THE MAP OF BMT IN BRAZIL: A PUBLIC ACCESS PANEL TO HEMATOPOIETIC STEM CELL TRANSPLANTATION DATA

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Short title: THE MAP OF BONE MARROW TRANSPLANTATIOND

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ABSTRACT

Brazil has a vast Hematopoietic Stem Cell Transplantation (HSCT) program with 126 teams and 86 Centers recognized by the Ministry of Health. Outcomes of these transplants are unknown. The objective of this work is to create a public database to help the public and health care professionals to find information on allogenic HSCT performed in Brazil. Methods: The team chose indicators, outcomes, and developed tools to accept secure data input using e-DBtC, Access, RedCap and excel spreadsheet. All data was inserted into the Virtual Analytics platform after careful validation and then presented as tables and graphics in separate portals for healthcare professionals and general public. Results: 29 HSCT centers participating in the project sent data on all consecutive allogeneic transplants performed between August 2019-2020. We gathered data from 943 transplants, with results arranged in graphs and tables, with the possibility of using various filters, so users can customize their search. In conclusion, more than 60% of all allogenic transplants performed in the country are now included in the Map of BMT, in an easy and accessible way to be searched. We hope to continue this initiative and extend it to other services, emphasizing great accomplishment of the Brazilian transplant community.

Keywords: Allografts. Data Collection. Disease-Free Survival. Hematopoietic Stem Cell Transplantation. Information Technology. Patient Access to Records. Registries. Survival Rate.

Thousands of patients undergo hematopoietic stem cell transplants (HSCT) in Brazil every year in public and private centers. [ABTO] Patients are usually treated according to international trials and guidelines published in peer reviewed journals and adapted to conditions and medications that are available in the country.

Two articles in this same volume of the Journal of Bone Marrow Transplantation and Cellular Therapy describe the beginning of the Brazilian BMT Registry using data reported to the Center of International Blood and Marrow Transplant Research (CIBMTR) and then reported back to the Brazilian Bone Marrow Transplant Society (Sociedade Brasileira de Terapia Celular e Transplante de Medula Óssea – SBTMO) as a consolidated unidentified Data Back to Center file. We are thrilled that the Brazilian summary slides are being published for the first time. This is an outstanding initiative to understand our results and to build up a solid database to develop several registry-based trials.

Another pioneer initiative was launched in 2020: the public and free website the "Map of Bone Marrow Transplantation" where primary physicians, transplant centers and the public can access the Brazilian HSCT activity in Portuguese and apply filters to look for the information of interest.[1]

The objective of this paper is to present this new website as an excellent tool to understand the Brazilian transplant activity.

METHODS

Training new data managers

Between 2019 and 2020, the Sao Paulo State Bone Marrow Association (Associação da Medula Óssea do Estado de São Paulo – Ameo), with funding from the Brazilian government (Programa Nacional de Apoio à Atenção Oncológica – Pronon - NUP 25000.001178/2017-55) and Ministry of Health, developed a program to provide online training for new data managers to understand the complex HSCT-related data and to be able to report it to the CIBMTR, as detailed elsewhere.[2,3] All centers already performing HSCT from unrelated donors were invited to participate.

The Brazilian Central Ethics Committee (Comitê Nacional de Ética em Pesquisa - Conep) was consulted and the Map of Transplants was interpreted as a registry as defined by Resolution CNS number 510 from 2016, Article 1 and the Brazilian Law number 12.527, of November 18, 2011, because patients cannot be identified and there is public access of the results so, neither a specific research project, nor specific consent form are needed. Likewise, lawyer consultants reassured that the portal is compliant with the Brazilian General Personal Data Protection Law (Lei Geral de Proteção de Dados Pessoais) and that no specific consent was needed.

One professional was appointed by each transplant center director to receive a scholarship, but the participation of other professionals was open and free. Public centers also received a laptop to work.

Building up the Center dataset

Each data manager, as part of their training, had to organize the information about all patients undergoing allogeneic transplants between August 2019 and August 2020 in the institutional to be reported. Centers were encouraged to use a surrogate institutional dataset to organize the patients' data and to have the items already translated into Portuguese in the same format they are entered in the CIBMTR portal. Centers were offered an Access and/or RedCAP database ready to be used. Transplant centers already reporting to the CIBMTR could use their "Data Back to Center" file to avoid duplicate work. Other centers chose to use a simple Excel file. Patient identifiers were coded by the institution never shared with AMEO and, once in the Virtual Analytics Platform, all data was encrypted. The variables initially collected are shown in Table 1

Importing data to the Virtual Analytics Platform

Unidentified but individualized patient data was sent from the transplant centers in four different formats: CIBMTR-Data Back to Center files, Access, RedCap and structured excel files. These was carefully checked for consistency before being entered into the Virtual Analytics platform, as shown in Figure 1.

Building the Map of Bone Marrow Transplantation PortaL

Three separate Portals were designed: Public, Professionals and a password protected Center Portal. The data selected to be presented in the portal is shown in Table 2. The portal "Map of BMT" was built as a free and reliable tool for the public to understand the number of transplants performed in each region, being able to filter it according to the age group, disease, donor source, and for professionals to access HSCT results shown as a Kaplan Meier graphic format. Centers can use the password protected access to check their own data within the portal.

Results

The training program for the new Brazilian Data Managers happened over 14 months, with 200 hours of online teaching, time to practice, in person teaching and audit of every center, later changed to online audit due to the Covid pandemic[2,4] A total of 66 data managers from 31 hospitals completed the training (Table 3).

Thirty centers sent the data of all consecutive allogeneic transplants performed between August 2019 and August 2020. Seventeen of the centers are public. Most centers are located in the Southeast region (23), followed by South (4) and Northeast (3). A total of 943 transplants were performed in 929 patients, 870 of them were the first allogeneic transplant.

The Map of BMT, hosted at the AMEO website (www.ameo.org.br) has three portals: Patients, Professionals and a password protected Transplant Center access (Figure 2).

Graphics included in the portal are number of allogeneic transplants according to age, gender, schooling, donor, underlying disease, graft source, number of participating public and private centers in the region. Results include number of allogeneic transplants in each region, time between diagnosis and transplant and the first appointment and transplant, overall survival, disease free survival and primary cause of death (Figure 3).

The majority of the transplants were performed in patients older than 18 years (605 in adults vs. 338 in children), as shown in Figure 4. However, there are profound differences in the age groups transplanted in the country: children (less than 18 years of age) are 20% of the patients undergoing HSCT in the Northeast, versus 35% in the Southeast and 56% in the South.

Information on education was specifically collected for the project and show that 25% of the patients had not completed all school years, as opposed to 36% who had already graduated from university (Figure 5)

The most common underlying diagnoses were acute leukemias, followed by non-malignant disease in pediatrics (Figure 6) and by myelodysplastic syndrome and lymphomas in adults (Figure 7).

The number of allogeneic transplants from matched sibling donors (MSD) is similar to the number of haploidentical (Haplo) transplants, followed by unrelated donors (URD; Figure 8)

However, in adults, 46% of the transplants are from MSD, followed by 33% Haplo and 22% from URD. In children, 41% are Haplo, 35% URD and only 23% of the transplants are from MSD. There are also regional differences: in the northeast, 60% of the transplants are from MSD, while in the south, 44% are haploidentical, followed by MSD and URD in the same proportion.

Bone marrow is used in over half of the transplants in all regions, but it is 78% of the graft sources for children and 40% for the adults. Only 10 cord blood transplants (1%) were reported (Figure 9).

There is a glossary of terms available in the Patient's Portal for them to search for medical terms (Figure 10) and the graphics are very straight forward and easy to be understood (Figure 11).

Patients may look for information on survival applying filters on underlying diagnosis, age group and donor source (Figure 12).

Overall survival is shown at the Patient's Portal as a table with the percentage of patients alive at 30 days, 100 days, 6 months at one year, calculated by the Kaplan-Meier method (Figure 13). Patients are encouraged to discuss their diagnosis and expected survival with their primary physician.

In the Professional's Portal data is further detailed (Figure 14), with more filters: underlying diagnosis, age (by decade), transplant number (1-3+), donor source, gender, donor age (</> 30 years) and center (public or private) (Figure 15).

Overall survival and disease free survival are presented as Kaplan-Meier graphics with both the median follow up time and patient censoring clearly shown (Figure 16). When the number of patients in a specific dataset is less than 25, graphics are not generated and a table is shown with the results.

Causes of death are detailed in the Professional's Portal and can be filtered according to age group, type of transplant and within 100 days post-transplant or later (Figure 17).

Infections are the most important cause of death (Figure 18) and responsible for over half of the deaths within and after the 100-day time point in all donor sources.

One clear limitation of our data is the short overall follow-up time of 138 days, further detailed in each Kaplan-Meier. This data can be used to show the transplant-related mortality and survival at 30 and 100 days, but longer follow-up was needed to understand survival at 6 months and one year. Since the dataset is intended to have updates every 6-months, so we may shortly have a longer follow-up time and more reliable survival data.

