5033-87532_Auto_Edited.docx.docx

WORD COUNT 4061
TIME SUBMITTED 30-NOV-2023 11:00AM
PAPER ID 104723015

Name of Journal: *World Journal of Transplantation*
Manuscript NO: 87532
Manuscript Type: MINIREVIEWS

Autologous hematopoietic stem cells transplantation conditioning regimens and chimeric antigen receptor T cell therapy in various diseases

Auto-HSCT and conditioning regimens

Shahzaib Maqbool, Maryam Farhan Baloch, Muhammad Abdul Khaliq Khan, Azeem Khalid, Kiran Naimat

Abstract

Conditioning regimens employed in Autologous Stem Cell Transplantation have been proven useful in various hematological disorders and underlying malignancies; however, despite being efficacious in various instances negative consequences have also been recorded. Multiple conditioning regimens were extracted from various literature searches from database like PubMed, Google scholar, EMBASE, and Cochrane. Conditioning regimens for each disease were compared by using various end points such as Overall Survival (OS), Progression Free Survival (PFS), and Leukemia Free Survival (LFS). Variables were presented on graphs and were analyzed to conclude more efficacious a conditioning regimen. In Multiple Myeloma the most effective regimen was high dose melphalan given at the dose of 200/mg/m^2. The comparative results of Acute Myeloid Leukemia (AML) were presented and the regimens that proved to be at an admirable position were BU+MEL regarding OS and BU+VP16 regarding LFS. In case of Acute Lymphoblastic Leukemia (ALL) busulfan, fludarabine and etoposide **(BuFluVP)** conferred good disease control with a paramount improvement not only in survival rate but also low risk of recurrence. However, for ALL chimeric antigen receptor (CAR) T cell therapy was treatment in context of better OS and LFS. With respect to Hodgkin's

Lymphoma MITO/MEL overtook BEAM in view of PFS and vice versa regarding OS. Non-Hodgkin's Lymphoma patients were administered MITO (60mg/m^2) and MEL (180mg/m^2) which showed promising results. Lastly, Amyloidosis was considered, and the regimen that proved to be competent was MEL200 (200mg/m^2). This review article demonstrates a comparison between various conditioning regimens employed in different diseases.

Key Words: Conditioning regimens; Multiple myeloma; Lymphoma; Hodgkin; Non-Hodgkin; Acute leukemia

Maqbool S, Baloch MF, Khan MAK, Khalid A, Naimat K. Autologous hematopoietic stem cells transplantation conditioning regimens and future directions to chimeric antigen receptor T cell therapy in various diseases. *World J Transplant* 2023; In press

Core Tip: This literature review study is based on real-world data collected from various published research introducing multiple conditioning regimens for different disorders. Comparison between regimens of an individual disorder were formed using variables such as Overall Survival (OS), Progression Free Survival (PFS), Complete Remission (CR) and Leukemia Free Survival (LFS) to conclude a laudable conditioning regimen having trivial adverse effects. The following article is designed to discuss the conditioning regimens employed in Autologous Stem Cell Transplantation of various diseases. The primary objective of conducting this review is to highlight the various conditioning regimens, and discuss both the positive and the negative consequences along with proposing a treatment that is both efficacious and harmless.

INTRODUCTION

This literature review study is based on real-world data collected from various published research introducing multiple conditioning regimens for different disorders. Comparison between regimens of an individual disorder were formed using variables such as Overall

Survival (OS), Progression Free Survival (PFS), Complete Remission (CR) and Leukemia Free Survival (LFS) to conclude a laudable conditioning regimen having trivial adverse effects. In Multiple Myeloma the most effective regimen was high dose melphalan given at the dose of 200/mg/m^2/day. However, for ALL CAR-T cell therapy was treatment in context of better OS and LFS. With respect to Hodgkin's Lymphoma MITO/MEL overtook BEAM in view of PFS and vice versa regarding OS. Non-Hodgkin's Lymphoma patients were administered MITO (60mg/m^2) and MEL (180mg/m^2) which showed promising results. Lastly, Amyloidosis was considered, and the regimen that proved to be competent was MEL200 (200mg/m^2). This article presents a descriptive picture of diseases and the regimens employed in them along with mentioning the most successful regimen.

