https://doi.org/10.46765/2675-374X.2025v7n1e314 SHORT COMMUNICATION

Post-transplant cyclophosphamide-based graft-versus-host disease prophylaxis and its impact on allogeneic hematopoietic cell transplantation donor selection: a summary of the SBTMO/ABHI joint session at the 2025 SBTMO annual meeting

Alberto Cardoso Martins Lima[1,2*], Antonio Martin Jimenez-Jimenez[3], Celso Arrais Rodrigues da Silva[4,5], Adriana Seber[6,7,8], Raquel Aparecida Salustriano Fabreti de Oliveira[9,10], Margareth Afonso Torres[11], Carmem Bonfim[12]

1. Universidade Federal do Paraná – Complexo Hospital de Clínicas – Curitiba (PR), Brazil.
2. Associação Fundo de Incentivo à Pesquisa – Instituto de Imunogenética – São Paulo (SP), Brazil.
3. University of Miami – Miller School of Medicine – Sylvester Comprehensive Cancer Center – Miami (FL), USA.
4. Universidade Federal de São Paulo – Programa de Pós-Graduação: Medicina (Hematologia e Oncologia) – São Paulo (SP), Brazil.
5. Rede DASA – Hospital Nove de Julho – São Paulo (SP), Brazil.
6. Universidade Federal de São Paulo – Instituto de Oncologia Pediátrica – São Paulo (SP), Brazil.
7. Rede DASA – Hospital Samaritano – São Paulo (SP), Brazil.
8. Grupo de Apoio ao Adolescente e à Criança com Câncer – Instituto de Oncologia Pediátrica – São Paulo (SP), Brazil.
9. Imunolab – Laboratório de Histocompatibilidade – Belo Horizonte (MG), Brazil.
10. Faculdade de Ciências Médicas de Minas Gerais – Programa de Pós-Graduação em Ciências da Saúde – Belo Horizonte (MG), Brazil.
11. Hospital Israelita Albert Einstein – São Paulo (SP), Brazil.
12. Duke University – Pediatric Transplant and Cellular Therapy Division – Durham (NC), USA.

***Corresponding author:** acml@ufpr.br

Section editor: Fernando Duarte Barroso

Received: Nov. 20, 2025 • **Accepted:** Feb. 17, 2026

ABSTRACT

This brief communication summarizes the joint session of the Brazilian Cellular Therapy and Bone Marrow Transplantation Society (SBTMO) and the Brazilian Histocompatibility and Immunogenetics Association (ABHI), held during the 2025 SBTMO Annual Meeting. The joint session focused on how post-transplant cyclophosphamide (PTCy) is redefining donor selection in contemporary allogeneic hematopoietic cell transplantation (HCT). In three lectures with experts in the field, several topics concerning PTCy were addressed, including the effectiveness of PTCy in overcoming the HLA barrier, the increased use of mismatched unrelated donors (MMUD) under PTCy, which significantly broadens HCT access for underserved ethnic minorities, and strategies for reducing the dose of PTCy. The impact of donor-specific HLA antibodies in allogeneic HCT, the importance of HLA serotypes (associated antigens) in improving the accuracy of virtual crossmatch during MMUD searches, and the utility of novel bioinformatics tools to enhance serotype evaluation for MMUD selection under PTCy were also discussed. Additionally, the present report outlines the discussions among the speakers, session chairs, and audience members.

Keywords: Donor selection; Hematopoietic cell transplantation; Post-transplant cyclophosphamide; Alternative donors; Virtual crossmatch; Donor-specific HLA antibodies.

