

Enhancing Pediatric Cancer Survival in Indonesia: The Role of CAR T Cell Therapy

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Pediatric cancer poses a major health challenge globally, especially in low-middle-income countries like Indonesia. The survival rate of pediatric cancer in many high-income countries (HICs) reaches 90%, while it only ranges from 5 to 60% in LMICs. Over 80% of children with cancer live in low-middle-income countries, indicating the urgency to improve the survival rate of pediatric cancer in LMICs [1]. In Indonesia, the prevalence of pediatric cancer was 43.5% in 2020, making it the highest among Southeast Asian countries [2]. According to Dharmais Cancer Hospital (2024), the national cancer referral center for all of Indonesia, the 5-year survival rate of high-risk pediatric acute lymphoblastic leukemia is only 48.8% (unpublished data).

One key factor contributing to the low survival rate of pediatric cancer in Indonesia is the lack of effective therapy options, especially for high-risk and relapsed or refractory patients. Several therapeutic approaches, such as immunotherapy, have been widely used in HICs but are still not very popular in Indonesia. CAR (Chimeric Antigen Receptor) T-cell therapy is one of the most promising immunotherapeutic approaches to treat pediatric cancer. Implementing CAR T Cell therapy in Indonesia offers promising prospects for improving the survival rates of pediatric cancer patients.

CAR T cell therapy utilizes the body's immune system to specifically target and eliminate cancer cells. This innovative therapy entails extracting a patient's T cells, genetically modifying them to express chimeric antigen receptors specific to tumor-associated antigens, and then reinfusing them into the patient. Once infused, these engineered T cells recognize and eliminate cancer cells bearing the targeted antigen, thereby offering a highly targeted and potentially curative treatment option [3]. This innovative therapy has demonstrated remarkable success in treating certain hematologic malignancies, including pediatric leukemia. The most extensively studied case in childhood patients involves CAR T cells that target CD19, a B cell surface receptor [4].

CAR T cell therapy holds great promise for improving survival rates among pediatric cancer patients in Indonesia. Children with refractory or relapsed leukemia, such as B-cell acute lymphoblastic leukemia (B-ALL), who have exhausted standard treatment options, can benefit

from CAR T cell therapy. Most relapsed or refractory pediatric cancer patients in Indonesia do not have effective therapy options to treat the disease. CAR T cell therapy emerges as a novel therapy that can significantly improve the survival of this subset of patients. Numerous studies have documented high remission rates (ranging from 70% to 90%) in adults and children diagnosed with refractory B-ALL [4]. A study by Maude et al. [5] reported high remission rates and durable responses in young adults and children with refractory or relapsed B-ALL treated with CAR T cells. Similarly, Park et al. [6] demonstrated long-term remissions and improved survival in pediatric leukemia patients receiving CAR T cell therapy. Several groups also have observed the persistence of CAR T cells and sustained remission lasting over six months in the majority of patients examined [4].

Efforts have been made to implement CAR T cells in Indonesia. Dharmais Cancer Hospital, as a National Cancer Center in Indonesia, has initiated this effort by collaborating with iCarTAB Biomed Inc., a China-based CAR T cell manufacturer with one of its manufacturing sites located in Malaysia. However, this approach involves sending patients' blood samples that have been processed through leukapheresis to Malaysia for CAR T cell manufacturing, followed by the shipment of the manufactured cells back to Indonesia for administration to patients. This process is impractical and incurs intangible costs such as transportation and cryopreservation, ultimately making it more expensive for patients. Regulatory issues related to the shipment of cells across borders in the region and early preparation of patients for CAR T cell therapy soon after relapse before they succumb to treatment-related mortality or relapse-related complications are also challenges that need to be addressed [7].

Reflecting on the abovementioned issue, CAR T cell therapy adoption in Indonesia faces significant challenges. Limited healthcare infrastructure, including specialized facilities for cell therapy manufacturing and administration, poses logistical hurdles. Moreover, cost remains a major barrier, as CAR T cell therapy is often expensive and inaccessible to many patients in Indonesia. Furthermore, the lack of local expertise in cellular immunotherapy may impede the successful implementation of CAR T cell therapy programs.

Efforts to address these challenges and maximize the potential of CAR T cell therapy in Indonesia are essential. This requires a multi-faceted approach involving investment in healthcare infrastructure, including establishing specialized centers equipped for CAR T cell therapy manufacturing and administration. Two alternative models have been proposed for manufacturing CAR-T cell therapy: centralized and decentralized models [8]. In the centralized manufacturing model, point of manufacturing and point of care are located in different geographical areas, while decentralized manufacturing focuses on establishing point of care and manufacturing in close proximity. A decentralized manufacturing model might be the best approach to be implemented in LMICs like Indonesia. Building hospital-based cellular therapy manufacturing reduces the need for transportation and cryopreservation. The decentralized system's geographic proximity improves communication between manufacturing and treatment teams, facilitating the creation of customized products based on a patient's phenotype. This setup also reduces administration time and the risk of delays and mix-ups compared to centralized manufacturing, making hospital-based cellular therapy manufacturing a potentially more cost-effective option [8].

In addition, initiatives to reduce the cost of therapy through partnerships with pharmaceutical companies, government subsidies, or philanthropic endeavors can improve affordability and access. Furthermore, capacity-building initiatives aimed at training local healthcare professionals in cellular immunotherapy techniques are essential for ensuring the successful implementation and sustainability of CAR T cell therapy programs in Indonesia. Collaboration between local institutions, international organizations, and industry stakeholders can facilitate knowledge transfer and technology transfer, fostering indigenous expertise in this cutting-edge treatment modality.

CAR T cell therapy represents a transformative approach to improving survival rates among pediatric cancer patients in Indonesia. By harnessing the power of immunotherapy, specifically tailored to target cancer cells, CAR T cell therapy offers hope for children with refractory or relapsed leukemia who have limited treatment options. Through continued research, collaboration, and investment in healthcare infrastructure, CAR T cell therapy potentially could greatly improve the prognosis and quality of life for pediatric cancer patients in Indonesia.

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