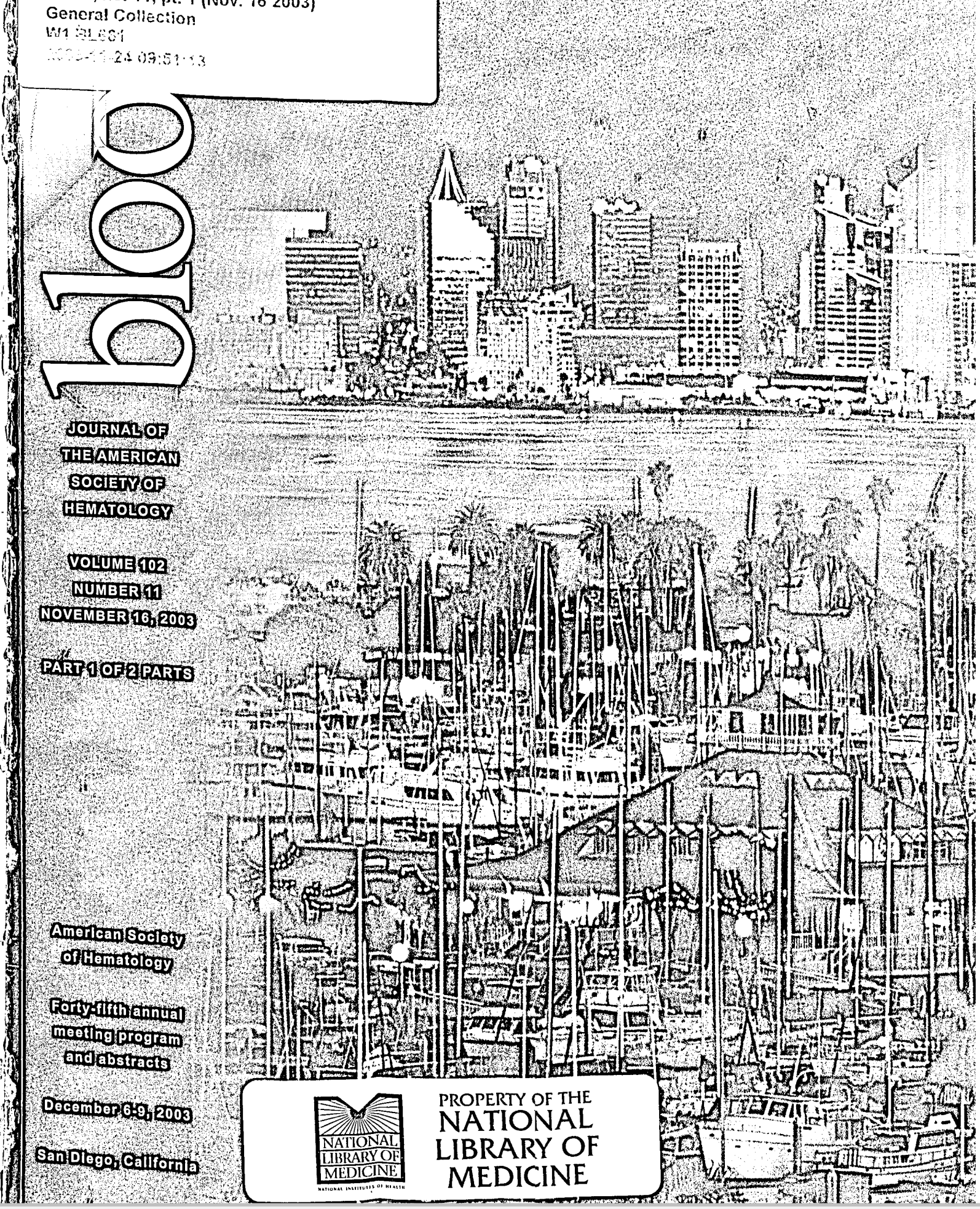

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PROGRAM OF THE 45th ANNUAL MEETING OF

