

## A new molecule to inhibit lymphoma growth

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Immunohistochemical analysis of diffuse large B cell lymphomas stained for the expression of the BCL2 protein (dark brown colour). Credit: Università della Svizzera italiana

The prestigious scientific journal Clinical Cancer Research has published



a study conducted by the research group led by Dr. Francesco Bertoni of the Institute of Oncology Research (IOR, affiliated to USI Università della Svizzera italiana), that have tested a new molecule that demonstrates its ability to inhibit lymphoma growth.

Lymphomas are tumors that originate from blood <u>cells</u>, more specifically from lymphatic tissue. There are numerous types of lymphomas and each have different characteristics, aggressiveness, evolution and prognosis. In most cases, the standard treatments include irradiation and chemotherapy, two therapies that can have important side effects. Innovative biological approaches and the discovery of new biological molecules are changing the therapeutic approach and increasing the chances of healing.

Cancer cells are able to elude physiological control and grow in uncontrolled manner. In fact, groups of "pro-tumor" proteins can get activated and no longer respond to the normal intracellular "anti-tumor" control mechanisms. Among the "pro-tumor" proteins, the network including the signal molecules "PI3K/AKT/mTOR" is well known to sustain the survival and proliferation of <u>cancer cells</u>. Importantly, the PI3K/AKT/mTOR signaling axis is active in lymphomas and blocking could represent a good strategy to fight <u>lymphoma cells</u>.

The IOR research group led by Dr. Francesco Bertoni (who is also Vicepresident of the SSAK Swiss Group for Clinical Cancer Research Project Group Lymphoma) with in particular Chiara Tarantelli and Eugenio Gaudio, has focused on the possibility to inhibit the PI3K/AKT/mTOR signaling with PQR309 (bimiralisib) in the lymphoma cells. PQR309 is a new molecule produced by a Swiss company that directly blocks multiple proteins driving the PI3K/AKT/mTOR signaling and has shown the ability to block the growth of lymphoma cells.



A drug (idelalisib) that acts by blocking only one specific type of protein in the "PI3K" family (PI3K delta) is already approved for clinical use, but many patients do not respond to this treatment. However, in the laboratory, PQR309 shows that it has anti-tumor activity even in lymphoma models that do not respond to idelalisib. PQR309 seems to act even better when combined with other novel anti-tumoral drugs. Furthermore, the mechanism of action of the drug PQR309 has been investigated and compared to that of other signaling inhibitors, obtaining results with implications in the design of novel treatment schemes for patients with lymphoma.

The results of this study, together with the ongoing clinical studies with PQR309, can lead to better treatments for people affected with lymphoma and to better understanding of the mechanisms of action of anti-lymphoma agents. Lymphomas are among the 10 most common cancers in adults and the third most frequent neoplasia in children and adolescents. Despite the great advancements made in their treatment, European statistics show that around 5 people per 100.000 still succumb to lymphoma every year.

**More information:** Chiara Tarantelli et al. PQR309 is a novel dual PI3K/mTOR inhibitor with pre-clinical antitumor activity in lymphomas as a single agent and in combination therapy, *Clinical Cancer Research* (2017). DOI: 10.1158/1078-0432.CCR-17-1041

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