that an improvement of function and adaptation to daily life routine took place during the second half year following completion of treatment.

Conclusions: Preoperative ILP combined with an aggressive surgical approach results in an excellent local control rate in high grade soft tissue sarcomas. Long-term limb salvage can be achieved in the overwhelming majority of our patients. Ranked by the patients themselves, functional results allow to maintain greater than 80% of preoperative routine activities.

Hematological malignancies

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Long-term follow-up of patients with newly diagnosed adult Acute Lymphoblastic Leukemia (ALL): A single institution experience of 378 consecutive patients over a 21-year period

X. Thomas[1], C. Danaïla[1], Q.H. Le[1], C. Sebban[1], J. Troncy[1], C. Charrin[2], V. Lhéritier[1], M. Michallet[1], J.P. Magaud[2], D. Fiere[1]. [1] *Service d'Hématologie Clinique;* [2] *Laboratoire d'Hématologie et de Cytogénétique, Hôpital Edouard Herriot, Lyon, France*

Purpose: Although the prospect of long-term leukemia-free survival (LFS) after treatment for adult ALL is widely accepted, few studies have reported long-term survival data. 378 ALL patients (pts), referred to our hospital from 1978 to 1999, were reviewed for long-term follow-up data.

Methods: The analysis included data on 351 pts treated by standard chemotherapy according to 11 different successive regimens.

Results: Complete remission (CR) was achieved in 299 pts (79%). Initial performance status, LDH level, immunophenotype, age, and risk group at diagnosis were of significant prognostic value for CR achievement. Median LFS was 14 months with a 3-year (y), a 5-y, and a 8-y LFS at 30%, 26%, and 24% respectively. LFS was better in T-lineage ALL than in B-lineage ALL ($p = 0.05$). Younger age was also a favorable prognostic factor for LFS ($p = 0.001$). Philadelphia-positive (Ph+) ALL displayed a poor outcome since median LFS was 7 months with only 13% of survival at 3 ys. Median overall survival (OS) of the entire cohort was 18 months with a 3-y, a 5-y, and a 8-y OS at 32%, 24%, and 22% respectively. Favorable prognostic factors for OS were younger age ($p < 0.0001$), and T-lineage ALL ($p = 0.001$). Among non T-lineage ALL, standard-risk ALL displayed a significant better outcome than high-risk ALL ($p = 0.0003$). All pts relapsing after 3 ys of CR were B- or non B non T-lineage ALL. Long-term survivors (LTS), defined as survival in CR $\geq$ 3 ys, represented 23% of evaluable pts. 83 pts remain alive in initial CR at >3 ys, while only 3 were LTS after a second CR. Regarding survival, a significant improvement was demonstrated in T-lineage ALL ($p = 0.03$). Furthermore, pts (aged less than 50 ys) transplanted while in first CR did significantly better than those receiving only chemotherapy as post-remission therapy ($p < 0.0001$). The 3-y OS, after allogeneic transplantation in first CR, was 74% in T-lineage ALL, while it was less than 50% in B-lineage ALL.

Conclusion: This single center study on a large cohort of unselected ALL pts reflects the degree to which ALL treatment remains unsuccessful in adults. Only T-lineage ALL outcome has improved over the ys. The results suggest a time (3 ys) at which it becomes reasonable to speak of potential cure, provided the pt is in CR.

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Treatment of patients with refractory, C-KIT positive, acute myeloid leukemia with SU5416, a novel receptor tyrosine kinase inhibitor

W. Fiedler[1], P. Staib[2], R. Kuse[3], U. Dührsen[4], M. Flasshove[5], V. Spataro[6], S. Kelsey[8], P. Scigalla[8], D.K. Hossfeld[1], W.E. Berdel[7]. [1] *University Hospital Hamburg-Eppendorf, Oncology/Hematology, Hamburg, Germany;* [2] *University Hospital, Oncology/Hematology, Cologne, Germany;* [3] *AK St. Georg, Hematology, Hamburg, Germany;* [4] *University Hospital (GHS), Hematology, Essen, Germany;* [5] *University Hospital (Cancer research), Oncology, Essen, Germany;* [6] *University Hospital, Oncology/Hematology, Bellinzona, Switzerland;* [7] *University Hospital, Oncology/Hematology, Münster, Germany;* [8] *Sugen Inc., South San Francisco, USA*

In acute myeloid leukaemia (AML) increased microvessel densities have been detected on bone marrow histologies. Endothelial cell (EC) proliferation is driven by VEGF released by AML blasts. Stem cell factor (SCF) secreted by activated ECs or AML blasts may promote AML growth. SU5416 represents a small molecule inhibitor of phosphorylation of VEGF receptor-1 and -2 and of c-kit, the SCF receptor. This possible mechanism represented the rationale to initiate a phase II trial of SU5416 in patients with refractory AML.

