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REVIEW ARTICLE

Practical issues in CAR T-cell therapy

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Abstract

Chimeric antigen receptor (CAR) T-cell therapy presents a revolutionary advancement in personalized cancer treatment. During the production process, the patient's own T-cells are genetically engineered to express a synthetic receptor that binds to a tumor antigen. CAR T-cells are then expanded for clinical use and infused back into the patient's body to attack cancer cells. Although CAR T-cell therapy is considered a major breakthrough in cancer immunotherapy, it is not without limitations. In this review, we discuss the barriers to effective CAR T-cell therapy in Korea.

Key Words CAR T-cell therapy, Korea, Patient access, Barrier

INTRODUCTION

Chimeric antigen receptor T-cell (CAR T-cell) therapy presents a revolutionary pillar in hematologic cancer treatment. Currently, six CAR T-cell therapies have been approved (axicabtagene ciloleucel, brexucabtagene autoleucel, idecabtagene vicleucel, lisocabtagene maraleucel, tisagenlecleucel, and ciltacabtagene autoleucel) by the United States Food and Drug Administration (US FDA) [1], but only one (tisa-cel) is available in Korea. In this review, we discuss the current barriers and complexities of CAR T-cell therapy in Korea, including the issues related to clinical unit set-ups, patient accessibility, cost issues, and reimbursement-related challenges.

CAR T-cell production and administration process

Tisa-cel, the only commercially available CAR T-cell product available in Korea, is a personalized autologous cellular therapy, and patients must first undergo leukapheresis procedures before providing T-cells. These cells are then sent to certified manufacturing centers (to other continents) within a strict timeframe for production. After manufacturing and quality assessment, the final products are released to hospitals for patient infusion [2]. This complexity of CAR T-cell production and the administration process itself is a significant barrier for patients. Since production is heavily dependent on the manufacturers' workforce, limited production slots sometimes thwart the execution of subsequent steps, while other times supply chain disruptions cause unexpected delays.

Another major problem in patient accessibility is the lack of certified CAR T-cell therapy centers. CAR T-cell therapy is already resource intensive, requiring multiple highly trained specialists and quality-assured infrastructure [3]. Specifically, a leukapheresis facility, adequate cell storage unit, structured clinical unit with well-established protocols to monitor and manage patients developing acute complications, and intensive care unit are required. In terms of medical personnel, hematologists, dedicated critical care medicine specialists, neurologists, and specialized nurses are needed around the clock. Moreover, per the "act on the safety of and support for advanced regenerative medicine and advanced biological products" and "enforcement decree of the act on the safety of and support for advanced regenerative medicine and advanced biologic products" [4], all centers intending to administer CAR T-cell therapy have to be assessed by the Korean Ministry of Food and Drug Safety. As such, only a handful of CAR T-cell therapy centers in Korea are geographically concentrated in Seoul, putting further constraints.

Cost and reimbursement issues

CAR T-cell therapies are associated with substantial costs, in hundreds of thousands of US dollars [5]. The high cost

of CAR T-cell therapies is exacerbated by contentious reimbursement issues and ambiguous regulations. With CAR T-cell therapies offering unprecedented cure opportunities for many patients across the globe, regulatory agencies should be cautious not to unnecessarily restrict or delay patient access.

CONCLUSION

In conclusion, the success of CAR T-cell therapy requires highly coordinated interaction between different specialists across various infrastructures within health establishments. On a macroscopic scale, the cross-functional collaboration of numerous stakeholders, ranging from industry to regulatory agencies, is crucial to provide solutions to the issues raised in this article.

Authors' Disclosures of Potential Conflicts of Interest

No potential conflicts of interest relevant to this article were reported.

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