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CURRENT USE AND OUTCOMES OF HEMATOPOIETIC STEM CELL TRANSPLANTATION: BRAZILIAN SUMMARY SLIDES

Anderson João Simione¹, Heliz Regina Alves das Neves^{2,29}, Cinthya Corrêa da Silva³, Paula Moreira da Silva Sabaini⁴, Bruna Letícia da Silva Santos Geraldo⁵, Marcelo C. Pasquini⁶, Vergilio Antonio Rensi Colturato¹, Samir Kanaan Nabhan², Vanderson Geraldo Rocha⁷, Adriana Seber ^{5,8,9}, Alexandre Silvério¹⁰, Maria Claudia Rodrigues Moreira¹¹, George Maurício Navarro Barros⁴, Claudia Caceres Astigarraga¹², Liane Esteves Daudt¹³, Maria Cristina Martins de Almeida Macedo^{14,15,25}, Ricardo Chiattone⁹, Yana Augusta Sarkis Novis¹⁶, Juliana Folloni Fernandes^{3,17}, Volney Assis Lara Vilela¹⁸, Decio Lerner¹⁹, Rodolfo Daniel de Almeida Soares²⁰, Phillip Scheinberg²¹, Gustavo Machado Teixeira²², Celso Arrais-Rodrigues²³, Marcos Paulo Colella²⁴, Roberto Luiz da Silva²⁵, Vaneuza Araújo Moreira Funke^{2,29}, Afonso Celso Vigorito²⁴, Leonardo Javier Arcuri^{3,19}, Nelson Hamerschlak³, Jayr Schmidt Filho²⁶, Vinicius Campos de Molla²⁷, João Samuel de Holanda Farias²⁸, Ricardo Pasquini ^{2,29}, Carmem Maria Sales Bonfim³⁰, Abrahão Elias Hallack Neto³¹, Rodolfo Froes Calixto³², Monique Ammi³³, Luis Fernando Bouzas³⁴, Fernando Barroso Duarte³⁵

1Hospital Amaral Carvalho, Jaú, SP, 2 Hospital de Clínicas – Universidade Federal do Paraná, Curitiba, PR, 3 Hospital Israelita Albert Einstein, São Paulo, SP, 4 Barretos Cancer Hospital, Barretos, SP, 5 Associação da Medula Óssea, São Paulo - AMEO , SP, 6 International Blood and Marrow Transplant Research (CIBMTR) and Medical College of Wisconsin, Milwaukee, WI, USA, 7 Hospital das Clínicas da Universidade de São Paulo, São Paulo, SP, 8 Grupo de Apoio ao Adolescente e à Criança com Câncer, São Paulo, SP, 9 Hospital Samaritano, São Paulo, SP, 10 CEPON – Centro de Pesquisas Oncologicas, Florianópolis, SC, 11 Complexo Hospitalar de Niterói, Niterói, RJ, 12 Associação Hospitalar Moinhos de Ventos, Porto Alegre, RS, 13 Hospital de Clínicas de Porto Alegre, Porto Alegre, RS, 14 Hospital Leforte Liberdade SA, São Paulo, SP, 15 Biosana's, São Paulo, SP, 16 Sociedade Beneficente de Senhoras Hospital Sírio Libanês, São Paulo, SP, 17 ITACI - Instituto da Criança do Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, SP, 18 Instituto de Cardiologia do Distrito Federal – Unidade Pietro Albuquerque, Brasília, DF, 19 Instituto Nacional do Câncer (INCA), Rio de Janeiro, RJ, 20 Hospital Natal Center, Natal, RN, 21 Real e Benemérita Sociedade de Beneficência Portuguesa de São Paulo, São Paulo, SP, 22 Hospital das Clínicas da Universidade Federal de Minas Gerais, Belo Horizonte, MG, 23 Universidade Federal de São Paulo, São Paulo, SP, 24 Universidade Estadual de Campinas, Campinas, SP; 25 IBCC – Instituto Brasileiro de Controle de Câncer, São Paulo, SP, 26 A.C. Camargo Cancer Center, São Paulo, SP, 27 Centro De Pesquisa Clínica Hospital 9 De Julho, São Paulo, SP, 28 Hospital Erasto Gaertner, Curitiba, PR, 29 Hospital Nossa Senhora das Graças – Instituto Pasquini, Curitiba, PR 30 Hospital Pequeno Príncipe – Curitiba, PR, 31 Hospital Universitario da Universidade Federal de Juiz de Fora, Juiz de Fora, MG, 32 Real Hospital Português, Recife, PE, 33International Blood and Marrow Transplant Research (CIBMTR), Minneapolis, MN, USA, 34 Hospital Unimed Volta Redonda, Rio de Janeiro, RJ, 35 Hospital Universitário Walter Cantídio, Fortaleza, CE,

Correspondence to: Anderson João Simione - ambtmo.anderson@amaralcarvalho.org.br - registrobrasileiro@sbtmo.org.br

