relapse. Five pts have died (median 9 months), 2 from graft-versus-host disease (GVHD), 2 infections, and 1 elected Hospice care after experiencing renal failure. Last disease responses were complete remission (n = 8), partial remission (n = 6), stable disease (n = 5), not-evaluated (n = 1). The incidences of grades II and III-IV acute GVHD were 60% and 15% respectively, and chronic GVHD was 46% at 1-year. Estimated 1-year rate of non-relapse mortality (NRM), relapse, progression-free (PFS), and overall survivals (OS) were 33%, 0%, 67%, and 67% respectively. Patients receiving peri-HCT rituximab had lower HR for relapse (HR:0, p = 0.001), comparable HR for NRM (HR:1, p = 0.9) and OS (HR:0.7, p = 0.45), and a trend for lower HR for PFS (HR:0.5, p = 0.07) compared to the historical control group. At day 84, median CD3 chimerisms were 99% *vs* 95% (p = 0.08), respectively.

After adjusting for the previous 4 significant covariates, PFS was better (HR:0.4, p = 0.04) among the rituximab group. Peri-transplant rituximab is a promising addition to nonmyeloablative HCT and may decrease early disease progression by allowing the generation of potent GVL effects.

231

LEUKEMIC TRANSFORMATION OF PHILADELPHIA-NEGATIVE MYELOPROLIFERATIVE NEOPLASMS: RESULTS OF A TREATMENT ALGORITHM EMPLOYING ALLOGENEIC TRANSPLANTATION USING RELATED AND UNRELATED DONORS

Kennedy, J.A.[1], Atenafu, E.G.[2], Messner, H.[3], Brandwein, J.M.[3], Craddock, K.J.[4], Lipton, J.H.[3], Minden, M.D.[3], Schimmer, A.D.[3], Schuh, A.C.[3], Yee, K.W.[3], Gupta, V.[3] [1] University of Toronto, Toronto, ON, Canada; [2] Princess Margaret Hospital, Toronto, ON, Canada; [3] Princess Margaret Hospital, Toronto, ON, Canada; [4] University Health Network, Toronto, ON, Canada

Leukemic transformation (LT) is a rare but fatal complication of Philadelphia-negative myeloproliferative neoplasms (MPNs) for which optimal treatment strategies are not known. LT is generally considered incurable with induction chemotherapy alone.

At our centre, we have adopted a treatment strategy for LT where patients within the transplant age group who have a reasonable fitness level are offered induction therapy. Subsequently, those who achieve complete remission (CR/CRi) or revert back to a chronic MPN (cMPN) state are considered eligible for allogeneic transplantation (allo-SCT) if a suitable related or unrelated donor is available. Alternatively, those who are not candidates for the aforementioned strategy are offered supportive therapy including clinical trials.

We evaluated clinical outcomes of this treatment approach in 75 patients with LT diagnosed between 1998 and 2011. Prior to LT, MPN diagnoses were: PV, 16%; ET, 16%; primary MF, 28%; post-PV/ET MF, 25%; and MPN-U, 15%. 39 (52%) patients were treated with curative intent (induction chemotherapy +/- allo-SCT) while the remainder were treated with non-curative intent. At the time of LT, the curative intent cohort differed from the non-curative group in terms of median age (57 vs. 72 yrs, P<0.0001), performance status (ECOG≤1 in 92% vs. 58%, p = 0.001), serum albumin (38 vs. 35 g/L, p = 0.008) and the frequency of normal cytogenetics (47% vs. 20%, p = 0.03) respectively.

Among all patients, the 2-year overall survival (OS) from the time of LT was 15%. Outcomes were significantly improved in individuals treated with curative vs. non-curative intent (2-year OS, 25% vs. 4%, P< 0.0001). Among the curative group, 30/39 achieved either CR (n = 19) or reversion to cMPN (n = 11). Suitable donors were identified for 24 (80%) of these responders and 17 (57%) underwent allo-SCT. Median time to transplant was 177 days. Survival of patients undergoing allo-SCT was significantly better compared to those who achieved CR/cMPN post-induction but were not transplanted (2-year OS, 46% (n = 17) vs. 15% (n = 13), P = 0.035). To avoid a time to transplant bias, a landmark analysis was done comparing survival between the transplant cohort and non-transplanted patients who survived at least 177 days (n = 13), and similar results were observed (2-year OS 46% vs. 15%, p = 0.035).

Our results demonstrate the curative potential of intensive induction therapy followed by allo-SCT in select patients with LT preceded by MPN.

