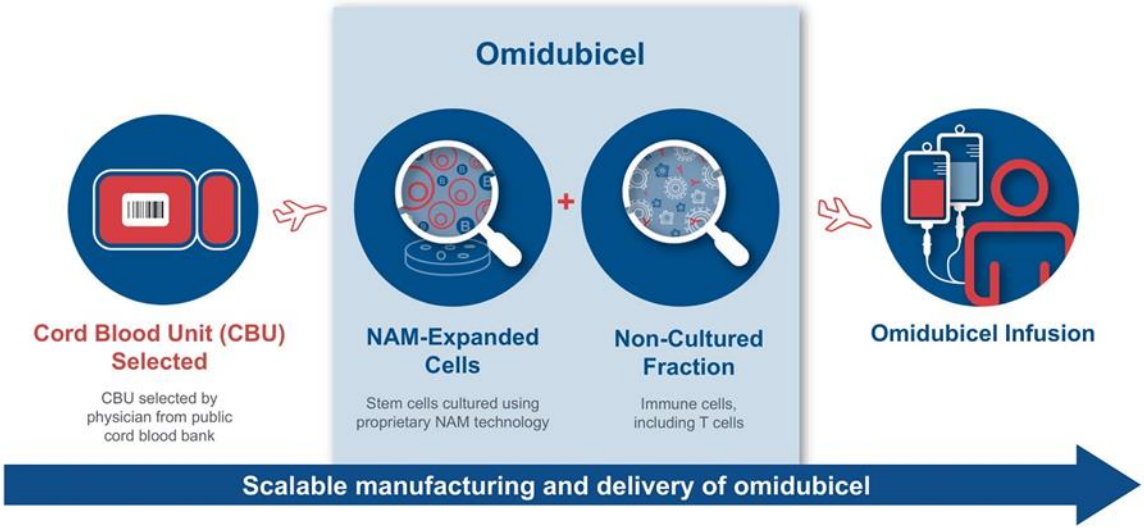
Omidubicel: A new approach to treating blood diseases



Umbilical cord blood (UCB) is recognized as an essential source of hematopoietic stem cells for use in allogeneic hematopoietic stem cell transplantation (allo-HSCT). However, cord blood transplantation is associated with challenges, including delayed hematopoietic recovery, prolonged hospitalization, and higher transplant costs than other donor sources. Recently, a new treatment method has been proposed to solve this problem. Omidubicel is an advanced nicotinamide-based cell therapy made from a single HLA-matched cord blood unit for each patient. This method is associated with rapid transplantation in patients with blood malignancies [(1, 2)]. For example, many sickle cell disease (SCD) patients do not have HLA-matched donors for hematopoietic stem cell transplantation (HSCT). Hence, unrelated cord blood (UCB) is an alternative transplantation option but is associated with a high rate of graft failure and insufficient cell dose. With the Omidubicel strategy, increasing the cord blood cell dose leads to improved engraftment in patients undergoing myeloablative HSCT for SCD [(2)].

Omidubicel is an ex-vivo expanded hematopoietic progenitor cell and is a product of expanded myeloid and lymphoid cells. This method preserves the function of stem cells to optimize cell homing, engraftment, differentiation, and self-renewal. According to a recent phase III clinical trial report, patients who received omidobicel had a faster time to neutrophil engraftment, faster platelet recovery, fewer infections, and shorter hospital stays than patients who received standard cord blood transplants. The clinical trial involved 125 patients with hematologic malignancies aged 12 to 65 years from more than 50 hospitals in different countries and is the most extensive study of an expanded cord blood cell product [(1, 3)].

