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MIKOŁAJA KOPERNIKA
W TORUNIU
Collegium Medicum
im. Ludwika Rydygiera w Bydgoszczy

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STRESZCZENIE ROZPRAWY DOKTORSKIEJ

Dyscyplina naukowa: Nauki medyczne i nauki o zdrowiu

Tytuł rozprawy doktorskiej: Skuteczność terapii innowacyjnych w onkologii dziecięcej w świetle wyników postępowania przeciwnowotworowego w najczęstszych nowotworach wieku dziecięcego

Streszczenie rozprawy doktorskiej w języku angielskim:

Despite the dynamic development and broad access to healthcare in Poland, malignant diseases remains one of the leading causes of death among children, ranking as the second most common in the 1-19 age group. Due to the high toxicity and the incomplete efficacy of conventional chemotherapy and radiotherapy observed in certain types of cancer, research into alternative treatment modalities, including approaches based on the patient's immune response, was initiated as early as in the 1960s. Currently, innovative therapies, including immunotherapy, are increasingly becoming an integral part of treatment in pediatric oncology.

This project aimed to evaluate the effectiveness of innovative therapies for selected childhood cancers in pediatric oncology. The project was conducted through statistical analysis of treatment outcomes in children aged 0-19 years treated at the Department of Pediatrics, Hematology and Oncology, University Hospital No. 1 in Bydgoszcz between January 1990 and December 2024. The analysis focused on the outcomes of innovative therapies, such as monoclonal antibodies, including antibody-drug conjugates and bispecific antibodies, immune checkpoint inhibitors, cellular therapies, and CAR-T cells. The results of individual analyses are presented in seven publications attached to the doctoral dissertation.

Immunotherapy has significantly improved outcomes in high-risk ALL patients. The use of CAR-T therapy in patients with primary refractory ALL or relapsed disease enabled complete remission in cases where standard second-line and subsequent treatments had failed. Monitoring immune response and CAR-T cell number allows for the identification of patients at risk of treatment-related complications. In the analyzed group, the fourth day after CAR-T cell infusion was associated with elevated plasma levels of most analyzed cytokines, which temporally correlated with the onset of CRS and ICANS.

Treatment outcomes in AML have significantly improved over the past 30 years. The introduction of allogeneic hematopoietic stem cell transplantation in high-risk patients

improved both 5-year overall survival and event-free survival. Further research should require international collaboration due to the small number of pediatric AML patients.

The introduction of response-adapted treatment evaluation in Hodgkin lymphoma therapy has enabled a reduction in the number of patients receiving radiotherapy. Limiting radiotherapy to selected patient groups allows for a reduction in long-term complications without compromising treatment outcomes. Treatment of relapsed disease with anti-CD30 monoclonal antibodies in combination with PD-1 checkpoint inhibitors may serve as an alternative to standard second-line therapy.

The five-year overall survival probability in anaplastic large cell lymphoma is higher than in T-cell lymphoblastic lymphoma. For rare lymphoma types, there are no established treatment guidelines. In EBV-associated non-Hodgkin lymphomas, patients may benefit from treatment with EBV-specific cytotoxic T lymphocytes.

In neuroblastoma therapy, high-risk patients treated with dinutuximab-beta following hematopoietic stem cell transplantation showed an improvement in 5-year overall survival from 0.0% to 41.1%. Among patients with relapsed disease, stem cell transplantation was statistically associated with improved overall survival.

Treatment outcomes for pediatric malignancies have significantly improved over the study period, mainly due to the introduction of new international treatment protocols, and innovative therapies, including cellular therapies and immunotherapy.