Discussion

To the best of our knowledge this is the first portal were professionals, patients, public and transplant centers can look for the results of the HSCT performed in the country. It is not meant to duplicate efforts or compete with registries as the Worldwide Network for Blood and Marrow Transplantation (WBMT), CIBMTR, European Blood and Marrow Transplant (EBMT) or Brazilian Organ Transplantation Registry (Registro Brasileiro de Transplantes - RBT) of the Brazilian Organ Transplantation Association (Associação Brasileira de Transplante de Órgaos – ABTO) or Brazilian Bone Marrow Transplantation Registry (SBTMO). This website is unique and provide carefully reviewed and valuable data to primary physicians, patients, and transplant centers to understand transplant results and to plan improvements in patient care.

The Brazilian Transplantation Registry (RBT) of the Brazilian Organ Transplantation Society (ABTO) has been collecting data on transplant activity in the country since 1995, including HSCT.[5] Reporting to the ABTO has significantly increased in the past decade with the partnership with the Brazilian Bone Marrow Transplant Society (Sociedade Brasileira de Terapia Celular e Medula Óssea – SBTMO) and many centers now also include data on patient survival.[6]

Reporting consecutive patient data to the CIBMTR is compulsory in the United States to have their national Stem Cell Therapeutic Outcomes Database (SCTOD). Patients may consent for their data to be also used by the CIBMTR for research. Each HSCT centers may choose to participate reporting the minimal obligatory Transplant Essential Data (TED) only, or being a Comprehensive Report Form Center.[7] Centers sign in a contract with the CIBMTR and the forms are electronically filled in, all in the English language. There are 93 different forms as of June, 2021, that may be filled in according to the center track, underlying disease and type of transplant.[8]

Brazilian centers reporting to the CIBMTR can simply export their Data Back to Center files to our Map of BMT, avoiding any duplicate entries and assuring the integrity of their data, due to the automatic online data check available in their FormsNet3 website.

Half of the transplant centers reporting to the RBT-ABTO also report to the CIBMTR: in 2019, 1,073 transplants from 23 Brazilian centers were reported to the CIBMTR (Simione AJ, in press in this volume) and 3,805 transplants from 62 institutions were reported to the RBT.[6] As of 2021, 32 transplant centers are affiliated to the CIBMTR and 74 to the RBT, so we expect to progressively increase the comprehensive report of our data.[9]

All transplant center leaders were invited to participate in our Scientific Council, that has already met couple of times do define the future directions of the portal. Since the platform launch on December 18, 2020, we will have now the first update and have data on 6-month and one year follow up.

Now, that we have the reporting system of the most complex and expensive transplants organized, we would like to scale the project up to include centers performing autologous and HSCT from related donors.

In conclusion, we strongly believe that this portal, the "Map of BMT" is a novel and important initiative that can be a model for other countries and for registries to improve transparency and access to HSCT demographics and results.

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TABLE 1: Indicators selected for data collection

	Description
Patient data	Gender, Age at HSCT, Consent, Blood Type, Date Of Birth, Race/Color, educational level, Private/SUS, Date 1st Consultation, Performance Status, History of IOT, History of Fungal Infection, Cytomegalovirus Status
Disease Data	Diagnosis, Date of diagnosis, Pre-HSCT disease condition, Pre-HSCT DRM assessment, Classification of diseases
Donor Data	Gender, Age, Blood Type, Relationship (Donor/Patient), HLA Compatibility, Cytomegalovirus Status
Transplant Data	Type of transplant, Transplant Subtype, Current Transplant Number, History of Previous Transplants, HSCT Date, Conditioning Protocol, Conditioning Classification, Prophylaxis for Graft Versus Host Disease, Cell Source, Infused Cell Count
Engraftment	Neutrophil Engraftment, Platelet Engraftment, Quimerism Assessments
Graft Versus Host Disease	Acute GVHD, Chronic GVHD
Outcomes	Current Status, Date of last follow-up, Date of death, Cause of death, Relapse, Date of Relapse, Graft Loss, Date of Loss, New Neoplasm, Date of New Neoplasm, New Neoplasia Diagnosis, Veno Occlusive Disease (VOD), Performed a Second transplantation

TABLE 2: Data selected to be presented in the portal

Presentation	Description
General Data	Total transplanted patients Total number of transplants
Graphics	Transplants by Age Transplants by Gender Transplants by Educational level Transplants by Donor Type Transplants by Diagnostic Transplants by Cell Source Number of centers per region Number of Public/Private Centers by region
Results	Number of transplants per region Time between diagnosis and HSCT Time between the first consultation in the HSCT center and the transplant date Global Survival Disease-free survival Mortality

TABLE 3: Participating centers, directors and data managers

Transplant Center	City	State	Type	Director HSCT Center	Data Manager	Occupation
Associação Paulista para o Desenvolvimento da Medicina-Hospital São Paulo	São Paulo	SP	Public	Profa.Dra.Sandra de Oliveira Campos/Dr. Celso Arraes/Dr. Viniciu	Raquel P.P.Montanari Gouvea/ Isaias Olive	Administrator
Bio Sana's Serviços Médicos	São Paulo	SP	Private	Dr. Roberto Luiz da Silva/Dra. Maria Cristina M de Almeida Mace	Denise Borges R. Minari	Nurse
Casa de Saúde Santa Marcelina	São Paulo	SP	Public	Dra. Katya Parisio	Adriana Rodrigues Oliveira	Clerck
Centro de Hematologia e Hemoterapia da Universidade Estadual de Campinas (UNICAMP)	Campinas	SP	Public	Profa.Dra.Margareth Castro Ozelo/Afonso Celso Vigorito	Larissa Codogno Guzelotto	Nurse
Complexo Hospitalar de Niterói - Ímpar Servicos Hospitalares S/A	Niterói	RJ	Private	Dra. Maria Claudia Rodrigues Moreira	Andreia Ribeiro de Almeida	Nurse
Hospital Samaritano Higienópolis	São Paulo	SP	Private	Dra. Maria Fernanda Carvalho de Camargo	Paola Azenha Milani Soriano	Physician
Fundação Antonio Prudente - Hospital A.C. Camargo	São Paulo	SP	Private	Dr. Jayr Schmidt Filho	Bruna Tirapelli Gonçalves	Nurse
Fundação Doutor Amaral Carvalho	Jaú	SP	Public	Dr. Alcindo Storti	Bruna Fernanda S. Mathias	Assistant
Fundação Faculdade de Medicina de São José do Rio Preto	São José do Rio Preto	SP	Public	Dr. João Vitor Piccolo Feliciano	Laila Toniol Cardin	Biologist
Fundação Felício Rocho	Belo Horizonte	MG	Public	Dr. Guilherme Campos Muzzi	Thais Cristina da Silva	Nurse
Fundação Pio XII - Hospital de Amor	Barretos	SP	Public	Dr. George Navarro	Paula Moreira da Silva	Nurse
Grupo de Apoio ao Adolescente e à Criança com Câncer (GRAACC) - Unifesp	São Paulo	SP	Public	Dr. Victor G. Zecchin/ Dra Renata Fittipaldi	Cintia Monteiro Lustosa	Nurse
Hospital das Clínicas da Faculdade de Medicina da USP	São Paulo	SP	Public	Dr. Vanderson Geraldo Rocha/Dra. Lívia Mariano Compt	Bruna Del Guerra C. Moraes	Nutricionist
Hospital de Clínicas da Universidade Federal de Minas Gerais	Belo Horizonte	MG	Public	Dr. Gustavo Machado Teixera	Glaucia Helena Martinho	Nurse
Hospital de Clínicas de Porto Alegre	Porto Alegre	RS	Public	Dra. Liane Esteves Daudt	Raquel Schultz / Priscila de Oliveira	Student
Hospital Israelita Albert Einstein	São Paulo	SP	Private	Dr. Nelson Hamerschlak	Mariana Clapis B. Velloso	Nurse
Hospital Leforte Sociedade Assistencial Bandeirantes	São Paulo	SP	Private	Dr. Ricardo Tscuotto/Dr. Rodrigo Santucci	Lucilene Jeronima da S. Souza	Nurse
Hospital Moinhos de Vento	Porto Alegre	RS	Private	Dra. Claudia Caceres Astigarraga	Valesca Scalei Cezar	Nurse
Hospital Nossa Senhora das Graças	Curitiba	PR	Private	Dra. Elenaide C. Nunes	Cristiano de Oliveira Ribeiro	Nurse
Hospital Pequeno Príncipe-Associação Hospitalar de Proteção à Infância	Curitiba	PR	Public	Dra. Gilmara Cristina Kuwahara	Priscila Panek	Nurse
Hospital Quinta D'Or	Rio de Janeiro	RJ	Private	Dr. Renato Castro	Beatriz Carvalho Espindola	Nurse
Hospital Universitario Clementino Fraga Filho (Universidade Federal do Rio de Janeiro)	Rio de Janeiro	RJ	Public	Dr. Rony Schaffel/Dr. Marcio Nucci	Valéria Vianna Santos	Biologist
Hospital Universitário Walter Cantídeo - Universidade Federal do Ceara	Fortaleza	CE	Public	Dra. Josenília Maria Alves Gomes/Dr. Fernando Barroso Duarte	Thaisa Marjore Viana	Pharmacist
Instituto de Tratamento do Cancer Infantil (ITACI)/ ICr-HC da Faculdade de Medicina da USP	São Paulo	SP	Public	Dra. Juliana Fernandes Folloni	Gislene Santana Tusani	Nurse
Instituto Nacional do Câncer José Alencar Gomes da Silva - CEMO (INCA)	Rio de Janeiro	RJ	Public	Dr. Décio Lerner/Dr. Renato Castro	Aline Sperandio/Jéssica Di Chiara Salgado	Assistant/ Nurse
Núcleo Oncoclínicas	Belo Horizonte	MG	Private	Dr. Wellington Azevedo	Raquel Di Mambro Castro	Nurse
Real Benemérita Associação Portuguesa de Beneficência (BP-Mirante)	São Paulo	SP	Private	Dr. José Ulysses Amigo Filho	Vinícius Vitor Barbosa	Student
Real TMO Clínica Médica (Hospital Português de Beneficência- Pernambuco)	Recife	PE	Private	Dr. Rodolfo Froes Calixto	Gizeli Braga M. dos Santos	Secretary
Santa Casa de Misericórdia de Belo Horizonte	Belo Horizonte	MG	Public	Dr. Saulo Levindo Coelho/Dr. Wellington Morais de Azevedo	Danielle Resende de Pádua	Nurse
Sociedade Beneficente de Senhoras Hospital Sírio Libanês	São Paulo	SP	Private	Dra.Yana Augusta Sarkis Novis	Simone Ojima Ferreira	Nurse
Terapia Celular de Natal (Hospital Natal Center)	Natal	RN	Private	Dr. Rodolfo Daniel de A. Soares	Nayane M.F. Alves	Nurse