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ABSTRACT

The first HSCT program in Latin America started in 1979 at the Federal University Hospital (Curitiba, Paraná). Over the years, the number of centers performing transplants in the country increased, generating the need to know the results of this modality of treatment. Understanding the HSCT scenario in Brazil is still challenging since not all Brazilian centers report data to the Center for International Blood and Marrow Research (CIBMTR). Although it has been improving over the last years, infrastructure and trained data managers are still lacking. The partnership between the Brazilian Cellular Therapy and Bone Marrow Transplant Society (SBTMO) and the CIBMTR, allowed the return of Brazilian data registered in the CIB-MTR, through the Data Back to Center (DBtC), in a standardized and organized way. With this database it was possible to know the demographic data and the outcomes of transplants performed in Brazil. Between 2012 and 2021, complete information of 7,982 transplants were reported to the CIBMTR from 31 Brazilian transplant centers. The consolidation of the Hematopoietic Stem Cell Transplantation Brazilian Registry (HSCTBR) using CIBMTR infrastructure, allowed the Brazilian Summary slides development and update. Despite the difference in the number of cases and of follow-up time, the results in this study were similar to those presented in the US Summary Slides.

Keywords: Data Management. Hematopoietic Stem Cell Transplant. Research Report.

INTRODUCTION

Hematopoietic stem cell transplantation (HSCT) is a therapy that can be the only option for curing many malignant and non-malignant hematological diseases, as well as extending the survival of many patients¹. Brazil has a large HSCT program, with 126 teams in 86 transplant centers recognized by the Brazilian Ministry of Health.

The first national results on this treatment modality were published in 1985². In 1997, a Brazilian center took part for the first time in an international multicenter study³. Over the following years, some national multicenter studies were developed. Back then, the initiatives for the creation of the Hematopoietic Stem Cell Transplantation Brazilian Registry (HSCTBR) had already begun⁴.

Until the publication of the First Brazilian Summary Slides in 2021⁵, the Brazilian Association of Organ Transplants (ABTO), created in 1995, was the only source of information about the number of Brazilian HSCT performed every year. According to ABTO, 3,826 transplants were performed in 2021: 1,547 allogeneic and 2,279 autologous⁶.

According to the CIBMTR, a total of 295,682 autologous and 287,972 related and unrelated allogeneic transplants were reported around the world between 1970 and 2021⁷. Despite the existence of the first summary slides⁸, the HSCT scenario in Brazil is still challenging, because not all Brazilian centers report data to the CIBMTR and there is a lack of infrastructure and trained data managers (DM). Therefore, over the years, through a working group composed of physicians and DM and with the collaboration of the CIBMTR and the SBTMO, strategies such as continuing education in data management and communication channels were developed to support DM and centers in affiliation process. These actions favor the increasing numbers of registered and active Brazilian centers in the CIBMTR⁹.

The partnership between SBTMO and CIBMTR allowed access through the tools available in the registry, such as the DBtC, which allows the return of the data sent by the Brazilian transplant centers to CIB-MTR. Part of the data inserted can return to the centers registered in a standardized and codified way, allowing the analysis of the outcomes of transplants performed in the country. The consolidation of the HSCTBR using CIBMTR infrastructure and the accessibility to these data is fundamental for public health administration.

OBJECTIVE

Our objective is to understand the demographic data and the outcomes of transplants performed in Brazil using the DBtC tool to retrieve the data registered in the CIBMTR in a standardized and organized way. Furthermore, make the data available to HSCT centers and maintain a routine to update the results.

METHODS

Data from 8,197 transplants performed between 2012 and 2021 were extract from the CIBMTR portal using the DBtC, with information from transplanted patients in 31 Brazilian centers that sent their data to the CIB-MTR. However, only 7,982 transplants had completed data for analysis (3,459 autologous and 4,523 allogeneic). For this reason, this was the total of HSCT considered in the analyses. The spreadsheet was imported into Power BI Desktop (PBI). Functions were updated to count the number of transplants performed and the number of participating centers, to translate some columns into Portuguese, to categorize disease classification, to group variables, and for calculating global survival analyses, and sheet relationships.

Patients were classified in pediatric (0-17 years of age) and adults (\geq 18 years of age). Allogeneic transplants were categorized as matched related donor, mismatch related donor (including haploidentical and related donors with one mismatch), and unrelated donor. Grafts were classified as Bone Marrow (BM), Peripheral Blood Stem Cells (PBSC) and umbilical cord blood (CB). The disease stage for acute leukemias was classified as 1st remission, 2nd or further remission and patients who underwent HSCT with active disease.

Patients with Myelodysplastic Syndrome (MDS) were divided into Early Stage, which is subdivided into refractory anemia (RA); refractory anemia with ring sideroblasts (RARS); refractory cytopenia with multilineage dysplasia (RCMD); and with MDS with del(5q) alone, or Advanced Stage, including refractory anemia with excess blasts (RAEB) and Chronic Myelomonocytic Leukemia (CMML). Patients with Lymphoma were categorized as chemosensitive and chemoresistant disease by the response to treatment prior to HSCT.

