

with CR/CRi. This report details the experience of 2 patients who received SGN-CD33A, had anti-leukemic benefit, and went to allogeneic SCT.

**Results:** Case 1: A 37-year-old male with AML (intermediate risk cytogenetics) achieved CR with standard induction/consolidation May 2013. He relapsed Dec 2013 and got decitabine before enrolling in SGN33A-001 Jan 2014 (20 mcg/kg). He had ECOG 1, G4 neutropenia, G3 thrombocytopenia, and 6-8% blasts. D15 marrow showed a hypocellularity with no evidence of leukemia. He remained pancytopenic and his marrow hypoplastic with no evidence of AML until residual leukemia was identified at 6.6% by flow cytometry in hypocellular marrow Mar 2014. He had a double cord transplant Apr 2014 with fludarabine, cytoxan, and TBI conditioning regimen. D30 and D100 posttransplant marrow had no AML and 100% donor chimerism. He is now 5 months posttransplant with no AEs related to SGN-CD33A.

Case 2: A 41-year-old male with normal karyotype AML (nucleophosmin cytoplasmic and IDH2 mutations) achieved CR with high-dose cytarabine + idarubicin induction Jul 2013 which was complicated by acute renal failure requiring hemodialysis. He had 4 cycles of idarubicin + cytarabine consolidation. He relapsed Apr 2014 and enrolled in SGN33A-001 (60 mcg/kg). He had ECOG 0, G3 neutropenia, and G2 thrombocytopenia. The marrow was 10-20% cellular with 50% CD33+ blasts. D15 marrow was <5% cellular without AML. He experienced cellulitis with lymphangitis, Staphylococcus aureus bacteremia, and persistent fever with cavitary pulmonary nodules. He had prolonged pancytopenia; D64 marrow was < 5% with pockets of hematopoiesis. He had fludarabine and busulfan conditioning regimen and MRD allo HSCT complicated by severe mucositis. He had neutrophil recovery by D16. D30 marrow had no AML and 100% donor chimerism. He is doing well at D75.

**Conclusions:** These case reports support the anti-leukemic activity of SGN-CD33A and enablement of allogeneic SCT. This trial is ongoing to define MTD and optimize dose and schedule. Combinations of SGN-CD33A with standard AML and MDS agents are planned.

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### Myeloablative Haploidentical Stem Cell Transplantation (MAC-HAPLO) with Post-Transplant Cyclophosphamide (PT-CY) As GVHD Prophylaxis in High Risk Leukemias/ Myelodysplastic Syndromes (MDS)

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**Introduction:** Allogeneic transplantation is the only curative option for patients with high risk leukemias or MDS. Only one third of them have an HLA identical sibling donor and around 60-70% will find an unrelated donor; that's why haploidentical stem cell transplantation (HAPLO-HSCT) offers a therapeutic option to most of these patients. Myeloablative conditioning (MAC) used to obtain better disease

control than reduced intensity conditioning regimens (RIC), but with higher toxicity, rendering long term similar results. **Patients and Methods:** We retrospectively evaluated the results in patients diagnosed with high risk leukemias or MDS of our MAC-HAPLO regimens (Fludarabine 30 mg/m<sup>2</sup> x5 days (-6 to -2), Cyclophosphamide 14.5 mg/kg x2 days (-6 to -5), IV Busulfan 3.2 mg/kg x 3 days (BUX3) on days -4 to -2, or Fludarabine 40 mg/m<sup>2</sup> x4 days (-6 to -2) and IV Busulfan 3.2 mg/kg x 4 days (BUX4)) with GVHD prophylaxis based on PT-CY (50 mg/kg on days +3 and +4) and a calcineurin inhibitor plus mycophenolate from day +5, performed in GETH centers.

**Results:** From Feb 2011, 24 MAC-HAPLO have been done in 7 centers. Median age was 37 years (15-65), 58% were males and all were in advanced disease phase or presented high risk features (AML 16/ALL 4/MDS 2/ CML-BC 1/ CMML 1). Previous HSCT had been employed in 21% (autologous in 1, allogeneic in 4), and in 79% the HAPLO-HSCT was their first transplant. Disease status at HAPLO-HSCT was morphologic CR in 83%, but with persistent disease (morphologic or MRD+ by flow or molecular markers) in 67%. BM was the graft source in 3 patients (12.5%) and PBSC in 21 (87.5%), non T-cell depleted in all cases. The haploidentical donor was the patient's mother (21%), father (12.5%), siblings (41.5%) or offspring (25%). MAC regimen was BUX3 in 8 (33%) and BUX4 in 16 patients (67%). Median infused CD34+ cells were 4.93x10<sup>6</sup>/kg (3,20-8,43). Median neutrophils engraftment was reached at day +16 (13-29) and platelets >20K at day +27 (11-131). Complete chimerism was obtained at a median of 22 days (13-44) in 21 evaluated patients. Cumulative incidence (CI) of non-relapse mortality (NRM) was 21.5% at 1 year. CI of grade II-IV acute GVHD was 45.5% at day +100, and grade III-IV was 9%. CI of chronic GVHD at 1 year was 35%, being extensive in 8%. No differences in acute or chronic GVHD CI were seen when comparing BUX3 against BUX4. After a median follow-up of 15 months (3-31), estimated 18-months event-free survival (EFS) and overall survival (OS) were 63% and 75% respectively. CI of relapse or progression was 19.5%. No significant differences in NRM, EFS, OS and relapse incidence were detected between BUX3 and BUX4. The effect of CR prior to MAC-HAPLO has not been appropriately assessed due to the limited number of events in our series.

