ORIGINAL ARTICLE

10.46765/2675-374X.2025V6N1P271

CURRENT USE AND OUTCOMES OF CELLULAR THERAPY: BRAZILIAN SUMMARY SLIDES-2025

Cinthya Corrêa da Silva[1] | Anderson João Simione[2] | Paula Moreira da Silva Sabaini[3] | Antonio Vaz de Macedo[4] | Heliz Regina Alves das Neves[5,6] | Monique Ammi[7] | Flavia Ferreira Costa[8] | Celso Arrais Rodrigues da Silva[9] | Adriana Mendes de Quadros Cavilha[5] | Rosana Rocha Concilio[10] | Phillip Scheinberg[10] | Nelson Hamerschlak[1] | Marco Aurelio Salvino[11] | Adriana Seber [12,13,14] | Yana Augusta Sarkis Novis[8] | Vanderson Geraldo Rocha[15] | Joaquim Gasparini dos Santos[15] | Lúcia Silla[16,17] | Ricardo Chiattone[14] | Andreza Alice Feitosa Ribeiro[1] | Vaneuza Araújo Moreira Funke[5,6] | Leonardo Javier Arcuri1[18] | Lucila Nassif kerbauy[1] | Jayr Schmidt Filho[19] | Maria Claudia Rodrigues Moreira[20] | Carmem Maria Sales Bonfim[21] | Cilmara Cristina Kuwahara [21] | Marcelo C. Pasquini[22] | Fernando Barroso Duarte[23, 24]

1. Hospital Israelita Albert Einstein, São Paulo, SP, 2. Hospital Amaral Carvalho, Jaú, SP, 3. Barretos Cancer Hospital, Barretos, SP, 4. Hospital da Polícia Militar, Belo Horizonte, MG, 5. Hospital de Clínicas – Universidade Federal do Paraná, Curitiba, PR, 6. Hospital Nossa Senhora das Graças – Instituto Pasquini, Curitiba, PR, 7. Center for International Blood and Marrow Transplant Research (CIBMTR), Minneapolis, MN, USA, 8. Hospital Sírio-Libanês, São Paulo, SP, 9. Hospital Nove de Julho, São Paulo, SP, 10. Real e Benemérita Sociedade de Beneficência Portuguesa de São Paulo, São Paulo, SP, 11. Universidade Federal da Bahia, Salvador, BA, 12. Associação da Medula Óssea, São Paulo - AMEO , São Paulo, SP, 13. Instituto de Oncologia Pediátrica, Graacc/Unifesp, São Paulo, SP, 14. Hospital Samaritano Higienópolis, São Paulo, SP, 15. Hospital das Clínicas da Universidade de São Paulo, São Paulo, SP, 16. Hospital de Clínicas de Porto Alegre, Porto Alegre, RS, 17. Universidade Federal do Rio Grande do Sul, Porto Alegre, RS, 18. Instituto Nacional do Câncer (INCA), Rio de Janeiro, RJ, 19. A.C. Camargo Cancer Center, São Paulo, SP, 20. Complexo Hospitalar de Niterói, Rio de Janeiro, RJ, 21.Hospital Pequeno Príncipe – Curitiba, PR, 22. Center for International Blood and Marrow Transplant Research (CIBMTR) and Medical College of Wisconsin, Milwaukee, WI, USA, 23. Hospital Universitário Walter Cantídio, Fortaleza, CE, 24. Hospital Monte Klinikum, Fortaleza, CE

Corresponding author: Cinthya Muniz Corrêa Rocha da Silva (e-mail: silvacinthya87@gmail.com)

Received: 16 Jun. 2025 • Revised: 21 Jun. 2025 • Accepted: 24 Jun. 2025

ABSTRACT

Chimeric antigen receptor T-cells (CAR T cells) are genetically modified cellular immunotherapies approved as a standard of care treatment for patients with lymphoma and leukemia worldwide. Here, we report the initial activity in Brazilian centers through the collaboration between the Brazilian Cellular Therapy and Bone Marrow Transplant Society (SBTMO) and the Center for International Blood and Marrow Transplant Research (CIBMTR). A total of 104 patients who received commercial and academic CAR-T cells in Brazil between January 2020 and April 2025 were included. The median age was 56 years (range 4-83). Indications were Non-Hodgkin Lymphoma (NHL; 75 cases; 72%), Acute Lymphoblastic Leukemia (ALL; 23 cases; 22%), Multiple Myeloma (MM; 4 cases; 4%) and Chronic lymphoblastic leukemia (CLL; 2 cases; 2%). Anti-CD19 commercial CAR-T were 82% of the total, 68 for NHL and 17 for ALL). Most deaths were due to disease progression or relapse (n=19), followed by infections (n=8). The overall survival after a median follow-up of 200 days was 73% (95% CI: 62-86; N=63) for NHL and 79% (95% CI: 63-99; N=19) for ALL. This report demonstrates the successful initial implementation of CAR-T cells in Brazil among centers that report to the SBTMO/CIBMTR. This infrastructure will assist in further capturing the activity, assessing the outcomes, and complying with regulatory requirements.

