

no cytotoxic potencial against HCT116 $luc$  cells (NY-ESO-1–/HLA-A\*02+), demonstrating target specificity. Next, we generated an in vivo melanoma model through subcutaneous injection of  $1 \times 10^6$  A375 $luc$  cells in NSG mice and after 6 days the animals (3–5 per group) were intravenously treated with  $7 \times 10^6$  engineered T cells or non-transduced T cells (NT T cells) (1 donor). Twenty days after the treatment, the tumor burden of 80% (4/5) of animals treated with TCR-T cells increased up to 1.5 times (average:  $4.5 \pm 7.7$  times) and in 80% (4/5) of the animals that received TCR+ shRNA- T cells this increase was  $\leq 3.4$  times (average:  $2.4 \pm 2.9$  times). However, the average tumor burden increased 39.9 times ( $\pm 35.3$ ) in animals treated with NT T cells and 824.1 times ( $\pm 1302.1$ ) in untreated mice. From day 20 to 34 post treatment only untreated animals (5/5) had tumors with volume  $\geq 2\text{cm}^3$  and were euthanized. Collectively, these data demonstrate the successful generation of T cells expressing high affinity TCR anti-NY-ESO-1:HLA-A\*02 with NY-ESO-1 specific and potent antitumor activity. These results lay the groundwork for the development of a new advanced cell therapy product for solid neoplasms and other NY-ESO-1+ malignancies.

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#### RECURRENT CYTOMEGALOVIRUS REACTIVATIONS: FREQUENCY, VIRAL DYNAMIC AND RISK FACTORS IN ALLOGENEIC STEM CELL TRANSPLANTATION.

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**Background:** Cytomegalovirus reactivation (CMVi) is a significant concern following allogeneic sStem Cell Transplantation (allo-SCT) and is associated with considerable morbidity and mortality. High immunosuppression increases the risk of CMV reactivation, leading to recurring episodes, and CMV viremia has been associated with high overall and non-relapse mortality rates. **Objective:** This study aims to describe the frequency, the differences in the viral dynamic compared to the first episode, and the risk factors for recurrent CMV (CMVrec). **Methods:** A prospective cohort of 260 allo-SCT transplants, enrolled between 2016 and 2023, underwent CMV screening using quantitative PCR (Qiagen/Abbott) in plasma. The screening began during the first week after SCT and was repeated weekly until D+100. Additional screenings were performed if immunosuppression continued beyond D+100. Recurrent CMV (CMVrec) was defined as a new viremia in a patient with a previous episode who had tested negative for the virus for at least four weeks. **Results:** Among the 260 allo-SCTs, the median age was 41 years (ranging from 2 to 76), and acute myeloid leukemia represented 36%, followed by acute

lymphocytic leukemia with 21%. The distribution of Haplo-identical (Haplo), Unrelated Donor (URD), and Related Donor (RD) was 110 (42%), 80 (31%), and 70 (27%), respectively. The median follow-up duration was 240 days. CMVi occurred in 189 transplants (73%), with 285 episodes. The frequencies of reactivation in URD, Haplo, and RD cohorts were similar (60%, 76%, and 81%, respectively;  $p = 0.007$ ). At least one CMVrec occurred in 63 (33%) transplants with CMVi. One, 2, 3, and 4 recurrent episodes were documented in 35 (13%), 20 (8%), 6 (2%), and 2 (1%) transplants, respectively. CMVrec showed lower peak viral load (median 115 vs. 1600 IU/mL;  $p < 0.001$ ) and shorter duration of viremia (median 8 vs. 37 days;  $p < 0.001$ ) but similar initial viral load (median 84 vs. 94 IU/mL;  $p = 0.098$ ) compared to the first episode. CMVrec was more frequent in RD transplants (43.4%) compared to URD (23.9%) and Haplo (32.7%) ( $p < 0.005$ ). The viral dynamic including first viral load (90 vs. 101 IU/mL;  $p = \text{NS}$ ), peak viral load (1297 vs. 1908 IU/mL;  $p = \text{NS}$ ), duration of viremia (37 vs. 36;  $p = \text{NS}$ ), the median time for the episode (D + 24 vs. D + 26;  $p = \text{NS}$ ) and frequency of treatment were similar (81% vs 86%  $p = \text{NS}$ ) in the first episode from transplants with or without recurrence. **Conclusion:** In our data, the frequency of recurrent CMV was high and the CMVrec episodes had different viral dynamics compared to the first episodes. Characteristics of the first episode were not associated with the frequency of recurrence, except for the type of donor.

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#### DESCRIPTIVE ANALYSIS OF HEMATOPOIETIC STEM CELL TRANSPLANTS PERFORMED IN A PUBLIC SERVICE BETWEEN 1984 AND 2023

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**Introduction:** Hematopoietic Stem Cell Transplantation (HSCT) is a treatment modality for some benign and/or malignant diseases that affect blood cells. The first successful HSCT took place in the USA in 1957 and later in Brazil in 1979. Several changes have occurred over the decades from scientific and technological advances. Studies that explore descriptive analysis are important in order to monitor trends and changes over time and generate knowledge for practice and actions in public policies. **Objective:** To describe the characteristics of transplants performed in a public HSCT center. **Material and methods:** This is a descriptive study carried out in a HSCT center that used an institutional database and the Center for International Blood and Marrow Transplant Research (CIBMTR) between July 1984 and June 2023 as a