The 2025 joint session of the Brazilian Cellular Therapy and Bone Marrow Transplantation Society (Sociedade Brasileira de Terapia Celular e Transplante de Medula Óssea [SBTMO]) and Brazilian Histocompatibility and Immunogenetics Association (Associação Brasileira de Histocompatibilidade e Imunogenética [ABHI]) was held on August 22 at the 2025 SBTMO Annual Meeting and focused on the impact of post-transplant cyclophosphamide (PTCy)-based graft-versus-host disease (GVHD) prophylaxis in allogeneic hematopoietic cell transplantation (allo-HCT) donor selection. It included Dr. Antonio Jimenez-Jimenez from the Sylvester Comprehensive Cancer Center at the University of Miami, Dr. Celso Arrais Rodrigues from Hospital 9 de Julho and Universidade Federal de São Paulo, and Dr. Alberto Cardoso Martins Lima from Instituto de Imunogenética (IGEN)/Associação Fundo de Incentivo à Pesquisa and Complexo Hospital de Clínicas/Universidade Federal do Paraná. Dr. Adriana Seber, the current vice-president of the SBTMO, Dr. Raquel Fabreti, the current president of the ABHI, and Dr. Margareth Torres chaired the joint session.

In the first presentation, Dr. Jimenez provided a comprehensive overview of how PTCy has revolutionized allo-HCT by mitigating the detrimental impact of the HLA barrier, thereby expanding transplant access to historically underserved ethnic minorities[1] and attenuating the disparity in outcomes between matched unrelated donor (MUD) and mismatched unrelated donor (MMUD).[2] In this context, Dr. Jimenez presented a large retrospective Center for International Blood and Marrow Transplant Research (CIBMTR) cohort analysis showing that PTCy transplants had better outcomes than those with standard GVHD prophylaxis. Within the PTCy arm, 8/8 MUD and 7/8 MMUD transplants yielded similar overall survival (OS) and GVHD-free/relapse-free survival results.[2] He also described two prospective studies from the National Marrow Donor Program (NMDP)/CIBMTR, which used only HLA-mismatched MMUD (HLA < 7/8), with either bone marrow (15-MMUD trial) or peripheral blood (ACCESS trial) as graft sources.[3,4] Remarkably, both trials exhibited low rates of severe acute and chronic GVHD and excellent survival outcomes, despite using highly HLA-MMUD. Next, Dr. Jimenez briefly described the OPTIMIZE trial (NCT06001385), which will assess the effectiveness of a reduced dose of PTCy and the occurrence of infections in the first 100 days after transplant as the primary endpoint, and introduced the new ACCELERATE clinical trial (NCT06859424). Finally, he discussed that the classical "sequential" donor search should be replaced by a "concurrent" donor search strategy, in which all donors are evaluated simultaneously and guided by the search prognosis online tool (https://search-prognosis.b12x.org/).[5]

In the second presentation, Dr. Arrais shared his group's experience with PTCy across various donor sources. The lecture began with a complex clinical case in which haploidentical HCT was ruled out due to very strong donor-specific HLA antibodies (DSAs) (mean fluorescence intensity [MFI] > 20,000), and the only available donors were MMUDs with several HLA mismatches. He presented data from several landmark studies showing the remarkable impact of PTCy in decreasing severe acute and chronic GVHD and improving non-relapse mortality (NRM).[6-8] Next, Dr. Arrais presented his experience with PTCy's dose reduction from the standard dose (100 mg/kg) to a reduced dose (80 mg/kg) of PTCy.[9] In this retrospective analysis, 158 patients were assessed, and donors were haploidentical in most cases (72%). The standard PTCy dose was administered to 114 patients (72%). Remarkably, compared with the standard-dose group, the reduced-dose group showed higher OS, lower NRM, and similar relapse rates. A propensity score-matched analysis was conducted, confirming the superior outcomes observed in the reduced-dose group.[9] Finally, Dr. Arrais revisited the clinical case, indicating that the patient found an 8/10 MMUD without DSA and underwent allo-HCT using PTCy, with satisfactory post-HCT results.