Keywords: Immunotherapy, Adoptive. Immunotherapy. Receptors, Chimeric Antigen. Data Management.

INTRODUCTION

Chimeric antigen receptor T cells (CAR-T cells) are genetically modified cellular immunotherapies directed against different antigens expressed in tumors cells. Brazil's National Health Surveillance Agency (Anvisa), as other national regulatory health authorities, require recipients of these therapies to be followed for 15 years for assessment of safety, including the development of subsequent neoplasms. All genetically modified cellular products carry the risk of subsequent malignancies, including insertional mutagenesis or replication of competent retrovirus or lentivirus[1].

Among the cellular immunotherapy products, the most used and currently approved as standard of care treatment are autologous CAR-T cells targeting CD19 and BCMA. The process involved in CAR-T cell therapies is multi-step, starting with the leukapheresis, manufacturing, lymphodepleting chemotherapy, infusion, treatment of the specific therapies and long-term follow-up. In 2019, the Centro de Terapia Celular do Hemocentro de Ribeirão Preto (CTC-USP) used for the first time in the country their academic CD19 CAR-T cells to treat patients with lymphoma and leukemia, who had exhausted all other treatment options. Many of these patients achieved remission and are still disease-free as of 2025.[2,3]

Since 2020, Anvisa has approved four commercial CAR-T products for leukemia, lymphoma, and myeloma treatment: Kymriah® (tisagenlecleucel; approval date February 23, 2022), Carvykti® (ciltacabtagene autoleucel, approval date April 1, 2022), Yescarta® (axicabtagene ciloleucel, approval date October 26, 2022), and Tecartus® (brexucabtageno autoleucel, approval date January 30, 2024).

With the publication of the first specific health regulations for Advanced Therapy Products (ATPs), Brazil has joined the countries with regulatory frameworks for the development and use of these innovative products.[4] There are nine Brazilian academic CAR-T cells initiatives. According to Anvisa, it is required to conduct a 15-year post-CAR-T cell

therapy follow-up. Industries may have different protocols or registries to comply with this follow-up.

The Brazilian Cellular Therapy and Bone Marrow Transplant Society (SBTMO) has a long experience of registering hematopoietic cell transplants (HCT) in partnership with the Center for International Blood and Marrow Transplant Research (CIBMTR), using the North American web-based infrastructure. The first Brazilian CAR-T cell therapy was registered at the CIBMTR in 2020. Over the years, the number of Brazilian centers reporting to the CIBMTR has increased, facilitating the establishment of a comprehensive database for also evaluating CAR-T cell therapy outcomes in the country. This growth has also contributed to the development of the Hematopoietic Cell Transplantation and Cellular Therapy Brazilian Registry (HCT-CT/BR). Data reported by Brazilian centers to the CIBMTR is aggregated and shared back with the SBTMO. The CAR-T cell therapy activities at Brazilian centers are published annually on the SBTMO website and Journal, providing a valuable resource for the community of advanced cell therapies in Brazil. This initiative enhances collaboration, data sharing, and the progress of cellular therapies in Brazil.

OBJECTIVE

Our objective is to report the CAR-T cell activities and outcomes in Brazilian centers in the past four years.

METHODS

Data Sources

Brazilian advanced cell therapy centers report their data to the CIBMTR, using the electronic FormsNet3 platform. Patients and/or parents gave informed consent for the report. Access is protected by double authentication for all users. The compiled, standardized, and codified data returns to SBTMO through the Data Back to Centers (DBtC) tool, enabling the analysis of CAR-T cell outcomes throughout the country.

Selection

Data from 104 CAR-T cells infused between January 2020 and April 2025 were extracted from the CIBMTR portal using the DBtC, gathering information from 11 Brazilian centers. There was complete information about the type of CAR-T cell and diagnoses.

The spreadsheet was imported into Power BI Desktop (PBI). Functions were created to count the number of CAR-T cell performed and the number of participating centers, to translate columns into Portuguese, categorize and classify diseases, and to group variables.

Definitions and Outcomes

Patients were classified as pediatric (0-17 years of age) or adults (≥18 years of age).

CAR-T cells were classified as non-commercial and commercial.

Treatment outcomes and causes of death were reviewed.

Statistical analysis

Descriptive statistics was used for categorical data, with the number of cases and percentage. Graphics were generated by PBI.

Ethical considerations

Ethics approval for utilization of the CIBMTR platform for the Brazilian Registry for research was obtained from the national Institutional Review Board (IRB) in 2019 (CONEP CAAE: 65575317.5.1001.0071, principal investigator Nelson Hamerschlak, MD). All procedures of the present study followed the ethical standards of the responsible committees of the institution and national guidelines and adhered to the revised version of the Helsinki Declaration of 1975 and the Resolution No. 466/2012, of the National Council of Health.