**Conclusions:** IV Busulfan based MAC-HAPLO with PT-CY in the treatment of high risk leukemias and MDS offers good disease control with manageable toxicity, with either BUX3 or BUX4.

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### Allogeneic Hematopoietic Stem Cell Transplantation (alloHSCT) Following Blinatumomab-Induced Remission in Pediatric Patients with Relapsed/Refractory (r/r) B-Precursor Acute Lymphoblastic Leukemia (ALL): Preliminary Results from a Phase I/II Study

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The prognosis for patients (pts) with r/r ALL is poor especially after transplantation. Blinatumomab, an investigational bispecific T-cell engager (BiTE<sup>®</sup>) antibody construct that re-directs T cells to CD19<sup>+</sup> B cells resulting in serial lysis, has shown antileukemia activity in pts with r/r ALL. We evaluated the transplantation rate after blinatumomab-induced remission, in pediatric patients with r/r ALL characterized by negative prognostic factors, such as refractory disease and prior alloHSCT.

In this single-arm study, eligible pts were 2–18 yrs old and had an M3 marrow with B-precursor ALL that was refractory, in  $\geq 2$ nd marrow relapse, or any marrow relapse after HSCT; and no CNS leukemia. A stepwise dose (wk 1: 5  $\mu\text{g}/\text{m}^2/\text{d}$ ; thereafter: 15  $\mu\text{g}/\text{m}^2/\text{d}$ ) of blinatumomab was given by continuous IV infusion (4 wks on/2 wks off) for up to 5 cycles. Primary endpoint was complete remission (CR) rate within 2 cycles. Secondary endpoints were alloHSCT rate, relapse-free survival (RFS), overall survival (OS), and adverse events (AEs). 39 pts received blinatumomab. Median (range) age was 9 (2–16) yrs. 69% of pts had  $\geq 50\%$  bone marrow blasts. 41% had 1 prior salvage, 41% had  $\geq 2$  prior salvages and 18% were primary refractory or had refractory relapse. 87% of pts enrolled had relapsed within 6 months after the last remission. Among pts with prior alloHSCT (64%), 16% had 1 relapse and 50% had  $\geq 2$  relapses. Of 12 pts (31%; 95% CI, 17%–48%) who reached CR within the first 2 cycles, 6 (50%) proceeded to alloHSCT. 5 pts who did not respond to blinatumomab received alloHSCT after treatment was ended. Donors included haploidentical parents (n=9), a sibling (n=1) and an unrelated donor (n=1). AlloHSCT were performed at 8 different centers. Conditioning regimens included 5 myeloablative, 5 reduced intensity, and 1 unknown regimen. Median (95% CI) RFS was 5.6 (2.6–12.1) months among blinatumomab responders and 6.5 (2.2–7.7) months among responders receiving alloHSCT (measured from the time of alloHSCT). At 6-month follow-up, median (95% CI) OS was 4.3 (3.6–8.1) months among all pts and 7.7 (0.45–NE) months among pts receiving alloHSCT (measured from the time of alloHSCT). 100-day mortality rate post alloHSCT was 10%. The most common AEs among all pts included pyrexia (74%), anemia (33%), nausea (31%), headache (28%) and hypertension (26%). Anemia (26%), pyrexia (21%), increased alanine aminotransferase or aspartate aminotransferase (18% each) and febrile neutropenia (15%) were the most common grade  $\geq 3$  AEs. 3 (8%) pts (2 with grade 3 events) had cytokine-release syndrome.

In this phase I/II study, blinatumomab has shown promising antileukemia activity in pediatric patients with r/r B-precursor ALL, most of whom had prior alloHSCT and/or were refractory. Half of pts who achieved CR in response to blinatumomab

proceeded to alloHSCT, suggesting that blinatumomab may provide a therapeutic option to bridge this patient population to alloHSCT.

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### Race Influences the Response to Conventional Induction Chemotherapy in Asian Patients with Acute Myeloid Leukemia

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**Background:** Though there has been significant improvement in the outcome of adult patients with acute myeloid leukemia (AML), much of this has been attributed to advance in supportive care. Response to therapy has been a key predictor of clinical outcome in patients with newly diagnosed AML. Published studies have identified prognostic factors in predicting treatment response for AML induction therapy but data is lacking in Asian population.

**Objectives:** To evaluate the response rates of conventional induction chemotherapy in patients with AML in a tertiary care hospital and to identify prognostic factors associated with primary resistant AML.

**Methods:** This retrospective study included newly diagnosed AML patients who received conventional induction chemotherapy at Singapore General Hospital between January 1999 and June 2013. Primary outcome of the study was to determine the response rates to treatment. Secondary outcomes included duration of CR, relapse rate, overall survival (OS), and pre-treatment prognostic factors associated with primary resistant AML. Primary resistant AML was defined as failure to achieve CR within two cycles of induction chemotherapy.

**Table 1**  
Racial distribution of study population

	Chinese	Malay	Indian	Others
Frequency	314	53	7	17
Percentage	(80.3%)	(13.6%)	(1.8%)	(4.3%)

**Table 2**  
Summary of primary and secondary outcomes

No of conventional induction chemotherapy	Patients who achieved CR		
	One cycle (n=245)	Two cycles (n=61)	> 2 cycles (Primary Resistant AML) (n=7)
CR rate (%)	65.7	15.6	1.8
Duration of CR (days)			
Median	273	209	206
Range	(183 – 468)	(114 – 562)	(173 – 301)
Relapse rate (%)	42.4	40.9	85.7
Undergone hematopoietic stem cell transplantation (%)	56.3	60.7	85.7