and clinical findings, chemotherapy related toxicities, and patient, tumor, and treatment related prognostic factors in patients with osteosarcoma. Patients with positive surgical margin had significantly worse PFS (p=0.0458). Conclusion: Our results achieved by multidisciplinary modalities are comparable with the literature. Extremity localization, necrosis rate and surgical margins were found to be important prognostic factors. Material and methods: One hundred and four patients with extremity osteosarcomas, seen at Regional cancer Centre, Trivandrum, India. Objectives: To confirm the initial previous pilot study concerning the outcome of RMS in this single center series - only 4 pts alive and disease-free (13%). The observed differences in outcome between subgroups are probably due to the small pt numbers. Introduction: RMS is common in childhood and adolescence. The embryonal RMS has a better outcome than the alveolar subtype and parameningeal RMS have the worst. Treatment guidelines for young adults and adults are similar to those of pediatric patients (pts). We reviewed the presentation and outcome of pts with RMS. Results: Between 1990 and 2004, 29 pts (14 males/15 females, median age 22 years, range 15–69) with RMS were treated at our hospital. Location was: head and neck (orbita 2); parameningeal 6, extremities 7, trunk 6 and genitourinary 3 (paratesticular 2). Twelve were embryonal RMS, 7 alveolar, 2 pleomorphic and 6 pts not specified. At diagnosis 3 pts (10%) had stage I, 4 (13%) stage II, 17 (58%) stage III and 5 (17%) stage IV disease. Treatment included surgery in 17 pts (58%), radiation in 14 (48%) and chemotherapy in 26 (48%). The most frequent chemotherapy regimens were VIP (30 pts) and VADRIYA (6 pts). In pts submitted to surgery, 9 had tumour free margins, 4 were left with microscopic residual disease and 4 with gross residual disease. At the end of the first treatment program, 10 pts (34%) achieved complete remission (CR), 5 (15%) partial remission and 14 (48%) had disease progression. The median time to progression was 5 months (range: 0–145+) at first treatment. Among CRs, 6 pts relapsed and 4 are alive and disease-free. The median duration of first response was 7 months. Twenty four pts have died (2 due to neurogenic siposis, 17 due to disease progression and 5 due to other causes) and one pt was lost to follow-up with disease progression. For the whole group the median overall survival is 18 months (range: 1–145+). For different RMS subtypes was 17 months (2–145+) for embryonal and 18 months (1–41) for alveolar, and for different RMS location was 21 months (1–77) for parameningeal, 18 months (5–104) for extremities and 10 months (0–121+) for head and neck non-parameningeal. Conclusion: As previously reported, we documented the poor prognosis of RMS in this single center series - only 4 pts alive and disease-free (13%). The observed differences in outcome between subgroups are probably due to the small pt numbers.

Rhabdomyosarcomas (RMS) in Adolescents and Adults: A Single Institution Retrospective Analysis

Ana H. Luza, Paula A. Veira, Isabel Sargento, Aires Fernandes, Margarida Ferreira Instituto Português de Oncologia de Lisboa Francisco Gentil, E.P.E., Medical Oncology, Lisboa, Portugal

Introduction: RMS is common in childhood and adolescence. The embryonal RMS has a better outcome than the alveolar subtype and parameningeal RMS have the worst. Treatment guidelines for young adults and adults are similar to those of pediatric patients (pts). We reviewed the presentation and outcome of pts with RMS. Results: Between 1990 and 2004, 29 pts (14 males/15 females, median age 22 years, range 15–69) with RMS were treated at our hospital. Location was: head and neck (orbita 2); parameningeal 6, extremities 7, trunk 6 and genitourinary 3 (paratesticular 2). Twelve were embryonal RMS, 7 alveolar, 2 pleomorphic and 6 pts not specified. At diagnosis 3 pts (10%) had stage I, 4 (13%) stage II, 17 (58%) stage III and 5 (17%) stage IV disease. Treatment included surgery in 17 pts (58%), radiation in 14 (48%) and chemotherapy in 26 (48%). The most frequent chemotherapy regimens were VIP (30 pts) and VADRIYA (6 pts). In pts submitted to surgery, 9 had tumour free margins, 4 were left with microscopic residual disease and 4 with gross residual disease. At the end of the first treatment program, 10 pts (34%) achieved complete remission (CR), 5 (15%) partial remission and 14 (48%) had disease progression. The median time to progression was 5 months (range: 0–145+) at first treatment. Among CRs, 6 pts relapsed and 4 are alive and disease-free. The median duration of first response was 7 months. Twenty four pts have died (2 due to neurogenic siposis, 17 due to disease progression and 5 due to other causes) and one pt was lost to follow-up with disease progression. For the whole group the median overall survival is 18 months (range: 1–145+). For different RMS subtypes was 17 months (2–145+) for embryonal and 18 months (1–41) for alveolar, and for different RMS location was 21 months (1–77) for parameningeal, 18 months (5–104) for extremities and 10 months (0–121+) for head and neck non-parameningeal. Conclusion: As previously reported, we documented the poor prognosis of RMS in this single center series - only 4 pts alive and disease-free (13%). The observed differences in outcome between subgroups are probably due to the small pt numbers.
Setting. An exhaustive collection of pathology data along with clinical data and follow up has been funnelled for all patients diagnosed with a sarcoma within the Rhone-Alpes region from March 2005 to Feb 2006. The principal objective of this new study is to show the link between medical practices, management and outcome of sarcomas patients.