INTRODUCTION

Over the years, many treatment regimens have been crafted for multifarious diseases, and consequently, endorsement of Hematopoietic Stem Cell Transplantation (HSCT) was a strategic approach for hematological disorders or underlying malignancy [1]. Hematopoietic Stem Cells have the potential to develop into all types of blood cells, including white blood cells, red blood cells, and platelets specifying them as an ideal choice [2]. The rationale behind the HSCT procedure is to replace the recipient's damaged cells with infused healthy stem cells and immune cells after exposure to a short course of chemotherapy or radiotherapy [3].

According to recent research, peripheral blood is 99% of the time used as a donor in autologous stem cell transplants [3]. In contrast, blood cells used in allogenic stem cell transplantation are taken from potential donors or cord blood units [4]. Today more than 50,000 HSCT procedures are performed annually worldwide. In Europe transplants that are performed are more than one-half autologous [5].

Conditioning regimens are devised in order to eradicate tumour cells and prevent graft rejection. In the 1970s, successful bone marrow transplantation (BMT) using cyclophosphamide (Cy) and total body irradiation (TBI) was reported [6]. BEAM

(carmustine, etoposide, cytarabine, and melphalan) is the most used conditioning regimen for Hodgkin's Lymphoma, and it has a lower mortality rate when compared to other regimens [7]. Conditioning regimens with low toxicity are now generally preferred for patients with primary immunodeficiency (PID) [8]. To eliminate the damaged cells in the body, HSCT conditioning requires chemotherapy and/or radiation, but this procedure can have life-threatening side effects, therefore HSCT is primarily used to treat malignant illnesses where its advantages outweigh its potentially deadly hazards [9]. As an alternative to the traditional conditioning regimen, a reduced intensity, and non-myeloablative conditioning regimen has been presented [10]. According to research from the Fred Hutchinson Cancer Research Center, patients undergoing nonmyeloablative conditioning (grades III–IV acute graft against host illness) had a considerably decreased incidence of severe acute graft *vs* host disease [11]. According to data from the Centre for International Blood and Bone Marrow Transplant Research (CIBMTR), with multiple myeloma and lymphoma being the most prevalent symptoms [3].

The following article is designed to discuss the conditioning regimens employed in Autologous Stem Cell Transplantation of various diseases. The primary objective of conducting this review is to highlight the various conditioning regimens, and discuss both the positive and the negative consequences along with proposing a treatment that is both efficacious and harmless.

HEMATOPOIESIS FROM HEMATOPOIETIC STEM CELLS

The discovery of induced pluripotent stem cells (iPSCs) by the reprogramming of human and mouse fibroblasts, in 2006 with traits like embryonic stem cells proved to be a landmark in the field of medicine [12]. This discovery ultimately paved way for modern and significant contributions to drug discovery, cell therapy, basic research, and the widespread use of autologous cell-based therapy [13]. Since the isolation of human embryonic stem cells (ESCs), valuable approaches have been made generally focused on directed differentiation to generate pluripotent hematopoietic stem and progenitor cells (HSPCs) to be manipulated in cellular therapy and to treat malignancies [14,15,16].

Since the very beginning, the stem cell concept has been crafted into a hierarchal tree-like model where the stem cells are sitting on the root of a branching family tree and the multipotent stem cells originate in an orderly branching fashion from their ancestorial root [17]. To summarize HSCs are immature embryonic stem cells that harbor the potential to differentiate into their lineage of cells including RBCs, WBCs, and platelets as shown in **figure 1**[18].

HEMATOPOIETIC STEM CELL TRANSPLANTATION

Hematopoietic Stem Cell Transplantation is the most widely used cellular immunotherapy, and is an indispensable treatment for many malignant, congenital, and acquired hematological ailments [19]. HSCT is a requisite after chemotherapy or radiotherapy to consolidate a patient's recovery and provide a lasting cure [20].

1: Autologous Stem Cell Transplantation (Auto-SCT)

In ASCT the stem cells are harvested from the recipient's own bone marrow, peripheral blood, or umbilical cord units. This mode of transplantation is effective since it reduces the occurrence of immunocompromise and transplant rejection [21].

