CellProtect

Nordic Pharmaceuticals AB

Developing innovative cell therapy treatments for incurable diseases

Karin Mellström, Dr Med Sci, founding CEO

www.cellprotect.se

Summary of CellProtect

- Phase I/II trial in newly diagnosed Multiple Myeloma (MM) patients with promising results on efficacy (biomarker)
- Validated GMP manufacturing method for autologous, activated NK-cell therapy product with
  - 48 months stability data on frozen product
  - COGS - No more than 25% of cost per treatment
- Patents covering manufacturing process, cell type and treatment with autologous ex vivo expanded and activated NK-cells
- Orphan drug designation with EMA and FDA ongoing
- Process development to support scale up of manufacturing of CellProtect.
- Potential to expand into other oncology indications and infection diseases.

CellProtect
Nordic Pharmaceuticals AB

CellProtect : autologous *ex vivo* expanded and activated NK cells

- NK cells can recognize and kill cancer cells
- In several types of cancer, including multiple myeloma, the tumor cells can evolve to evade and suppress the NK cells killing activity
- Blood is taken from the patient at diagnosis and the anti-cancer effect of NK-cells is ***restored*** by Cell Protects patented process ***and then frozen***
- Activated NK cells is given back to patients after first line treatment - ***when the patient needs the treatment!***

CellProtect
Nordic Pharmaceuticals AB

Multiple Myeloma is an incurable and progressive hematologic cancer

First line treatment high dose chemotherapy followed by autologous stem cell transplant (only younger and fit patients)

- *prolong remission but does* not cure
- *residual disease is the problem*
- *5 year survival 50 %*

CellProtect complements the existing treatments, and has the potential to eradicate residual tumor

Research findings

CellProtect
Nordic Pharmaceuticals AB

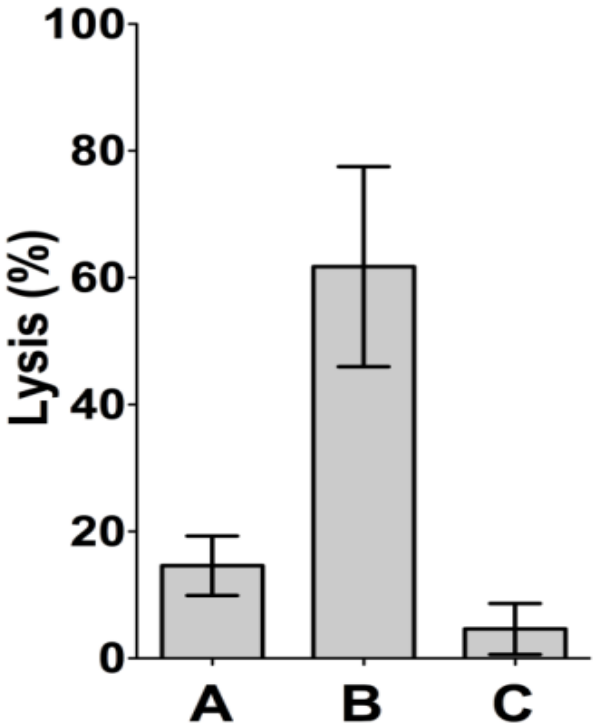
NEOPLASIA

Autologous antitumor activity by NK cells expanded from myeloma patients using GMP-compliant components

Evren Alici,[1,2] Tolga Sutlu,[1] Bo Björkstrand,[1] Mari Gilljam,[1] Birgitta Stellan,[1] Hareth Nahi,[1] Hernan Concha Quezada,[1,2] Gösta Gahrton,[1] Hans-Gustaf Ljunggren,[2] and M. Sirac Dilber[1]

[1]Department of Medicine, Karolinska Institutet, Karolinska University Hospital Huddinge, Stockholm; and [2]Center for Infectious Medicine, Department of Medicine, Karolinska Institutet, Karolinska University Hospital Huddinge, Stockholm, Sweden

Multiple myeloma (MM) is an incurable plasma cell malignancy with poor outcome. The most promising therapeutic options currently available are combinations of transplantation, targeted pharmacotherapy, and immunotherapy. Cell-based immunotherapy after hematopoietic stem-cell transplantation has been attempted, but with limited efficacy. Natural killer (NK) cells are interesting candidates for new means of immunotherapy; however, their potential clinical use in MM has not been extensively studied. Here, we explored the possibility of expanding NK cells from the peripheral blood of 7 newly diagnosed, untreated MM patients, using good manufacturing practice (GMP)–compliant components. After 20 days of culture, the number of NK cells from these patients had expanded on average 1600-fold. Moreover, expanded NK cells showed significant cytotoxicity against primary autologous MM cells, yet retained their tolerance against nonmalignant cells. Based on these findings, we propose that autologous NK cells expanded ex vivo deserve further attention as a possible new treatment modality for MM. (Blood. 2008;111:3155-3162)



