Conclusions: Allogeneic transplantation with CD45 lymphocytes RA depletion resulted on encouraging results, with a very low incidence of acute and chronic GVHD, but preserving the GVL effect by infusing CD45 RA- donor lymphocytes.
Conflict of interest: Miguel Angel Diaz, Marta Gonzalez-Vicent, Blanca Molina, Elena Sebastian, Josune Zubicaray, Julian Sevilla: Nothing to disclose.
Keywords: CD45RA depletion, Allogeneic transplant, Children

289

Class I Graft-Versus-Host Mismatch Based on Predicted Indirectly Recognizable HLA Epitopes (PIRCHES) Is Associated with Worse Post-Transplant Outcomes in Patients Receiving Peripheral Blood, T-Cell Replete Haploidentical Hematopoietic Cell Transplantation with Post-Transplant Cyclophosphamide

***Joseph Rimando MD*[1]**, *Michael Slade MD, MSCI*[2], *Feng Gao MD*[3], *Rizwan Romee MD*[4], *Chang Liu MD, PhD*[5]. [1] *Department of Medicine, Washington University School of Medicine, St. Louis, MO;* [2] *Bone Marrow Transplantation & Leukemia Section, Division of Oncology, Washington University School of Medicine, St. Louis, MO;* [3] *Division of Public Health Sciences, Section of Oncologic Biostatistics, Department of Surgery, Washington University School of Medicine, St. Louis, MO;* [4] *Department of Hematologic Malignancies, Dana-Farber Cancer Institute and Harvard Medical School, Boston, MA;* [5] *Pathology and Immunology, Washington University School of Medicine, St. Louis, MO*

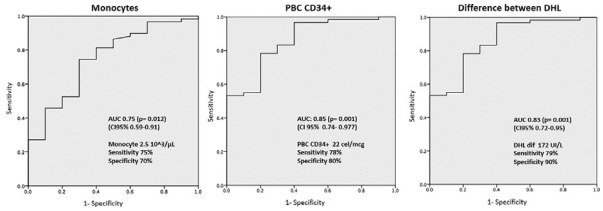
Introduction: High dose post-transplant cyclophosphamide has improved the outcomes and expanded the use of haploidentical hematopoietic cell transplantation (haplo-HCT). The impact of HLA disparity in this setting, however, is unclear and is traditionally measured at the antigen or allele level. The Predicted Indirectly Recognizable HLA Epitopes (PIRCHES) model provides a novel tool to calculate the number of mismatched HLA peptides between donor and host that can be processed and presented by shared HLA antigens for T cell recognition. No data exist on the relationship between PIRCHES mismatch and clinical outcome in haplo-HCT with post-transplant cyclophosphamide.
Methods: 148 patients who received a peripheral blood, T-cell replete haplo-HCT with post-transplant cyclophosphamide at a single center between 2009 and 2016 were retrospectively analyzed. The PIRCHES mismatch load was calculated using the PIRCHES matching tool online and was categorized by class and vector. The primary outcome was incidence of relapse. The association between PIRCHES mismatch and outcome was analyzed using the Cox proportional hazard model or Gray's subdistribution method for competing risk as appropriate. This study was approved by the Institutional Review Board.
Results: The median follow-up for survivors was 34.0 months (range, 14.5-78.3 months). One-hundred (67.6%) patients were deceased and 61 (41.2%) patients relapsed during follow-up. Class I graft-versus-host (GvH) PIRCHES mismatch had a median of 11 with a range of 0 to 56. Class II GvH PIRCHES mismatch had a median of 29 with a range of 0 to 122. Class I GvH PIRCHES mismatch was associated with worse acute graft-versus-host disease (aGvHD) (grades II-IV) (HR 1.021 per unit PIRCHES mismatch increase; 95% CI 1.001-1.040; p=0.036). Class I GvH PIRCHES mismatch was not associated with treatment-related mortality (TRM), but was associated with a trend towards worsened overall survival (OS) (HR 1.015 per unit PIRCHES mismatch increase; 95% CI 0.999-1.033; p=0.073). Class I host-versus-graft (HvG) PIRCHES mismatch was associated with worse relapse-free survival (RFS) (HR 1.018; 95% CI 1.001-1.035; p=0.036) and worse OS (HR 1.018; 95% CI 1.001-1.035; p=0.036) but not relapse. Class II PIRCHES mismatch was not associated with relapse, OS, RFS, TRM, or aGvHD. Both class I and II PIRCHES mismatch were not associated with chronic GvHD or engraftment.
Discussion: Class I GvH PIRCHES mismatch was associated with greater aGvHD and a trend towards worsened OS, while class I HvG PIRCHES mismatch was associated with worsened RFS and OS. Class II PIRCHES mismatch was not associated with outcomes and appears to be tolerated by this patient cohort. PIRCHES mismatch represents a novel strategy to predict clinical outcome in haplo-HCT. Further studies using registry data and prospective studies are needed to validate these findings.