2: Allogenic Stem Cell Transplantation (Allo-SCT)

Allogenic Transplantation uses fresh HSCs so the collection from the donor as well as the conditioning of the patient occurs at the same time and reduces the risk of cell reduction *via* thawing or freezing [22]. Patients who undergo Allogenic STC require a longer period of immunosuppression in-order to avert the likelihood of transplant rejection.

DISEASES TREATED BY AUTOLOGOUS STEM CELL TRANSPLANTATION (AUTO-SCT)

Owing to the great advancements in the field of medicine Auto-SCT has now been regarded as an established therapeutic approach for many Haemato-oncologic, immunological and hereditary conditions with the potential of cure. In 2012 the number of Auto-SCT transplants performed reached over one million [21]. There are following

disease for which the ASCT is being performed more frequently and are mentioned in the **figure 2**.

AUTOLOGOUS STEM CELL TRANSPLANTATION CONDITIONING REGIMENS IN VARIOUS DISEASES

1: Autologous hematopoietic stem cell transplantation conditioning regimens in Multiple myeloma (MM):

Multiple myeloma is an incurable, malignant B-cell neoplasm characterized by uncontrolled, destructive growth of mutated plasma cells along with the dissemination of multiple tumor cells throughout the bone marrow [23]. With the progress in the field of medical oncology, various drugs of paramount significance have been developed for the treatment of multiple myeloma (e.g proteasome inhibitors and immunomodulatory drugs) [24].

The process of Auto-SCT is carried out in four basic steps: the mobilization, apheresis of mobilized stem cells, utilization of conditioning regimen and, finally reinfusion [25]. According to a retrospective study by *Annamaria et al (2018), involving 187* patients of multiple myeloma and a comparison of high dose Melphalan 200 mg/m^2 (MEL200) and low dose Melphalan 140mg (MEL140) conditioning regimens were made. The MEL 200 was used in 112 (60%) and MEL 140 was used in 75 (40%) of the patients. According to this study OS was found higher among patients treated with MEL 200 as compared to those who were given MEL200 or MEL140 (66% *vs* 51% at 5 years) [26].

According to a study by *Taiga Nishihori et al (2011)* reviewing the effectiveness of various treatment modalities in MM also showed promising benefits by utilization of Bortezomib along with high dose MEL [27].

During the last decade, genetically engineered chimeric antigen receptor (CAR)-T cell therapy has been identified with the identification of several target antigens like CD19, CD38, CD138, and B-cell maturation antigen (BCMA) [28]. However, CAR-T cell targeting CD19 is the most identified CAR-T cell that is being used in hematological malignancies and BCMA-targeted CAR-T cells are being evaluated to be used against MM. These new

treatment strategies have brought a ray of hope to cure MM with reduced mortality rates and improved overall survival [29].

2: Autologous hematopoietic stem cells transplantation conditioning regimens in Acute Myeloid Leukemia (AML):

In recent years the therapeutic and prognostic profile of AML has been improved due to recent advances in chemotherapeutic agents and the rising trend of autologous Hematopoietic stem cells transplantation (ASCT) to consolidate adult patients with AML [30]. AML is a rare diagnosis, still, due to high neoplasm potential it is associated with large number of leukemia-associated deaths with reduced overall survival rate. The presence of balance translocation between chromosome 8 and 21 t (8;21), inversion of chromosome 16, and translocation between chromosome 15 and 17 t (15;17) has also been implicated in acute promyelocytic leukemia pathogenesis along with some genetic and epigenetic alterations [31]. Though recent advances have been paving an excellent pathway for halting the disease progression and improvement in overall survival rate, still AML is posing some serious therapeutic challenges to be treated.