The classification of conditioning was based on the agents and doses used, Myeloablative Conditioning (MAC) for patients who received total body irradiation (TBI) \geq 500 cGy in a single dose or >800 cGy in fractionated doses; busulfan >9 mg/kg oral or \geq 7.2 mg/kg IV or melphalan >150 mg/m² as a single agent or in combination with other drugs. The other conditionings that did not fill the criteria for MAC were classified as Reduced Intensity/Non-Myeloablative (RIC/NMA)^{10,11}. The causes of death were classified using the standard classification from DBtC. The main causes of death between 2017-2021 were separated between deaths 0-100 days and deaths >100 days up to 3 years after HSCT. For the analysis

of overall survival (OS), patients who underwent 1st HSCT were selected, and those who were without follow-up update after transplantation or had error in survival time were excluded (table 1).

The charts were generated in the PBI and exported to PowerPoint for publication. Global survival analyses were performed by the Kaplan Meier method (Comparison between groups by long-rank test) using the R program (Version 4.1.0).

The use of this data was ethically enabled by the national Institutional Review Board (IRB) approval in 2019 (Conep CAAE: 65575317.5.1001.0071, principal investigator Dr. Nelson Hamerschlak).

RESULTS

Between 2012 and 2021, 7,982 transplants were reported from 31 transplant centers in Brazil (table 2), 16 (52%) located in the state of São Paulo; 4 in Paraná, 2 in Rio de Janeiro; 2 in Rio Grande do Sul; 2 in Minas Gerais and 1 center in each state: Ceará, Distrito Federal, Rio Grande do Norte, Pernambuco and Santa Catarina.

The number of CIBMTR active centers keeps increasing along the last years, reaching 26 active centers in 2020 (figure 1), which have contributed to the increase in the total number of Brazilian transplants registered in the CIBMTR since 2016, reaching 1,177 transplants in 2019. However, there was a decrease in the number of HSCT registered in 2020 and 2021, because of the Sars-CoV-2 pandemic (figure 2).

Between 2012 and 2021, 43.2% of the allogeneic transplants performed in Brazil used a matched related donor, followed by an unrelated donor (31.2%), and a mismatch related donor (25.6%). In the last 2 years, the main type of allogeneic transplant performed in the country used a mismatched related donor (figure 3).

Regarding the graft source for allogeneic transplants, BM was used in most pediatric transplants, while in adults the main source was PBSC from 2018 on (table 3).

Mismatched related donors were used to treat acute myelogenous leukemia (AML; 30.2%), followed by non-malignant diseases (25.7%) and acute lymphoblastic leukemia (ALL; 23.1%); 50.6% of them used MAC and 49.4% used RIC/NMA.

The main global indications for HSCT in Brazil between 2019-2021 were Multiple Myeloma (861; 26%), followed by AML (536, 16%), ALL (405; 12%), non-Hodgkin lymphoma (NHL; 383; 11%) and Hod-gkin disease (HD; 336; 10%) (figure 4). In pediatric allogeneic HSCT, the main diseases were ALL (36%), other Non-Malignant (22%) and AML (18%). In adults, the main indications for allogeneic transplants were AML (35%), ALL (18%) and MDS (11%).

Acute leukemias continue to be the main indication for allogeneic transplantation, but from 2016 on, there was an increase in indications for MDS/MPN and Lymphomas. The main indications for autologous HSCT remain Multiple Myeloma and Lymphomas.

In patients with acute leukemias, 50.5% of those with AML and 46.7% with ALL were in the 1st remission. Most HSCT were from matched related donor in both AML (48.4%), as well as in ALL (38.5%) (table 4).

Infections were the leading cause of death in the first 100 days after all transplants: autologous (68%), matched related donor (54%), unrelated donor (57%), and mismatch related donor (61%). The most common cause of death more than 100 days after HSCT was the primary disease: autologous (67%), matched related donor (46%), unrelated donor (43%) and mismatch related donor (49%).

For the analysis of OS, the median follow-up was 23 months in allogeneic and 13 months in autologous HSCT. Patients with acute leukemia who underwent transplantation with advanced stage had lower survival rates compared to the other stages (table 5).

Adults had a better survival after HSCT from matched sibling donors when having HSCT for AML (p=0.085; figure 5) and ALL (p=0.008; figure 6), but donor source had no impact in pediatric patients with acute leukemias.

The 2-year survival for MDS was similar despite disease risk and donor source (figure 7). Patients with CML had a 2-year OS of 60.4% with a matched related donor, 51.0% with a mismatch related donor and 60.5% with an unrelated donor (p=0.712) (figure 8). Patients with Myelofibrosis had a survival of 61.4% in 2 years (figure 9). Donor source had no impact in children with Aplastic Anemia, different from adults who had a better survival after HSCT from matched sibling donors (p=0.002) (figure 10).

Patients undergoing autologous HSCT to treat chemosensitive Lymphomas had a significantly better 2-year OS than chemoresistant disease: 88.2% versus 74.7% in HD (p=0.038) and 75.3% versus 52.8% in NHL (p<0.001) (figure 11). In Multiple Myeloma, the 2-year OS was 82.0% (figure 12).

DISCUSSION

Our study, using DBtC data, demonstrated a greater number of allogeneic than autologous transplants reported to the CIBMTR, but according to ABTO there is a greater number of autologous transplants in the country. The explanation for this difference is due to the larger number of affiliated centers in the CIBMTR that perform allogeneic transplants.