Results. To date, 547 novel incident sarcoma cases were declared by 33 pathology labs. More than 400 patients matching the inclusion criteria will be analyzed. The first year of the EMS project yielded and accrued which was 3-fold that expected (6/100000/year). The most frequent histotypes were GIST (17%), and liposarcomas (16%). Given the large and unexpected accrual, it was decided to prolong the investigation over an additional 2 year period, and to address additional questions on the distribution of molecular alterations.

Conclusions: The first year of inclusion enabled to show an incidence of sarcoma three fold higher than reported in the published literature, with a description and cartography of the different histotypes. Before the assessment of the primary end point, this first step shows the feasibility and relevance of this approach to explore cancer, causes, treatments and outcome for patients. Financial support: Merck KGaA, La Ligue and CONCITANET network.

<table>
<thead>
<tr>
<th>Tumor type</th>
<th>Age</th>
<th>Primary site</th>
<th>Best response</th>
<th>TTP mos.</th>
</tr>
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<tbody>
<tr>
<td>STS synovial</td>
<td>29</td>
<td>Gluteal</td>
<td>Partial response(PR)</td>
<td>5.1</td>
</tr>
<tr>
<td>STS liposarcoma myxoid</td>
<td>69</td>
<td>Lower limb</td>
<td>PR</td>
<td>14.8</td>
</tr>
<tr>
<td>STS synovial</td>
<td>29</td>
<td>Chest wall</td>
<td>PR/unc</td>
<td>6.4</td>
</tr>
<tr>
<td>STS synovial</td>
<td>29</td>
<td>Lower limb</td>
<td>PR/unc</td>
<td>5.3</td>
</tr>
<tr>
<td>STS leiomyosarcoma</td>
<td>57</td>
<td>Retroperitoneal</td>
<td>PR/unc</td>
<td>9.4</td>
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<tr>
<td>EFT</td>
<td>26</td>
<td>Lower limb</td>
<td>PR</td>
<td>10.5</td>
</tr>
<tr>
<td>EFT</td>
<td>17</td>
<td>Chest wall</td>
<td>PR</td>
<td>6.3</td>
</tr>
<tr>
<td>RMS</td>
<td>24</td>
<td>Femur</td>
<td>PR/unc</td>
<td>3.4</td>
</tr>
</tbody>
</table>

Most common toxicities were mild to moderate fatigue (60%) and nausea (50%). Although one patient died of drug related febrile neutropenia, complicated myelosuppression was observed in less than 5% of cases, reversible grade 3/4 liver function test increases were experienced in nearly all pts (90% ALT, 77% AST). Conclusions: As a 3-h infusion is a well-tolerated and active agent in STS but not in RMS. Further studies are necessary in RMS.

Introduction: Thymic tumor, one of the tumors of the anterior mediastinum, is generally slow-growing tumor. Thymomas may be associated with paraneoplastic syndromes, particularly with myasthenia gravis.

Material and method: Sixteen patients who applied to Ankara Oncology Training and Research Hospital were included in the study. Eleven thymoma and five rhabdomyosarcoma patients who had been documented histologically were evaluated.

Results: Median age was 42 years for thymoma patients and 29 years for thymic carcinoma patients. In thymoma group one patient was in stage 2, seven in stage 3, and three in stage 4B. One patient was in stage 1, one in stage 2, one in 4A, and two in stage 4B in thymic carcinoma group. Follow up was 24 months and 30 months for thymoma and thymic carcinoma patients, respectively. Paraneoplastic syndrome was found in 5 patients in thymoma group (3 myasthenia gravis, 1 anemia, 1 anemia and thrombocytopenia) and in 1 patient (1 myasthenia gravis) in thymic carcinoma group. One patient in thymic carcinoma group was treated with total resection and other five patients in the same group were treated with subtotal resection. Only biopsy was performed in only one thymoma patient. Total resection was performed in two patients in thymic carcinoma group while two patients had subtotal resection. Biopsy was performed in one patient in this group. Cisplatin based chemotherapy was given both groups (cisplatin, vincristine, adriamycin, cyclophosphamide).

