Development of a humanized immunocompetent mouse model to study the relapse vaccine DCP-001

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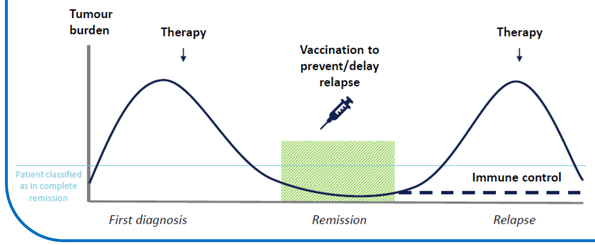
Abstract

DCP-001 is an off-the-shelf whole cell-based relapse vaccine, aimed to provide immune control over residual disease in order to prevent or delay relapse after initial treatment of haemato-oncological malignancies. A Ph I clinical study in post-remission treatment of patients with acute myeloid leukemia (AML) demonstrated that DCP-001 is safe, feasible and generates both cellular and humoral immune responses. It is currently being studied in an international Ph II trial. To further study DCP-001 as a vaccine in the preclinical setting, a humanized tumor mouse model was developed.

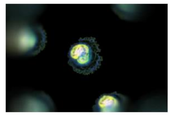
We showed that DCP-001 vaccination efficiently suppressed tumor growth in this mouse model.

DCP-001: a relapse vaccine based on the DCOne® platform

Relapse vaccine window in cancer treatment

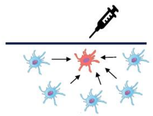


DCOne®



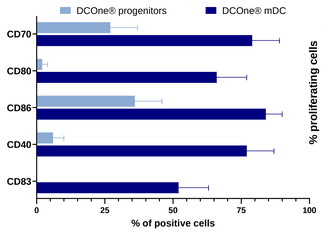
- DCOne® myeloid leukemic cell line
- Shifted towards a mature dendritic cell (mDC) phenotype in proprietary manufacturing process

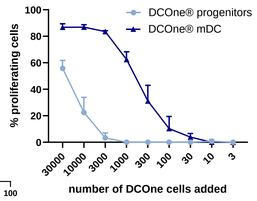
DCP-001

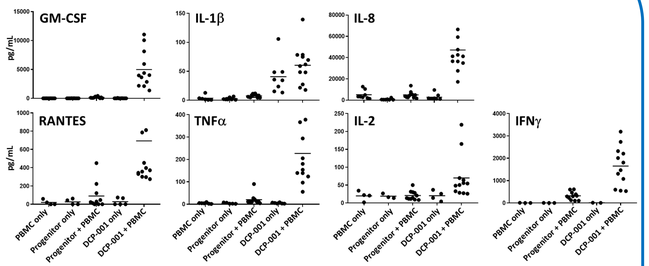


- Highly immunogenic vaccine carrying multiple endogenous tumor-associated antigens (TAA)
- Off-the-shelf product
- Administered via intradermal injection
- Developed as relapse vaccine in post-remission window

Immunogenic character of DCP-001 results in multifunctional immune response





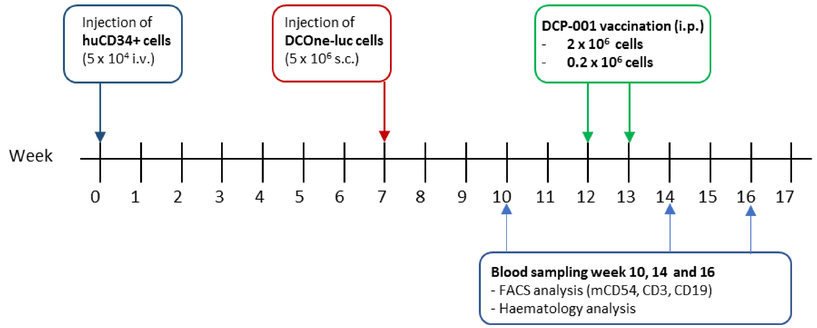


Left: Phenotype of DCOne progenitors and DCOne mDCs. Right:Peripheral blood lymphocytes (PBL) were co-cultured with increasing amounts of DCOne mDC (DCOne DC) or DCOne progenitor cells and PBL proliferation was analyzed in a mixed lymphocyte reaction (MLR).

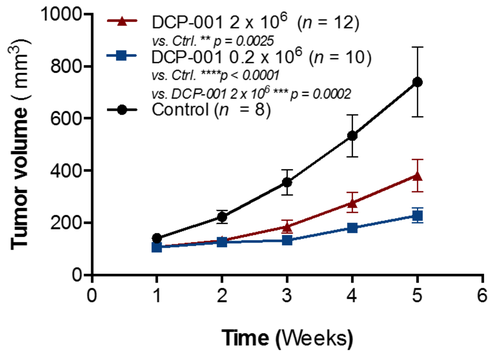
PBMCs derived from healthy donors (n=8) were co-incubated with DCP-001 in a 1:1 ratio in 96 wells plates for 6 days. Supernatants were analyzed for cytokine release by Luminex analysis. Horizontal lines represent the mean.

Generation of a humanized mouse model for DCP-001 vaccination

NSGS mice were reconstituted with human CD34+ hematopoietic progenitors. After 7 weeks, DCOne progenitor cells expressing luciferase (DCOne^{luc}) were injected as a model tumor. DCP-001 vaccine was administrated intraperitoneally at 5 and 6 weeks after the tumor injection.



DCP-001 vaccination significantly suppresses tumor growth



Lower dose (0.2 x 10^6 cells) of DCP-001 showed stronger suppression of tumor growth as compared to higher dose (2 x 10^6 cells)

Conclusions and Perspectives

- The newly developed humanized AML mouse model is a highly valuable tool to study DCP-001 vaccination
- This model provides the basis for further preclinical research including DCP-001 in combination with other therapeutic modalities
- These data support the rationale of DCP-001 as relapse vaccine providing immune control over residual disease