We observed an increase in the number of transplants with mismatch related donor since 2012, and a decrease in unrelated CB transplants in the same period, probably due to the use haploidentical donors with cyclophosphamide after transplantation.

Comparing our data with the American summary slides published in the CIBMTR website¹², the matched related donor is the main type of transplants performed in Brazil, while in the United States (USA), it is unrelated BM/PBSC.

In pediatric patients, the main source was BM in Brazil, following the same trend in the USA; in adult, while in Brazil the use of PBSC has been increased over the years and has become the main source used since 2018, in the three modalities of allogeneic donors, in the USA the main source was PBSC since 2000.

In Brazil, in recent years, the main indications for HSCT were MM, AML, ALL, NHL, and HD, while in the USA in 2020 were MM, AML, NHL, MDS/MPN and ALL.

Another important comparison was the cause of early death, 0 to 100 days after transplantation: in Brazil, the main cause of early mortality was infection for autologous, matched related donor, mismatch related and unrelated donors, while in the USA, it was the primary disease for autologous and unrelated donors, and organ failure to matched and mismatch related donor.

Comparing the 2-year OS in our study with the 3-year OS in the US Summary Slides, the Brazilian data is similar to the survival rates reported by American centers (table 6), despite the socioeconomical differences.

The Brazilian Summary slides can be fully accessed by active centers in the HSCTBR, through the SBTMO data request flow (figure 13).

4

CONCLUSION

The partnership between SBTMO and CIBMTR made the HSCTBR possible through the availability of the DBtC. The analysis of the data from Brazil, allowed us to develop a Brazilian Summary Slides to better understand the transplants outcomes, making them available to centers as a national and international benchmarking. The Brazilian Summary is updated twice a year and published at the SBTMO website. Despite the difference in the number of cases and follow-up time, the results in this study were similar to those presented in the US Summary Slides.

The initiatives for the HSCTBR consolidation had positive results, such as the increase in the number of Brazilian centers affiliated to the CIBMTR and the qualification of DM. However, there is still a lot to be done. It is necessary to upgrade the commitment of the HSCT centers, in order to improve the registry of transplants, the accomplishment of long-term follow-up and the DM continuing education, stimulating the data quality improvement in the national registry. It is also essential to receive the support of the government (resources, infrastructure and qualification). The union of strength and perseverance will allow the consolidation of the HSCTBR, allowing the provision of better care to patients.

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REFERENCES

- Kanate AS, Majhail NS, Savani BN, et al. Indications for Hematopoietic Cell Transplantation and Immune Effector Cell Therapy: Guidelines from the American Society for Transplantation and Cellular Therapy. Biol Blood Marrow Transplant. 2020;26(7):1247-56. doi: 10.1016/j. bbmt.2020.03.002.
- 2 Ferreira E, Dulley FL, Morsoletto F, et al. Bone marrow transplantation in Brazil. Hum Immunol. 1985;14(3):324-32. doi: 10.1016/0198-8859(85)90240-x.
- 3- Gluckman E, Rocha V, Boyer-Chammard A, et al. Outcome of cord-blood transplantation from related and unrelated donors. Eurocord Transplant Group and the European Blood and Marrow Transplantation Group. N Engl J Med. 1997;337(6):373-81. doi: 10.1056/ NEJM199708073370602.
- 4 SBTMO. Reportar é preciso: em webinar, SBTMO apresenta novos dados do Registro Multicêntrico Brasileiro de TCTH [Internet]. Rio de Janeiro; 2022 [cited 2022 Jul 7]. Available from: https:// sbtmo.org.br/reportar-e-preciso-em-webinar-sbtmo-apresenta-novos-dados-do-registro-multicentrico-brasileiro-de-tcth/.
- 5 Simione AJ, Neves HR, Silva CC, et al. Current use and outcomes of hematopoietic stem cell transplantation: The first Brazilian summary slides. JB-MTCT. 2021;2(2):p99. doi: 10.46765/2675-374X.2 021v2n2p99.
- 6 ABTO. Dimensionamento dos transplantes no Brasil e em cada estado [Internet]. São Paulo; 2022 [cited 2022 Jul 7]. Available from: https:// site.abto.org.br/publicacao/xxvii-no-4/
- 7 CIBMTR. FACTS AND FIGURES July 2020 June 2021 [internet]. Milwaukee: Medical College of

Wisconsin; 2021 [cited 2022 Jul 7]. Available from: https://www.cibmtr.org/About/Admin-Reports/Documents/Facts%20and%20Figures%202021%20FINAL.pdf

- 8 Simione AJ, Neves HR, Silva CC, et al. Use of a Business Intelligence Tool for Multicentric Analysis in Hematopoietic Stem Cell Transplantation in Brazil with Data Extracted from the Data Back to Center – CIBMTR. Transplant Cell Ther. 2021;27(3):S101–3. doi: 10.1016/S2666-6367(21)00131-7
- 9 Silva CC, Neves HR, Simione AJ, et al. Challenges and strategies used to increase the report of Brazilian Hematopoietic Stem Cell Transplantation (HSCT) data to the Center for International Blood and Marrow Transplant Research (CIBMTR). JBMTCT. 2020;1(1):46–52. doi: 10.46765/2675-374X.2020v1n1p46-52.

