Lack of consensus on optimal use of ASCT in patients with AL amyloidosis. A randomized phase II study involving 91 patients comparing high-dose intravenous melphalan (HDM) followed by ASCT with a course of oral melphalan 10 mg/m^2 given once daily and dexamethasone 40 mg given once daily for the first 4 days of a 28 day cycle for up to 18 cycles. At a median follow-up of 3 years, median overal survival (OS) in the HDM arm was significantly worse than those taking high dose melphalan and dexamethasone (22.2 versus 56 months). Clinical studies using modern induction regimens and strict selection criteria emphasize an improved outlook on early survival outcomes in transplantation. . The HOVON104 study evaluated ASCT after four cycles of bortezomib-based induction in 50 patients reported an estimated 3-year OS in the 86% and 72% cardiac response rate in evaluable patients at 2 years.

https://doi.org/10.1016/j.htct.2024.11.086

05

CAR-T CELL THERAPY IN LYMPHOMAS: EXPANSİON OF INDICATIONS AND NEW APPROACHES

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CAR-T (chimeric antigen receptor T-cell) therapy represents a revolutionary advance in treating hematologic cancers, offering promising outcomes for lymphoma patients, especially those with relapsed or refractory disease. Initially approved for diffuse large B-cell lymphoma (DLBCL), CAR-T therapy is expanding to address a broader range of lymphomas, including other B-cell and T-cell subtypes. As CAR-T technology evolves, researchers are exploring innovative delivery strategies and engineering methods to enhance efficacy and address the unique challenges of treating different lymphoma types. CAR-T cell therapy works by genetically modifying a patient's T cells to express a receptor targeting specific cancer cell antigens. In B-cell lymphomas, CD19 has proven an effective target, with CAR-T therapies such as axicabtagene ciloleucel and tisagenlecleucel demonstrating remarkable responses. Recent studies reveal high remission rates in DLBCL, mantle cell lymphoma, and follicular lymphoma when using CD19-targeted CAR-T therapy, even in patients who have exhausted other treatment options. The success of these therapies has catalyzed research into additional lymphoma subtypes and new antigen targets, allowing CAR-T cell therapy to benefit an expanding patient population (Denlinger et al., 2022). One notable development is the investigation of CAR-T cell therapy in T-cell lymphomas. T-cell lymphomas pose unique challenges due to their antigen overlap with healthy T cells, leading to risks like T-cell fratricide, where CAR-T cells inadvertently destroy each other. To address this, researchers are designing CAR-T cells targeting less common antigens, such as CD30, which is often overexpressed in Hodgkin lymphoma and some T-cell lymphomas, but not in normal T cells. CD30-directed CAR-T therapies have shown early success in clinical trials, offering hope for relapsed Hodgkin lymphoma patients who lack other viable options (Brudno et al., 2024, Ramos et al., 2020). Localized CAR-T cell therapy is another emerging strategy, particularly for lymphomas affecting the central nervous system (CNS). CNS lymphomas present an additional barrier because CAR-T cells administered intravenously may struggle to cross the blood-brain barrier (BBB) and reach tumor cells. Direct intrathecal CAR-T administration, which bypasses the BBB, has shown promising early results for CNS lymphoma, providing high CAR-T cell concentrations directly within the CNS and improving patient outcomes. This approach may reduce systemic side effects like cytokine release syndrome (CRS) and neurotoxicity, although localized neurotoxicity remains a concern (Sagnella et al., 2022). Engineering advancements are also helping address antigen escape, where cancer cells evade CAR-T cells by losing the targeted antigen. Dual-target CAR-T cells can recognize multiple antigens, reducing the risk of relapse due to antigen loss. For example, dual CD19/CD22 CAR-T therapies are being studied for their ability to sustain long-term remission by targeting two markers common to B-cell lymphomas, thus enhancing durability and reducing escape mutations. Also combining CAR-T with immune checkpoint inhibitors improve CAR-T cell efficacy. (Roddie et al., 2023). In summary, CAR-T cell therapy has transformed the lymphoma treatment landscape, extending beyond DLBCL to address Hodgkin lymphoma, follicular lymphoma, and other challenging subtypes. As new approaches evolve—such as local delivery for CNS lymphoma, dual-target CAR-T constructs, and novel T-cell lymphoma strategies—CAR-T therapy's role continues to expand, offering new hope to patients with previously untreatable lymphomas. Continued innovation will be crucial for refining CAR-T technology, overcoming barriers, and realizing its full potential across diverse lymphoma types.

https://doi.org/10.1016/j.htct.2024.11.087

06

PROFESSOR DOCTOR SEREF INCEMAN'S BIOGRAPHY AND LEGACY

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Dr Inceman was born in Istanbul in 1919. He completed his primary education at Galatasaray High School (1940). He graduated from Istanbul University Faculty of Medicine (1940-1946). After graduation, he started his residency at the Internal Medicine Clinic (Capa) of the same faculty. He completed his military service in Erzincan (1949-1950). He worked in the clinic of Professor Jean Bernard, who conducted studies on leukemia and immunohematology at the University of Paris (1950-1951). in 1951, he stayed with Professor Swen Moeschlin at the Internal Medicine Clinic of the University of Zurich, Switzerland for a month. He was promoted to Associate Professor in 1956 and to Professor in 1966. Between 1963 and 1986, he directed the Hematology Department and served as its chairman. He was one of the founding members of THD in 1967 and was its first president. His research interest in the