In the third lecture, Dr. Lima discussed how HLA serotypes can enhance the accuracy of virtual crossmatch and, ultimately, optimize the selection of unrelated donors in the PTCy era. Dr. Lima showed that DSA is strongly associated with higher risks of graft failure and lower survival.[10,11] Thus, avoiding DSA is a primary selection criterion in the contemporary NMDP/CIBMTR donor selection guidelines.[5] The DSA testing using Single Antigen Beads panels, however, has limitations that can lead to false-negative virtual crossmatch results.[12] Indeed, a key limitation discussed was the HLA antigen composition of the Single Antigen Beads panels, which is particularly relevant in the context of the highly admixed Brazilian population.[13] Another drawback is that thousands of new HLA alleles identified by next-generation sequencing typing, many of which are non-common and well-documented, still lack defined serological equivalents,[14] which can severely compromise virtual crossmatch

assessment. To address these issues, a new nomenclature of HLA serotypes has been recently proposed[15] and validated.[16] Then, Dr. Lima explained the "determining epitopes" concept, the HLA Allele To Serotype software, and the HLA serotype designation.[15,16] He also presented two online tools (https://www.igen.org.br/marco/ and https://sorotipos18ws-v2.igen.org.br/en-US) created by IGEN's Bioinformatics Team to support the use of HLA serotypes in routine virtual crossmatch analysis for allo-HCT. Lastly, Dr. Lima presented two clinical cases of MMUD allo-HCT with PTCy, demonstrating that misleading virtual crossmatch results, with false-negative DSA assignment, can occur without detailed consideration of HLA serotypes and additional Single Antigen Beads testing.[12]

The chairs initiated the discussion with the audience, and the first question concerned the impact of B-leader matching on the selection of haploidentical donors.[17] Both speakers agreed that B-leader matching could be used as a tie-breaker when multiple young, DSA-negative haploidentical donors are available.[18] However, Dr. Lima cautioned that the B-leader model has been studied only in patients with acute leukemia and myelodysplastic syndrome, and its applicability should not be extended to other contexts (e.g., nonmalignant diseases).[17] Additionally, it was mentioned that a multicenter European Society for Blood and Marrow Transplantation (EBMT) study, involving patients with acute myeloid leukemia receiving peripheral blood stem cell grafts, failed to validate the B-leader utility.[19]

Likewise, it was asked whether non-inherited maternal antigens (NIMA) play a role in the selection of haploidentical donors. Dr. Lima and Dr. Torres emphasized that there is a paucity of data regarding NIMA in haploidentical transplants with PTCy[18]; therefore, this parameter should not be used for donor prioritization. In the context of haploidentical HCT with PTCy for nonmalignant diseases, specific donor characteristics may be more important depending on the patient's diagnosis (e.g., ABO matching is prioritized in sickle cell disease).[20]

The utility of C1q testing in allo-HCT was questioned,[21] and Dr. Lima highlighted that the literature shows that DSAs with MFI > 10,126 are highly predictive of C1q positivity, with an area under the curve of 0.99, 100% sensitivity, and 99% specificity.[22] He also mentioned that the high cost of this test limits its widespread use in Brazil. Subsequently, Dr. Jimenez mentioned that he uses C1q in his routine DSA assessment but avoids DSA whenever possible, regardless of whether the DSA is C1q-negative but still presents moderate to high MFIs (e.g., MFI ≈ 8,000). Dr. Lima and Dr. Torres stated their preference for using flow cytometry crossmatch with serial dilutions (titration) over C1q testing for DSA risk stratification in their HLA laboratories.[23]

Next, Dr. Arrais raised an interesting discussion about choosing a highly mismatched MMUD (< 5/8) with PTCy versus selecting a well-matched, high-dose umbilical cord blood unit (CBU). In response, Dr. Jimenez stated that he would prefer a highly mismatched MMUD rather than a CBU, citing his center's experience with MMUDs under PTCy. However, all speakers and panelists agreed that HLA-mismatched sources are helpful and that their use should be tailored to the patient's specific needs and the center's experience.[5] Dr. Arrais also asked Dr. Jimenez about the lowest HLA-mismatch degree used in his practice with MMUD with PTCy. Dr. Jimenez mentioned that a 4/8 MMUD had been employed with PTCy, resulting in positive post-HCT outcomes.[3,4] Of note, Dr. Adriana Seber highlighted that evidence on highly mismatched MMUD transplantation with PTCy in the pediatric setting remains scarce,[24] and MMUD cases are assessed on a case-by-case basis.[25]

Continuing the MMUD topic, Dr. Lima asked Dr. Jimenez about his perspective on the conflicting results between recent CIBMTR and EBMT registry studies evaluating HLA mismatching under PTCy-based prophylaxis.[2,26] Dr. Jimenez replied that the U.S. and European cohorts differed in several relevant characteristics (e.g., use of anti-thymocyte globulin, types of malignancies included, chronic GVHD definitions, etc.), which limit direct comparisons of the studies' findings. In addition, Dr. Lima inquired whether the impact of the peptide-binding motif (PBM) model would be studied in the ACCESS trial,[26,27] and Dr. Jimenez stated that details on HLA mismatching, including the PBM model, will be evaluated and provided in the ACCESS final trial report.