RESULTS

From January 2020 to April 2025, a total of 104 autologous CAR-T cell infusions were reported from 11 Brazilian centers (Table 1). A total of 64 patients (62%) had not undergone a previous HCT. There was a notable increase in the number of procedures performed in the country and registered in the CIBMTR: one patient registered in 2020, one in 2021, four in 2022, 43 in 2023, 44 in 2024 and 11until April 2025 (Figure 1). Seventy three percent (76) were performed in the state of São Paulo, 16% (17) in the state of Paraná, 10% (10) in the state of Rio de Janeiro and 1% (1) in Ceará. Adults were 86% (90) of the cases, with a median age of 60 years (range 18-83). The median age at diagnosis was 61 years (21-83) for NHL, 58 (37-74) for (MM), 10 (4-45) for ALL, and

68 (66-69) for CLL. The predominant age group was between 60 and 69 years (Figure 2). The indications were NHL (75 cases; 72%), ALL (23 cases; 22%), MM (4 cases; 4%) and CLL (2 cases; 2%) (Figure 3).

Among the 104 infusions, 82% were commercial (68 NHL and 17 ALL), and 18% were academic (7 NHL, 6 ALL, 4 MM and 2 CLL) (Figure 4). Previous HCT was reported in 83% of patients with ALL, 50% of MM, 50% of CLL, and 24% of the patients with NHL (Figure 5). Commercial products (n=85) were 64% (n=54) Kymriah® (n=37 for NHL and n=17 for ALL) and 36% (n=31) Yescarta® for NHL.

The median follow-up of patients who are alive after CAR-T cell was 243 days (range 25-731). Of the 63 patients treated for NHL with a reported follow-up, overall survival at 200 days was 73% (95% CI: 62-86) (Figure 6) and 79% (95% CI: 63-99) for ALL, n=19 (Figure 7).

Disease progression and/or relapse accounted for most deaths (63%, n=19), followed by infectious complications (27%, n=8), (Figure 8).

DISCUSSION

This report demonstrates a notable increase in the number of Brazilian centers participating in the CIBMTR for CAR-T cell therapy. The number of registered cases had increased substantially over the years, starting with one case per year in 2020 and reaching 104 patients by April 2025.

Over these years, only eight centers contributed to the initial summary of CAR-T cell therapies, increasing to eleven centers in this update, indicating increased involvement and collaboration among the Brazilian institutions in this innovative treatment approach. The predominant indication for adults was NHL (75) and ALL (14) for pediatric patients. These number, however, demonstrate an enormous unmet need for the patients who might benefit from these therapies.

When comparing the main indications for CAR-T therapy between Brazil, USA, Canada, and Israel, a similar profile is observed, with a prevalence of NHL, followed by ALL. Most CAR-T cells infusions reported to the CIBMTR are commercial, with only 6% reporting academic products.[5]

Despite the short follow-up, OS of NHL, and ALL at the median of 200 days was 73% (95% CI: 62-86) and 79% (95% CI: 63-99), far superior to the dismal outcomes of these relapsed diseases.

In this cohort, disease progression or relapse was the leading cause of death (63%, n=19), followed by infectious complications (27%, n=8), (Figure 8).

Efforts should be made to notify and engage participating centers to ensure accurate and comprehensive reporting of outcomes, which is essential for meaningful analyses and quality improvements.

The Brazilian Summary Slides are published yearly and fully available to active centers in the HCT-BR through the SBTMO data request flow (Figure 9).

CONCLUSIONS

The partnership between SBTMO and CIBMTR led to the creation of the Hematopoietic Cell Transplantation and Cellular Therapy Brazilian Registry (HCT-CT/BR). Analyses of the Brazilian CAR-T cell data have resulted in the development of the Brazilian Summary Slides, contributing to a deeper understanding of national CAR-T cell outcomes, and providing centers with a national and international reference. These Brazilian summaries are updated annually and published in the Journal of Bone Marrow Transplantation and Cellular Therapy (JBMTCT). Despite differences in the number of cases, the results of this study are like the US Summary Slides. Consolidation of the registry is promising, as evidenced by the growing number of Brazilian centers affiliated to the CIBMTR and the enhancing qualifications of the Data Managers (DMs) nationwide. Nevertheless, significant work remains ahead. Enhancing the commitment of CAR-T cell centers to report the data is paramount to optimize the transplant registry, as well as ensuring long-term follow-up, and providing continuous education to DMs, thus fostering the retrieval of high-quality data within the national registry. Governmental support, including resources, infrastructure, and training, is indispensable to attain these objectives. Sustained and unwavering dedication in this endeavor holds the potential for ongoing improvements within in the SBTMO data registry, ultimately resulting in better care to our patients. Our current challenge now is to help all Brazilian centers involved in CAR-T cell

therapies to register data with the CIBMTR-SBTMO, so that this national initiative can be strengthened, as already done with HCT data.