According to a retrospective analytical study involving 952 patients of AML by *Nagler et al* (2014), the median age of patients was 50.5 years with 56% of the population (n = 531) consisted of the male population and the effectiveness of intravenous busulfan in ASCT was ascertained in this study and comparison was made with oral busulfan utilization in patients undergoing ASCT. Intravenous conditioning regimens based mainly on busulfan (12.8mg/kg) combined with cyclophosphamide (120mg/kg) were administered in about 517 patients, similarly, the combination of intravenous busulfan (12.8mg/kg) and melphalan (140mg/kg) was given to 234 patients, a combination of intravenous busulfan and etoposide was tried in (82) patients finally the intravenous busulfan and idarubicin were administered in 46 patients and outcomes in terms of two years OS, LFS and relapsed incidence were assessed. But to over surprise the effectiveness of all combinations was higher in patients aged less than 50 as compared to older patients and OS was 67±2%, leukemia free survival was 53±2%, and relapse incidence was 40±2%. Out of all the combinations discussed herein, the combination of intravenous busulfan

(12.8mg/kg) with melphalan (140mg/kg) was significantly associated with improved OS as compared to other three combinations, validating the effectiveness of IV busulfan and melphalan a regimen of choice when compared with other regimens used either IV route and also with oral busulfan that was actually was showing the greater toxicity profile than IV busulfan administration with less incidence of veno-occlusive disease [32].

The conditioning regimens are now considered the real estate of Auto-SCT success because it not only creates the space to transplant the HST but also eradicate the disease itself. A study conducted by *Gorin et al (2017)* using the data from a registry of the European Society for Blood and Marrow Transplantation (EBMT) to compare the effectiveness of two standard conditioning regimens like BUMEL and BUCY in Auto-SCT of AML patients. The first regimen consisted of busulfan (12.8mg/kg) and melphalan (140mg/kg) combined (BUMEL) and the second regimen used in comparison consisted of busulfan (12.8mg/kg) and cyclophosphamide (120mg/kg) (BUCY). This study involved 853 patients with available cytogenetics of AML and BUMEL therapy was used in 30% of the patients (n = 257), while 70% of the patients (n = 596) were administered with BUCY therapy and the outcomes were evaluated in terms of relapse incidence (RI), LFS and finally OS. The findings were truly mandating the utilization of the BUMEL regimen against BUCY due to reduced RI (39.5% *vs* 52.2%; P = 0.003), better LFS (55.4% *vs* 44.6%; P = 0.005) and finally better OS rate (73.8% *vs* 63%; P = 0.0007) validating the higher effectiveness of BUMEL regimen in ASCT [33]. When the OS is compared between other conditioning regimens used *vs* BUMEL ASCT of patients with AML, the BUMEL regimen was found to be highly effective on all grounds, making it the conditioning regimen of choice with excellent ultimate outcomes.

The construction of a CD-70 CAR-T cell can prove to be a breakthrough in the field of oncology and medicine. CD70 is a type 2 transmembrane glycoprotein and a member of the tumor necrosis factor (TNF) ligand family that is now increasingly being utilized as a therapeutic target for the treatment of AML, however, still there is very much to discover about this therapeutic approach. The antitumor activity of a CD70-specific monoclonal antibody along with hypomethylating agents for the treatment of patients with AML has

been showing promising benefits [34]. Therefore, we can hope that in the future designing of CAR-T cells will be conducive to the treatment of hematological malignancy with minimal myelotoxicity.

3: Autologous hematopoietic stem cell transplantation conditioning regimens in Acute Lymphoblastic Leukemia (ALL):

Acute lymphoblastic leukemia is a familiar paediatric carcinoma marked by chromosomal translocations and somatic mutations [35].

Lee JW *et al* (2015) carried out a retrospective study using a myeloablative therapy. They inducted 44 patients from March 2009 to January 2014 and the efficacy was assessed by complete remission (CR). These patients underwent HSCT using a once-daily IV conditioning regimen. The regimen included busulfan (120mg/m^2 for patients >1 year of age and 80 mg/m^2 for patients <1 year of age), fludarabine 40mg/m^2 and etoposide 20 mg/kg. Results showed 28 (63.6%), 12 (27.3%), and 1 (2.3%) patient were in 1st, 2nd, and 3rd complete remission (CR), respectively; while 2 (4.5%) patients had no remission at the time of HSCT. The complications reported in this study included elevated AST and/or ALT or total bilirubin [36].