Dr. Torres emphasized that several common HLA alleles in the Brazilian population are not covered by the three commercially available Single Antigen Beads panels.[13] In her comment, she emphasized the necessity of 11-loci, high-resolution donor HLA typing when performing virtual crossmatch analysis in allo-HCT. She

also provided examples demonstrating how virtual crossmatch can be compromised if only HLA-A, -B, -DRB1, and -DQB1 at medium resolution are available.[12] Dr. Daniele Oliveira from REDOME Registry stated that providing DSA results for REDOME's requests can expedite the search process,[5] especially for patients who have experienced graft failure and are undergoing a MUD/MMUD search for a salvage transplant.

Concluding this discussion, Dr. Lima emphasized the importance of organizing a future webinar between ABHI, SBTMO, REDOME, and the General Coordination of the National Transplantation System to address the current challenges of virtual crossmatch in allo-HCT. This joint webinar is expected to discuss the shared responsibilities, required qualifications, and practical procedures to implement an effective virtual crossmatch strategy for MUD/MMUD selection in Brazil. Lastly, the chairs thanked the audience for their attendance and adjourned the joint session.

CONFLICTS OF INTEREST

Nothing to declare.

DECLARATION OF USE OF ARTIFICIAL INTELLIGENCE TOOLS

The authors declare that generative artificial intelligence tools were not used in the creation of the present manuscript.

FUNDING

Not applicable.

DATA AVAILABILITY STATEMENT

Not applicable.

AUTHORS CONTRIBUTION

Conceptualization: Lima ACM, Jimenez-Jimenez AM, Silva CAR, Seber A, Oliveira RASF, Torres MA, Bonfim C. **Writing:** Lima ACM, Seber A. **Supervision:** Bonfim C. **Final Approval:** Lima ACM, Jimenez-Jimenez AM, Silva CAR, Seber A, Oliveira RASF, Torres MA, Bonfim C.

ACKNOWLEDGEMENTS

Dr. Andresa Melo and Dr. Fernando Barroso Duarte are acknowledged for the initial discussion on the topic of the SBTMO/ABHI joint session. We also thank Tatiana Almeida, Igor Dias, and Valeria Duarte for organizing the logistics with the speakers.

REFERENCES

1. Chowdhury AS, Maiers M, Spellman SR, Deshpande T, Bolon YT, Devine SM. Existence of HLA-mismatched unrelated donors closes the gap in donor availability regardless of recipient ancestry. Transplant Cell Ther. 2023;29(11):686.e1-686.e8. https://doi.org/10.1016/j.jtct.2023.08.014
2. Shaffer BC, Gooptu M, DeFor TE, Maiers M, Bolaños-Meade J, Abboud R, et al. Post-transplant cyclophosphamide-based graft-versus-host disease prophylaxis attenuates disparity in outcomes between use of matched or mismatched unrelated donors. J Clin Oncol. 2024;42(28):3277-86. https://doi.org/10.1200/JCO.24.00184
3. Shaw BE, Jimenez-Jimenez AM, Burns LJ, Logan BR, Khimani F, Shaffer BC, et al. National Marrow Donor Program-sponsored multicenter, phase II trial of HLA-mismatched unrelated donor bone marrow transplantation using post-transplant cyclophosphamide. J Clin Oncol. 2021 Jun 20;39(18):1971-82. https://doi.org/10.1200/JCO.20.03502