ACKNOWLEDGEMENTS

- Nelson Hamerschlak, MD, Vergilio Antonio Rensi Colturato, MD and Fernando Barroso Duarte, MD have been influential advocates for the progress of HCT and CAR-T cell in Brazil, having catalyzed significant advances in the field since 2016.

- Marcelo Pasquini, MD facilitates direct collaboration with the CIBMTR, ensuring that the latest research updates and best practices are disseminated within the Brazilian community.

- Monique Ammi has played an active role facilitating the affiliation of Brazilian centers and has been pivotal in educating and supporting data managers involved in HCT and CAR-T cell initiatives.

- The multidisciplinary CAR-T cell teams across the country, through their dedicated efforts, directly contribute to the ongoing development and success of this specialized field of medicine.

- Data managers of the HCT and CAR-T units, whose ongoing contributions have been essential to the accurate documentation and reporting of data in both national and international registries.

- Mary Flowers, MD is recognized for her valuable participation in the HCT-CT/BR Committee, contributing directly to the advancement of national and international research.

- Finally, the invaluable contribution of patients who have undergone CAR-T cell cannot be overstated, as their willingness to share data and participate in scientific research is critical to advancing knowledge and improving outcomes in this important area of healthcare.

TABLE 1. CAR-T cell centers

Center name
A.C. Camargo Cancer Center
Albert Einstein Hospital
Centro De Pesquisa Clinica Hospital 9 De Julho
Complexo Hospitalar de Niterói
CTMO-HCFMUSP
Hospital Nossa Senhora das Graças - IP
Hospital Pequeno Príncipe
Hospital Samaritano
Hospital Sírio Libanês
Monte Klinikum Hospital
Real e Benemérita Sociedade de Beneficiência Portuguesa de São Paulo

