Harnessing the power of natural killer cells for cancer immunotherapy

By leveraging its unique and versatile production-platform technology, Glycostem has developed highly pure and active cancer-fighting cell therapy products that are safe and effective for allogeneic transplantation in patients with hematological cancers and solid tumors.

Natural killer (NK) cells are critical immune cells in the fight against cancer and have recently been explored as a promising therapeutic alternative to T-cell-based approaches. In particular, NK cells play a critical role in eliminating circulating cancer stem cells with high metastatic potential. Moreover, engineered NK cells are considered less risky for patients than their T-cell counterparts because NK cells have never been thought to cause graft-versus-host disease. NK cells are cleared from circulation more rapidly after mediating their anticancer effects and unlike chimeric antigen receptor expressing T-cells, are less likely to produce potentially fatal cytokines, besides providing a failsafe mechanism when cytotoxic T-cells are unable to recognize tumors. Because NK cells are highly dysfunctional and reduced in number in cancer patients compared with those in healthy individuals, the transfer of large numbers of NK cells represents a promising therapeutic strategy.

However, transplantation studies in which autologous NK cells are removed, expanded to large numbers ex vivo, and transferred back into the patient, have not demonstrated significant clinical benefit because of the problem of self-tolerance, which allows tumor cells to escape immunological control mechanisms. In addition, autologous cell transplantation is not off-the-shelf and is associated with limited expansion, poor anticancer efficacy and high costs. Because of these limitations, development efforts have focused on safe and effective allogeneic NK cell transfusion procedures, in which a patient receives cells from a genetically unrelated donor.

Glycostem is a clinical-stage company on a mission to harness the power of allogeneic cell products in the field of cellular immunotherapy. The European-based biotech company, which was founded in 2007, recently tested its lead candidate oNKord for safety in a phase 1 study in subjects with acute myeloid leukemia. oNKord, which comprises highly pure and cytolytic NK cells generated ex vivo from umbilical cord blood progenitor cells, did not cause toxicity or graft-versus-host disease, further expanded and matured in vivo, migrated to the bone marrow, and killed leukemic blasts. Initial observations after treatment with a single dose of oNKord suggest that one could expect a strong reduction of residual disease as well as prolonged progression-free survival and overall survival.

This revolutionary NK-cell-based therapy has been granted Orphan Drug Designation by the US Food and Drug Administration and the European Medicines Agency for the treatment of acute myeloid leukemia, and conditional product approval is expected in Europe in 2020 or 2021. Further, oNKord also has the potential to treat multiple myeloma and other hematological cancers, as well as solid tumors such as colorectal cancer, cervical cancer, epidermoid cancer, head and neck cancer, lung cancer, and breast cancer. After the successful completion of the phase 1 clinical trial, Glycostem began to set up automated, closed-system good manufacturing practice (GMP)-certified manufacturing facilities to initiate multi-center clinical trials for acute myeloid leukemia, multiple myeloma, and solid tumors.

“At Glycostem, we believe that natural killer cells will become the new star in the domain of cellular immunotherapy,” said the company’s chairman and CEO, Troels Jordansen. “By developing a suite of innovative natural killer cell products, we are setting the stage to make a considerable impact on the future treatment of cancer.”

Versatile platform technology

Glycostem is opening new horizons in allogeneic NK-cell-based immunotherapy, thanks in large part to its cutting-edge platform technology. In recent years, Glycostem’s platform technology has enabled a closed-system cell-culture process for the large-scale expansion of CD34+ hematopoietic stem and progenitor cells, derived mainly from umbilical cord blood. Umbilical cord blood is advantageous because it is a rich source of stem cells, its use is not restricted by ethical considerations, and it is commercially available for large-scale use at excellent quality, reliability, and cost.

Glycostem’s state-of-the-art platform technology, which uses a proprietary, fully synthetic cell-culture medium and a patented combination of growth factors, allows further differentiation of these hematopoietic stem and progenitor cells into fully functional immune cells, including NK cells and antigen-presenting cells such as dendritic cells.

“Over the last 10 years, Glycostem has established a reproducible and efficient closed-production process protected by six patent families,” Jordansen said. “This makes Glycostem the leading cellular immunotherapy company focused on developing a safe and cost-effective allogeneic approach with the promise of providing the first truly off-the-shelf products.”

Glycostem’s unique, versatile production-platform technology is able to create a multitude of off-the-shelf products to treat various types of cancer. Moreover, Glycostem is developing second-generation products with dedicated functionality, such as gene-modified NK cells, and NK cells engineered to express chimeric antigen receptors that target specific tumor antigens.

Currently, Glycostem is initiating additional partnerships to further explore the potential of combining their NK cell products with antibodies, small molecules, or chemotherapy to enhance therapeutic responses against cancers. “There are growing opportunities to augment the cancer-fighting capabilities of NK cells,” Jordansen said. “Through future collaborations with academic and industrial partners offering innovative technologies, we hope to spearhead the development of novel therapeutic strategies that will maximize the anticancer effects of natural killer cells.”