290

Difference between Recollection Day and Basal DHL As a Predictor of Apheresis CD34+ Yield

***Paola Santana-Hernández MD*[1]**, *Andrés Gómez- De León MD*[1], *Perla Rocío Colunga-Pedraza MD*[1], *Rosario Salazar-Riojas MT*[1], *Mayra Judith Valdes-Galvan MT*[1], *David Gómez-Almaguer MD*[2]. [1] *Hematology, Hospital Universitario Dr. José Eleuterio González. Universidad Autónoma de Nuevo León, Monterrey, NL, Mexico;* [2] *Hematology, Universidad Autónoma de Nuevo León, Hospital Universitario "Dr. José Eleuterio González", Monterrey, NL, Mexico*

Introduction: The preapheresis peripheral blood CD34+ cell count (PBCD34) is the most important predictor of a good mobilization. Flow cytometry is not always immediately available in our country, therefore looking for another surrogate marker to predict CD34+ counts would be useful. Lactate dehydrogenase (LDH) has been correlated to higher PCBCD34.
Objective: We aim to investigate if LDH difference is a reliable tool to predict a poor mobilization in our patients.
Methods: We included all patients who receive an autologous transplant from January 2015 to September 2018. Demographic and laboratory characteristics were obtained, including complete blood count, preapheresis PBCD34 and DHL (table 1). Poor mobilization was defined as a final PBCD34+ count $<2 \times 10^6$/kg. The association between these parameters was assessed, Spearman's correlation was used and ROC curves calculated.
Results: Seventy four patients were included. Median age was 43 years (11-72 years), 48% female, diagnosis were 31 myeloma multiple, 19 non Hodgkin lymphoma, 7 Hodgkin disease, 17 others. An adequate yield of CD34+ cells/kg was collected in 64 patients (86%). Preapheresis PBCD34+ had a stronger correlation with the difference of recollection minus basal LDH (Rho = 0.44, p = 0.001) than with monocytes (Rho = 0.189, p = 0.119). The area under the curve for LDH difference was 0.83 (p = 0.001, CI95% 0.72-0.95) (figure 1).
Conclusion: LDH difference is a good predictor of poor mobilization, with the main advantage that is a fast, cheap and easy marker to perform. It would be useful particularly in centers with poor access to flow cytometry or where the CD34+ count is delayed.



	Good mobilizers	Poor mobilizers	p
Basal DHL	303 (160–592) UI/L	359 (199–501) UI/L	0.41
Apheresis day DHL	614 (169–2268) UI/L	455 (265–683) UI/L	0.006
Difference between DHLs	286 (–103–1925) UI/L	142 (–98–339) UI/L	0.001
PBCs CD34+	40.3 (1.38–3478) cel/µ	10.5 (0.73–37) cel/µ	< 0.001
WBC count	32 (3.4–58.8) x10³/µL	36 (0.34–109) x10³/µL	0.34
Monocytes	4.2 (0.13–13.9) x10³/µL	2.1 (0.37–5.7) x10³/µL	0.012
Lymphocytes	2.13 (0.1–7.2) x10³/µL	2.5 (0.6–4.1) x10³/µL	0.93