FIGURE 1: Data processing for the Portal "Map of BMT"

FIGURE 2: The Map of Bone Marrow Transplantation Portal
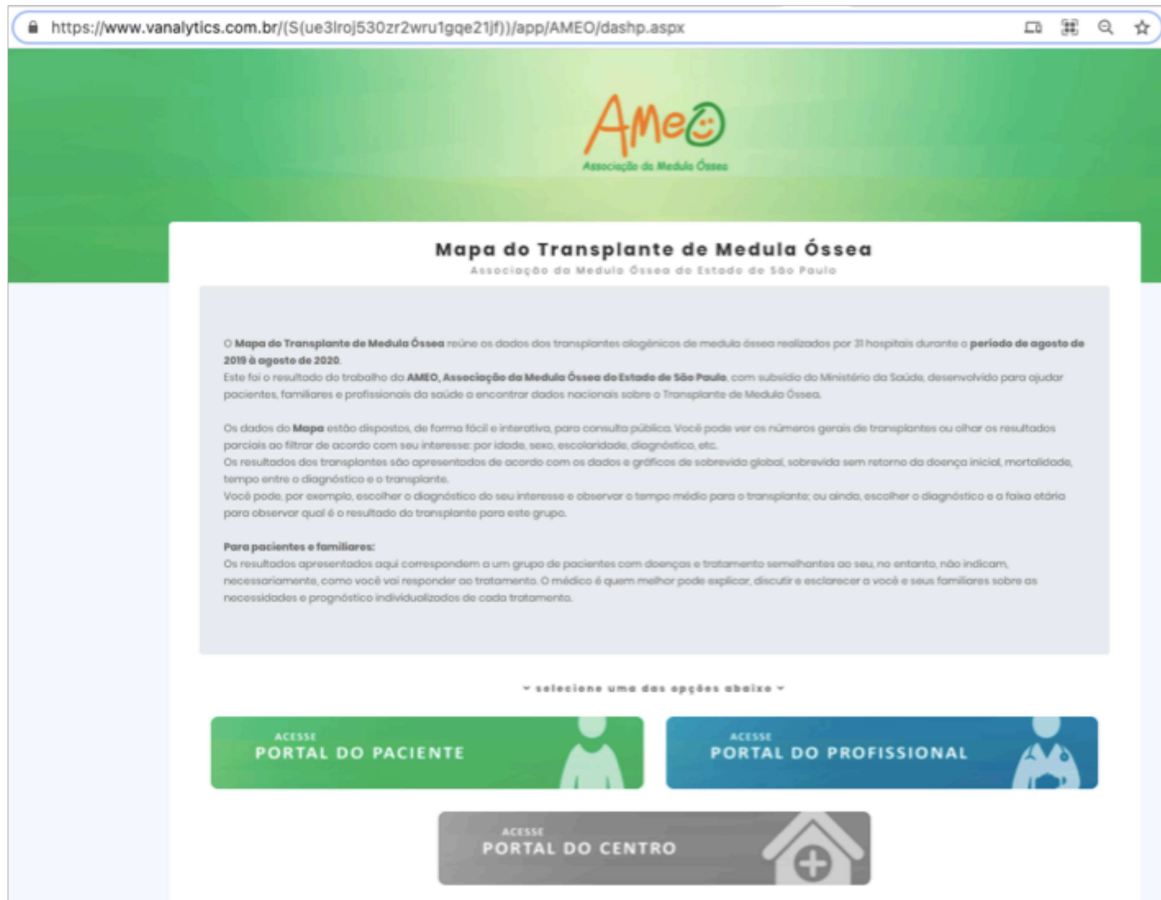

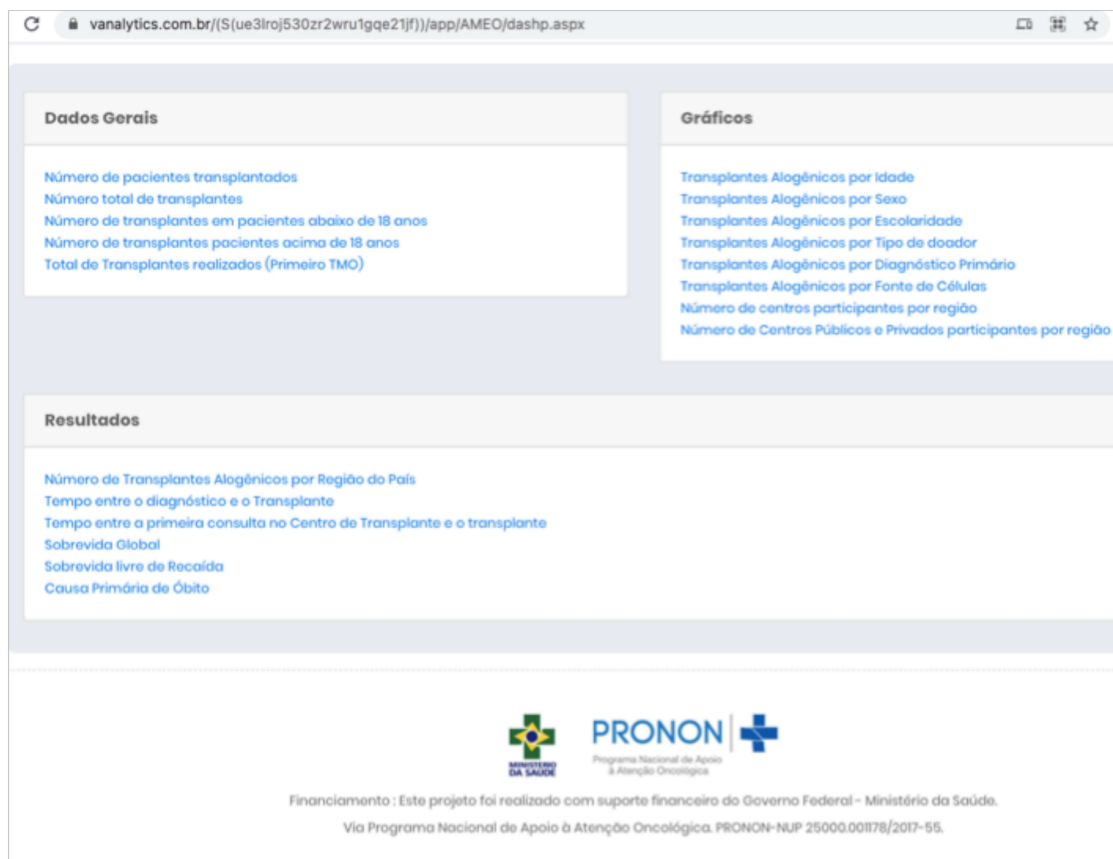**FIGURE 3:** Transplant data presented in the portal