source of information. The characteristics related to the transplants used were: 1) Total number of transplants performed, as well as the median in each of the four decades; 2) Total number of autologous and allogeneic transplants; 3) Types of allogeneic transplants; 4) Sources of hematopoietic stem cells used in transplants; and 5) Main diseases with indication for HSCT. For the evaluation of the characteristics, absolute numbers and percentages (%) were used in the indicated period and medians for the decades. **Results:** In almost four decades of service activities, 2,592 hematopoietic stem cell transplants were performed, of which 1,517 (58%) were allogeneic and 1,075 (42%) were autologous. Of the allogeneic transplants performed, 1,131 (75%) are related, 282 (19%) are unrelated, 94 (6%) are haploidentical and 10 (1%) are syngeneic. The medians of transplants performed in the first (1984–1993), second (1994–2003), third (2004–2013) and fourth (2014–2022) decades were 25, 73, 86 and 83, respectively. The most used source in allogeneic transplants was Bone Marrow (BM) 78% followed by Peripheral Blood (PB) 17% and Umbilical and Placental Cord Blood (UPCB) 5%. Considering allogeneic HSCT, the main diseases with indication for transplants were Acute Myeloid Leukemia (AML) with 355 cases (27%), Acute Lymphoid Leukemia (ALL) with 309 cases (24%), Chronic Myeloid Leukemia (CML) with 294 cases (22%), Severe Aplastic Anemia (SAA) with 216 cases (16%) and Myelodysplastic Syndrome (MDS) with 150 cases (11%). In relation to autologous, the main diseases were Hodgkin's Lymphoma (HL) with 357 cases (35%), Multiple Myeloma (MM) with 345 cases (33%), Non-Hodgkin's Lymphoma (NHL) with 256 cases (25%), Testicular Germ Tumor (TGT) with 41 cases (4%) and Neuroblastoma with 29 cases (3%). **Conclusion:** This descriptive study provided an understanding of the characteristics of transplants performed. An increase in the number of HSCT was observed from the second decade onwards, being mostly allogeneic using the BM as a source. The two most transplanted diseases were AML and HL. Although the study contributed to our current understanding, we recognize that the main limitation was the analysis of characteristics in a single period 1984–2023, without stratification into smaller periods, which prevents the understanding of changes and differences over the years. The findings of this study have practical implications for the HSCT area and pave the way for future investigations to better understand the characteristics of transplants performed in the public health service.

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#### O PAPEL DAS CÉLULAS MESENQUIMAIS NO TRANSPLANTE DE MEDULA ÓSSEA: PREVENÇÃO E TRATAMENTO DA DOENÇA DO ENXERTO CONTRA O HOSPEDEIRO

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**Objetivos:** Reunir as informações mais atuais sobre o uso das Células-Tronco Mesenquimais (CTMs) como aliada do

Transplante de Medula Óssea (TMO) na prevenção e tratamento da Doença do Enxerto Contra o Hospedeiro (DECH). **Material e métodos:** Foi realizada uma revisão integrativa da literatura nas bases de dados PubMed, SciELO, BVS e Google Acadêmico. A busca foi direcionada a artigos publicados nos últimos 5 anos, utilizando-se os descritores: “Mesenchymal stem cells”, “Bone marrow transplantation” e “Graft versus host disease”. Foram selecionados sete estudos publicados em inglês, incluindo revisões sistemáticas e metanálises, ensaios pré-clínicos e clínicos. Por fim, para garantir a qualidade da revisão, foram adotados critérios de exclusão que compreenderam artigos sem acesso ao texto completo e com restrições de acesso pago, bem como aqueles que não estavam diretamente relacionados ao tema central ou que apresentaram duplicações. **Resultados:** Foi encontrado que as Células-Tronco Mesenquimais (CTMs) possuem importante ação imunomoduladora e, por isso, têm sido consideradas uma terapia celular promissora na prevenção e tratamento da DECH refratária às medicações de primeira linha. O uso de CTMs umbilicais e infusão após o TMO mostrou uma redução da incidência de DECH crônica e aumento da enxertia medular, além de aumentar a sobrevida global e a resposta completa em pacientes com DECH aguda. Ademais, foi vista uma resposta terapêutica diferente a depender da fonte de CTMs utilizada. As CTMs derivadas da medula óssea não apresentaram redução da incidência de DECH crônica nem melhoria da enxertia medular, porém, é necessária a realização de mais estudos a fim de investigar as diferentes respostas a partir das fontes de CTMs. Também foi avaliada a possibilidade de aplicação das CTMs em co-infusão com o TMO alogênico, indicando redução da incidência de DECH crônica e aumento da enxertia de neutrófilos e plaquetas, sem alterações na mortalidade. **Discussão:** As CTMs são células multipotentes com propriedades imunomoduladoras e alta capacidade de diferenciação e de autorrenovação. Alguns mecanismos de imunomodulação incluem a secreção de mediadores que suprimem a diferenciação de monócitos em células dendríticas, a atuação em linfócitos T CD4+ por meio do interferon- $\gamma$  e do Fator de Transformação do crescimento- $\beta$  (TGF- $\beta$ ), além de interações com linfócitos B e células NK4. As CTMs não expressam o Antígeno Leucocitário Humano (HLA) de classe 2 e outras moléculas co-estimulatórias, por isso são capazes de evitar a resposta imune do hospedeiro e viabilizar a infusão de CTMs alogênicas sem rejeição. Devido a isso, a terapia para a DECH com CTMs tem se mostrado eficaz, principalmente por apresentar pouco ou nenhum efeito colateral e resultar em sobrevida superior a 2 anos após o TMO. **Conclusão:** As CTMs são uma terapia celular promissora no manejo da DECH refratária às opções de primeira linha, sendo a imunomodulação o principal mecanismo terapêutico. Além disso, permite a infusão de CTMs alogênicas sem rejeição devido à ausência de expressão do HLA de classe 2 e outras moléculas.

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