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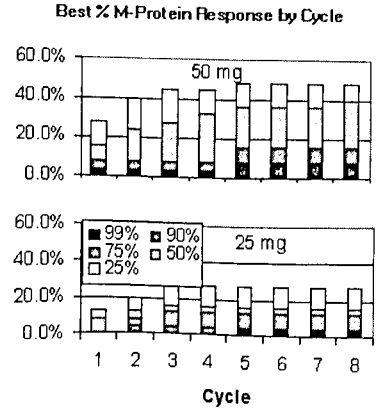
mAb B-B4, targeting CD138, conjugated with DM1 (B-B4-DM1) against a panel of CD138+ MM cells (MM.1S, OCI-My5 and MM.1R) and CD138- cells (the Waldenstrom's macroglobulinemia cell line WSU-WM and the lymphoma line SUDHL4) in vitro. Following 48 h of treatment, B-B4-DM1 significantly decreased survival of CD138+ MM cells (IC50: 10-50 nM), assessed by viable cell number, MTT and proliferation assays, compared to CD138- WSU-WM or SUDHL4 cells (IC50 not reached). In contrast, cytotoxicity of unconjugated DM1 was equivalent in both CD138+ and CD138- cells (IC50 < 10 nM). The exposure of cells to equimolar concentrations of unconjugated mAb B-B4 alone for 96 h did not induce any cytotoxicity. We examined the effects induced by B-B4, B-B4-DM1 and DM1 on proliferation of OCI-My5 and SuDHL4 cells adherent to bone marrow stromal cells (BMSCs). Unconjugated mAb did not induce any detectable effect, whereas B-B4-DM1 showed specific activity against CD138+ cells. DM1 alone induced toxicity in both lines including BMSC. We further evaluated activity of BB4-DM1 against CD138+ MM cells cultured with CD138- cell lines or peripheral blood cells, or against CD138+ primary MM cells adherent to patient BMSCs. B-B4-DM1 was selectively able to deplete CD138+ tumor cells. Propidium iodide profiling confirmed that B-B4-DM1 treatment of MM cells results in reduction of S-phase, G2 arrest, and apoptotic cell death. Finally, antitumor activity of B-B4-DM1 was evaluated in vivo in a murine MM xenograft model. Mice bearing OPM2 human MM cells were treated with B-B4-DM1 (75 µg/Kg or 150 µg/Kg), huC242-DM1 (150 µg/Kg) unreactive with MM cells or vehicle only for a total of 5 days. Inhibition of tumor growth and improvement in median overall survival were observed in B-B4-DM1-treated mice ($p<0.005$) compared to control groups. In conclusion, our data demonstrate that B-B4-DM1 has in vitro and in vivo anti-MM activity, suggesting its potential utility for treatment of MM.

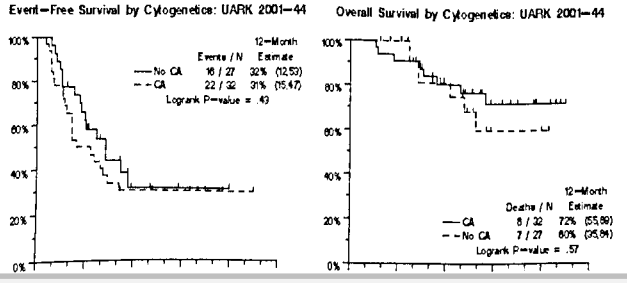
Abstract# 1642 **Poster Board #-Session: 754-I**

Revimid 25 mg (REV 25) x 20 Versus 50 mg (REV 50) x 10 q 28 Days with Bridging of 5 mg x 10 Versus 10 mg x 5 as Post-Transplant Salvage Therapy for Multiple Myeloma (MM). Maurizio Zangari,[1] Bart Barlogie,[1] Joth Jacobson*,[2] Jerome B. Zeldis,[3] Elias J. Anaissie,[1] Raymond Thertulien,[1] Athanasios Fassas,[1] Choon-Kee Lee,[1] John D. Shaughnessy,[1] Guido J. Tricot.[1] *[1]Myeloma Institute for Research and Therapy, University of Arkansas for Medical Sciences, Little Rock, AR, USA; [2]Cancer Research And Biostatistics, Seattle, WA, USA; [3]Celgene Corporation, Warren, NJ, USA.*

58 patients with advanced and refractory MM were enrolled in this randomized phase II trial. Patient characteristics included age ≥ 60 in 54%, abnormal cytogenetics in 54% including del 13 in 33%; prior therapy > 5 years in 41%; prior autotransplants in 86% including tandem transplant in 48%; prior thalidomide exposure in 93% of patients. Cumulative response rates after monthly REV cycles are depicted according to the levels of M protein reduction specified, which were higher with REV 25 than REV 50 (Cycle 8 50% or greater response: 40% vs 15% p=0.041).



Dose limiting toxicity was cytopenia, especially thrombocytopenia with 55% of patients with pre-REV platelet levels ≥ 100,000/µL developing grade > 2 thrombocytopenia (< 50,000/µL) as opposed to 90% when pre-REV platelet levels were < 100,000/µL (p=.001).



REV was not associated with sedative or neurotoxic side effects. Estimated 12-month EFS and OS rates are 30% and 61%, respectively, independent of cytogenetic abnormalities (CA) and REV dose. Serial gene expression profiling (GEP) studies prior to and 48 hr after REV revealed similar but not identical GEP changes as observed after thalidomide. Clinical outcome data will be presented in the context of these GEP data.

Abstract# 1643 **Poster Board #-Session: 755-I**

Primary Treatment of Mutiple Myeloma with Thalidomide, Vincristine, Liposomal Doxorubicin and Dexamethasone (T-VAD Doxil): A Phase II Multicenter Study. Konstantinos Zervas*, Meletios Athanasios Dimopoulos, Eleni Hatziharisi*, Athanasios Anagnostopoulos*, Maria Papaioannou*, Chrisanthi Mitsouli*, Panos Panagiotidis*, Ioannis Korantzis*, Michael Tzilianos*, Alice Maniatis*. *Greek Myeloma Study Group, Athens, Greece.*

Introduction: We and others have shown that VAD-doxil is an outpatient regimen which is effective in two-thirds of previously untreated patients with multiple myeloma. Recent data also indicate that thalidomide with dexamethasone is a highly active primary treatment for myeloma patients. Thus, we studied the efficacy and toxicity of the combination of VAD-doxil with thalidomide as initial cytoreductive treatment in previously untreated patients with symptomatic myeloma.