- 10 Bacigalupo A, Ballen K, Rizzo D, et al. Defining the intensity of conditioning regimens: working definitions. Biol Blood Marrow Transplant. 2009;15(12):1628-33. doi: 10.1016/j. bbmt.2009.07.004
- 11 Giralt S, Ballen K, Rizzo D, et al. Reduced-intensity conditioning regimen workshop: defining the dose spectrum. Report of a workshop convened by the center for international blood and marrow transplant research. Biol Blood Marrow Transplant. 2009;15(3):367-9. doi: 10.1016/j. bbmt.2008.12.497.
- 12 Phelan, R., Arora, M., Chen, M. Current use and outcome of hematopoietic stem cell transplantation: CIBMTR summary slides, 2020 [Internet]. Milwaukee: Medical College of Wisconsin; 2021 [cited 2022 Jul 7]. Available from: http://www.cibmtr.org

TABLE 1. Exclusion criteria for overall survival

Exclusion criteria	n
Patients without follow-up update	1,186
Error in survival time	34
2 nd HSCT or more	706

TABLE 2. HSCT centers

Participants Centers
A.C. Camargo Cancer Center
Albert Einstein Hospital
Associação Hospitalar Moinhos de Vento
Bio Sana's Serviços Médicos
Bio Sana's São Camilo
Centro De Pesquisa Clinica Hospital 9 De Julho
Centro de Pesquisas Oncológicas Dr. Alfredo Daura Jorge (CEPON)
Complexo Hospitalar de Niterói
CTMO-HCFMUSP
Fundação Pio XII - Hospital de Câncer de Barretos
Hospital Amaral Carvalho
Hospital de Clínicas - UFPR
Hospital de Clínicas de Porto Alegre
Hospital Erasto Gaertner
Hospital Leforte Liberdade
Hospital Nossa Senhora das Graças - IP
Hospital Pequeno Príncipe
Hospital Samaritano
Hospital Sírio Libanês
Hospital Universitario da Universidade Federal de Juiz de Fora
Hospital Universitário Walter Cantídio/UFC
Instituto da Criança - Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo (ITACI)
Instituto de Cardiologia do Distrito Federal - Unidade de TMO Pietro Albuquerque
Instituto de Oncologia Pediátrica - GRAACC
Instituto Nacional de Câncer
Natal Hospital Center
Real e Benemérita Sociedade de Beneficiência Portuguesa de São Paulo
Real Hospital Português
UFMG Hospital das Clínicas Servico de Transplante de Medula Óssea
UNICAMP - HEMOCENTRO
Universidade Federal de São Paulo - Hospital São Paulo

	2012	2013	2014	2015	2016	2017	2018	2019	2020	202
Patients <18 Yes	ars									
Matched R	Related Do	nor								
PBSC	2%	4%	2%	3%	9%	5%	9%	8%	3%	15%
BM	89%	80%	93%	94%	91%	93%	83%	90%	97%	85%
CB	9%	16%	5%	3%	0%	2%	8%	2%	0%	0%
Unrelated 1	Donor									
PBSC	5%	3%	16%	13%	8%	8%	12%	4%	26%	28%
BM	55%	74%	78%	74%	84%	87%	80%	88%	70%	62%
CB	40%	23%	6%	13%	8%	5%	8%	8%	4%	10%
Mismatch	Related D	onor								
PBSC	24%	10%	28%	14%	29%	22%	33%	26%	23%	22%
BM	76%	90%	72%	86%	71%	78%	67%	74%	77%	78%
Patients ≥18 Ye	ars									
Matched R	Related Do	onor								
PBSC	49%	47%	43%	52%	46%	53%	53%	56%	64%	65%
BM	51%	53%	57%	48%	54%	47%	47%	44%	36%	35%
CB	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
Unrelated 1	Donor									
PBSC	40%	31%	39%	53%	50%	47%	58%	55%	57%	80%
BM	43%	62%	61%	43%	50%	53%	42%	44%	39%	20%
CB	17%	7%	0%	4%	0%	0%	0%	1%	4%	0%
Mismatch	Related D	onor								
PBSC	18%	33%	40%	36%	40%	42%	59%	67%	74%	73%
BM	82%	67%	60%	64%	60%	58%	41%	33%	26%	27%

