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ORAL ABSTRACTS

721.ALLOGENEIC TRANSPLANTATION: CONDITIONING REGIMENS, ENGRAFTMENT AND ACUTE TOXICITIES

Addition of Inotuzumab Ozogamicin to the Conditioning Regimen of Allogeneic Stem Cell Transplantation (allo-SCT) for Relapsed CD22 (+) Lymphoid Malignancies: Long-Term Survival Results

Issa F. Khouri, MD[1], *Kamal Alzahrani*[1], *Alison Gulbis*[2], *Koji Sasaki, MD*[3], *Nitin Jain, MD*[3], *Nicholas J. Short, MD*[3], *Tapan M. Kadia, MD*[3], *May Daher, MD*[4], *Hind Rafei, MD*[1], *Jin S Im*[1], *David Marin, MD*[1], *Amanda L. Olson, MD*[1], *Uday R. Popat, MD*[1], *Muzaffar H. Qazilbash, MD*[1], *Jeremy Ramdial, MD*[1], *Gabriela Rondon, MD*[1], *Samer A. Srour, MD*[1], *Partow Kebriaei, MD*[1], *Elizabeth J. Shpall, MD*[1], *Hagop M. Kantarjian, MD*[3], *Richard E. Champlin, MD*[1], *Elias Jabbour, MD*[5]

[1] Department of Stem Cell Transplantation and Cellular Therapy, The University of Texas MD Anderson Cancer Center, Houston, TX
[2] Division of Pharmacy, The University of Texas MD Anderson Cancer Center, Houston
[3] Department of Leukemia, The University of Texas MD Anderson Cancer Center, Houston, TX
[4] Stem Cell Transplantation and Cellular Therapy, MD Anderson Cancer Center, Houston, TX
[5] University of Texas M.D. Anderson Cancer Ctr., Houston, TX

Background: Inotuzumab ozogamicin (InO) is a humanized antibody-drug conjugate that targets CD22+ B-cells. InO demonstrated antitumor activity and manageable toxicity in phase 1/2 trials for the treatment of B-cell non-Hodgkin lymphoma (NHL) as a single agent and in combination with rituximab. In order to improve outcomes in patients with relapsed CD22 (+) NHL, or chronic lymphocytic leukemia (CLL) who failed targeted therapies and were candidates for allo-SCT, we prospectively studied the addition of InO to our standard chemo-conditioning of BFR (bendamustine, fludarabine and rituximab-Khouri Blood 2014). Herein we report long-term survival outcomes. **Methods:** InO was infused intravenously (iv) on day -13 outpatient, with a dose cohort of 0.6, 1.2 or 1.8 mg/m2. Bendamustine 130 mg/m ^{2} iv daily on days -5 to -3 together with 30 mg/m ^{2} iv of fludarabine on days -5 to -3 were given prior to transplantation. Rituximab was given at a dose of 375 mg/m ^{2} iv on days -6, +1, and +8. Tacrolimus and mini-methotrexate were used for graft versus host disease (GVHD) prophylaxis. **Results:** The study included 26 patients. Median age was 59 (range, 26-70) years. Disease types: ***CLL*** [n=11 (27%) ; 64% with *TP53* mutations (either alone, or with other mutations such as *BTK, CDH2, ZMYM3*); 22% with complex cytogenetics; 75% with unmutated IGHV; mantle cell lymphoma (***MCL***) [n=8 (31%); 83% had Ki 67 >30%; 25% *TP53* mutation; and 25% blastoid histology]; ***Follicular***lymphoma (n=5, 19%), and diffuse large b cell (***DLBCL***[n= 2; (8%)]. Median # prior treatments was 2.5 (range, 1-6). Patients with CLL/MCL were previously treated with ibritunib (n=10), venetoclax (n=5), idelalisib (n=2), nivolumab (n=1) and CAR T (n=1). At study entry, 18 (69%) patients were in CR, 7 (27%) in PR, and 1 (4%) had SD. Eleven (42%) received their transplants from matched sibling donors (MSDs) and 15 (58%) from matched unrelated donors (MUDs). The number of patients who received the 0.6, 1.2 or 1.8 mg/m2 of InO were 4, 2 and 20 patients, respectively. No DLT was observed. Forty-two percent of patients never experienced severe neutropenia and 77% never experienced platelet counts < 20K x 10 ^{9}/L. Only 1 patient developed veno-occlusive disease, confounded by the simultaneous manisfestation of hyper-acute GVHD related to prior nivolumab pre-alloSCT. Treatment-related mortality (TRM) at 2-years was 12%. With a median follow-up of 48.7 months (range, 3.6-82.8), the 5-year overall survival (OS) and progression-free survival rates (PFS) were 84% and 80%, respectively. Seven of 8 (87.5%) patients with PR/SD at study entry converted to CR after allo-SCT. There was no significant difference in OS or PFS by histology subtype. Patients who received a transplant from MSDs had OS and PFS rates of 100% v 79% ($P = .060$) and 64% ($P = .032$) for those who received MUDs, respectively (Figure 1). We compared results of this trial to a group of patients (n=56) with relapsed lymphoid malignancies who received allo-SCT at our center in a preceding prospective trial using BFR conditioning without InO and the same GVHD prophylaxis (clinicaltrials.gov #NCT00880815) which was previously published. There was no statistically significant difference in patients, disease (including histology, disease status pre-transplant) or transplant characteristics between the 2 groups. We found no statistically significant differences in engraftment times, incidence and grades of liver toxicity, TRM, risk of acute grade II-IV or III-IV GVHD. However, the study group containing InO had a higher incidence of extensive chronic GVHD (mainly *de novo*) than the control group (50% vs 25%, $P = .019$), respectively. There was a trend in patients with NHL to have a better 5-year OS (93% vs 68%) and 5-year PFS (93% vs 58%, Figure 2) in the

