Chimeric antigen receptors (CAR) T-cells for acute lymphoblastic leukemia treatment
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A
cute lymphoblastic leukemia (ALL) is a very aggressive disorder caused by
malignant transformation of lymphoid cell lineage progenitors in bone
marrow. Classically, ALL can be originated from B-cell precursor lineage
(BCL-ALL) which comprehends majority cases, or T-cell precursor lineage
(TCL-ALL) (1). ALL is a most common type cancer in childhood and large
presence of blasts is found in peripheral blood (PB) and bone marrow (BM).
In this topic, Cortelazzo details related reviews main features of ALL, including
incidence, risk factors, genetic alterations in both BCL-ALL and TCL-ALL,
clinical presentations, and others interesting point (2).

Conventional treatment strategy is based on intensive multi-drug
chemotherapy according different protocols. First-rate drugs include
vincristine, cyclophosphamide, cytarabine, methotrexate, prednisone,
thioguanina, nitrosoureas, anthracyclines, and others. There are various
papers published describing therapeutic strategies for the specific
manifestations of the disease (3-7). These therapies are important for the
destruction of cancer cells, resulting in decreased blasts counting in patients.
However, several problems associated with conventional chemotherapy are
observed. For example, most chemotherapy treatments do not reach the
brain and marrow areas, so it may be necessary to inject it directly into the
cerebrospinal fluid to kill cancer cells in that area. Furthermore, toxicity is a
serious side effect observed in the chemotherapy strategy, because the drugs
do not selectively act on the cancer cells. Additional effects include hair loss,
nausea, vomiting, hemorrhage, diarrhea and susceptibility to infections. Due
to the debilitating effects of chemotherapy, new strategies which eliminate or
minimize these bad effects are necessary. Thereby, cancer immunotherapy has
recently developed as a promising tool for therapeutic strategies. Important
advantage of immunotherapy is to enable selectivity to cancer cells and thus
avoid many side effects observed in conventional therapies.

Chimeric antigen receptors (CAR) T-cells have recently emerged as an
immunotherapy component designed to specifically act on a target antigen.
In anti-cancer immunotherapy, a CART T cell is a T lymphocyte extracted
from own patient, then genetically modified to harbor a recombinant
receptor specific against a target tumor antigen and finally infused back into
the patient. Most tests using this strategy are currently in clinical phase of
study. The results in clinical trials were promising, but side effects have been
observed. In a review published in June, Luskin and DeAngelo discusses
CAR T cell therapy for ALL and ongoing efforts to improve efficacy and
decrease side effects, such as toxicity (8). Significantly limited described
in clinical trials include neurotoxicity, toxicity "on target, off organ" (when
target antigen is present in other organs), genotoxicity, hypersensitivity
reactions, and other problems, all with varying intensity and frequency.

In this year, Food and Drug Administration (FDA) announced the first
approval of a CAR-T cell therapy for kids and young adults with B-cell ALL.
This approval was much celebrated and brought new hope for a more specific
and efficient therapy for ALL. This result has come through many years of
research and is expected to improve the quality of treatment of patients. It
is worth noting that in addition to side effects, the high cost of treatment is
still an obstacle and the side effects. Although there are challenges to be
overcome as in any innovative research, CART T cell therapy seems to be
the most promising therapeutic tool against cancer, including ALL, since
chemotherapy introduction in the 1940s.

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