Cytotoxicity against primary autologous cells from the bone marrow of 7 patients with MM. A) Day 0 NK cells against MM cells
B) Day 20 NK cells against MM cells
C) Day 20 NK cells against non-MM cells in the bone marrow
(adapted from Alici et al. 2008)

CellProtect
Nordic Pharmaceuticals AB

CellProtect is safe and complementarity to existant treatments

Patient-derived

CellProtect does not cause Graft versus host reactions

Selective

In vitro cytotoxicity clearly shows that CellProtect selectively kills tumor cells.

Does **not** affect non-tumor cells.

Safe

Safety and tolerability is extensively explored in the current phase I/II clinical study

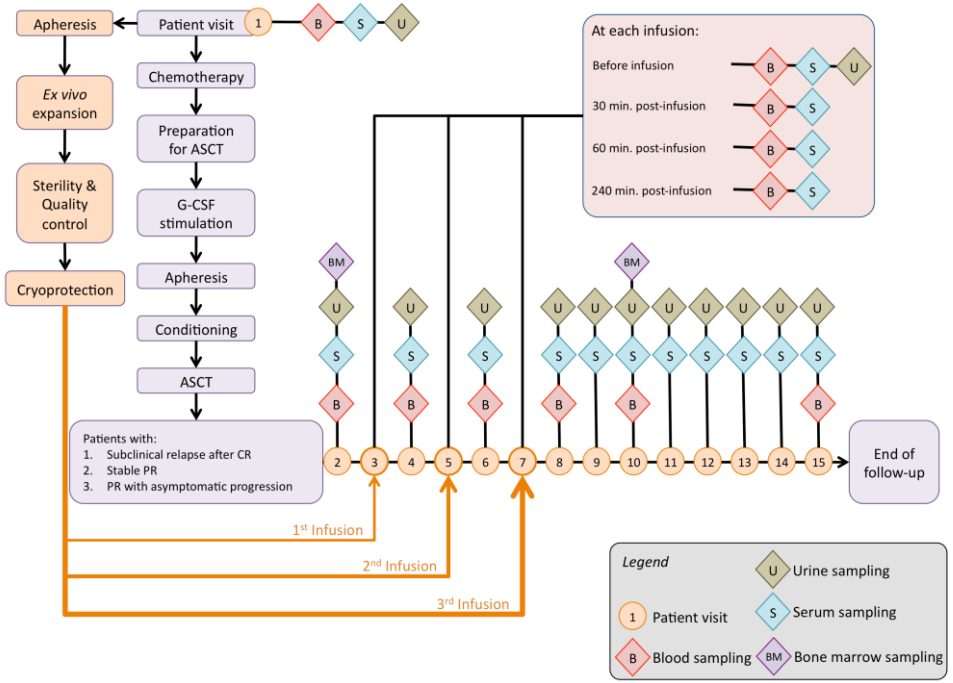
Efficacy

Efficacy is being explored in the phase I/II clinical study

Ongoing Phase I/II, first –in- man therapeutic exploratory clinical study in newly diagnosed MM patients