FIGURE 4: Age distribution of allogeneic transplants performed in 30 Brazilian centers between August 2019 and August 2020
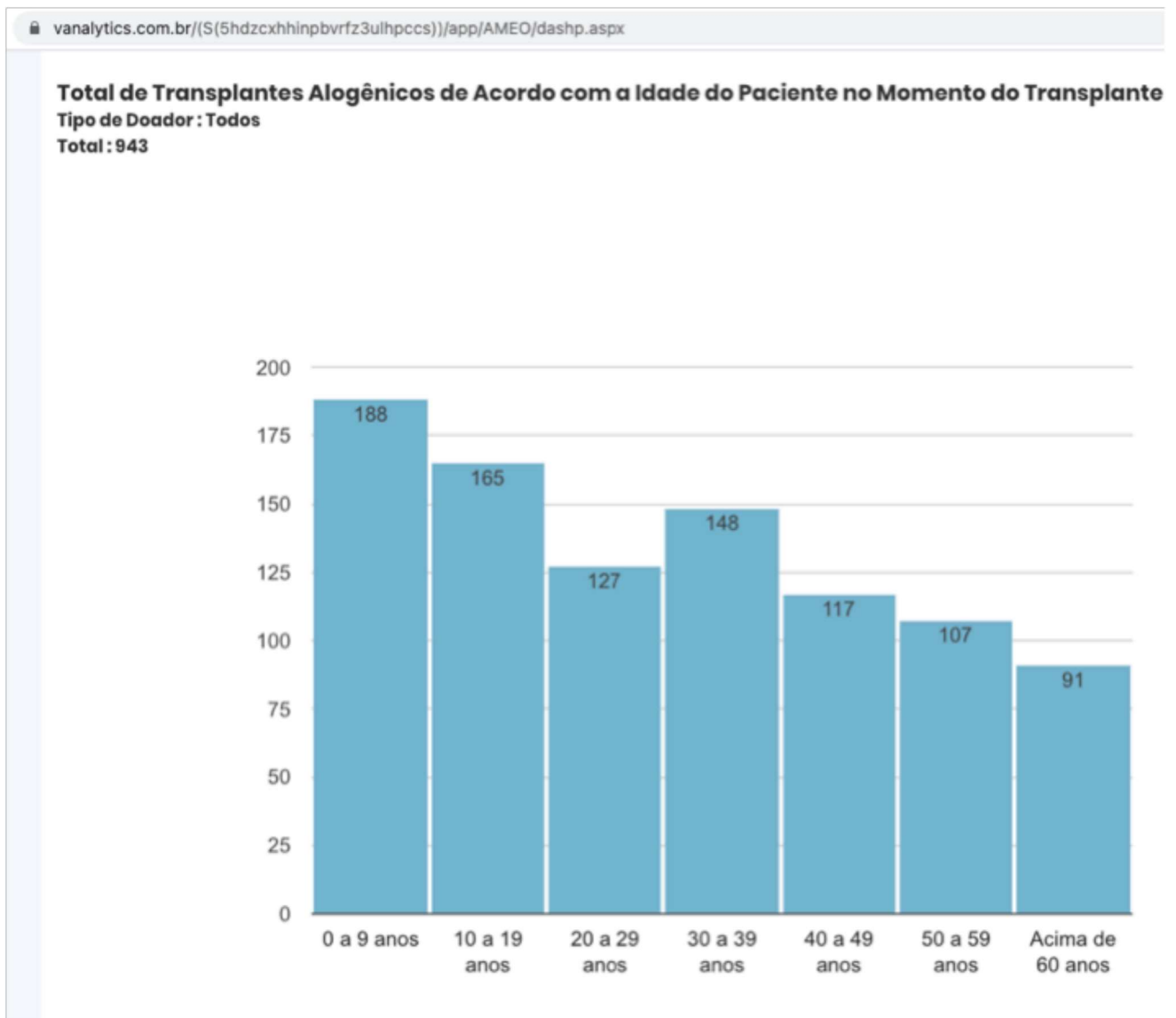
FIGURE 5: Education among 282 patients older than 18 years of age undergoing allogeneic HSCT in 30 Brazilian centers between August 2019 and August 2020
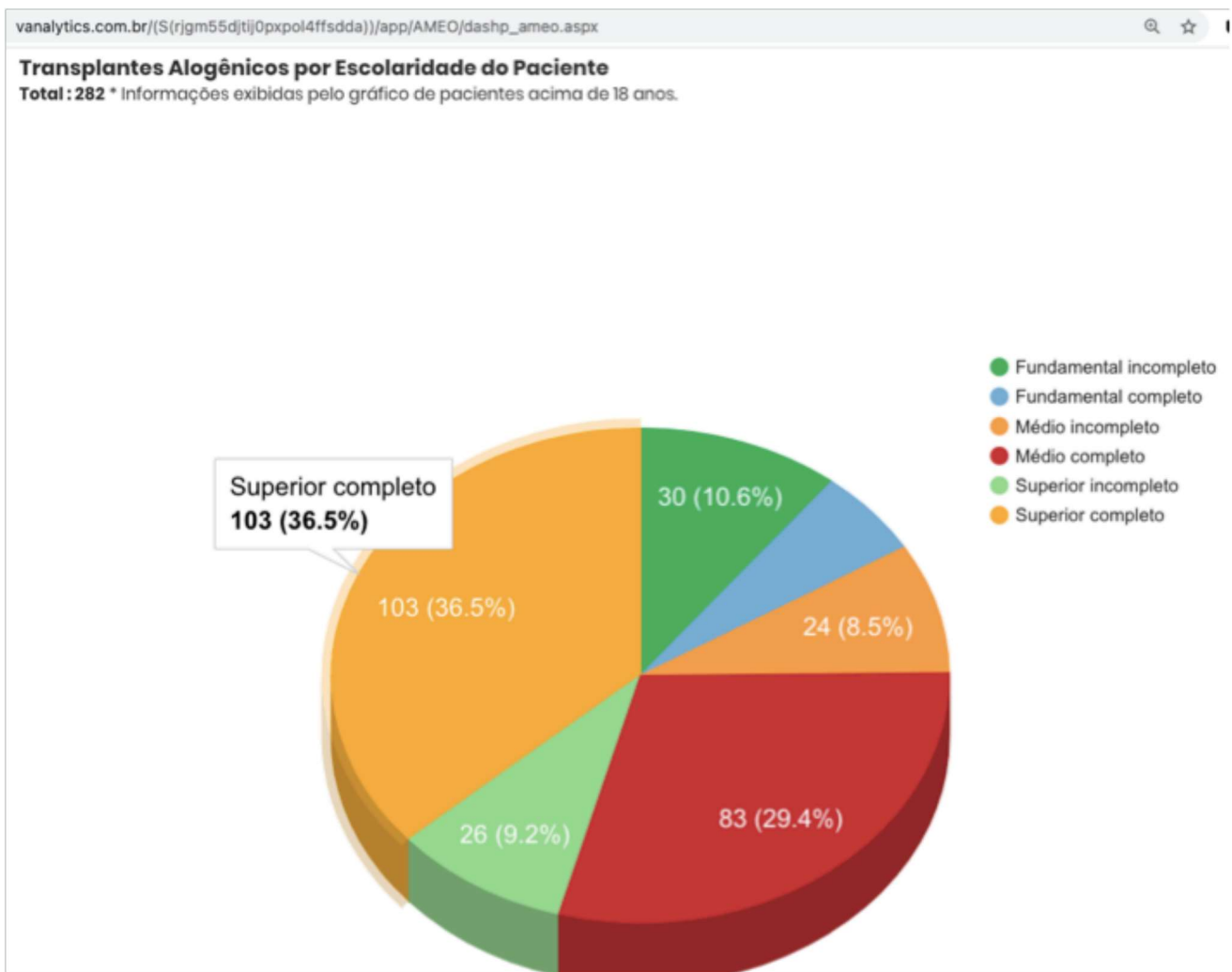