291

Differential Outcomes for *Ex Vivo* Versus *In Vivo* Alloreactive T-Cell Depletion Strategies in Haploidentical HSCT

Steve M. Devine[1], *Stephan Mielke MD*[2,3], *Eduardo Olavarria*[4], *Bert Tuk*[5], *Kees Meewisse*[6], *Andrew Sandler*[6], *Denis-Claude Roy*[7]. [1] *Center for International Blood and Marrow Transplant Research, Minneapolis, MN;* [2] *Karolinska Institutet and University Hospital, Stockholm, Sweden;* [3] *Hematology and Oncology, University Medical Center of Wuerzburg, Wuerzburg, Germany;* [4] *Hammersmith Hospital, Imperial College Healthcare NHS Trust, London, United Kingdom;* [5] *TCIM B.V., Willemstad, Netherlands;* [6] *Kiadis Pharma, Amsterdam, Netherlands;* [7] *Université de Montréal, Hôpital Maisonneuve-Rosemont, Montreal, QC, Canada*

Introduction: In haploidentical allogeneic hematopoietic stem cell transplantation (haplo-HSCT), different strategies are used to eliminate alloreactive T cells, one of which can be performed in vivo early after T-cell-replete haplo-HSCT using post-transplant cyclophosphamide (PTCy). Currently under development is T-cell-depleted haplo-HSCT supplemented with T-lymphocytes that are depleted ex vivo of their alloreactive component (ATIR101; Kiadis Pharma). Both strategies are promising, but comparisons of clinical outcomes obtained in similar patient populations have not been performed.

Methods: Data from published retrospective studies were analyzed to assess clinical outcomes of haplo-HSCT plus PTCy, and 1-year outcomes were compared with a pooled analysis of 2 phase II clinical trials of a single dose of ATIR101 in 37 AML/MDS/ALL patients. Studies in which PTCy was used in patient populations with >50% AML/MDS/ALL were identified (Table). The 1-year rates of relapse, relapse-related mortality (RRM), non-relapse mortality (NRM), graft-versus-host disease (GVHD), and overall survival (OS) for the ATIR101 clinical trials were compared with the weighted average of these outcomes for the identified studies. Differences in disease risk index (DRI) between PTCy and ATIR101 study populations were adjusted according to the relationship between DRI and OS. Finally, PTCy studies reporting GVHD-free and relapse-free survival (GRFS) were identified. One-year GRFS rates from 2 haplo-HSCT plus PTCy studies reporting DRI status were also normalized according to the DRI profile in the ATIR101 clinical trials to allow comparison.

Results: The weighted average of PTCy outcomes in populations with >50% AML/MDS/ALL vs ATIR101 patient outcomes were 29% vs 8% for relapse; 18% vs 8% for RRM; 22% vs 33% for NRM; 5% vs 5% for acute GVHD grade III/IV; 24% vs 3% for chronic GVHD; and 60% vs 58% for OS. The OS in DRI-adjusted studies for PTCy was similar to that in ATIR101 clinical trials (63% vs 58%, respectively, Table). One-year GRFS rates for PTCy were 33% (95% CI: 25–41) (Solh 2016), 45% (95% CI: 40–50) (McCurdy 2017), and 33% (average) (Santoro 2017). The DRI profile was more favorable than in the ATIR101 studies and the normalized 1-year GRFS rates were reduced to 30% (Solh 2016) and 40% (McCurdy 2017). In patients intended to receive a single dose of ATIR101 after haplo-HSCT, 1-year GRFS estimate was 53% (95% CI 39–72).

Conclusion: Although not a head-to-head comparison, these cross-study analyses provide first insights into a potential advantage of *ex vivo* (ATIR101) over *in vivo* (PTCy) depletion of alloreactive T cells, including but not limited to rates of relapse, chronic GVHD, and GRFS. A large, phase III, randomized control trial is underway to assess the relative safety and efficacy of ATIR101 after T-cell-depleted haplo-HSCT versus PTCy after T-cell-replete haplo-HSCT (CR-AIR-009 HATCY; NCT02999854).

