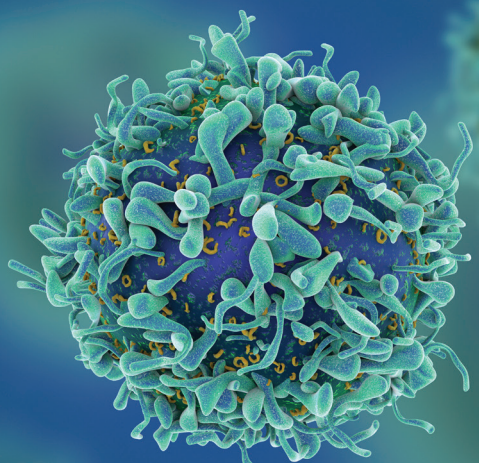
glycostem
innovative cellular therapy

Introduction

Glycostem is a clinical stage company focused on cellular immunotherapy utilising allogeneic Natural Killer (NK-cells).



March 2018

Over the last 10 years Glycostem has established a reproducible and efficient, closed production process, protected by 6 patent families and 'knowhow'. This makes Glycostem the leading cellular immunotherapy company with focus on safe and cost effective allogeneic approach with the promise of providing 'off-the-shelf' cellular products.

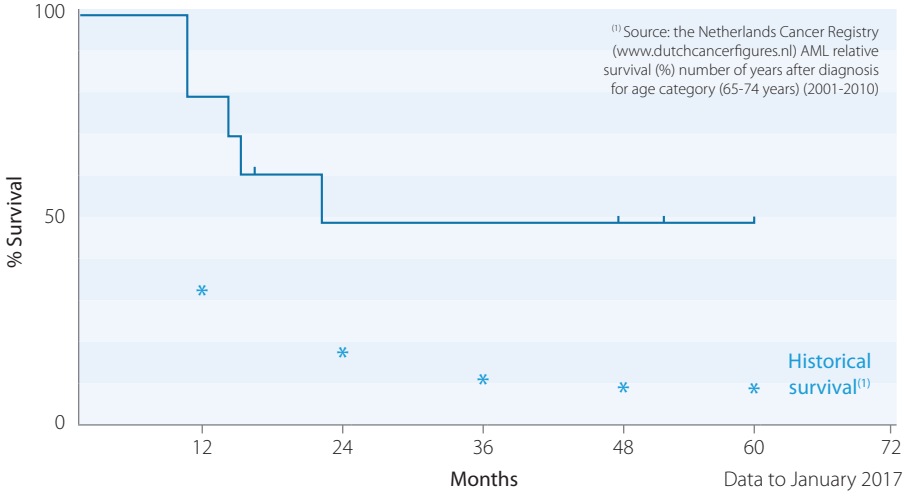
A recent published phase I clinical trial provided much encouragement by way of positive safety data and strong indication of efficacy, please see below Kaplan Meyer's Plot. By 2019 Glycostem will have certified GMP product facilities and initiate the pivotal phase I/II clinical trial in AML patients in Europe for which Glycostem has Orphan Drug Designation. Compassionate use will be initiated at the same time.

Management

Glycostem has appointed a highly specialised and experienced Executive Management Team consisting of:

- **Troels Jordansen**, CEO
  20 years' experience with cellular therapy and public listed company experience
- **Jan Spanholtz**, PhD, CSO
  15 years background in stem cell biology, immunology, translational clinical research and process development
- **Volker Huppert**, COO
  21 years of experience with NK-cells and closed system production
- **Hareth Nahi**, MD, CMO
  Associated professor and hematologist at Sahlgrenska in Stockholm
- **Jeroen Pieper**, Regulatory Manager
  10+ years in Regulatory Affairs
- **Richard van der Linden**, Quality Manager
  10+ years in Quality Assurance
- **Marty Wulferink**, IP Manager
  Strong background in cell biology and immunology and patent attorny

Treatment with oNKord® indicates dramatic impact on overall survival in elderly AML patients