FIGURE 1. Number of CAR-T cell infusions per years

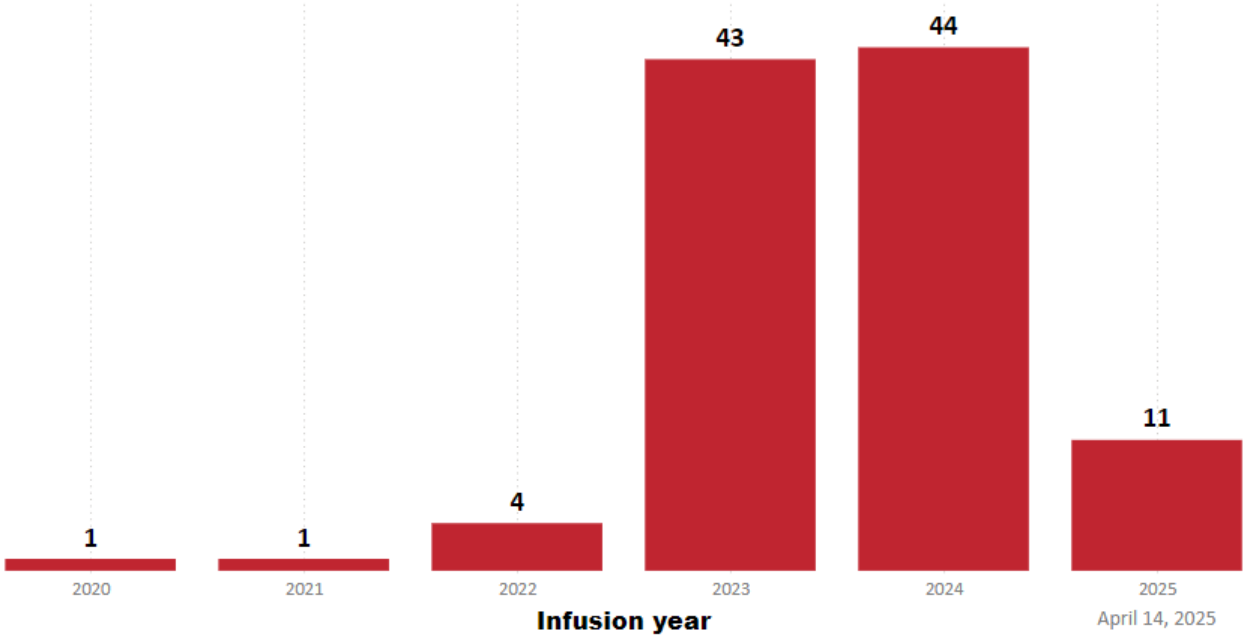


FIGURE 2. Patients' age at CAR-T cell infusion

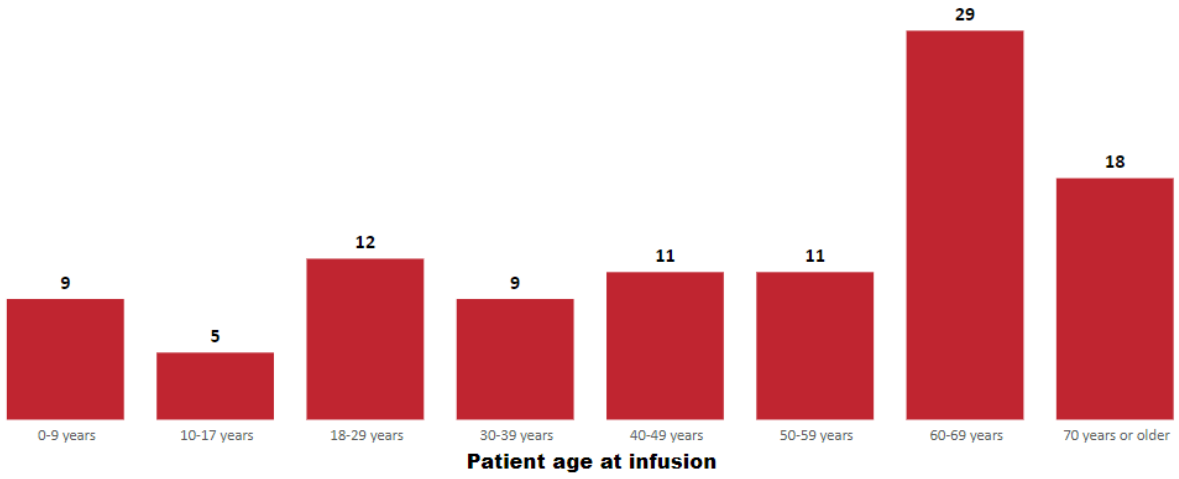


FIGURE 3. Indications for CAR-T cell therapies

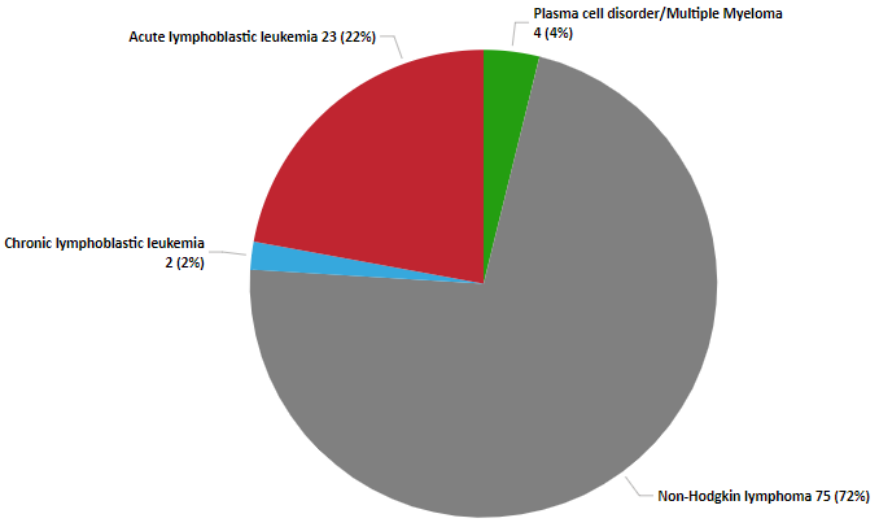


