wk×4) and all patients IFRT (20-30 Gy) post AutoSCT. Three patients did not proceed onto RI AlloSCT (1 HD parental withdrawal, 1 Burkitts PD, and 1 Burkitts too early post autoSCT) 9/12 proceeded to RI AlloSCT.. RI: Fludarabine 30 mg/m2 × 5d, Busulfan 3.2 mg/kg × 2d, and R ATG 2 mg/kg × 4d (UCB recipients) + AlloSCT (1 related 6/6 PBSC, 1 related 5/6 PBSC, 1 8/10 MUD, 1 5/6 UCB, 5 4/6 UCB). GVHD prophylaxis: tacrolimus (0.03 mg/kg CIVI) on day-1- ±60 and MMF (15 mg/kg IV/PO q12h) day +1 &luAmn;28 as previously reported (Osunkwo/Cairo et al BBMT 2004). Six HD (3 stage IIA, 1 stage IIB, 1 stage IIIB, 1 stage IVB) and 3 NHL ( ALCL n = 1, lymphoblastic n = 1, DLBCL n = 1, ) have been treated. MA AutoSCT + RI AlloSCT were well tolerated in all patients. Median time to RI AlloSCT after MA AutoSCT was 130 days. Median F/U is 924 days. Toxicity: grade 3 hematuria (n = 1), grade 3/4 infection without neutropenia (n = 4), grade 4 infection with neutropenia (n = 2), grade 4 pulmonary fibrosis (n = 1), grade 4 hearing loss (n = 1), and grade 4 thrombocytopenia (n = 1), grade 4 neurotoxicity (n = 1). All patients achieved 100% donor chimerism. GVHD: grade II-III aGVHD (2/8), cGVHD (3/8). Four of 6 HD patients: are NED; 2 patients died; PD n = 1 and cGVHD n = 1. Two of 3 NHL: are NED, 1 died of PD. There has been one death (NRM) from infection day +632. The estimated OS at 1 year is 56.2%. In summary, MA AutoSCT followed by IFRT, targeted monoclonal antibody therapy, and RI AlloSCT is feasible and well tolerated in pediatric patients with relapsed HD/NHL. A larger controlled study with longer follow up is required to determine if this approach will reduce relapse, MDS, long-term toxicity, and improve EFS.

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### BORTEZOMIB PRIOR TO AUTOLOGOUS TRANSPLANT IN MULTIPLE MYELOMA: EFFECTS ON MOBILIZATION, ENGRAFTMENT, AND MARKERS OF IMMUNE FUNCTION

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To explore the potential role of bortezomib (VELCADE®) in the frontline treatment of multiple myeloma, we conducted a study of bortezomib administered prior to autologous transplant. The primary objective was to determine the effects of bortezomib on cytokine based mobilization and engraftment. Given the critical role NF-κB in lymphocyte development and survival, we also sought to determine the effects of bortezomib on markers of immune function. Following induction, two cycles of bortezomib 1.3 mg/m$^2$ were administered on days 1, 4, 8, and 11 of a 21-day treatment cycle. Peripheral blood stem cells were mobilized with G-CSF 10 mcg/kg/day for 5 days and harvested by large volume apheresis (20 L/day) until a minimum of 2.5 × 10$^6$ CD34+ cells/kg were collected. High-dose melphalan 200 mg/m$^2$ was administered followed by autologous stem cell transplant with GM-CSF 250 mcg/m$^2$/day support until neutrophil engraftment. Peripheral blood was collected at baseline (cycle 1, day 1) and after treatment with bortezomib (cycle 2, day 18) for analysis of lymphocyte subsets and serum cytokines. Forty patients were enrolled with 37 continuing on to autologous transplant. Prior to receiving bortezomib, 20 patients had been previously treated with an anthracycline, 22 with thalidomide, and two patients had no induction therapy. Stem cell collection was successful in 37 of 38 patients (97%) with the median first collection of 4.24 × 10$^6$ CD34$^+$cells/kg. Following transplant, all patients engrafted with a median time to neutrophil engraftment (ANC ⩾ 500/mm$^3$) of 11 days (range 9-14 days) and platelet engraftment (platelet count ⩾ 20,000/mm$^3$) of 11 days (range 9-31 days). In an intention-to-treat analysis at 100 days post-transplant, we observed a CR in 6 patients (15%), a near CR in 10 patients (25%) and a PR in an additional 19 patients (48%) for an overall response rate of 88%. Following treatment with bortezomib, we observed a 38% decrease in CD56$^+$ NK cells ($P$ = .02) and a 26% increase in CD4/CD8 ratio ($P$ = .0006) with a 18% decrease in CD8$^+$ cytotoxic T-cells ($P$ = .054). No significant changes were detected in either Th1 or Th2 serum cytokine levels: IL-2 ($P$ = .116), TNF-alpha ($P$ = .854), IFN-γ ($P$ = .070), IL-4 ($P$ = .240), IL-6 (0.236), IL-10 (0.151). We conclude that pretransplant bortezomib does not adversely impair stem cell mobilization or engraftment. Bortezomib also decreases NK and cytotoxic T cell subsets without measurable change in serum Th1 and Th2 cytokines.