To compare the efficacy of TBI plus etoposide and myeloablative regimen (including fludarabine, thiotepa, and IV busulfan/treosulfan) Peters C *et al* in 2021 conducted a multi-centre and randomized trial in high-risk ALL patients. Efficacy was measured in terms of TRM. They inducted 417 patients and randomly assigned them to the two cohorts. Cohort 1 included TBI and IV etoposide (60 mg/kg) while cohort 2 included fludarabine (30mg/m^2) once daily, thiotepa (5mg/kg) twice daily, and treosulfan (14 g/m^2)/busulfan once daily. Following the TBI-based regimen and Myeloablative regimen, the two-year TRM was 0.02 (95%CI,0.01 to 0.05) and 0.09 (95%CI, 0.05 to 0.14), respectively [37]. Thus, showing that TBI plus etoposide regimen had good disease control.

For hematologic malignancies, CAR-T cell therapy has been unfolded as an efficacious therapeutic option. Its mechanism of action involves the patient's own T-cells that in turn express receptors modified to recognize specific epitopes of tumor-associated antigens

on the target cell surface [38]. Numerous trials have been carried out to investigate the efficacy of this therapy. Subklewe M *et al* (2019) conducted "the pivotal global ELIANA trail" (NCT02435849) using genetically modified CD19-directed T-cell products, 'Tisagenlecleucel' [39]. In another Phase 1 trial (NCT01044069), Davila ML *et al* (2014) pointed out the plausibility of CAR-T cell therapy. In this phase 1 trial, 16 patients were enrolled and given a 19-28z infusion of CAR-T cells after salvage chemotherapy. This blatantly boosted the overall complete response rate to 88% which is higher than that expected with salvage chemotherapy alone [40].

To sum up, the introduction of CAR T cell therapy has provided new directions to the field of oncology and medicine, however, ASCT is widely preferred because of being inexpensive. Moreover, CAR-T cell therapy needs further evolution by health professionals.

4: Autologous hematopoietic stem cell transplantation conditioning regimens in Hodgkin Lymphoma (HL):

Hodgkin lymphoma (HL) is a unique hematopoietic neoplasm characterized by cancerous Reed Sternberg cells in an inflammatory background. Patients in their 20s and 30s who have supra-diaphragmatic lymphadenopathy and frequently have systemic B symptoms are frequently identified [41]. In order to be collected by apheresis, hematopoietic stem cells must first be recruited into the circulation because they typically circulate in extremely small amounts in peripheral blood [42].

According to a retrospective, multi-center study by Mahmut *et al* (2020) involving 142 patients of HL undergoing ASCT showed the comparison of two conditioning regimens with end point represented by OS and PFS. The two conditioning regimens used were BEAM (carmustine 300mg/m^2 given at day -6, etoposide 200mg/m^2 between day -5 to -2, cytarabine 200mg/m^2 between day -5 to -2, melphalan 140mg/m^2 at day -1) was administered in 108 patients and 34 patients were administered with mitoxantrone (MITO) 60mg/m^2 in 3 divided doses at day -5 along with melphalan (MEL) 180mg/m^2 in 3 divided doses at day -2 constituting a group with MITO/MEL [43].

According to a study by Chen *et al* (2015) involving 1012 patients of HL BEAM and CBV^{low}, CBV^{high} were the most used regimens with 3 years OS of 79% and PFS of 62% in BEAM group, OS of 73% and PFS of 60% in CBV^{low}, OS of 68% and PFS of 57% in CBV^{high} group [44]. However, BEAM-based regimen was most effective in HL with better OS and PFS as compared to other regimens.

Chimeric antigen receptor (CAR) T-cell therapy of B-cell malignancies has proved to be effective. *Carlos A. Ramos et al* showed how the same approach of CAR T cells specific for CD30 (CD30.CAR-Ts) can be used to treat Hodgkin lymphoma (HL) [45].

5: Autologous hematopoietic stem cell transplantation conditioning regimens in Non-Hodgkin Lymphoma (NHL):

Non-Hodgkin lymphomas (NHL) are a diverse collection of lymphoproliferative tumors with a greater propensity to expand to extra-nodal sites than Hodgkin's lymphomas. Both nodal and extra-nodal regions are involved in the majority of NHL cases and chronic antigen stimulation [46]. The mobilization of hematopoietic stem cells is followed by apheresis of the mobilized stem cells, use of a conditioning regimen, and finally reinfusion [47].