Thirty-two patients (pts) with c-kit positive AML which was either refractory or occurred in patients older than 60yrs not judged medically fit enough for induction therapy, were treated twice weekly with 145 mg/m² SU5416 as a 60-minute infusion via a central venous device. From July 2000 to April 2001 15 female and 17 male patients with a median age of 68yrs (range 27-79) were enrolled. Treatment was generally well tolerated and toxicity was mild. Side effects included severe bone pain in 3 pts, liver failure with gastric hemorrhage and fatal shock (1 pt), grade IV pancreatitis (1 pt). Leukemia related side effects were: fatal thrombocytopenic hemorrhage (2pts), pneumonia/pyrexia/sepsis (6pts). 19 patients are evaluable for response: one patient with morphological remission (absence of blasts in peripheral blood and in bone marrow <5% without normalisation of peripheral blood thrombocytes and granulocytes), 7 pts with PR (reduction of blasts in blood and bone marrow by at least 50%) with a duration of 1-5 months, 11 pts were Non-responders after 4 weeks of therapy. 10 patients were non evaluable due to a treatment of less than two weeks caused by rapid disease progression after one infusion or serious adverse events due to underlying disease. 3 pts are too early to assess.

Treatment of c-kit positive AML with SU5416 represents a novel therapeutic approach. Administration of SU5416 was fairly well tolerated and toxicity was mild. Morphological and partial remissions were observed in a subgroup of patients. Future research is necessary to further identify the subgroup of AML patients where SU5416 shows activity.

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Troxatyl is effective in non-lymphoid blastic phase chronic myeloid leukemia (CML-BP)

F. Giles[1], M. Talpaz[1], C. Bivins[1], J. Jolivet[2], H. Kantarjian[1]. [1] *University of Texas MD Anderson Cancer Center, Departments of Leukemia and Bioimmunotherapy, Houston, USA*

Troxatyl(TM) (troxacitabine) is the first dioxolane nucleoside with potent antitumor activity. In a Phase I study of Troxatyl in patients (pts) with refractory acute myeloid or lymphocytic leukemia, myelodysplastic syndromes or CML-BP, mucositis and hand-foot syndrome were DLTs (Giles et al, JCO 2001). The Phase II single agent dose was defined as 8 mg/m2/day daily for 5 days. Seventeen pts (10 F, 7 M; median age: 52 years, range: 23-80) with CMLBP have been treated at the recommended dose. Nine pts had failed prior therapy for CMLBP which included topotecan-based therapy - 5 pts, allogeneic SCT - 3 pts, 6 thioguanine - 1 pt, homoharringtonine - 2 pts, mitoxantrone/ara-C - 1 pt, STI571 - 6 pts, donor lymphocyte infusions - 1 pt, 2-CDA/cyclophosphamide/VP16 - 1 pt, hCVXD - 1 pt, clofarabine/decitabine - 1 pt, liposomal daunorubicin/ara-C - 1 pt, CVAD - 1 pt. Toxicities included Grade 2 skin rash - 5 pts, hand-foot syndrome Grade 2 - 4 pts, Grade 3 - 3 pts, Grade 2 mucositis - 1 pt, Grade 4 mucositis - 2 pts. Six pts (35%) have returned to a second chronic phase. The durations of 2nd chronic phase in these pts are 3 to 18 plus months. In a recent analysis of results in 162 pts following first salvage therapy for non-lymphoid CML-BP treated at MDACC between 1986 to 1997 (Sacchi et al, Cancer 1999), 36 pts (22%) had an objective response and the median overall survival was 22 weeks. The median survival in the Troxatyl-treated CML-BP patients is 52+ weeks at the present time ($p < 0.01$). Troxatyl is being studied as a single agent in a multicenter Phase II study of pts with CML-BP including STI571 (Glivec) failures. Initial data from this study will be presented.

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Zevalin radioimmunotherapy offers safe and effective therapy for relapsed or refractory, B cell non-Hodgkin's lymphoma (nhl)

M. Saleh[1], C.A. White[2], T.E. Witzig[3], L. Gordon[4], G.A. Wiseman[3], C. Emmanouilides[5], J.L. Murray, J. Lister, R. Landin[2], P.S. Multani[2]. [1] *UAB Cancer Center and Georgia Cancer Specialists, Birmingham/Atlanta, USA;* [2] *IDEC Pharmaceuticals, San Diego, USA;* [3] *Mayo Clinic, Rochester, USA;* [4] *Northwestern Univ, Chicago, USA;* [5] *UCLA, Los Angeles, USA*

Zevalin consists of the anti-CD20 murine monoclonal antibody ibritumomab covalently bound to tiuxetan, which chelates 90Y for therapy. Zevalin therapy includes pretreatment with 2 doses of rituximab (250 mg/m2) 1 week apart to clear peripheral blood B cells and provide improved targeting. A total of 349 patients with relapsed or refractory low grade, follicular, or CD20+ transformed or intermediate grade B-cell NHL were treated with 90Y Zevalin on five clinical trials: a Phase I/II dose finding trial, a