TABLE 3. Source of cells used by donor type, age and year of HSCT

TABLE 4. Acute Leukemia by disease stage, donor type and HSCT year

	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
ML										
Disease Stage										
1 st complete remission	36%	46%	48%	45%	59%	50%	52%	55%	52%	55%
2 nd or subsequent complete remission	36%	26%	38%	41%	31%	30%	29%	25%	31%	25%
Relapsed disease/Never in CR	28%	28%	14%	14%	10%	20%	19%	20%	17%	20%
Donor Type										
Matched Related Donor	51%	58%	68%	48%	50%	50%	48%	46%	44%	38%
Mismatch Related Donor	16%	7%	8%	17%	22%	23%	29%	29%	40%	46%
Unrelated Donor (BM/PBSC)	28%	26%	20%	34%	28%	27%	22%	25%	16%	15%
Unrelated Donor (CB)	5%	9%	4%	1%	0%	0%	1%	0%	0%	1%
LL										
Disease Stage										
1 st complete remission	45%	42%	52%	59%	53%	42%	51%	39%	41%	46%
2 nd or subsequent complete remission	51%	52%	40%	40%	37%	50%	34%	48%	49%	44%
Relapsed disease/Never in CR	4%	6%	8%	1%	10%	8%	14%	13%	10%	10%
Donor Type										
Matched Related Donor	44%	56%	50%	45%	42%	37%	38%	31%	33%	26%
Mismatch Related Donor	7%	2%	3%	7%	15%	26%	26%	29%	40%	51%
Unrelated Donor (BM/PBSC)	31%	34%	46%	42%	42%	37%	34%	35%	25%	22%
Unrelated Donor (CB)	18%	8%	1%	6%	1%	1%	2%	5%	2%	1%

TABLE 5. Overall survival of AML/ALL patients

	N	OS in 2 years (%)	р		Ν	OS in 2 years (%)	р
AML				ALL			
Patients Age 0-17 Years				Patients Age 0-17 Years			
Donor Type				Donor Type			
Matched Related Donor	69	48,9% (35,0-61,4)		Matched Related Donor	105	60,4% (48,9-70,2)	
Mismatch Related Donor	56	63,3% (45,3-76,7)	0.440	Mismatch Related Donor	93	46,1% (32,6-58,6)	0.149
Unrelated Donor	70	55,7% (42,2-67,2)		Unrelated Donor	208	60,7% (53,0-67,5)	
Patients Age ≥18 Years				Patients Age ≥18 Years			
Donor Type				Donor Type			
Matched Related Donor	439	54,6% (49,3-59,5)		Matched Related Donor	260	57,0% (50,2-63,2)	
Mismatch Related Donor	188	43,2% (33,2-52,9)	0.085	Mismatch Related Donor	110	47,4% (35,7-58,2)	0.008
Unrelated Donor	187	53,3% (45,0-60,9)		Unrelated Donor	143	44,0% (34,8-52,7)	
Matched Related Donor				Matched Related Donor			
Patients Age 0-17 Years				Patients Age 0-17 Years			
Disease Stage				Disease Stage			
1st complete remission	34	54,4% (33,7-71,2)		1st complete remission	32	71,9% (52,9-84,3)	
2nd or subsequent complete remission	23	50,6% (27,0-70,2)	0.756	2nd or subsequent complete remission	58	51,9% (36,1-65,5)	0.405
Relapsed disease/Never in CR	12	-		Relapsed disease/Never in CR	15	-	
Patients Age ≥18 Years				Patients Age ≥18 Years			
Disease Stage				Disease Stage			
1st complete remission	294	63,7% (57,4-69,3)		1st complete remission	194	66,0% (58,2-72,6)	
2nd or subsequent complete remission	82	37,2% (25,0-49,4)	< 0.001	2nd or subsequent complete remission	54	30,1% (17,5-43,8)	< 0.001
Relapsed disease/Never in CR	63	31,0% (18,4-44,4)		Relapsed disease/Never in CR	12	-	
Mismatched Related Donor				Mismatched Related Donor			
Patients Age 0-17 Years				Patients Age 0-17 Years			
Disease Stage				Disease Stage			
1st complete remission	20	74,8% (45,4-89,9)		1st complete remission	17	75,5% (46,9-90,1)	
2nd or subsequent complete remission	25	70,3% (40,6-87,1)	0.992	2nd or subsequent complete remission		42,7% (27,7-57,0)	0.232
Relapsed disease/Never in CR	11	-		Relapsed disease/Never in CR		-	
Patients Age ≥18 Years				Patients Age ≥18 Years			
Disease Stage				Disease Stage			
1st complete remission	107	49,0% (34,4-62,1)		1st complete remission	65	57,2% (41,7-69,9)	
2nd or subsequent complete remission	53	47,1% (30,6-62,0)	0.003	2nd or subsequent complete remission	38	39,3% (21,0-57,1)	0.233
Relapsed disease/Never in CR	28	10,5% (0,8-35,0)		Relapsed disease/Never in CR	7	-	
Unrelated Donor				Unrelated Donor			
Patients Age 0-17 Years				Patients Age 0-17 Years			
Disease Stage				Disease Stage			
1 st complete remission	28	73,1% (48,4-87,3)		1st complete remission	62	73,7% (59,9-83,4)	
2nd or subsequent complete remission	26	59,3% (37,1-75,8)	0.133	2nd or subsequent complete remission	127	57,1% (47,2-65,8)	0.021
Relapsed disease/Never in CR	16	-		Relapsed disease/Never in CR	19	-	
Patients Age ≥18 Years				Patients Age ≥18 Years			
Disease Stage				Disease Stage			
1st complete remission	73	67,7% (53,9-78,2)		1st complete remission	84	48,0% (35,9-59,2)	
2nd or subsequent complete remission	77	55,6% (42,8-66,7)	< 0.001	2nd or subsequent complete remission	49	40,3% (25,6-54,5)	0.233
Relapsed disease/Never in CR	37	18,3% (6,4-35,1)		Relapsed disease/Never in CR	10	-	