FIGURE 6: Underlying diagnoses in children undergoing allogeneic HSCT in 30 Brazilian centers between August 2019 and August 2020
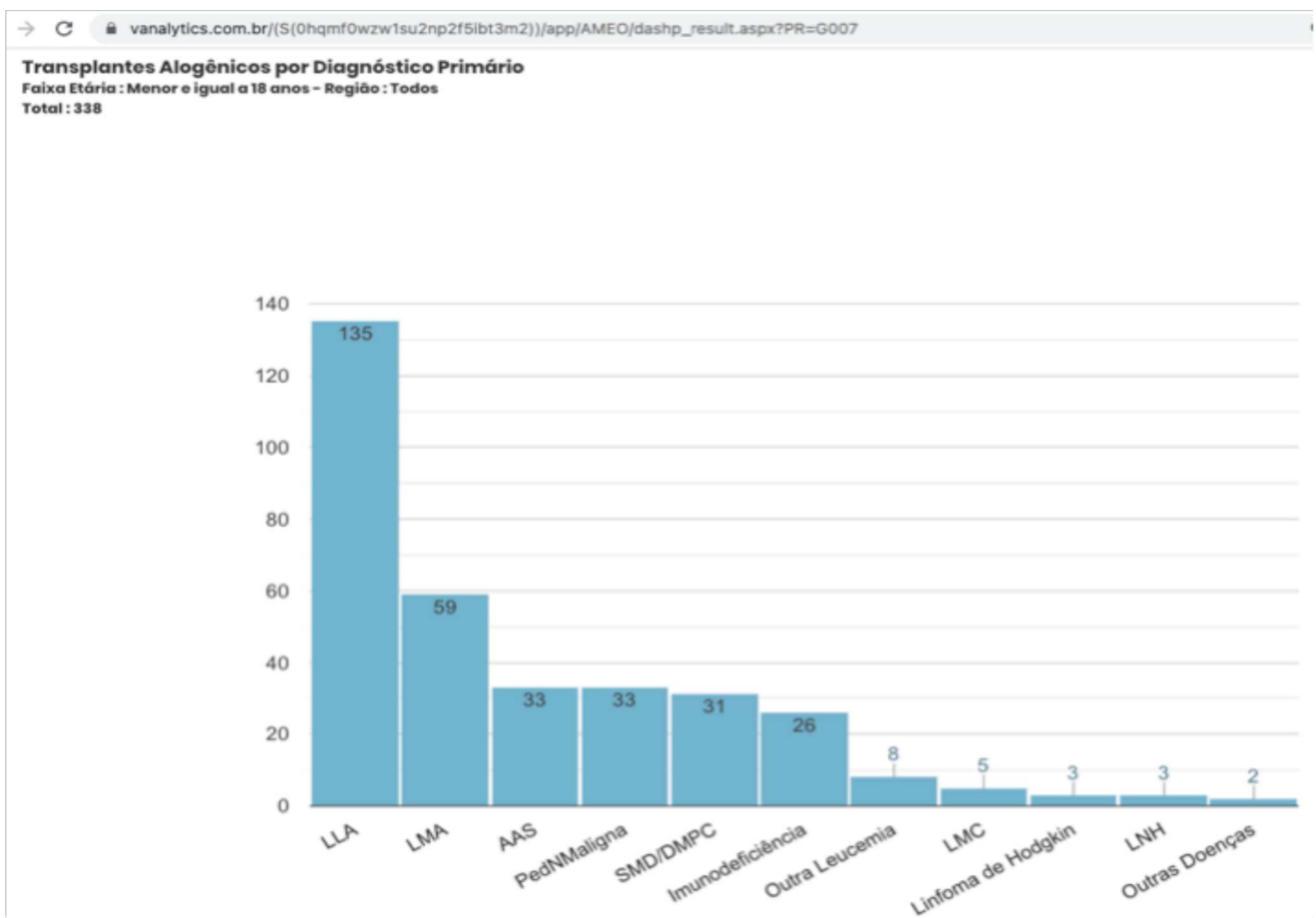
FIGURE 7: Underlying diagnoses in adults undergoing allogeneic HSCT in 30 Brazilian centers between August 2019 and August 2020
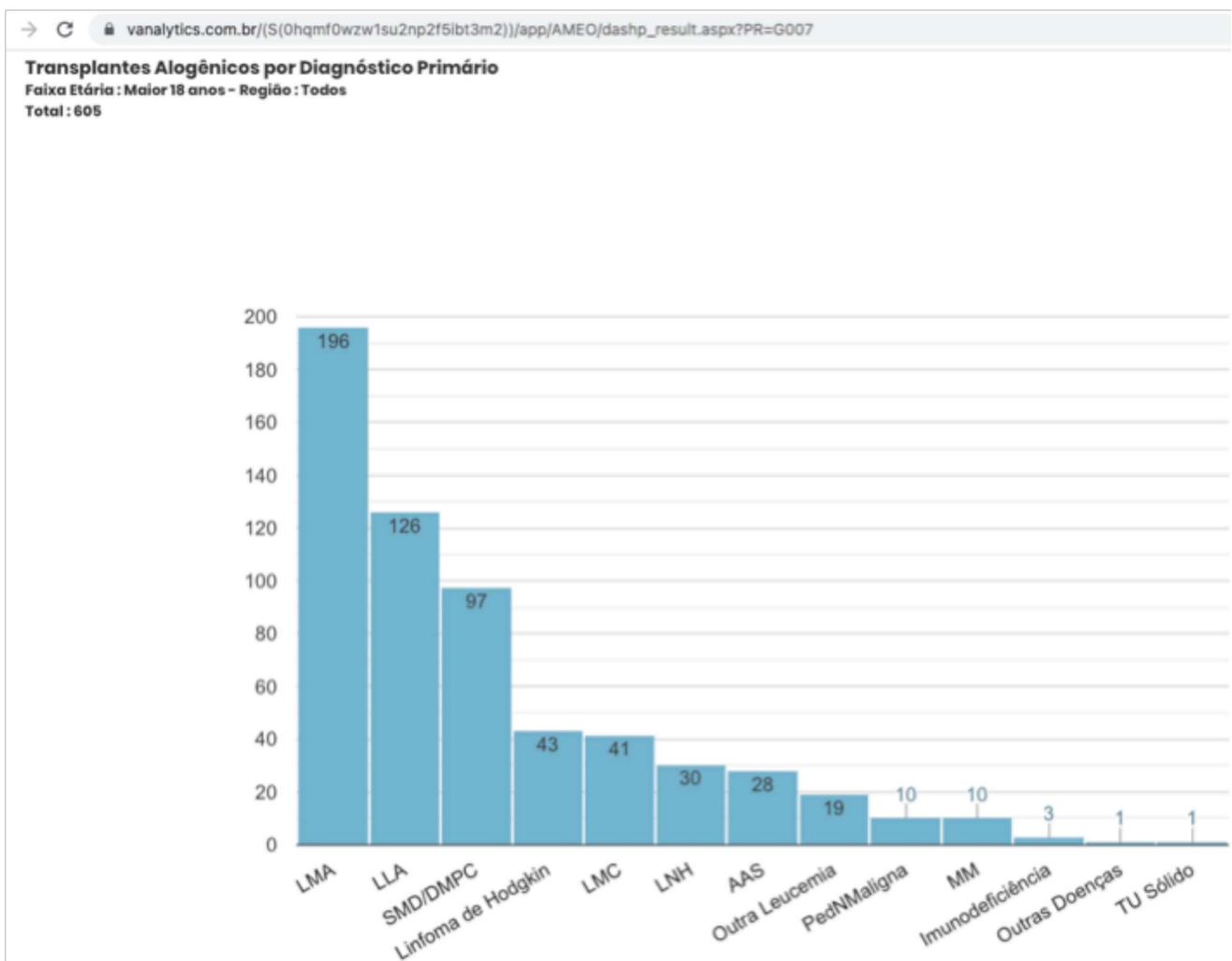