232

LOW DAY 100 TRANSPLANT-RELATED MORTALITY (TRM) FOLLOWING CLOFARABINE (CLO) IN COMBINATION WITH CYTARABINE AND TOTAL BODY IRRADIATION (TBI), MYELOABLATIVE CONDITIONING (MAC) AND ALLOGENEIC STEM CELL TRANSPLANTATION (ALLOSCT) IN CHILDREN, ADOLESCENTS AND YOUNG ADULTS (CAYA) WITH POOR-RISK ACUTE LEUKEMIA

Radhakrishnan, K.[1], Ricci, A.M.[2], Geyer, M.B.[3], Harrison, L.[1], Duffy, D.[1], Ozkaynak, F.[1], Satwani, P.[2], Cheerva, A.C.[4], Talano, J.[5], Moore, T.B.[6], Gillio, A.P.[7], Baxter-Lowe, L.A.[8], Cairo, M.S.[1] [1] New York Medical College, Valhalla, NY; [2] Columbia University, New York, NY; [3] Harvard Medical School, Boston, MA; [4] University of Louisville, Louisville, KY; [5] Medical College of Wisconsin, Milwaukee, WI; [6] University of California at Los Angeles, Los Angeles, CA; [7] Hackensack University Medical Center, Hackensack, NJ; [8] University of California at San Francisco, San Francisco, CA

Background: CAYA with ALL or AML in third complete remission (CR3), refractory relapse (RR) or induction failure (IF) have an extremely poor prognosis, <20% EFS (Gaynon, BJH, 2005, Wells et al, JCO, 2003). MAC prior to AlloSCT is associated with high TRM and is donor dependent: 5-20% for matched sibling, 10-40% for matched unrelated, and 20-52% for cord blood transplants. CLO, an inhibitor of DNA polymerase and ribonucleotide reductase, has been shown to be safe and induce durable remissions, both in conjunction with busulfan in poor-risk AML (Magenau et al., Blood, 2011) and with Melphalan in poor-risk hematologic malignancies in adults (van Besien et al, ASH,2009). CLO has significant activity in CAYA with relapsed ALL/AML (Jeha et al., JCO 2006,2009) and synergy with cytarabine (Faderl et al, Blood, 2005). We sought to determine safety, day-100 TRM, and overall survival (OS) of CLO, cytarabine and TBI followed by AlloSCT in CAYA with poor-risk ALL/AML.

Methods: This is an ongoing multi-center phase I/II trial of a novel conditioning regimen of CLO (dose escalation: 40mg/m^2 [n = 3], 46 mg/m^2 [n = 3], 52 mg/m^2 [n = 17]) x5d, sequential (4 hrs later) cytarabine 1000 mg/m^2 x6d and TBI (1200cGy) followed by AlloSCT from matched related or unrelated donors in CAYA with ALL/AML in CR3, RR or IF. Pts with unrelated grafts received R-ATG. GVHD prophylaxis consisted of tacrolimus and MMF (Bhatia/Cairo et al., BBMT, 2009). Kaplan-Meier method was used to determine the probabilities of engraftment, GVHD, TRM and OS.

Results: 23 pts, median age: 10.8 yrs (1.5-20.7); M:F: 17:6, ALL/AML: 20:3 (9 CR3, 3 RR, 11 IF), 9 related donors, 14 unrelated donors (8 BM/PBSCs, 6 UCB). Median TNC and CD34 dose was 4.76x10^8/kg and 4.84x10^6/kg for BM/PBSCs and 4.0x10^7/kg and 2.8x10^5/kg for UCB, respectively. Probabilities of neutrophil and platelet engraftment and grade II-IV aGVHD were 100%, 92.8% and 50.8%, respectively. All except one achieved 100% whole blood donor chimerism by day 30. CLO dose was tolerable at 52mg/m^2/d x5d without dose limiting toxicity. Probability of Day 100 TRM was only 5%. Probability of 1-yr PFS and OS were 45% (CI_{95}: 24-83%), and 44.6% (CI_{95}: 24-68%) respectively.

Conclusions: Preliminary results suggest this novel MAC regimen followed by AlloSCT is safe and well tolerated in CAYA with poor-risk ALL/ AML with CLO dose of 52 mg/m^2. Early results are encouraging with respect to low risk of day 100 TRM with this conditioning regimen in this poor-risk population.

233

OUTCOMES OF ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION (HCT) IN CHRONIC LYMPHOCYTIC LEUKEMIA (CLL): IMPACT OF MYELOABLATIVE (MA) VS. REDUCED-INTENSITY CONDITIONING (RIC) REGIMENS, AND IMPACT OF TOTAL BODY IRRADIATION (TBI)-BASED MA VERSUS CHEMOTHERAPY (CT)-BASED MA CONDITIONING

Leis, J.F.[1], Sabloff, M.[2], Sobecks, R.M.[3], Maziarz, R.T.[4], Ahn, K.W.[5], Zhu, X.[5], Kalaycio, M.E.[3], Cortes, J.[6], Saber, W.[5] On Behalf of the CIBMTR Chronic Leukemia Working Committee [1] Mayo Clinic Arizona & Phoenix Children's Hospital; [2] The Ottawa Hospital Blood & Marrow Transplant Program; [3] Cleveland Clinic Foundation; [4] Origon Health and Science University; [5] CIBMTR, Medical College of Wisconsin; [6] M.D. Anderson Cancer Center

There has been a marked change in transplant approaches of the CLL patient. MA conditioning has been shown to provide high