TABLE 6. Comparison overall survival – Brazil and USA

	Brazilian N	Registry (2012-2021) OS in 2 years (%)	US Summary Slides (2009-2019) N OS in 3 years (%)		
AML Matched Related Donor					
Patients Age 0-17 Years Disease Stage					
1 st complete remission	34	54.4% (33-71)	391	69% (65-74)	
2nd or subsequent complete remission	23	50.6% (27-70)	133	68% (60-77)	
Relapsed disease/Never in CR Patients Age ≥18 Years	12	-	75	30% (21-43)	
Disease Stage 1st complete remission	294	63.7% (57-69)	5,317	58% (57-60)	
2nd or subsequent complete remission	82	37.2% (25-49)	1,226	54% (51-57)	
Relapsed disease/Never in CR	63	31.0% (18-44)	1,721	31% (29-33)	
Unrelated Donor					
Patients Age 0-17 Years					
Disease Stage 1st complete remission	28	73.1% (48-87)	368	66% (61-71)	
2nd or subsequent complete remission	26	59.3% (37-75)	212	64% (57-71)	
Relapsed disease/Never in CR	16	-	118	34% (26-44)	
Patients Age ≥18 Years					
Disease Stage	73	67 70/ (52 70)	7.441	560/ (55 57)	
1 st complete remission 2nd or subsequent complete remission	73	67.7% (53-78) 55.6% (42-66)	7,441 1,940	56% (55-57) 54% (52-57)	
Relapsed disease/Never in CR	37	18.3% (6-35)	2,463	31% (30-33)	
Mismatched Related Donor Patients Age 0-17 Years		(,			
Disease Stage					
1 st complete remission 2nd or subsequent complete remission	20 25	74.8% (45-89) 70.3% (40-87)	172 99	63% (56-72) 61% (51-73)	
2nd or subsequent complete remission Relapsed disease/Never in CR	25	70.3% (40-87)	99 71	61% (51-73) 37% (27-50)	
Patients Age ≥18 Years	11	-	71	5770 (27-50)	
Disease Stage					
1st complete remission	107	49.0% (34-62)	1,977	53% (50-55)	
2nd or subsequent complete remission	53	47.1% (30-62)	572	55% (51-60)	
Relapsed disease/Never in CR	28	10.5% (0,8-35)	706	28% (25-32)	
Matched Related Donor Patients Age 0-17 Years					
Disease Stage					
1 st complete remission 2nd or subsequent complete remission	32 58	71.9% (52-84) 51.9% (36-65)	317 464	79% (74-84) 70% (66-74)	
Relapsed disease/Never in CR	15	-	38	57% (43-76)	
Patients Age ≥18 Years				()	
Disease Stage					
1 st complete remission	194	66.0% (58-72)	2,302	64% (62-66)	
2nd or subsequent complete remission	54 12	30.1% (17-43)	640 249	45% (41-49)	
Relapsed disease/Never in CR Unrelated Donor Patients Age 0-17 Years	12	-	249	37% (31-44)	
Disease Stage					
1 st complete remission	62	73.7% (59-83)	312	80% (75-84)	
2nd or subsequent complete remission	127	57.1% (47-65)	421	64% (60-69)	
Relapsed disease/Never in CR	19	-	40	68% (54-84)	
Patients Age ≥18 Years Disease Stage					
1 st complete remission	84	48.0% (35-59)	2,425	64% (62-66)	
2nd or subsequent complete remission	49	40.3% (25-54)	765	46% (43-50)	
Relapsed disease/Never in CR	10	-	253	36% (30-42)	
Mismatched Related Donor					
Patients Age 0-17 Years Disease Stage					
1st complete remission	17	75.5% (46-90)	137	75% (67-83)	
2nd or subsequent complete remission	67	42.7% (27-57)	233	63% (57-70)	
Relapsed disease/Never in CR	9	-	23	28% (14-57)	
Patients Age ≥18 Years					
Disease Stage		55 004 (41 60)		(00) ((5 50)	
1 st complete remission 2nd or subsequent complete remission	65 38	57.2% (41-69) 39.3% (21-57)	771 344	69% (65-73) 47% (42-54)	
Relapsed disease/Never in CR	7	-	99	28% (20-39)	
MDS (Adults)	,			2010 (20 55)	
Matched Related Donor					
Disease Stage					
Low risk	91	58,9% (47-68)	677	52% (48-56) 46% (44-49)	
High risk Unrelated Donor	90	55,8% (43-66)	1,693	46% (44-49)	
Disease Stage					
Low risk	43	52,3% (35-66)	1,133	49% (46-52)	
High risk	40	43,1% (25-59)	2,997	46% (44-48)	
Aplastic Anemia Patients Age 0 17 Veers					
Patients Age 0-17 Years Donor type					
Matched Related Donor	54	80,8% (67-89)	504	98% (96-99)	
Mismatched Related Donor	49	70,5% (54-82)	110	86% (80-93)	
Unrelated Donor	65	84,2% (72-91)	337	90% (95-99)	
Patients Age ≥18 Years					
Donor type Matched Related Donor	133	84 20/ (76 00)	625	840/ (01 07)	
Matched Related Donor Mismatched Related Donor	42	84,3% (76-89) 75,2% (58-85)	625	84% (81-87) 80% (74-86)	
ALL REAL REAL REAL POINT	69	58,1% (44-69)	581	77% (74-80)	