FIGURE 8: Number of transplants from HLA-identical siblings, haploidentical and unrelated donors
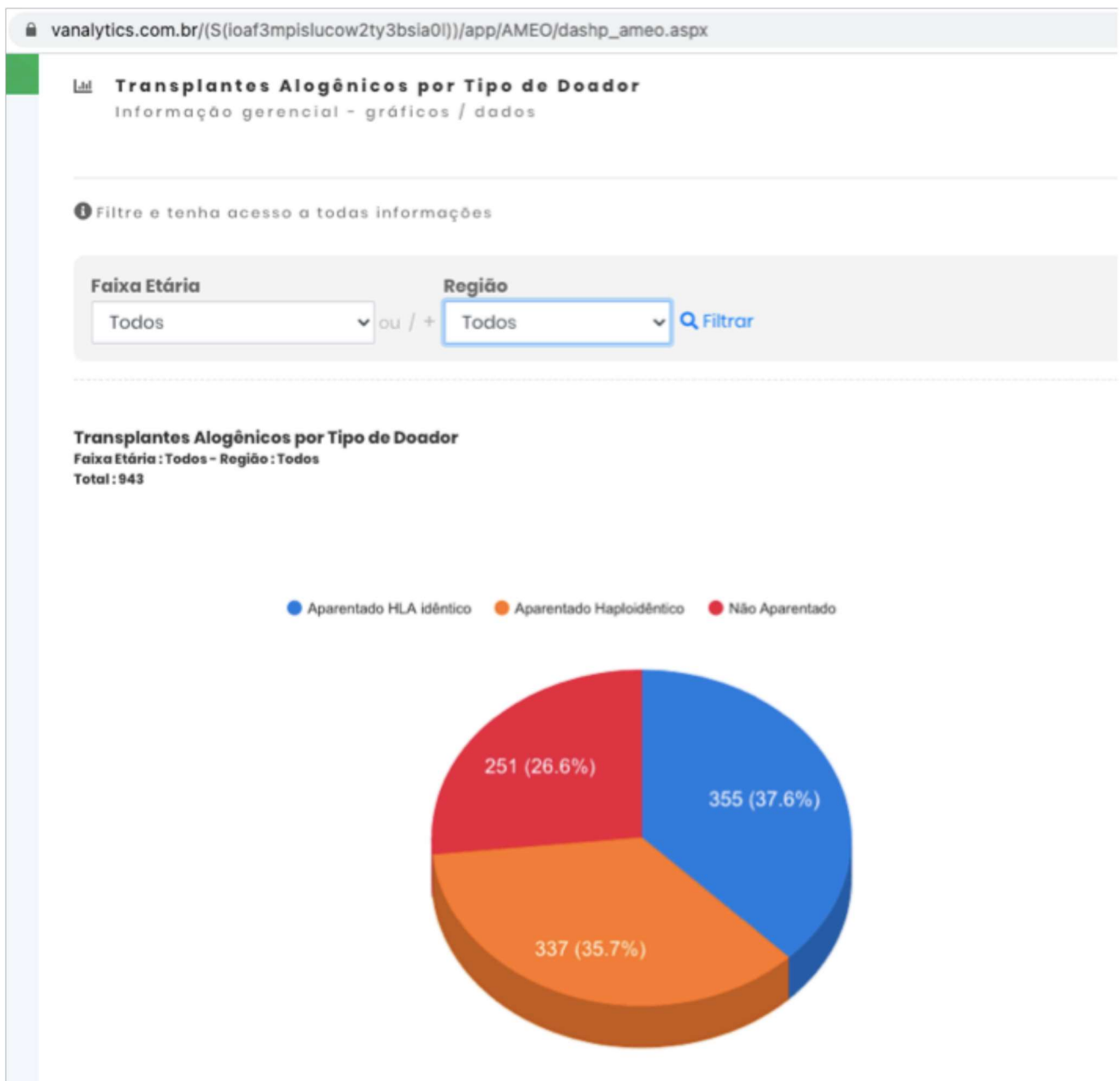
FIGURE 9: Source of stem cells for allogeneic transplants in 30 Brazilian centers between August 2019 and August 2020
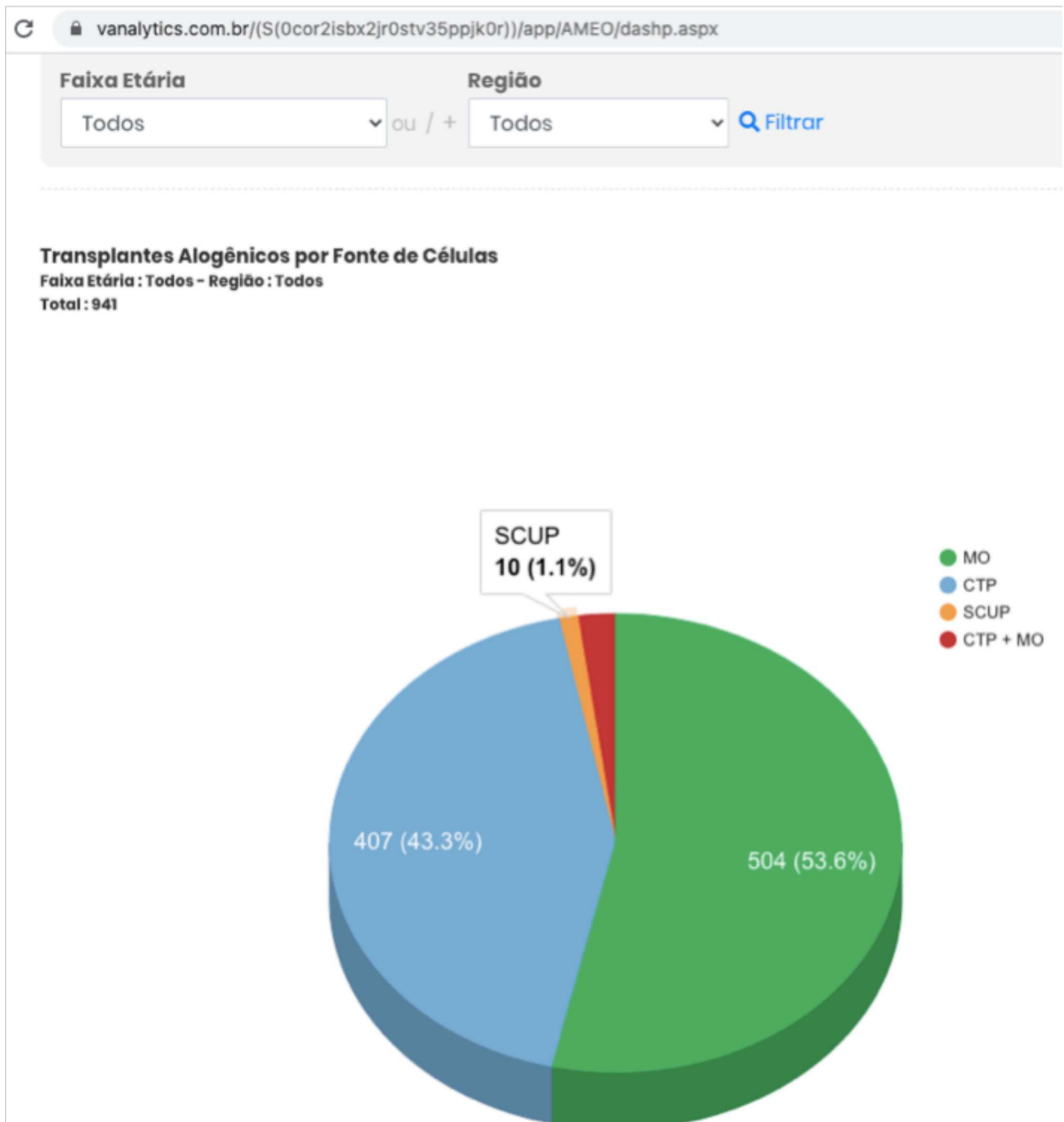
FIGURE 10: Glossary in the Patient's Portal