FIGURE 4. CAR-T cell indications by commercial and non-commercial product

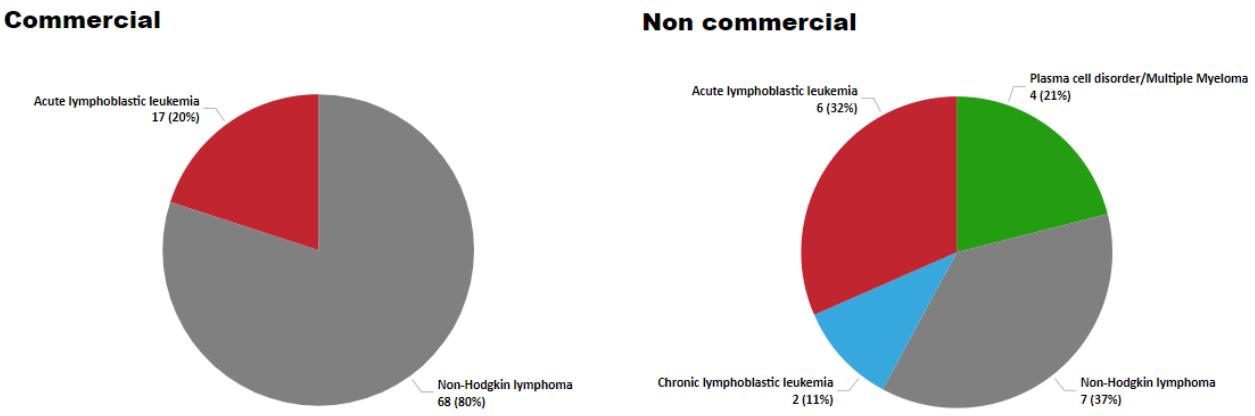


FIGURE 5. **Proportion of patients undergoing HCT prior to CAR-T infusion**

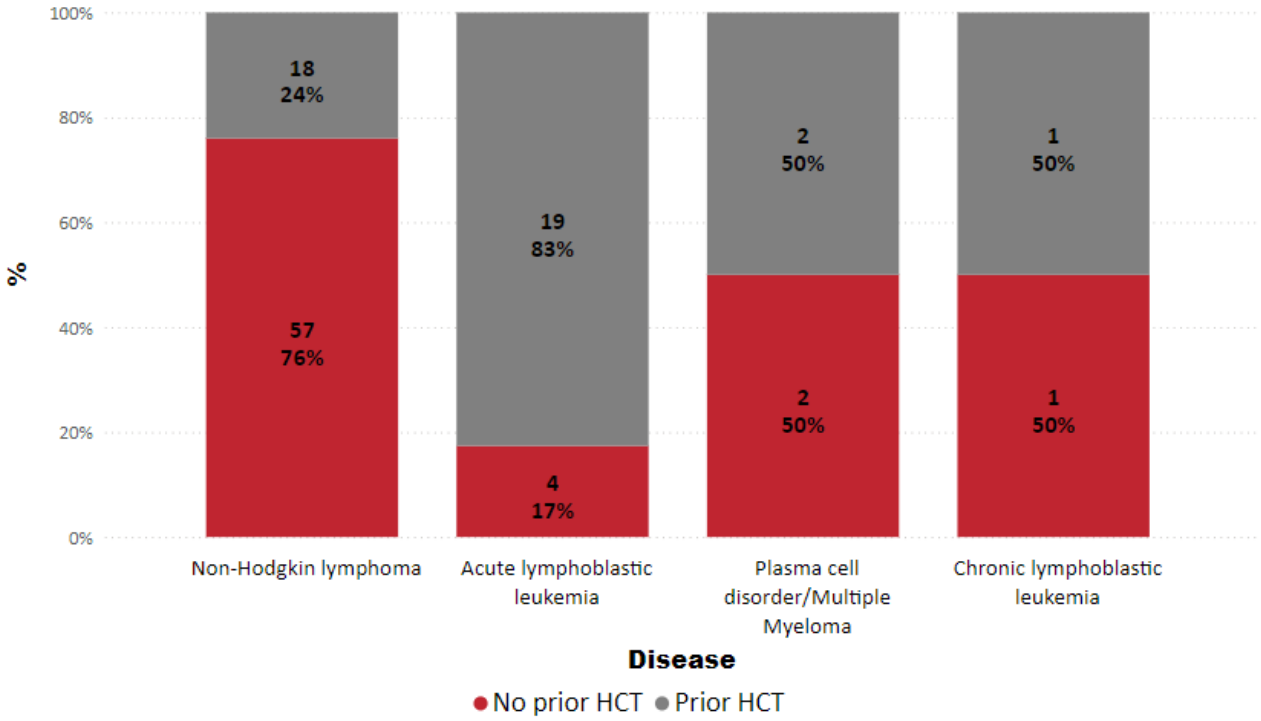


FIGURE 6. **Overall Survival of patients treated for non-Hodgkin lymphoma (at 200 days): 73% (95% CI, 62-86).**