Discussion: In treatment of the thymomas or thymic carcinomas, surgery is the main choice for the local tumors. Postoperative radiotherapy may be helpful to locally control. Cisplatin based chemotherapy may be helpful for treatment for metastatic disease.

Background: Trabectedin (T) is a marine-derived minor groove binder active in ovarian cancer & sarcoma. The final results of a trial using a 3-h schedule in different sarcoma subtypes [osteosarcomas (OS), adult-type soft tissue (STS), Ewing-type (EFT) and rhabdomyosarcoma (RMS)] are presented.

Methods: Eligible patients (pts) had measurable disease progressing despite prior therapy (with anthracycline and anthamide for STS), PS 0-1 and adequate organ function. Tumor types were: STS n=25 ( leiomyosarcoma 6, synovial sarcoma 4, others 5), EFT n=23, RMS n=8 and OS n=19. Pts with EOCG PS 0 were 84, 76, 65 and 63% respectively. Median age ranged from 24 yrs for OS to 42 yrs for STS; prior radiotherapy: EFT 77%, STS 60%, OS 21%. T was infused over 3-h q21d at 1.5 or 2.0 mg/m2 depending on prior therapy with a median cumulative dose 2.6 mg/m2 (1.1–3.9). Pre-medication included anti-emetics and dexamethasone.

Results: 75 pts are evaluable for safety, 69 for activity (RECIST criteria). 8 pts experienced clinical benefit (table below), none in the OS subset. Time to progression at 6 months for EFT and STS pts was 19.05% (95% CI: 2.3–35.8) and 26.2% (95% CI: 7.8–44.6) respectively; all pts in the RMS and OS subsets progressed quickly (TTP <2 months). Pre-medication included anti-emetics and dexamethasone.

Conclusions: T as a 3-h infusion is a well-tolerated and active agent in STS but not in RMS and OS. Further studies are necessary in RMS and OS.
with good performance status and without severe comorbidities. No toxicity was observed. Treatment of toxicity requires close monitoring of liver enzymes.

Conclusion: Our experience with the Kirkwood protocol is satisfactory. No severe adverse events have occurred so far. The high-dose protocol in the treatment regimen improves both immediate and short-term results of metastatic melanoma treatment. The study is ongoing.

Results: Since 2004 thirty-four patients have been enrolled. The results in arm A were as follows: no complete responses, 4 (22.2%) partial responses, stable disease in 7 (38.9%) and disease progression in 7 (38.9%) patients. Arm B presented with 2 (11.1%) CRs, 27.8% PDs and 5 (27.8%) SDs. The median survival was 6.2 and 9.9 months in arms A and B respectively. Grade 3-4 vomiting rate in arms A and B was actually the same: 27.8% and 33.3% of the cases respectively. No other grade 3-4 toxicity was observed in arm A. Additional morbidities related to Roncoleukin administration were grade 3-4 fever in 7 (38.9%) patients, grade 3 hypotension and grade 3 pulmonary edema in 1 (5.6%). No other manifestations of grade 3-4 toxicity were registered. All the toxic reactions were controlled with standard medical agents.

Conclusion: Roncoleukin administered at a dose of 9 mg/m2 is tolerated fairly well. The inclusion of high-dose Roncoleukin in the treatment regimen slightly improves the overall survival and the quality of life of patients.

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Conclusion: Roncoleukin administered at a dose of 9 mg/m2 is tolerated fairly well. The inclusion of high-dose Roncoleukin in the treatment regimen slightly improves the overall survival and the quality of life of patients.
Gokhan Gedikoglu, Gulten Tekuzman

Objective: Osteosarcoma (OS) is encountered infrequently in adults. Multidisciplinary evaluation of these patients and enrollment into clinical trials is essential in the treatment of OS. For the purpose of our study, we retrospectively analyzed the clinical characteristics, treatment modalities and outcomes of 11 patients with OS of the head and neck region, treated between January 1995 and April 2006 at the Hacettepe University, Faculty of Medicine, Department of Medical Oncology, were evaluated retrospectively.

Methods: Hospital records of 11 adult patients with osteosarcoma of the head and neck region, treated between January 1995 and April 2006 at the Hacettepe University, Faculty of Medicine, Department of Medical Oncology, were evaluated retrospectively.