FIGURE 11: Graphics and Tables in the Patient's Portal
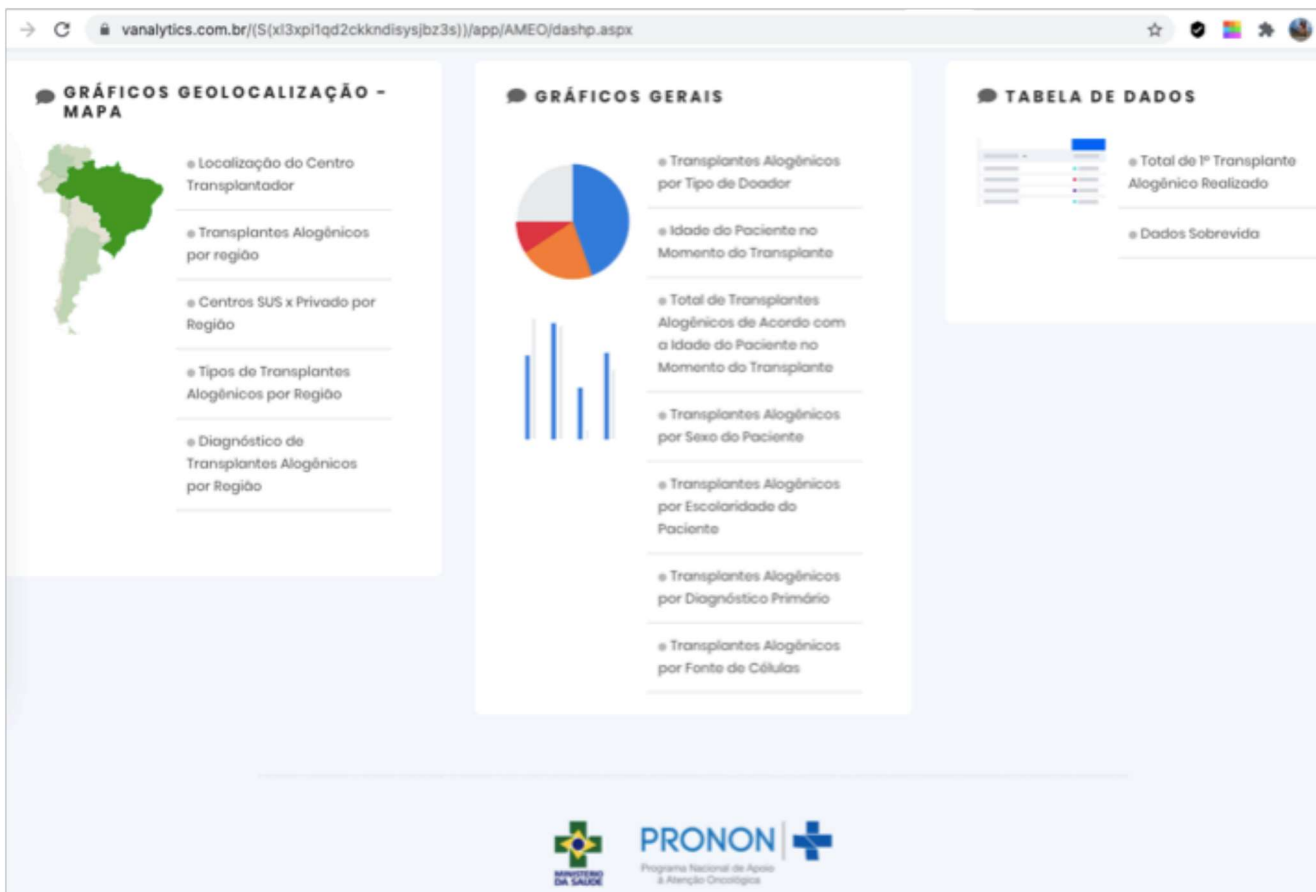
FIGURE 12: Filters that can be used by patients to build the survival table: diagnosis, age group, donor source
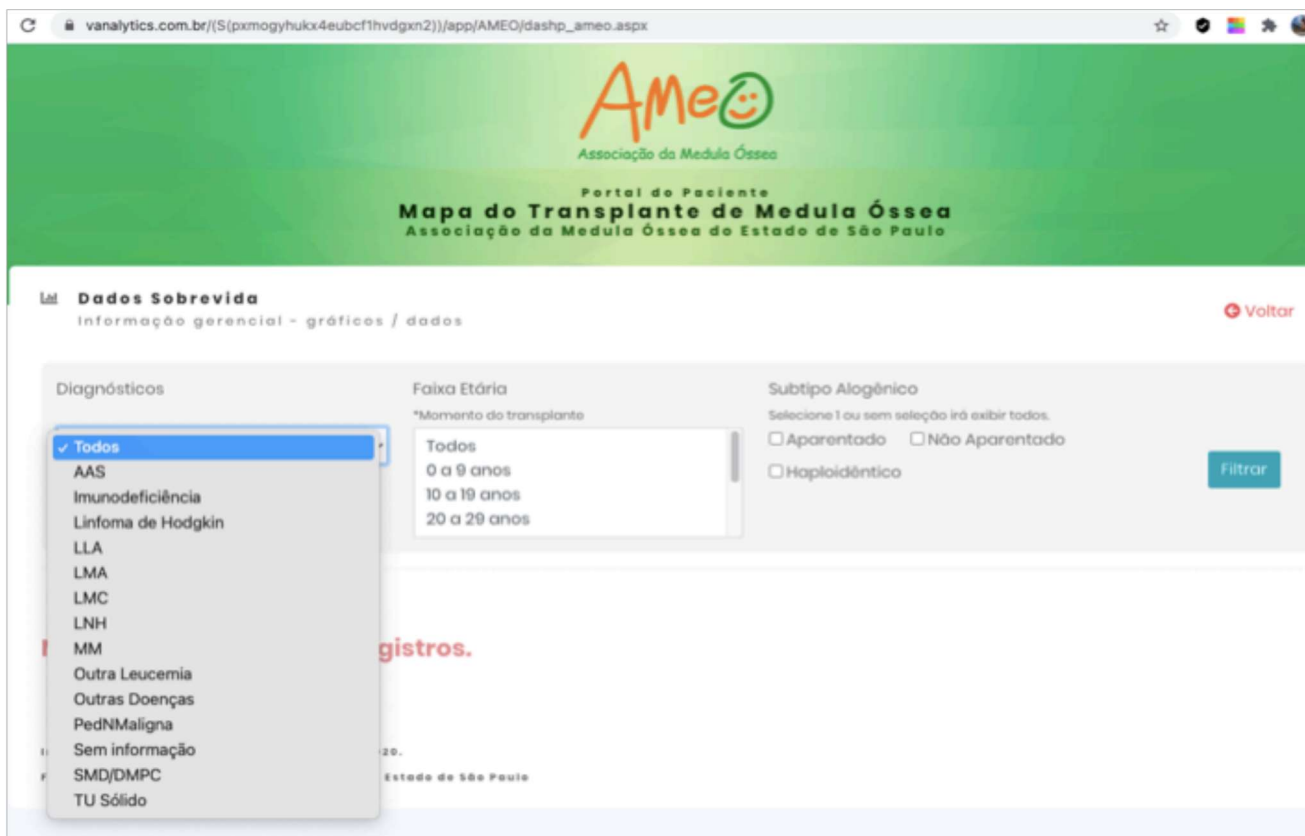
FIGURE 13: Survival of 817 patients at 30 days, 100 days, 6 months and one year after the first allogeneic transplant performed in 30 Brazilian centers between August 2019 and August 2020.
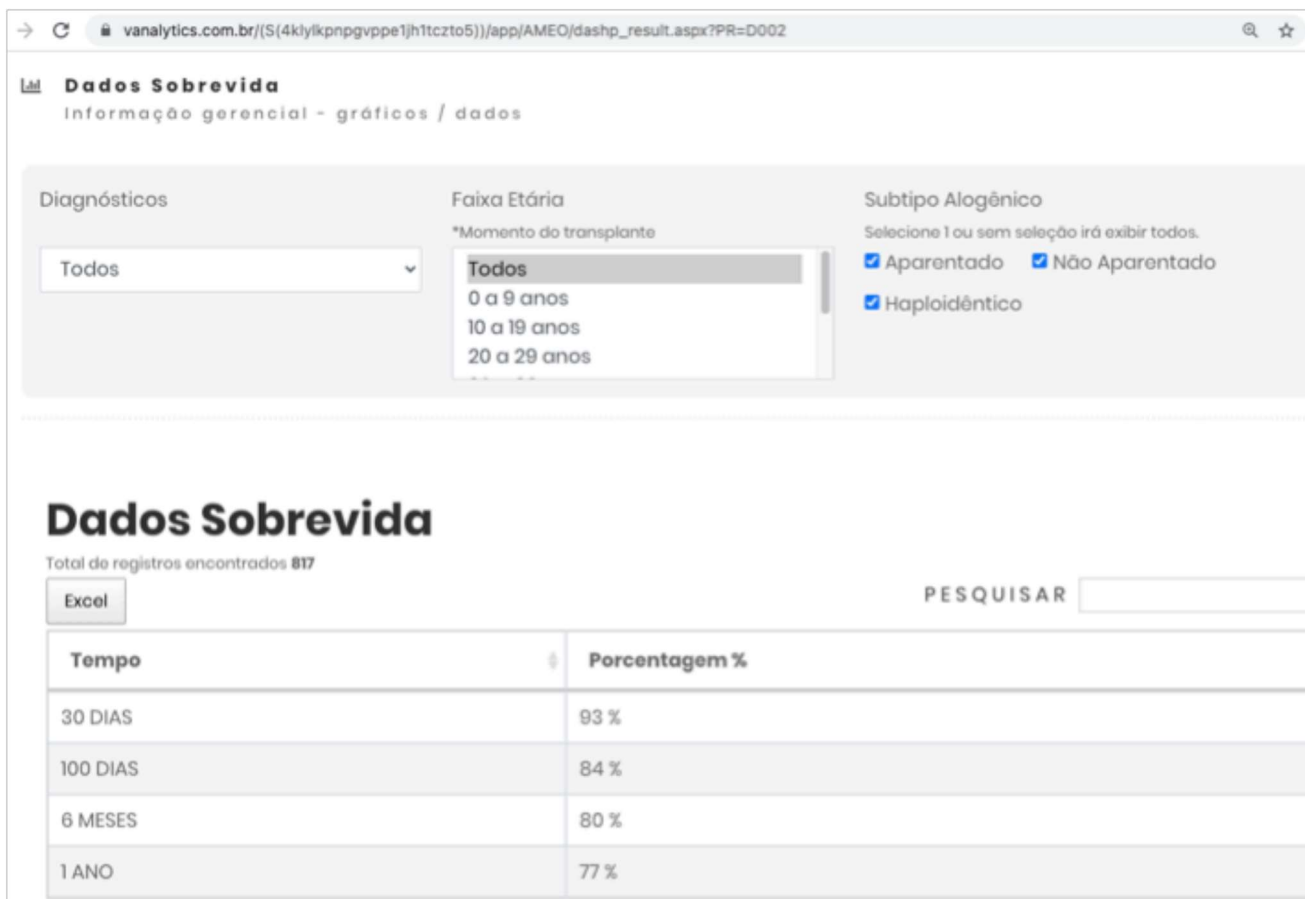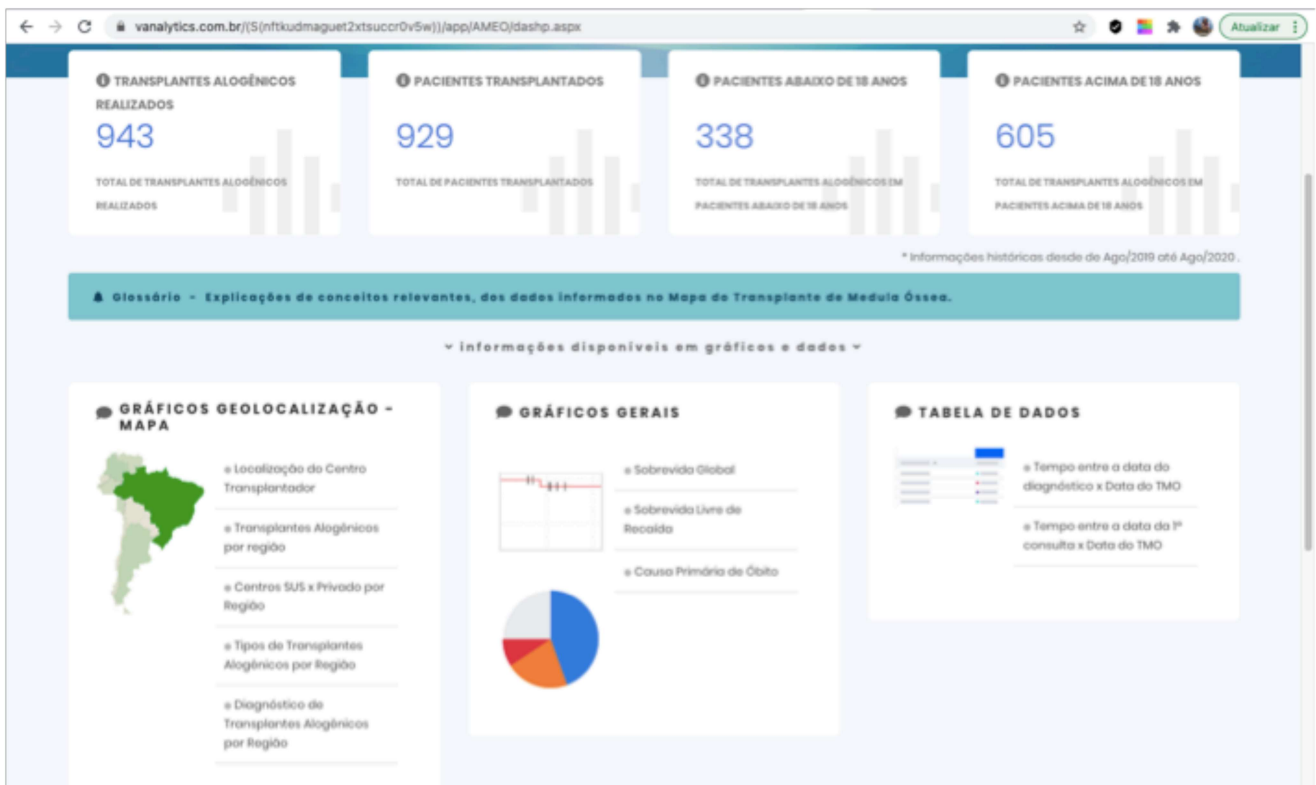
FIGURE 14: Professional's Portal