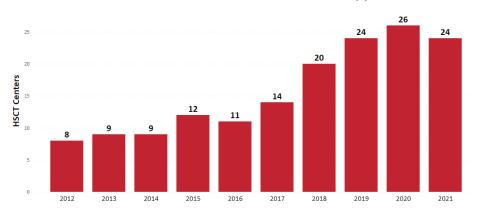


FIGURE 1. Brazilian active centers in the CIBMTR by year

FIGURE 2. Transplants performed in Brazil and reported in the CIBMTR

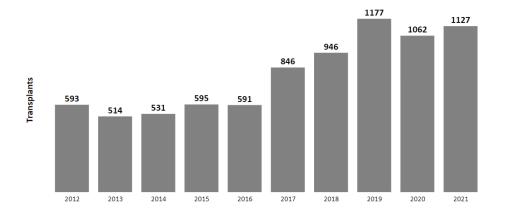
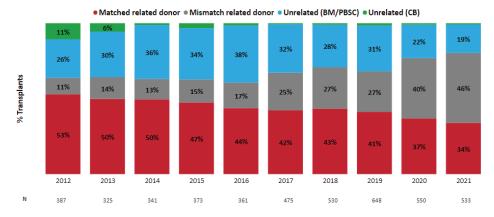


FIGURE 3. Relative proportion of allogeneic HSCT in Brazil by donor type



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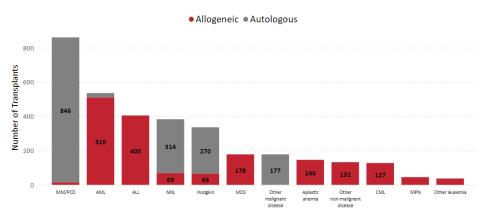


FIGURE 5. AML, overall survival after 1st allogeneic HSCT by donor type

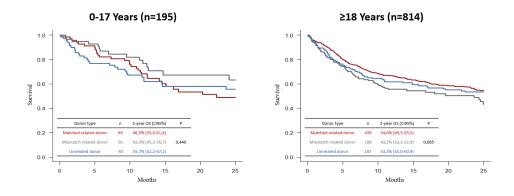
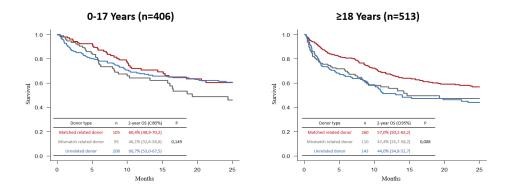


FIGURE 6. ALL, overall survival after 1st allogeneic HSCT by donor type





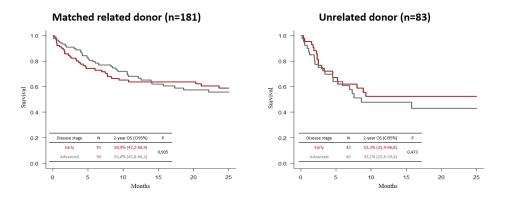
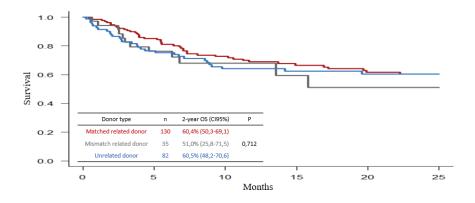
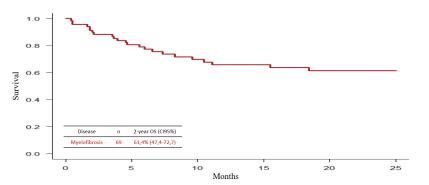


FIGURE 8. CML, overall survival after 1st allogeneic HSCT by donor type







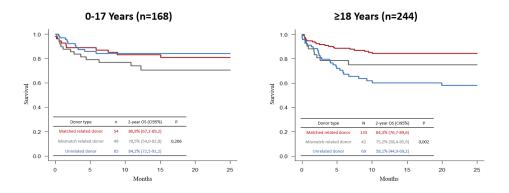


FIGURE 10. Aplastic Anemia, overall survival after 1st allogeneic HSCT by donor type

FIGURE 11. Lymphomas, overall survival after 1st autologous HSCT

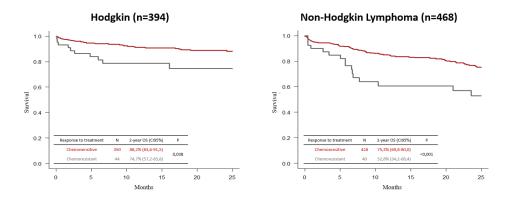
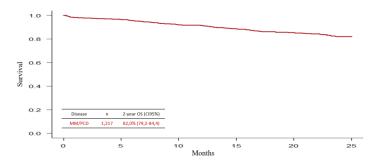


FIGURE 12. Multiple Myeloma/ Plasma Cell Leukemia, overall survival after 1st autologous HSCT



13

FIGURE 13. Data requesting flow