4. Al Malki MM, Bo-Subait S, Logan B, Olson J, Kou J, Smith S, et al. Post-transplant cyclophosphamide-based graft-versus-host disease prophylaxis after mismatched unrelated donor peripheral blood stem cell transplantation. J Clin Oncol. 2025 Jun 16;JCO2500856. https://doi.org/10.1200/JCO-25-00856

5. Jimenez Jimenez AM, Spellman SR, Politikos I, McCurdy SR, Devine SM, Malki MMA, et al. Allogeneic hematopoietic cell donor selection: contemporary guidelines from the NMDP/CIBMTR. Transplant Cell Ther. 2025 Jul 5;31(12). https://doi.org/10.1016/j.jtct.2025.07.004

6. Battipaglia G, Labopin M, Kröger N, Vitek A, Afanasyev B, Hilgendorf I, et al. Posttransplant cyclophosphamide vs antithymocyte globulin in HLA-mismatched unrelated donor transplantation. Blood. 2019 Sep 12;134(11):892-9. https://doi.org/10.1182/blood.2019000487

7. Broers AEC, de Jong CN, Bakunina K, Hazenberg MD, van Marwijk Kooy M, de Groot MR, et al. Posttransplant cyclophosphamide for prevention of graft-versus-host disease: results of the prospective randomized HOVON-96 trial. Blood Adv. 2022 Jun 14;6(11):3378-85. https://doi.org/10.1182/bloodadvances.2021005847

8. Bolaños-Meade J, Hamadani M, Wu J, Al Malki MM, Martens MJ, Runaas L, et al. Post-transplantation cyclophosphamide-based graft-versus-host disease prophylaxis. N Engl J Med. 2023 Jun 22;388(25):2338-48. https://doi.org/10.1056/NEJMoa2215943

9. Araujo TFN de, Rocha LP dos S, Oliveira CF de, Ferreira C de F de M, Souza BA de, Puls ML, et al. Impact of reduced-dose of post-transplantation cyclophosphamide (PTCy) in HLA-identical and haploidentical hematopoietic stem cell transplantation: a retrospective analysis. Blood. 2024 Nov 5;144(Suppl 1):7324. https://doi.org/10.1182/blood-2024-211512

10. Xie Y, Parekh J, Tang Z, Wu D, Wu X. Donor-specific antibodies and primary graft failure in allogeneic hematopoietic stem cell transplantation: a systematic review and meta-analysis. Transplant Cell Ther. 2021 Aug;27(8):687.e1-687.e7. https://doi.org/10.1016/j.jtct.2021.04.030

11. Huang Y, Luo C, Wu G, Huang X, Ding Y, Huang Z, et al. Effects of donor-specific antibodies on engraftment and long-term survival after allogeneic hematopoietic stem cell transplantation: a systematic review and meta-analysis. Bone Marrow Transplant. 2023 May;58(5):544-51. https://doi.org/10.1038/s41409-023-01932-6

12. Sullivan HC, Jaramillo A, Gaitonde S, Murphey C, Pandey S, Liu C, et al. Virtual crossmatching: principles, practices, and the path forward – an American Society for Histocompatibility and Immunogenetics/College of American Pathologists collaborative. Am J Transplant. 2025 Jun 21;25(10). https://doi.org/10.1016/j.ajt.2025.06.018

13. da Silva JS, Visentainer JEL, Fabreti-Oliveira RA, de Souza FCB, Silva MNP, da Costa Sena A, et al. Common, intermediate and well-documented HLA alleles in the Brazilian population: an analysis of the Brazilian Bone Marrow Donor Registry (REDOME). HLA. 2025 Feb;105(2):e70051. https://doi.org/10.1111/tan.70051

14. Holdsworth R, Hurley CK, Marsh SGE, Lau M, Noreen HJ, Kempenich JH, et al. The HLA dictionary 2008: a summary of HLA-A, -B, -C, -DRB1/3/4/5, and -DQB1 alleles and their association with serologically defined HLA-A, -B, -C, -DR, and -DQ antigens. Tissue Antigens. 2009 Feb;73(2):95-170. https://doi.org/10.1111/j.1399-0039.2008.01183.x