Between May 19, 2015, and September 15, 2016, Locke *et al* (2019) carried out a single-arm, multicenter, phase 1-2 experiment in which 119 patients were enrolled and 108 were given axicabtagene ciloleucel. Seven patients participated in phase 1, while the remaining 107 were enrolled in phase 2 studies. After receiving intravenous (IV) fludarabine and cyclophosphamide as conditioning chemotherapy, participants received one dose of axicabtagene ciloleucel. Only pronounced adverse events, such as neurological events, hematological events, infections, autoimmune disorders, and secondary malignancies were documented after three months [48].

Between February 25, 2011, and April 3, 2014, Michele Cavot *et al* selected 1503 previously untreated patients for this randomized, open-label, phase 3 research. The forecasts for overall survival over five years, survival without disease, and survival without events were 81.9%, 46.5%, and 41.4%, respectively. All patients displayed neutropenia and thrombocytopenia. All individuals had nausea, mucositis, and vomiting [49]. Logan Hahn

et colleagues (2021) assessed successive Hodgkin's lymphoma patients who received BEAM HDCT and BeEAM followed by ASCT between 2015 and 2019. BEAM had a 3-year OS of 78.1% while BeEAM had a 3-year OS of 71.0%. BEAM had a 3-year PFS of 71.3% while BeEAM had a 3-year PFS of 74.1% [50].

Chimeric antigen receptor T-cell therapy (CAR-T) has emerged as a standard of care for treating a number of disorders in recent years, overcoming any potential drawbacks associated with conventional therapies. Clinical trials of anti-CD19 CAR-T cell therapy for the treatment of refractory or relapsed B-NHL have produced encouraging effective outcomes [51].

6: Autologous hematopoietic stem cell transplantation conditioning regimens in Amyloidosis (AL):

Amyloidosis is a clonal plasma cell dyscrasia characterized by the accumulation of misfolded fibrillar proteins in extracellular tissues, leading to organ failure and eventually death. Though associated with high treatment-related mortality, for nearly 20 years AHSCT has been used and demonstrated improved survival and a prolonged treatment-free interval [52].

According to a study by Tandon *et al* (2017), involving 457 diagnosed cases of light chain amyloidosis (AL) undergoing AHSCT were selected and two conditioning regimens one with full dose melphalan (200mg/m^2) and the other with low or reduced intensity melphalan (100mg/kg) were compared. Complete response was observed in high dose Melphalan group (53% *vs* 37%, P = 0.003), and the PFS was also validating the effectiveness of high dose melphalan regimen when compared with low dose melphalan group (55% *vs* 31%; P< 0.001) [53].

Similarly, a trial labelled SWOG (S0115) conducted by Sanchorawala *et al* (2013) involved 93 patients diagnosed with amyloidosis either light chain (AL), myeloma associated (AM), and host-based high-risk myeloma (hM) with 59, 9 and 25 patients in each group were evaluated with sequential doses of modified melphalan (100mg/m^2). The estimated 2- and 5- year OS was 69%, 56%, and 80%, and 56%, 42%, and 55% for AL, ALM, and hM, respectively. 5-year estimated PFS was 50%, 30%, and 50% in AL, ALM and hM,

respectively [54]. Between July 1994 and June 2002, Skinner *et al* (2004) evaluated 701 consecutive patients with AL amyloidosis. 56% (394) of the patients met the eligibility criteria for high dose melphalan treatment. Overall median survival was 4.6 years and 56% of the patients remained alive. 5-year estimated survival rate was 47%. [55].

Strategies for the treatment of hematologic malignancies have evolved like the use of Immunotherapy is an attractive approach. *M. Rosenzweig et al (2017)* provided preclinical data evaluating bone marrow specimens for BCMA and CS1 expression in 10 AL patients. All the AL samples expressed high levels of CS1 (76.5 ± 4.7%) but low levels of BCMA (4.9 ± 0.8%). The study reported the unique nature of plasma clonal cells in AL patients because of the scarcity of BCMA expression [56].