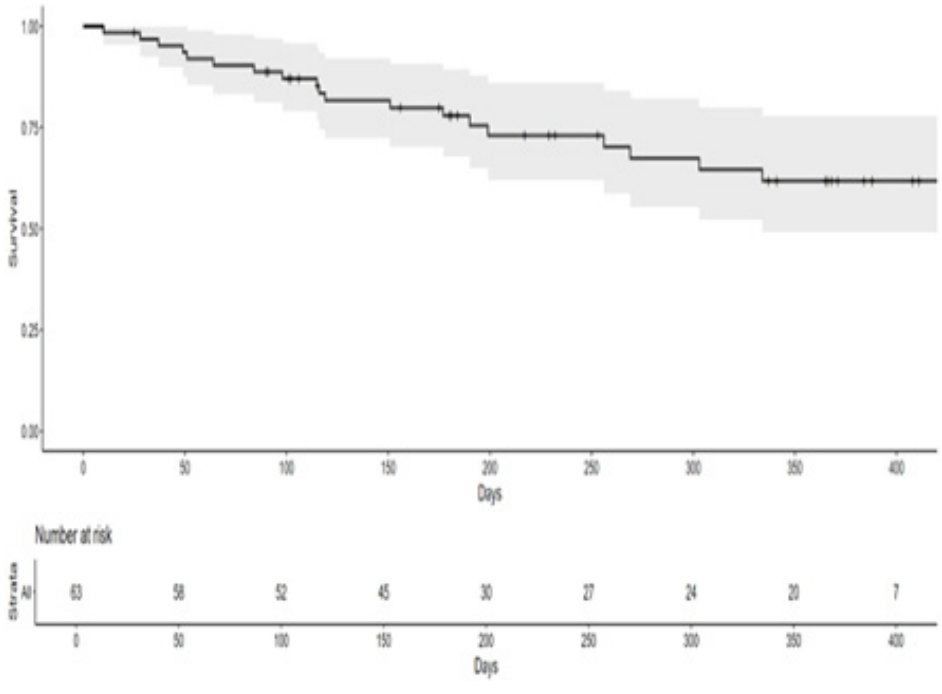


FIGURE 7. Overall Survival of patients treated for Acute Lymphoblastic Leukemia (at 200 days): 79% (95% CI, 63-99).

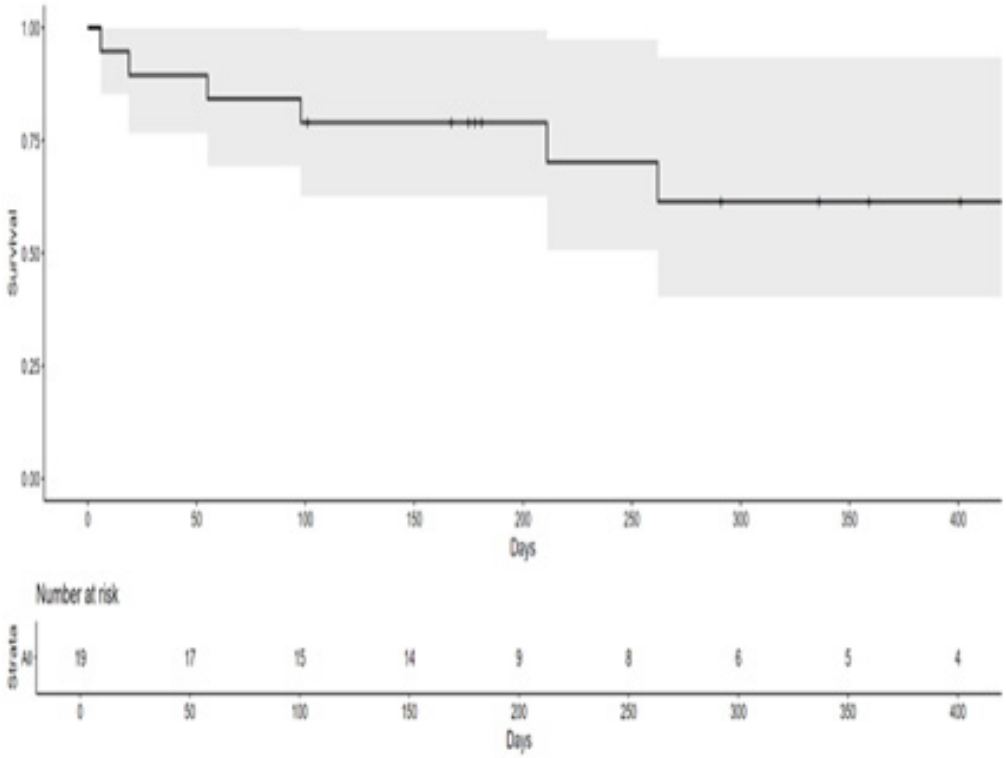


FIGURE 8. Causes of death.

