Ref: OT-43

Title:

A new agent for the treatment of lymphoid neoplasias.

Summary:

The present invention claims the use of a micro RNA (miR-28) for the treatment of mature B cell neoplasias, including Burkitt lymphoma (BL), diffuse large B cell lymphoma (DLBCL), follicular lymphoma (FL) and chronic lymphocytic leukemia (CLL). The patent application also claims different miRNA compositions, as well as compounds that mimic the miRNA activity of miR-28, including pharmaceutically acceptable carriers and the route of administration.

It is estimated that about 60,000-80,000 new cases of Non-Hodgkin Lymphoma (NHL) are diagnosed every year in Europe alone, most of which are mature B cell neoplasias. While a significant fraction of aggressive B cell lymphomas can be cured with current therapies, these are often highly intensive treatments, requiring admission to the hospital. In addition, almost half of the DLBCL and BL cases are resistant to these therapeutic approaches, or relapse within 5 years of treatment (LSS). Indeed, close to 30,000 people die for NHL in Europe per year, and close to 10,000 for DLBCL alone.

The inventors from CNIC have demonstrated that miR-28 impairs tumour growth in xenograft models of BL and DLBCL. Moreover, they have shown that compositions of synthetic miR-28 sequence, display antitumoral activity in BL xenografts both when delivered intra-tumorally or intravenously. In addition, miR-28 shows negligible toxicity in the assays performed.

Innovative aspects:

The key scientific findings that confer an innovative approach for the treatment of lymphoid neoplasias are that inventors have found that 1) miRNA-28 is a negative regulator of the germinal center reaction 2) miRNA-28 is downregulated in germinal center-derived neoplasias. The expression of miRNA28 reduces cell number, reduces proliferation and promotes apoptotic cell death of the cell lymphoma cultures assayed 3) miR-28 expression suppresses established lymphomas of human and murine origin in established xenografts. 4) miR-28 does not show toxicity in mouse fibroblasts or human T cell lines.

Therefore, researchers have demonstrated that compositions comprising a miR-28 mimic or a vector (such as a viral vector) comprising miR-28 can be efficiently administered to a subject suffering from a mature B-cell neoplasm and results in the inhibition of tumour cell proliferation and the promotion of tumour cell death. The administering may also prevent, stop or slow metastatic progression. The administering may extend the overall survival time of the subject. The administering may extend progression-free survival of the subject.

Competitive advantages:

Combination chemotherapy with rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone (R-CHOP) administered every 21 days is considered the established standard treatment, although there are several other treatment alternatives being tested. Nowadays, the great majority of new products in this area are chemotherapy-derived chemicals. However, different miRNAs are now being tested to treat different pathological scenarios, but all of them act as antagonists of the target molecule. There is only one miRNA (miRNA 34) that is being tested as replacement therapy in cancers such as hepatocarcinoma (MRX34©). In addition, our experimental approach is expected to be used in non-responsive patients, a tremendous competitive advantage and miRNA mimics are very effective, selective and low toxic compounds.

Key words: Mature B-cell neoplasms, Burkitt lymphoma (BL), diffuse large B cell lymphoma (DLBCL), follicular lymphoma (FL) and chronic lymphocytic leukemia (CLL), microRNA, miRNA28, miR-28, miRNA mimics

Contact:
Technology Transfer Office- CNIC
tto@cnic.es