Results: Five (45%) of the patients were male and 6 (55%) were female. Median age was 33 years (range, 23–43 years). The most common symptoms were persistent pain and swelling. All patients had primary OS except one whose OS was secondary to radiotherapy. Seven (64%) patients were classified as osteoblastic osteosarcoma. Patients were staged according to the American Joint Committee on Cancer staging system. One (9%) patient had stage I and 9 (82%) had stage II disease. Surgical excision was performed in all cases. Of the 11 patients, 6 (55%) had complete resection and 5 (45%) had either microscopic or macroscopic residual disease. Preoperative chemotherapy was given to 3 (27%) of the patients whereas 10 received postoperative chemotherapy (adjuvant chemotherapy to 5 and chemotherapy with intent to treat residual disease to 5 patients). Six (55%) patients received postoperative chemotherapy consisting of cisplatin and doxorubicin. Other patients were given different chemotherapy regimens. Chemotherapy related major side effects were nausea, vomiting and hematological toxicity. Palliative and postoperative radiotherapy was given to 9 patients. Median follow-up was 109 months (range, 26–145 months). Median overall survival was 52 months (95% confidence interval [CI] = 32.3–81.8) and median progression free survival was 46 months (95% CI = 14.4–78.6). Because of the small number of cases, there was no statistical significance between prognosis and stage, histopathologic subtypes and therapies.

Conclusion: Osteosarcoma of the head and neck region is encountered infrequently in adults. Multidisciplinary evaluation of these patients and enrollment into clinical trials will increase data and experience on this disease.

Sadik Muialhuoglu, Gungor Utkan, Murat Kocer, Golhan Celenkoglu, Saadet Tokluoglu, Ayse G. Durnal, Uku Y. Arslan, Ibrahim Tek, Murat Ozturk, Necati Alcis

**INTRODUCTION:** Dermatofibrosarcoma protuberans (DFSP) is a rare type of the sarcoma with low to intermediate grade malignancy. It compromises less than 0.1% of all cancers and about 1% of all soft tissue sarcomas. However, the cellular origin of DFSP is not entirely clear. Of the newly diagnosed cases, 90% occur in the skin and subcutaneous tissue with a peak incidence in the second and third decades of life. The most common location in our cases is the lower extremity. DFSP is characterized by slow and indolent growth and a low incidence of metastases. The optimal treatment for DFSP is resection with wide margins; the local control of the disease with this procedure exceeds 90%. The probability of regional or distant metastases is <1%. Patients with positive or close surgical margins have an elevated risk of local recurrences after resection alone, however, postoperative radiotherapy results in local control rates of >85% in such patients.

Sadik Muialhuoglu, Gungor Utkan, Murat Kocer, Ayse G. Durnal, Uku Y. Arslan, Ibrahim Tek, Murat Ozturk, Saadet Tokluoglu, Necati Alcis

**INTRODUCTION:** Malignant Fibrous Histiocytoma (MFH) is one of the most common soft tissue sarcomas (STS) of the adult patients. Five histologic subtypes have been described including storiform-pleomorphic which is the most common, myxoid, giant cell, inflammatory and angiomatoid subtypes.

Material and method: We investigated retrospectively 33 patients with MFH who were admitted to the Ankara Oncology Training and Research Hospital between January 1997–January 2003. The median age was 57 years (ranging from 28 to 70) with a sex ratio of 1.75 (21 men, 12 women). Primary site was extracranial in 69% (n=23) of patients, intraabdominal in 15% (n=5) of patients, head and neck in 2% (n=6) and trunk in 9% (n=3). The median tumor size was 10.5 cm (ranging from 2.3 to 25); 51% (n=17) patients had had grade 2 and 49% (n=16) patients had had grade 3 lesions. After pathologic subarachnoid examination 16 patients (48%) were found pleomorphic type, 4 patients (12%) mixed type and 1 patients (3%) giant cell tumor while subgroup could not be determined in 12 patients (35%). At diagnosis, 7 patients (21%) had stage 2 disease, 19 patients (57%) stage 3 disease and 6 patients (18%) stage 4 disease. All distant metastasis site in stage 4 patients were lung and it was lung and gastrointestinal system in one patient. Treatment was surgical in 24 patients. Seventeen patients were palliative and six patients were inoperable because of lung metastasis at the time of the diagnosis. Three patients were irresectable. All irresectable lesions were intraabdominal. Fifteen patients have been taken adjuvant chemotherapy (4 patients vincristine, cyclophosphamide, adriamycin, dacarbazine and 11 patients ifosfamide, mesna, adriamycin). Six patients have been taken palivacic chemotherapy (fatidium, mesna, adriamycin). Eighteen patients have been taken palliative radiotherapy.