IP Protection

Glycostem has 6 patent families, which are described below:

IP1 – GRANTED

- Method claims for the expansion of progenitor or stem cells;
- Product claims (culture medium); and
- claims the use of modified glycans and glycosaminoglycans for expanding progenitor or stem cells

IP2 – GRANTED

- Method claims for culture medium and expanding stem cells

IP3 – GRANTED

- Method claims for expanding progenitor cells; and
- Product claims directed to a collection of cell obtained by the method

IP4 – UNDER FINAL REVIEW

- Method covers a method for expanding progenitor cells; and
- Medical use of the obtained/used NK-cells

IP5 – UNDER FINAL REVIEW

- Use of IL-12 in low doses in the generation of NK cells; and
- Medical use of the obtained/used NK-cells

IP6 – PCT Phase

- Claims are directed to cancer treatment; and
- Immunotherapy using allogeneic NK cells

The exact composition of Glycostem's proprietary and fully synthetic expansion and differentiation media is covered by knowhow.

Science

Glycostem has developed a platform technology to select, expand and differentiate NK-cells from CD34+ cells, derived from umbilical cord blood and upgraded into a large scale GMP platform for clinical implementation (oNKord®). oNKord® was infused at up to 30 x 10^6 cells/kg/bodyweight in elderly AML patients, resulting in strong safety data. oNKord® showed active migration to the marrow and further matured in the absence of any exogenous cytokine injections.

This confirms previous findings from a preclinical model, showing migration to the bone marrow and upregulation of KIRs and CD16a *in-vivo* as well as antileukemic activity. oNKord® is well characterized and was found to have a increased functionality and similar gene expression profile as activated pheriphial blood NK-cells. Furthermore, oNKord® is highly cytotoxic against solid tumor targets such as cervical cancer cells, in which killing was independent of HLA expression levels, tumor histology and HPV types, or colorectal cancer cells, in which killing was independent of tumor EGFR levels, and RAS and RAF mutations, thus paving the way for oNKord® as immunotherapy for advanced solid tumors.

Clinical strategy

Based on the successful phase I clinical trial, Glycostem plans to initiate further clinical trials.

- Phase I/II – refractory/relapsed AML
  - AML trial is expected to include 31 patients in a multi-centre study without a control arm
- Phase I/II – Multiple Myeloma
  - This trial is expected to recruit 20 patients in a multi-centre study without a control arm
- Phase I/II – Defuse tumours

Development / Production

Glycostem has published[1], that their NK-cell generation technology will see the original stem cell population expanded upto 50,000 fold and that we achieve a purity of 99% (+/- 1%) of NK-cells in the final product. The starting point is CD34+ cells, isolated from fresh umbilical cord blood, are expanded and differentiated into NK-cells, which finally are washed and prepared for infusion. All of this takes place in state-of-the-art closed system which is set-up at our facilities in the Netherlands.

Research

The research focus is to develop novel oNKord® products with dedicated functions (CAR-NK products). To reach this goal, Glycostem is establishing several collaborations:

1. German company: developing of anti-tumor antibodies and novel CAR-NK constructs
2. To combine oNKord® process with lenti- and retroviral platform to develop CAR-NK

Our research department is, however, also looking for new and more effective ways collecting, expanding and differentiating NK-cells. Glycostem is looking internationally for collaboration partners (industry and academic) with innovative technology also regarding immune checkpoints or immunosuppressive strategies.

Product Pipeline

Product	Indication	Product development	Pre-clinical	Phase I	Phase II
oNKord®	AML - Refractory/Relapsed				
	Multiple Myeloma				
	Solid tumours				
CAR-NK-cells	Solid and liquid cancers				
NK-cells and antibodies	Solid and liquid cancers				

[1] Spanholtz et al. PlosOne 2010

oNKord® patients shows better survival than population in general

Finance

Glycostem is funded until 2019 to finalise the production development programme.

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