FIGURE 15: Filters that can be used in the Professional's Portal to generate Overall and Disease Free Survival Kaplan-Meier graphics
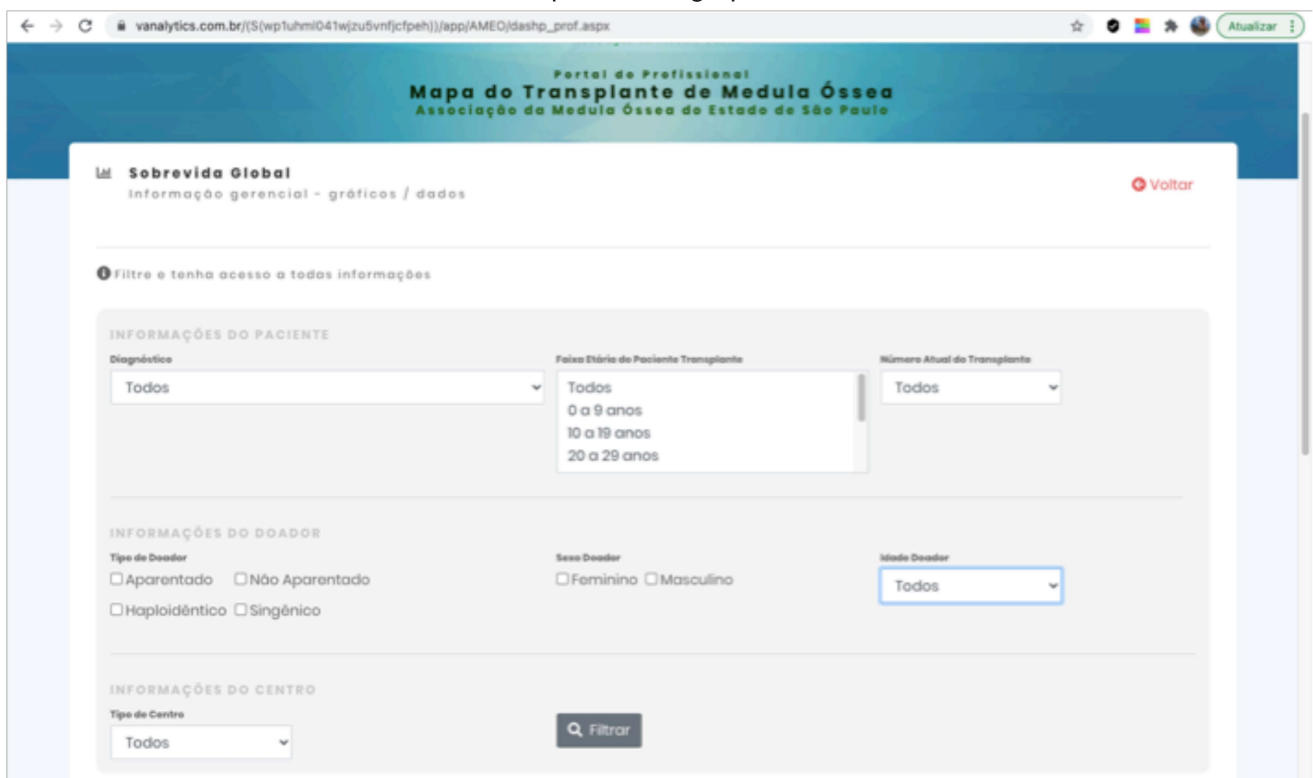
FIGURE 16: Overall survival of 789 allogeneic transplants performed in 30 Brazilian institutions between August 2019 and August 2020
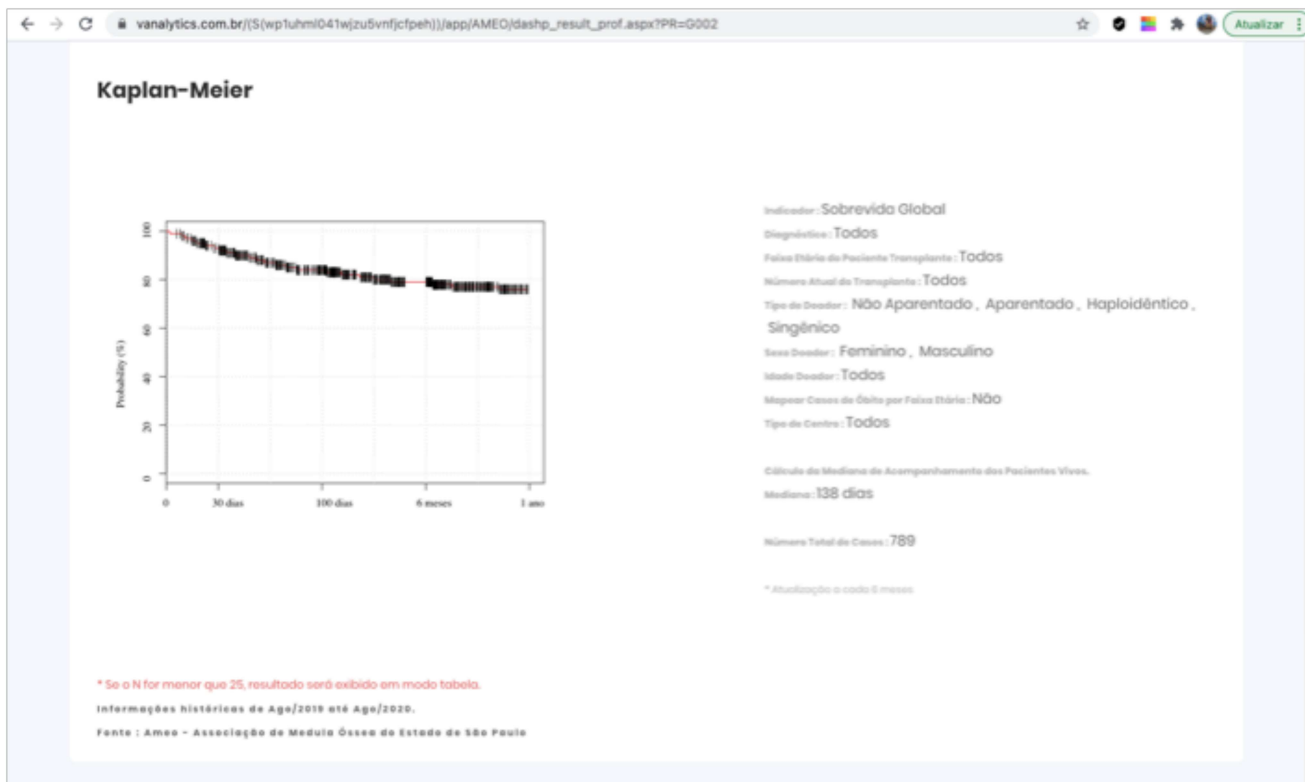

FIGURE 17: Filters that can be used to search causes of death among patients undergoing allogeneic transplants

FIGURE 18: Causes of death after all allogeneic transplants