NEW THERAPEUTIC APPROACH AGAINST B-CELL LEUKEMIA AND LYMPHOMAS

Targeted mechanism based on polymeric nanoparticles with chemotherapeutic payload

1. Unmet need

Lymphomas and leukemia are two types of cancers affecting white blood cells and they are respectively the 7th and the 11th most common cancers worldwide. Cancer therapy against these diseases depends on the specific type and the stage, and it generally involves a combination of treatments such as chemotherapy, radiotherapy, immunotherapy, or bone marrow transplantation. Chemotherapy is the major form of therapy and can be administered in different treatment protocols comprising combinations of multiple drugs. Despite current treatment approaches have greatly improved the prognosis for survival, some patients remain refractive to these therapeutic regimens. Hence, in addition to reducing the long-term side effects of therapeutics for all patients, there is an urgent need for novel therapeutic strategies for difficult-to-treat cases. Due to the cytotoxicity of drugs, the major challenge currently is to deliver the therapeutic agents to tumor cells while preserving the viability of non-malignant cells.

2. Technology

The research group from the University of Trieste is proposing a novel therapeutic approach to treat leukemia and lymphomas, based on the use of polymeric nanoparticles (NPs) featuring a targeting monoclonal antibody (mAb) and a chemotherapeutic payload. The NPs are composed of biocompatible and biodegradable polymers (FDA-approved) and loaded with a combination of two drugs, chlorambucil and hydroxychloroquine, which showed a synergistic killing effect against neoplastic B-cells. Moreover, the antiCD20 mAb allows to target the NPs toward the CD20 antigen, which is expressed by most cancers related to B-cells neoplasia, including chronic lymphocytic leukemia (CLL) and several non-Hodgkin lymphomas.

3. Main advantages

The proposed drug delivery system is advantageous compared to the present chemotherapy treatments because, by loading two toxic agents within a biocompatible protecting scaffold, it consents the safe and targeted delivery of a high-dose of chemotherapeutics to tumor cells, reducing the necessary administered dose and the toxic side effects on healthy tissues. Furthermore, it exploits the biodistribution properties of targeted nanoparticles and their ability to cross cellular barriers and afford intracellular delivery of toxic insoluble drugs with a modified pharmacokinetic profile. Finally, the solution would allow to perform the therapeutic treatment avoiding invasive chirurgical and radio-therapeutic procedures.
4. Stage of development

The group has completed a thorough characterization of targeting NPs loaded with chlorambucil and hydroxychloroquine both in vitro, on human and canine primary cells and cell lines, and in vivo, on murine models of CD20+ lymphoma. Studies on in vivo models of CLL and Burkitt lymphoma have proved the safe toxicological profile of the NPs, their good internalization in CD20+ B-cells, their targeted biodistribution at the tumor site, the pharmacokinetics and therapeutic efficacy of the encapsulated drugs. The technology has reached this stage of development with the employment of the polymeric NPs developed by Seria Inc. Preliminary investigations on other types of NP have been also carried on, but they are not yet at this level of development.

The further step is to move into a clinical phase on dogs spontaneously affected by these type of tumors, due to the similarity of dog’s clinical, immunological and molecular characteristics to human pathologies. The animal trials will be fundamental for the commercial development of the technology in veterinary and its translation into human clinical trials.

5. Intellectual property

The method to produce the employed polymeric NPs has been developed by LNK Chemsolution, Inc and is protected by a patent family. The targeting mechanism developed by the research group is instead not patented.

6. Target Markets

Dog B-cell malignancies represent the most reasonable market for the immediate future, but the dimension remains to be evaluated because of the absence of public data.

Human Chronic lymphocytic leukemia (CLL), which accounts for 35% of all leukemia cases, will have a market growth from $1.3 bn in 2014 to a peak of $2.2 bn in 2023, at a compound annual growth rate (CAGR) of 6.1%, as a result of increasing CLL incidence and of the uptake of new branded drugs, in addition to the launch of mAbs in the recent past.

The global market of human non-Hodgkin lymphoma is expected to grow from $6.2 bn in 2015 to $9.1 bn by 2020 (CAGR of 8%), out of which the B-cell lymphoma segment represents one third of the market value and will amount to $3.5 bn in 2025, growing at CAGR of 5.6% from 2016.

7. Potential Partners

Potential partners for this technology are pharmaceuticals companies developing drugs and chemotherapeutics against leukemia and lymphoma (in particular drugs that target B-cells and CD20), and which are interested in promoting this solution into clinical phases. Pharmaceutical companies active in the veterinary field could be potentially highly interested to co-develop this technology and support the group in the in vivo therapeutic trials on dogs spontaneously affected by the disease. Other partners could be manufacturers of nanoparticles for drug delivery interested in investigating this targeting mechanism on their substrates.