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glycostem
innovative cellular therapy

Natural killer cells making better cancer immunotherapies

By harvesting stem cells from umbilical cord blood and differentiating them into natural killer cells, Glycostem has developed oNKord, an affordable off-the-shelf cell therapy product indicated for oncology therapies that is ready to ship worldwide within 48 hours.

Glycostem Therapeutics is at the forefront of efforts to develop safer, more affordable cell therapies which are available off-the-shelf. Instead of working with T cells, Glycostem is developing naked and engineered natural killer (NK) cells, eliminating the logistical complexity and safety concerns associated with existing therapies.

NK cells have innate advantages over T cells currently used as chimeric antigen receptor T (CAR-T) therapies on the market. CAR-T cells can cause cytokine release syndrome and for NK cells, clinical reports indicate that this is not a problem, suggesting a more advantageous safety profile than CAR-T cells.

Glycostem uses stem cells harvested from umbilical cord blood and expands and differentiates them into NK cells. These NK cells are further cryopreserved, resulting in an off-the-shelf cell therapy product called oNKord (Fig. 1). Glycostem can 1-day ship oNKord around the world within 48 hours of receiving an order. The cost of manufacturing is significantly lower than for CAR-Ts and patients would get their treatment sooner.

Those benefits of NK cells are widely recognized but the cells also have limitations that have stopped them coming to market. Notably, NK cells must undergo significant expansion to achieve a therapeutic dose. Glycostem has overcome that barrier by establishing a proprietary medium and process that expands cell populations by up to 50,000 fold. This has allowed Glycostem to work with feeder-free processes.

> **Glycostem wants to remain a leading light in NK cell therapies**

Validating naked NK cells

Glycostem used the expansion technology to manufacture doses for a phase 1 trial in acute myeloid leukemia (AML). The trial was designed primarily to assess safety and dosing—and generated positive data in those areas—but it also gathered encouraging efficacy results. After 1 year, 80% of patients were alive. Glycostem expected to see a 1-year survival of around 35%.

The clinical data enabled Glycostem to raise money to support the next stage of its development. Glycostem has set up new state-of-the-art R&D laboratories in the Netherlands and built a good manufacturing practice (GMP)-licensed, fully closed and large-scale production system.

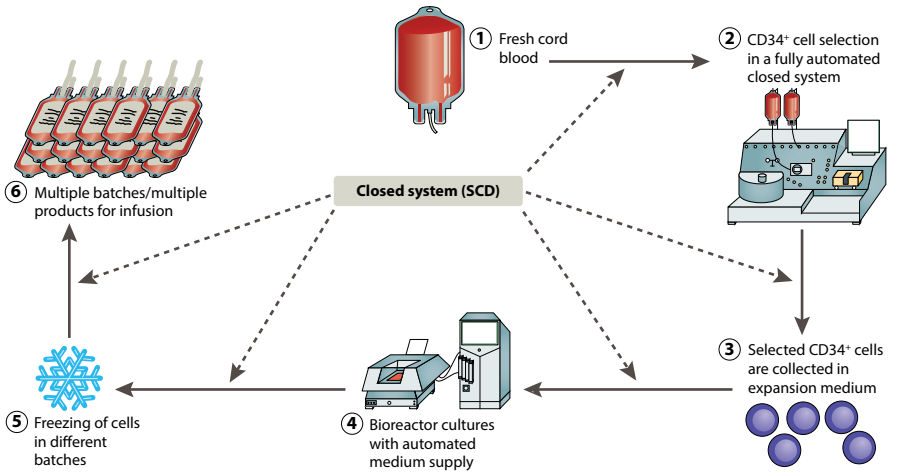

Fig. 1 | The closed oNKord system.

Working out of the GMP facility, which Glycostem thinks is the first of its kind, the team is making cell therapies for a series of planned clinical trials. Glycostem is preparing to run a phase 1/2a clinical trial in minimal residual disease-positive patients with AML. The trial will enrol 33 patients across its two phases, in five countries and eight clinical centres.

In parallel with the AML trial, Glycostem will initiate a phase 2a trial to start testing oNKord in 14 patients with multiple myeloma, which will put Glycostem on track to file for conditional approval of oNKord in two indications in 2023.

Glycostem also plans to initiate a clinical trial of oNKord in solid tumors in 2020. The basket trial will dose patients with NK cells every 3 weeks. The repeat dosing schedule is made possible by the safety of NK cells and the relatively low cost of production. The same trial will shed light on new and improved pre-conditioning agents as well.

A Korean company has licensed the rights to oNKord in its home market and Japan. Glycostem is taking the asset forward in Europe and the USA.

Opening up new indications

The pre-clinical and clinical data generated to date have given Glycostem confidence that naked NK cells work in some indications. However, the company recognizes that it may be necessary to engineer NK cells to treat certain other cancers, such as those affecting the liver, kidney, breast and prostate.

That recognition led Glycostem to hire a team of scientists and task them with genetically modifying NK cells to specifically target tumor cells. These CAR-NK therapies could be powerful enough to cure cancer or turn it into a manageable chronic disease.

Other companies are also developing CAR-NKs but Glycostem thinks its extensive experience making and testing naked NK cells will enable it to lead the field. That confidence is validated by deals. Glycostem has a three-asset CAR-NK deal with MolMed and a one-asset agreement with a Korean company, as well as multiple internal programs.

As it advances that extensive product pipeline, Glycostem plans to increasingly align itself with the US market. Preparations for a pre-investigational new drug (pre-IND) meeting with the US Food and Drug Administration are underway, and Glycostem is also looking to tap into the US market for raw materials. Further down the line, Glycostem may seek US investment.

The planned alignment with the USA reflects Glycostem's ambitions. Glycostem wants to remain a leading light in NK cell therapies and, as such, has set its sights on the mature, world-leading US market.

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