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### IMMUNOTHERAPY WITH RITUXIMAB/INTERLEUKIN 2 (IL-2) FOLLOWING AUTOLOGOUS PERIPHERAL BLOOD STEM CELL TRANSPLANT (ASCT) AS TREATMENT FOR CD20 POSITIVE NON-HODGKIN'S LYMPHOMA

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Relapse of NHL remains a problem after ASCT. Early after ASCT, the immune system is not very active and the addition of immunotherapy may decrease the incidence of relapse and prolong survival. In an initial phase I/II trial at our center, the immunemodulator IL-2 increased NK and LAK activity in vitro. Since Rituximab can lyse CD20+ cells by ADCC, adding Rituximab to IL-2 should boost its effectiveness. From January 2000, 20 patients with CD20+ NHL received ASCT followed by Rituximab/IL-2 therapy. The pathology at the time of ASCT included: follicular small/large cleaved (n = 2), diffuse large/T cell rich B cell (n = 8), mantle cell (n = 4) and transformed from indolent to diffuse (n = 6). The disease status was primary refractory (n = 3), relapse 1(PR) (n = 5), remission 1 (n = 3), remission 2 (n = 8) and relapse 2/refractory (n = 1). The median age of the patients was 46 years (range 31-70). The median time to initiation of the therapy was 79 days after transplant (range 49-100). The treatment schema was: IL-2 0.6 × 10$^6$ IU/m$^2$/day sc times 12 weeks, followed by 1.4 × 10$^6$ IU/m$^2$ sc three times/week for an additional 12 weeks (for a total of 24 weeks of IL-2 therapy). Rituximab was given iv at 375 mg/m$^2$ for a total of 4 doses: beginning one day prior to starting IL-2, then between days 25-30, 50-55 and 75-80 post beginning IL-2. NCI Common Toxicity Criteria were used to evaluate adverse events. Most common grade 3 /4 toxicities were neutropenia (n = 9), pneumonia (n = 2), hypothyroidism (n = 1), hypokalemia (n = 1) and pulmonary dysfunction (decreased DLCO) (n = 1). Neutropenia responded to G-CSF. There were 11 infectious episodes, pneumonia (influenza n = 1) and pneumococcus strept (n = 1), oral thrush (n = 2), herpes simplex (n = 1), urinary tract infection (n = 1), zoster (n = 1) and upper respiratory infection (n = 4). Most common side effects were fatigue, ertyheyma/indurationa/discomfort at IL-2 injection sites and flu-like symptoms. Seven patients stopped therapy before completing 24 weeks due to subdural hematoma and progression of NHL (n = 1), pneumonia (n = 2), decreased DLCO (n = 1) and at own or physician's choice without grade 3/4 toxicity (n = 3) at 9, 13, 14.5 weeks. With a median follow-up of 45 months (range 14-64), 18 patients remain alive and in compete remission. The combination of IL-2/ Rituximab can be administered with acceptable toxicity and has a high response rate. A randomized trial has been initiated to address whether this combination therapy is beneficial to patients.

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### HIGH RATES OF REACTIVATION OF VARICELLA ZOSTER VIRUS (VZV) ASSOCIATED WITH BORTEZOMIB (VELCADE) WHEN GIVEN PRE AND POST HIGH DOSE CHEMOTHERAPY (HDCT)

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We evaluated the tolerability and efficacy of the proteasome inhibitor bortezomib administered to multiple myeloma (MM) patients both prior to, and as consolidation therapy following HDCT, in a prospective pilot study. Patients received 2 cycles of bortezomib 1.3 mg/m$^2$ on days 1, 4, 8, and 11 of every 21 days, prior to stem cell collection and melphalan 200mg/m$^2$, followed by six cycles of consolidation bortezomib 1.3 mg/m$^2$ given once weekly for 4 of every 5 weeks, 90–120 days following transplantation. Of 40 enrolled patients, 33 have received at least one post transplantation cycle of consolidation bortezomib. Patient and