Table 1
Safety and efficacy of alloreactive T-cell depletion performed *ex vivo* (ATIR101) after T-cell-depleted haplo-HSCT versus *in vivo* (PTCy) after T-cell-replete haplo-HSCT

Average, %	ATIR101 (Two phase II trials: CR-AIR-007 & CR-AIR-008; N=37)	PTCy (Ciurea 2015, Piemontese 2017, Solomon 2012, Ciurea 2012, Devillier 2015, Di Stasi 2014, Esquirol 2016, Sugita 2015; total N=571)
Relapse	8%	29%
RRM	8%	18%
NRM	33%	22%
aGVHD (grade III/IV)	5%*	5%
cGVHD	3%	24%
OS	58%	60%

	ATIR101 (Two phase II trials; N=37)	PTCy: adjusted for DRI (McCurdy 2017, Ciurea 2015, Devillier 2015, Sugita 2015; total N=561)
OS	58%	63%†

	ATIR101 (Two phase II trials; N=37)	PTCy		
		Solh 2016 (N=128)	McCurdy 2017 (N=372)	Santoro 2017 (N=208)
DRI	L: 0%; I: 57%; H: 43%	L: 19%; I: 39%; H: 40%	L: 14%; I: 67%; H: 19%	NA
One-year GRFS (95% CI)	53% (39–72)*	33% (25–41)	45% (40–50)	33%
Normalized 1-year GRFS‡	–	30%	40%	NA

aGVHD, acute graft-versus-host disease; cGVHD, chronic graft-versus-host disease; H, high and very high; I, intermediate; L, low; NA, not available. * All grade III aGHVD; † Adjusted according to the relationship between DRI and OS (Armand 2014); ‡ In patients intended to receive a single dose of ATIR101 after haplo-HSCT, Kaplan–Meier estimate of 1-year GRFS; ‡ Normalized according to the DRI profile in the ATIR101 clinical trials to allow comparison.

292

Double-Unit Cord Blood (CB) Transplantation (dCBT) Supplemented with Haplo-Identical CD34+ Cells May be Associated with Enhanced Neutrophil Recovery but Successful Myeloid Bridging Is Strongly Influenced By Haplo CD34+ Cell Dose and Haplo-Winning CB Unit HLA-Match

Ioannis Politikos MD[1], *Sean M. Devlin PhD*[2], *Christopher Mazis*[1], *Molly A. Maloy M.S.*[1], *Kristine Naputo*[1], *Aishat Afuye*[1], *Scott T. Avecilla MD, PhD*[3], *Hugo Castro-Malaspina MD*[1], *Parastoo B Dahi MD*[1], *Sergio A. Giralt MD*[2], *Craig S. Sauter MD*[1], *Michael Scordo MD*[1], *Brian C. Shaffer MD*[1], *Gunjan L. Shah MD, MS*[1], *Roni Tamari MD*[1], *Miguel-Angel Perales MD*[2], *Andromachi Scaradavou MD*[4,5], *Richard J. O'Reilly MD*[4], *Christina Cho MD*[1], *Boglarka Gyurkocza MD*[1], *Katharine C. Hsu MD, PhD*[1], *Ann A. Jakubowski MD, PhD*[1], *Esperanza B. Papadopoulos MD*[1], *Marcel R.M. van den Brink MD, PhD*[2], *James W. Young MD, FACP*[1], *Doris M. Ponce MD*[1], *Juliet N. Barker M.B.B.S (Hons), FRACP*[1]. [1] *Department of Medicine, Adult Bone Marrow Transplant Service, Memorial Sloan Kettering Cancer Center, New York, NY;* [2] *Memorial Sloan Kettering Cancer Center, New York, NY;* [3] *Department of Laboratory Medicine, Memorial Sloan Kettering Cancer Center, New York, NY;* [4] *Department of Pediatrics, Bone Marrow Transplant Service, Memorial Sloan Kettering Cancer Center, New York, NY;* [5] *New York Blood Center National Cord Blood Program, New York, NY*