15. Osoegawa K, Marsh SGE, Holdsworth R, Heidt S, Fischer G, Murphey C, et al. A new strategy for systematically classifying HLA alleles into serological specificities. HLA. 2022 Sep;100(3):193-231. https://doi.org/10.1111/tan.14662

16. Osoegawa K, Yim K, Jeracki M, Nguyen TN, Wang L, Cho A, et al. A new strategy for systematically classifying HLA alleles into serological specificities: update and refinement. HLA. 2024;104(4):e15702. https://doi.org/10.1111/tan.15702

17. Fuchs EJ, McCurdy SR, Solomon SR, Wang T, Herr MR, Modi D, et al. HLA informs risk predictions after haploidentical stem cell transplantation with posttransplantation cyclophosphamide. Blood. 2022 Mar 10;139(10):1452-68. https://doi.org/10.1182/blood.2021013443

18. Ciurea SO, Al Malki MM, Kongtim P, Fuchs EJ, Luznik L, Huang XJ, et al. The European Society for Blood and Marrow Transplantation (EBMT) consensus recommendations for donor selection in haploidentical hematopoietic cell transplantation. Bone Marrow Transplant. 2020 Jan;55(1):12-24. https://doi.org/10.1038/s41409-019-0499-z

19. Kharfan-Dabaja MA, Labopin M, Ayala E, Bazarbachi A, Blaise D, Vydra J, et al. Significance of degree of HLA disparity using T-cell replete peripheral blood stem cells from haploidentical donors with posttransplantation cyclophosphamide in AML in first complete hematologic remission: a study of the Acute Leukemia Working Party of the EBMT. HemaSphere. 2023 Jul;7(7):e920. https://doi.org/10.1097/HS9.0000000000000920

20. Kassim AA, de la Fuente J, Nur E, Wilkerson KL, Alahmari AD, Seber A, et al. An international learning collaborative phase 2 trial for haploidentical bone marrow transplant in sickle cell disease. Blood. 2024 Jun 20;143(25):2654-65. https://doi.org/10.1182/blood.2023023301

21. Kongtim P, Vittayawacharin P, Zou J, Srour S, Shaffer B, Shapiro RM, et al. ASTCT consensus recommendations on testing and treatment of patients with donor-specific anti-HLA antibodies. Transplant Cell Ther. 2024 Dec;30(12):1139-54. https://doi.org/10.1016/j.jtct.2024.09.005

22. Wiebe C, Gareau AJ, Pochinco D, Gibson IW, Ho J, Birk PE, et al. Evaluation of C1q status and titer of de novo donor-specific antibodies as predictors of allograft survival. Am J Transplant. 2017 Mar;17(3):703-11. https://doi.org/10.1111/ajt.14015

23. Bettinotti MP. Evolution of HLA testing for hematopoietic stem cell transplantation: importance of the candidate's antibody profile for donor selection. Hum Immunol. 2022;83(10):721-9. https://doi.org/10.1016/j.humimm.2022.04.012

24. Eyrich M, Schulze H. HLA matching in pediatric stem cell transplantation. Transfus Med Hemother. 2019;46(5):348-55. https://doi.org/10.1159/000502422

25. Doherty EE, Krance RA. Should posttransplant cyclophosphamide be considered standard of care for pediatric transplantation of acute leukemia? Hematology Am Soc Hematol Educ Program. 2023 Dec 8;2023(1):171-4. https://doi.org/10.1182/hematology.2023000522

26. Arrieta-Bolaños E, Bonneville EF, Crivello P, Robin M, Gedde-Dahl T, Salmenniemi U, et al. Human leukocyte antigen mismatching and survival in contemporary hematopoietic cell transplantation for hematologic malignancies. J Clin Oncol. 2024;42(28):3287-99. https://doi.org/10.1200/JCO.24.00582

27. Crivello P, Arrieta-Bolaños E, He M, Wang T, Fingerson S, Gadalla SM, et al. Impact of the HLA immunopeptidome on survival of leukemia patients after unrelated donor transplantation. J Clin Oncol. 2023 May 1;41(13):2416-27. https://doi.org/10.1200/JCO.22.01229