study group vs the control groups. We did not observe such a trend in patients with CLL (5-year PFS 62% vs 59%): this could be related to small #patients, level of expression of CD22, more adverse mutations in the study group.

Conclusions: Our results show that InO is safe when combined with an allo-SCT conditioning regimen and may improve survival outcomes in patients with CD22 (+) NHL. This needs to be validated in a larger number of patients. An ongoing trial at our center involves fractionating InO dose pre-and post-allo-SCT in patients with lymphoma or acute lymphoblastic leukemia receiving a reduced-intensity conditioning, and adding post-transplant cyclophosphamide to decrease the risk of GVHD.

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OffLabel Disclosure: inotuzumab ozogamicin in allogeneic transplantation

Figure 1: PFS according to donor type after allo-SCT with InO-containing conditioning.

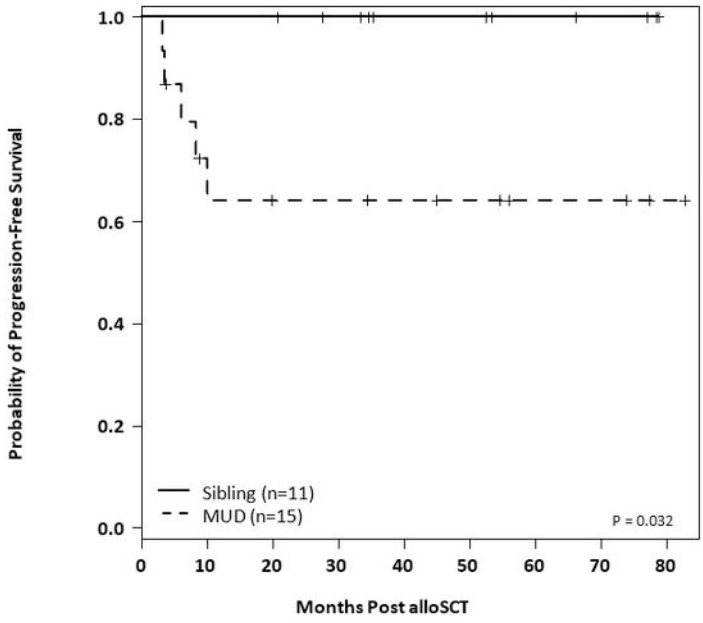

Figure 2: Patients with lymphoma who received InO+BFR tended to have a better PFS than those who received BFR alone.

Median follow-up InO group: 48.7 months (range, 3.6-82.8 months)

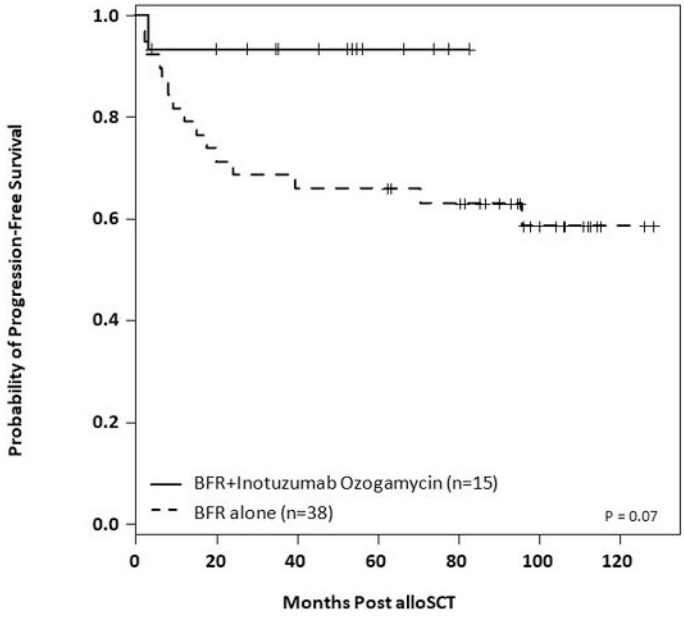

Figure 1

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