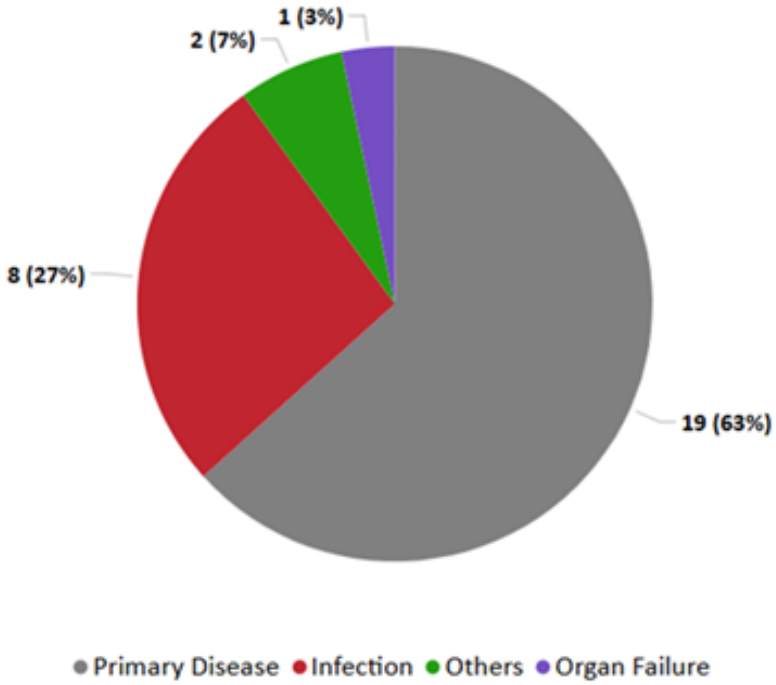
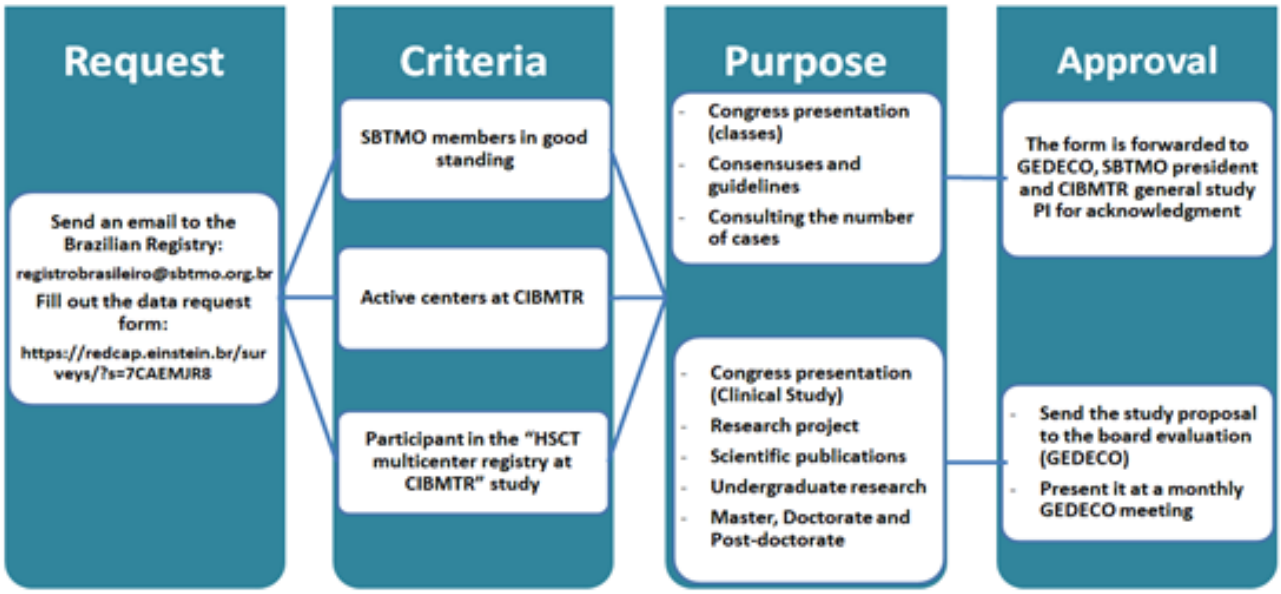


FIGURE 9. **Data request flow**



REFERENCES

1. June CH, O'Connor RS, Kawalekar OU, et al. CAR T cell immunotherapy for human cancer. Science. 2018;359(6382):1361-5.

2. Hemocentro RP. A história da terapia CAR-T: 60 anos de evolução e pioneirismo em direção à cura do câncer [Internet]. Ribeirão Preto; 2025 [cited 2025 Jun 15]. Available from: https://www.hemocentro.fmrp.usp.br/a-historia-da-terapia-car-t-60-anos-de-evolucao-e-pioneirismo-em-direcao-a-cura-do-cancer/

3. Donadel CD, Santis GC, Gonçalves TE, et al. Safety and efficacy of a new academic CD19-directed CAR-T cell for refractory/relapsed non-Hodgkin lymphoma and acute lymphoblastic leukemia in Brazil. Bone Marrow Transplant. 2024;59(7):1040-2.

4. Anvisa. Anvisa autoriza pesquisa clínica com células CAR-T no Brasil [Internet]. Brasília; 2023 [cited 2025 Jun 15]. Available from: https://www.gov.br/anvisa/pt-br/assuntos/noticias-anvisa/2023/anvisa-autoriza-pesquisa-clinica-com-celulas-201ccar-2013-t201d-no-brasil#:~:text=Terapias%20avan%C3%A7adas%20no%20Brasil,por%20empresas%20farmac%C3%AAuticas%20biotecnol%C3%B3gicas%20internacionais

5. CIBMTR. Summary Slides & Report [Internet]. Milwaukee; 2025 [cited 2025 Jun 15]. Available from: https://cibmtr.org/CIBMTR/Resources/Summary-Slides-Reports