CONCLUSION

This literature review study is based on real-world data collected from various published research introducing multiple conditioning regimens for different disorders. Comparison between regimens of an individual disorder were formed using variables such as Overall Survival (OS), Progression Free Survival (PFS), Complete Remission (CR) and Leukemia Free Survival (LFS) to conclude a laudable conditioning regimen having trivial adverse effects. In Multiple Myeloma the most effective regimen was high dose melphalan given at the dose of 200/mg/m^2/day. However, for ALL CAR-T cell therapy was treatment in context of better OS and LFS. With respect to Hodgkin's Lymphoma MITO/MEL overtook BEAM in view of PFS and vice versa regarding OS. Non-Hodgkin's Lymphoma patients were administered MITO (60mg/m^2) and MEL (180mg/m^2) which showed promising results. Lastly, Amyloidosis was considered, and the regimen that proved to be competent was MEL200 (200mg/m^2). This article presents a descriptive picture of diseases and the regimens employed in them along with mentioning the most successful regimen.

5033-87532_Auto_Edited.docx.docx

ORIGINALITY REPORT

9%
SIMILARITY INDEX

PRIMARY SOURCES

1	pubmed.ncbi.nlm.nih.gov Internet	74 words — 2%
2	ashpublications.org Internet	39 words — 1%
3	Michael Rosenzweig, Ryan Urak, Miriam Walter, Laura Lim, James F. Sanchez, Amrita Krishnan, Stephen Forman, Xiuli Wang. "Preclinical data support leveraging CS1 chimeric antigen receptor T-cell therapy for systemic light chain amyloidosis", Cytotherapy, 2017 Crossref	26 words — 1%
4	docplayer.net Internet	23 words — 1%
5	www.zora.uzh.ch Internet	23 words — 1%
6	Amin Islam, Md. Mahabubur Rahman, Paul Cervi, J H Yeo. "Hodgkin's Lymphoma- a Review: Future Directions in the Era of Targeted Therapy", Haematology Journal of Bangladesh, 2020 Crossref	22 words — 1%
7	Kyung Taek Hong, Hyoung Jin Kang, Jung Yoon Choi, Che Ry Hong et al. "Favorable Outcome of Post-Transplantation Cyclophosphamide Haploidentical	17 words — < 1%

Peripheral Blood Stem Cell Transplantation with Targeted Busulfan-Based Myeloablative Conditioning Using Intensive Pharmacokinetic Monitoring in Pediatric Patients", Biology of Blood and Marrow Transplantation, 2018
Crossref

8	thalassaemia.org.cy Internet	17 words — < 1%
9	A. Bazinet, G. Popradi. "A general practitioner's guide to hematopoietic stem-cell transplantation", Current Oncology, 2019 Crossref	16 words — < 1%
10	Sunita Nathan, Antonio M. Jimenez, Alfonso D. Moreno, John Maciejewski, Henry C. Fung. "Severe Mucositis with Bendamustine Etoposide Ara-C and Melphalan (Be-EAM) As Conditioning Regimen in Non-Hodgkin Lymphoma (NHL) Patients Undergoing Autologous Stem Cell Transplantation (AutoSCT)", Biology of Blood and Marrow Transplantation, 2015 Crossref	16 words — < 1%
11	stemcellres.biomedcentral.com Internet	16 words — < 1%
12	www.haematologica.org Internet	15 words — < 1%
13	cttjournal.com Internet	14 words — < 1%
14	www.1radionews.com Internet	14 words — < 1%
15	www.ncbi.nlm.nih.gov Internet	13 words — < 1%

16 Frederick L Locke, Armin Ghobadi, Caron A Jacobson, David B Miklos et al. "Long-term safety and activity of axicabtagene ciloleucel in refractory large B-cell lymphoma (ZUMA-1): a single-arm, multicentre, phase 1–2 trial", The Lancet Oncology, 2018
Crossref

12 words — < 1%

17 journals.lww.com
Internet

12 words — < 1%

18 www.nature.com
Internet

12 words — < 1%

EXCLUDE QUOTES	ON	EXCLUDE SOURCES	< 12 WORDS
EXCLUDE BIBLIOGRAPHY	ON	EXCLUDE MATCHES	< 12 WORDS