Patients and methods: The treatment consisted of vincristine 2mg IV, liposomal doxorubicin 40mg/m2 IV, administered as single dose on day 1, and dexamethasone 40mg PO daily for 4 days. Dexamethasone was also given on days 15-18 of the first cycle of treatment. The regimen was administered every 4 weeks for 4 courses. Thalidomide was given daily at a dose of 200 mg at bedtime. Response to treatment was evaluated after 4 cycles of treatment. After completion of 4 cycles the patients were allowed to proceed to high dose chemotherapy or to receive two additional cycles of the same treatment.

Results: Thirty-nine previously untreated patients were included in this phase II multicenter trial. Their median age was 68 years, median serum albumin 3.2g/dl and median serum b2 microglobulin 3.9mg/dlOn an intention-to-treat basis, 29 of the 39 patients (74%) responded to treatment. Four patients (10%) achieved complete and 25 (64%) partial response. Three patients (8%) showed minor response and 7 (18%) were rated as non responders. The time to response was short and at least 50% reduction of monoclonal protein was noted within 2 months of treatment in 80% of responding patients. Major grade 3 or 4 toxicities consisted of neutropenia (15%), thrombocytopenia (15%), deep vein thrombosis (10%), constipation (10%), skin rash (5%) and peripheral neuropathy (5%). Two patients (5%) experienced early death due to infection. Event-free and overall survival at 22 months were 55% and 74% respectively.

Conclusions: The combination of vincristine, liposomal doxorubicin, and dexamethasone (VAD doxil) with thalidomide is an effective and relatively well tolerated initial cytoreductive treatment for symptomatic patients with multiple myeloma. Prospective randomized studies are required in order to assess the effect of this regimen on the long-term outcome of this disease.

Abstract# 1644 **Poster Board #-Session: 756-I**

Doxorubicin and Dexamethasone (AD) Followed by Thalidomide and Dexamethasone (TD) as Initial Therapy for Symptomatic Patients with Multiple Myeloma. Raymond L. Comenzo,[1] Hani Hassoun,[1] Lilian Reich*,[1] Virginia Klimek,[1] Tarun Kewalramani,[1] Madhav Dhodapkar,[1] Lisa Drake*,[1] Cyrus Hedvat*,[2] Julie Teruya-Feldstein*,[2] Martin Fleisher*,[3] Daniel A. Filippa*,[2] Stephen D. Nimer.[1] *[1]Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY, USA; [2]Pathology, Memorial Sloan-Kettering Cancer Center, New York, NY, USA; [3]Clinical Laboratories, Memorial Sloan-Kettering Cancer Center, New York, NY, USA.*

The addition of thalidomide to doxorubicin-containing regimens has been associated with high response rates and a 25% incidence of venous thromboembolic complications in patients with multiple myeloma (NEJM 2001;344:1951-2; Blood 2001;98:1614-5; Blood 2002;100:1168-71). This risk has been increased in patients with myeloma exhibiting the 11q+ chromosome abnormality. To maintain the beneficial effects of these agents and minimize thromboembolic complications, we are examining the use of these agents in a temporally separated fashion for symptomatic stage II and III patients. Doxorubicin and dexamethasone (AD; A=9mg/m²/day, Days 1-4; D=40mg/day, Days 1-4, 9-12, 17-20) are given for 3 months followed by thalidomide and dexamethasone (TD; T=200mg nightly; D=as above) for 2 months with prophylactic antibiotics and daily aspirin (325g). At any point in therapy patients achieving complete responses (CR; immunofixation negative) are permitted to forgo further induction therapy and proceed with autologous stem cell transplantation (SCT). As of 7/03 we have enrolled 27 patients (16M, 11W) with a median age of 58 years (range, 38-79); 10 had myeloma with plasmacytomas extending into soft tissues. Median β2 microglobulin was 2.2mg/L (ND-10.5) and hemoglobin 11.3g/dl (8.3-14.3). Fluorescent in situ hybridization (FISH) studies of baseline bone marrows, searching for abnormalities of chromosomes 11, 13 and 14, are available for 23 patients. Abnormalities of 14 were detected in seven patients, of 11 in five patients, of 11, 13 and 14 in two, of 11 and 13 in one, and of 11 and 14 in one. Seven patients had no abnormalities of 11, 13 or 14 by FISH. Five patients are currently in treatment and two have been removed from study, one for a DVT that occurred during cycle 5 and the other for a myocardial infarction after cycle 1. Two patients developed DVT on or just after therapy with thalidomide (2/21; 10%; 1/2 with 11q+), which seems to be less than the incidence of DVT (6/21; 29%; 4/6 with 11q+) noted in initial versions of this trial incorporating thalidomide and doxorubicin together in each cycle. Twenty patients are currently evaluable for response. Nineteen have responded to therapy (95%), including 5 complete responses (25%), 6 very good partial responses (30%)