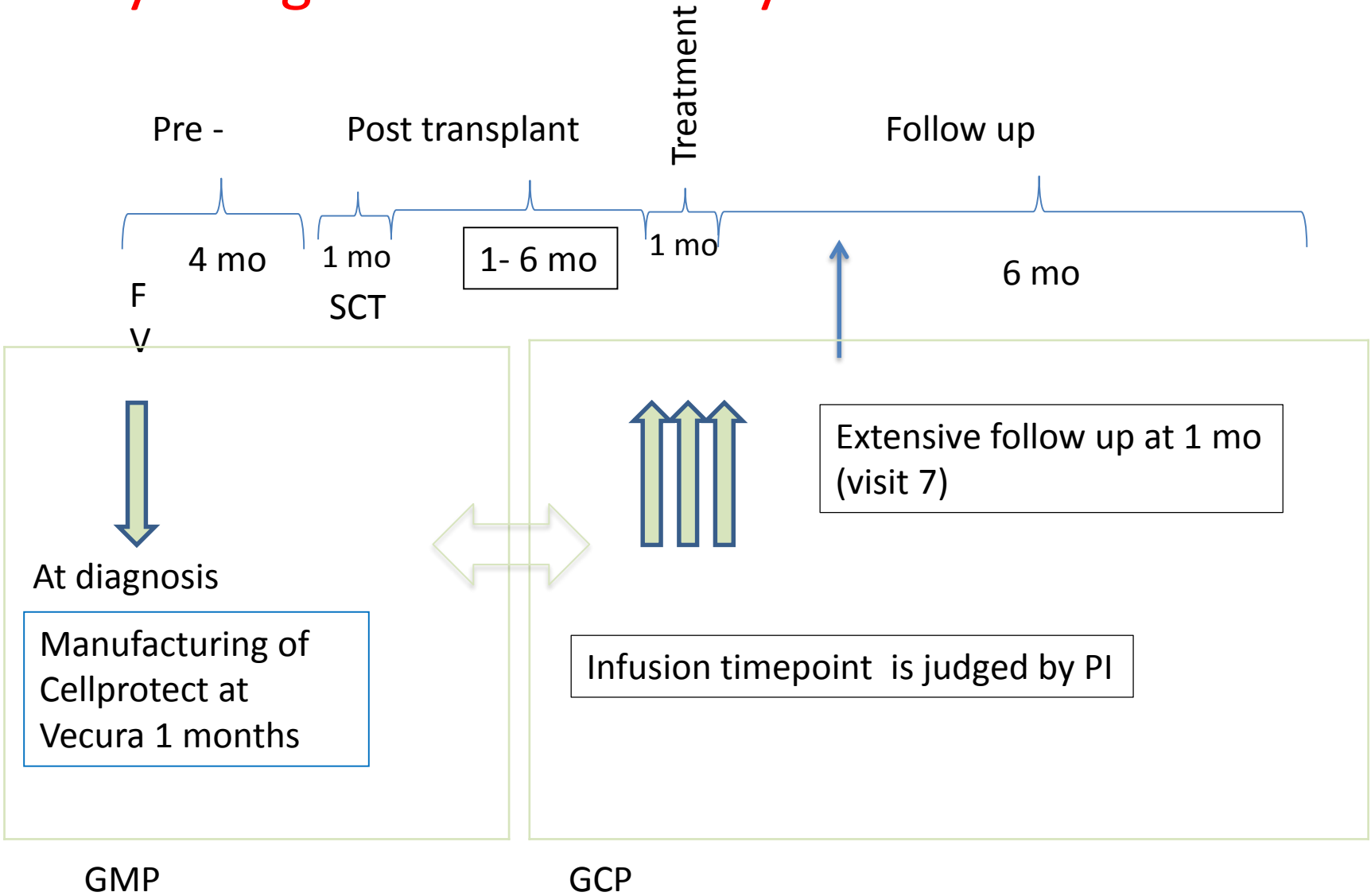
ACP-001

- First-in-man, Phase I/II
- Open, single arm study
- Primary objective:
  - Safety and tolerability
- Secondary objective:
  - Effect on serum Ig levels (M-component) as indicator of biological effect
- Inclusion:
  - MM patients eligible for ASCT
- 3 escalating infusions/patient (Weekly)
  - 10^6, $50x10^6$ and $100x10^6$ cells/kg
- Evaluation:
  - 4 weeks after infusion,
  - 6 months follow up



CellProtect
Nordic Pharmaceuticals AB

Study design allows for early clinical observations



CellProtect
Nordic Pharmaceuticals AB

Status Phase I/II study - ACP001

GMP manufacturing

- Nine (9) batches CellProtect produced
- Four (4) batches has been CellProtect QP released.
- Two (2) batcher that fullfills the release criteria are stocked at the GMP facility pending QC analyses of QP release.

GCP CellProtect infusions

- Four (4) patients infused with CellProtect
- Three (3) patients evaluated at visit 7.

Next decision point: Interim analyses of 6 evaluated patients expected **Q3 2016**

Early clinical results give strong signals on efficacy

CellProtect
Nordic Pharmaceuticals AB

- The CellProtect treatment is hitherto safe and tolerable; no severe adverse events observed.
- Signals of clinical efficacy observed in two patients with stable detectable serum M component after ASCT
- Indications that serum M component levels remains low during follow up.

CellProtect
Nordic Pharmaceuticals AB

Path forward

- Sucessfully complete the phase I/II clinical study
- confirm the regulatory strategy
- Scale up manufacturing procedure with service providers

***app* 10 million SEK**

- Pivotal Phase II (app 200 patients)
- Registration and partnering

app 100 million SEK

Market CellProtect after phase II via conditional approval as an Orphan Drug

CellProtect
Nordic Pharmaceuticals AB

We are seeking

- Commercial partner for further clinical development
- Funding / VC capital for further clinical development and commercialization of CellProtect
  - First step to prepare for phase II (10MSEK)
  - To accomplish a phase II clinical trial (100MSEK)