Streszczenie w języku angielskim

Regulation of CD20 antigen expression by the phosphatidylinositol 3-kinase and AKT kinase signaling pathway in B-cell-derived cancer cells

Most therapeutic regimens used in the treatment of non-Hodgkin's lymphomas rely on anti-CD20 monoclonal antibodies, the most commonly used being rituximab. One of the determinants of rituximab efficacy is the expression of the CD20 antigen, which serves as its therapeutic target. Modulating the levels of CD20 protein on the surface of malignant cells derived from B lymphocytes remains among crucial strategies to enhance the antitumor efficacy of rituximab. One of the most promising pathways that may influence CD20 expression is the PI3K/AKT, which has a well-described role in the pathogenesis of lymphoproliferative malignancies. The PI3K/AKT pathway can be activated by various drugs, often as an incidental finding, reflecting the pleiotropic property of the pharmaceutics.

The primary aim of this study was to verify the hypothesis of CD20 regulation via the PI3K/AKT pathway. A secondary, post-hoc aim was to validate salinomycin *in vitro* as an agent enhancing rituximab efficacy through this mechanism.

The research was experimental and conducted in vitro using established cancer cell lines representing various types of B-cell-derived malignancies. The impact of SYK, BTK, PI3K, and AKT kinase inhibitors used in clinical and preclinical studies, on the surface levels of CD20 in B-cell-derived cancer cells and the efficacy of anti-CD20 monoclonal antibodies via the CDC mechanism was evaluated in subsequent experimental steps. Activation and silencing of the PI3K pathway resulted in increased and decreased CD20 expression, respectively. Following a systematic literature review, salinomycin was identified as a model compound with already proven anticancer activity and potential effects on the PI3K/AKT pathway. Subsequent validation confirmed the positive impact of salinomycin on PI3K/AKT pathway activation, increased CD20 expression, and the cytotoxicity of rituximab and ofatumumab via this mechanism.