Conclusion: MFH approximately accounts for 20% soft tissue sarcomas. Extrremities was the most common location in our cases. Pleomorphic type was documented the most common type and approximately half of the patients was documented grade 3.
Results: 23 patients were diagnosed to have Ewing sarcoma, median age 11 years (range 3-18 years), and median follow up period 12 months (range 1 month–30 months), 13 males and 10 females. 82.6% (19 patients) were of bone origin and 17.3% (4 patients) were of soft tissue origin. Site of origin, 47.8% lower limbs, 17.3% upper limbs, 21.7% spine and pelvis, 8.6% abdomen (one originate from the kidney) and from the 4.3% mediastinum. 69.5% (16 patients) were localized and 30.4% (7 patients) have metastasis at diagnosis, all of them have metastasis to the lung, 3 to the bone and one to the bone marrow. 95% received chemotherapy (one died before starting chemotherapy), 65.2% received local radiotherapy part of local control, and surgery done in 69.5%. Overall survival 82.6%, event free survival 78.2%. Overall survival for the localized group 94.7% and event free survival 94.7%. Overall survival for metastatic group 71.4% and event free survival 57.1%.

Conclusion: During the study period, 23 patients were diagnosed to have Ewing Sarcoma, more males affected than females, majority are of bone origin, in most of the time it originate from the long bones of the lower limbs, one of our patient had PNET of the kidney, a rare site of origin. Ewing sarcoma family of tumors have good prognosis when its localized, but still prognosis is poor when its metastatic at diagnosis, and novel chemotherapy is needed for this group of patients.

ALVEOLAR SOFT PART SARCOMA (ASPS), EXPERIENCE OF THE INSTITUT GUSTAVE ROUSSY (IGR)
Rodrigo Ruiz-Soto1, Angela Cioffi1, Sylvie Bonvalot2, Daniel Varne2, Cecile Le Péchoux4, Philippe Terrier5, Julien Domont1, Axel Le Cesne1
1Institut Gustave Roussy, Medicine, Villejuif, France, 2Institut Gustave Roussy, Surgery, Villejuif, France, 3Institut Gustave Roussy, Radiology, Villejuif, France, 4Institut Gustave Roussy, Radiotherapy, Villejuif, France, 5Institut Gustave Roussy, Pathology, Villejuif, France

Background: ASPS is a rare malignancy, representing less than 1% of all soft tissue sarcomas, characterized by slow growth and indolent behavior.

Methods: We report the clinicopathological characteristics of 19 ASPS patients (pts) treated at the IGR during the period 1980–2005.

Results: Pts were divided in localized disease (12 pts AJCC stage I, one pt stage II) and advanced disease (6 pts stage IV). Localized disease. Seven females, median age 27 years (16–47 years), median tumor size at diagnosis of 6 cm (3–15 cm). The most common localization was the lower extremity (n=6). Tumor grade grade was grade 1 in 5, grade 2 in 6 and grade 3 in 3. All underwent surgery treatment, 2 received neoadjuvant chemotherapy (CT) and 2 adjuvant CT. The type of surgery was R0 (n=5), R1 (n=7) and R2 (n=1). Five pts were re-operated and residual cells were found in one. Response to neoadjuvant chemotherapy was measured as 80% and 0% necrosis. Seven pts relapsed, 1 locally, 3 local/metastatic and 3 metastatic. The median time to relapse was 29 months (1–127 months). With a mean follow up of 78 months (4–188), 8 pts are alive and all deaths related to PD (5 yr OS 50%). Advanced disease. All females, median age 29 years (21-49), primary tumor in the lower extremity (n=4). All had synchronous metastasis (mets), 4 solitary mets localized to the lung and 2 pts multiple mets (lungs and bones). Treatment was surgery (n=2), surgery and CT (n=1), surgery and CT-radiotherapy (n=1) and CT alone (n=2). CT regimen included anthracyclines. Treatment response was CR in 3 pts, SD in 1 and PD in 2. All pts in CR relapsed after a median time of 16 months (0-41). With a median follow-up of 56 months (14–108 months), 4 pts are alive (median survival 49 months).

Conclusions: Advanced disease is more prevalent in women. Cerebral metastasis were not as common as stated in the literature. Because of the small number of pts we can not conclude if chemotherapy treatment has a role in the treatment of ASPS, surgery appears to be the most important treatment.