This product was produced for the first time by Gamida Cell. In this method, cells are obtained after ex-vivo selection of CD133+ from a cord blood unit for 21 days in the presence of small molecules of nicotinamide and other growth factors. CD133 cells are isolated, and the remaining cord blood unit is frozen. CD133 cells are cultured and then frozen to produce the NiCord®/Omidubicel product. Finally, both frozen products are transported to the hospital to be cryopreserved and used for transplantation. Nicotinamide (NAM) is an allosteric inhibitor of NAD-enzymes and a form of vitamin B3. NAM plays an essential role in increasing stem cells, increasing progenitor cells, inhibiting differentiation, migration, blood supply to the bone marrow, increasing the ability of CD34+ progenitor cells to implant in the bone marrow, and increasing the efficiency of transplantation. Nicotinamide also maintains cell function and phenotype [4, 5].

Based on the analysis, NAM modulates transcription factors (TFs). For this reason, it plays an essential role in activating HSC differentiation, apoptosis, and migration pathways. Also, the signaling of NF-κB, C-Jun, LXR/RXR, PPARα/RXRα, and mTOR in CD34+ cells treated with NAM is significantly reduced compared to the control group [6]. Importantly, omidubicel has a lower T-cell content. However, post-transplant T-cell recovery in this method compared with standard UCB showed a lower risk of viral infections during the first year after transplantation. The reduced risk of viral infections for omidubicel recipients was an unexpected finding and may be attributed to more vital NK cell regeneration [3, 7].

Discussion

Several techniques have been developed to expand UCB stem and progenitor cells. However, Omidubicel (formerly known as NiCord) is the first drug to complete a Phase 3 trial, with results showing safety and efficacy. A recent study confirmed that omidubicel overcomes the limitation of UCBT, which is the delay in hematopoietic recovery. Omidubicel reduces neutrophil recovery time by ten days and average platelet recovery time by 13 days. It also effectively reduces the incidence of infectious complications and the number of days spent in the hospital after transplantation [3]. Given that the number of cord blood transplants is less than that of other cell sources, we hope that the increase in the transplantation rate in expanded cord blood cell products will lead to greater use of this valuable source. Omidibucel, on the FDA approval list, will soon become a standard method in treating blood diseases.

Written By: Mehregan Babamohamadi

References

1. Majhail NS, Miller B, Dean R, Manghani R, Sivaraman S, Galamidi-Cohen E, et al. Hospitalization and Healthcare Resource Use of Omidubicel Vs Cord Blood Transplantation for Hematological Malignancies in a Global Randomized Phase III Clinical Trial. Blood. 2021;138:4036.
2. Parikh S, Brochstein JA, Galamidi E, Schwarzbach A, Kurtzberg J. Allogeneic stem cell transplantation with omidubicel in sickle cell disease. Blood advances. 2021;5(3):843-52.
3. Horwitz ME, Stiff PJ, Cutler C, Brunstein C, Hanna R, Maziarz RT, et al. Omidubicel vs standard myeloablative umbilical cord blood transplantation: results of a phase 3 randomized study. Blood, The Journal of the American Society of Hematology. 2021;138(16):1429-40.
4. Islam P, Horwitz ME. Small-molecule nicotinamide for ex vivo expansion of umbilical cord blood. Experimental Hematology. 2019;80:11-5.
5. Peled T, Shoham H, Aschengrau D, Yackoubov D, Frei G, Lerrer B, et al. Nicotinamide, a SIRT1 inhibitor, inhibits differentiation and facilitates expansion of hematopoietic progenitor cells with enhanced bone marrow homing and engraftment. Experimental hematology. 2012;40(4):342-55. e1.
6. Yackoubov D, Steinhardt Y, Ashengrau D, Bitansky A, Maliutina A, Cohen S, et al. Nicotinamide (NAM) Modulates Transcriptional Signature of Ex Vivo Cultured UCB CD34+ Cells (Omidubicel) and Preserves Their Stemness and Engraftment Potential. Biology of Blood and Marrow Transplantation. 2020;26(3):S258-S9.
7. Szabolcs P, Levy S, Yackoubov D, Pato A, Galamidi-Cohen E, Horwitz ME. Hematopoietic Stem Cell Transplantation (HSCT) with Omidubicel Is Associated with Robust Immune Reconstitution and Lower Rates of Severe Infection Compared to Standard Umbilical Cord Blood Transplantation. Blood. 2021;138:333.