European Commission

SHOWCASING EU-FUNDED PROJECTS DEVELOPING THERAPIES FOR RARE DISEASES

Vaccine therapy for acute myeloid leukaemia

Acute myeloid leukaemia (AML) is a deadly rare disease that affects both children and adults. Approximately 45% of younger AML patients treated are cured, and in older patients, 85% relapse and die within 2 years. This is because of minimal residual disease (MRD) – a small amount of leftover cancerous cells. Immunotherapy has great potential for treating MRD, in particular cell therapy.

AML-VACCiN

Clinical development of a vaccine therapy for acute myeloid leukaemia

Led by Amsterdam University Medical Centre, the Netherlands
EU grant: €6 million - funded under **Horizon 2020** topic **New Therapies for rare diseases**
Duration: January 2016 to March 2020
CORDIS: https://cordis.europa.eu/project/id/667713
Project website: https://www.amlvaccin.eu

The AML-VACCiN project is working on clinical development of a highly innovative DC vaccine (DCP-001). Three innovative companies and internationally renowned scientists representing nine European medical institutes are working together to bring the AML vaccine closer to the clinical practice. The goal is to conduct a clinical study to demonstrate its safety and efficacy. AML-VACCiN is also developing biomarkers to better follow how the treatment works and to more selectively enrol patients into the future studies.

The collaboration has so far brought many successful results. The DCP-001 vaccine was demonstrated to be safe and capable of inducing an immune response and the biomarkers to follow how treatment works were developed. The ambition of AML-VACCiN is to build sufficient evidence to apply for conditional approval of the AML vaccine in Europe. The impact this research could have and its future applications appear very significant and have a strong potential for personalised AML therapy.

Gene Therapy for Fanconi anemia

Fanconi anemia is a rare inherited syndrome characterised by early bone marrow failure and increasing predisposition to cancer with age. Cell transplantation is the only curative therapy, although it is associated with complications, for example carcinoma. The genetic correction of imature blood forming cells (called hematopoietic stem cells or HSCs) from matching donors with viral vectors constitutes a recent and safe alternative for the treatment of various genetic diseases. But the success of Fanconi anemia gene therapy trials

conducted 17 years ago in the USA was limited by several challenges, for example by difficulties in the collection of sufficient numbers of HSCs from Fanconi anemia patients.

The EUROFANCOLEN consortium of researchers tackled these challenges over the 6 years of the project and has been very successful. The main achievement was to develop and carry out a clinical trial for gene therapy for Fanconi anemia patients across several countries. For this, EUROFANCOLEN researchers developed and used a novel viral vector to genetically correct the patients' HSCs, accompanied by comprehensive and ground-breaking safety and efficacy patient monitoring studies.

EUROFANCOLEN

Phase I/II Gene Therapy Trial of Fanconi anemia patients with a new Orphan Drug consisting of a lentiviral vector carrying the FANCA gene: a coordinated international action

Led by Research Centre for Energy, Environment and Technology (CIEMAT), Spain
EU grant: €5.3 million - funded under **FP7** topic **Preclinical and/or clinical development of substances with a clear potential as orphan drugs**
Duration: January 2013 to December 2018
CORDIS: https://cordis.europa.eu/project/id/305421
Project website: https://www.eurofancolen.eu/apps/

For the first time, a clinical trial in patients with Fanconi anemia demonstrated the safety and efficacy of the novel gene therapy approach. The first results were published in 2019 in Nature Medicine[1]. EUROFANCOLEN also initiated very active networking activities among Fanconi anemia patient associations across Europe (France, Germany, Italy, Spain, United Kingdom), and globally.

The EUROFANCOLEN ended in 2018, but activities continue. Long-term data obtained in this clinical trial opens new expectations and supports the gene therapy approach as an innovative and low-toxicity treatment for the haematological component of this devastating disease. The proposed gene therapy should not increase the incidence of solid tumours. The next ambition is to develop a global gene therapy trial both in Europe and in the USA.

An Innovative steroid-like Intervention on Duchenne Muscular Dystrophy

The rare disease Duchenne muscular dystrophy (DMD) is an incurable, muscle wasting disease that occurs primarily in males. Boys progressively weaken, lose the ability to walk and death occurs by early adulthood. The VISION-DMD project aims to advance the development of an innovative steroid-like drug vamorolone (VBP15), as a new therapy to revolutionise care for all patients with DMD. Building on positive previous results, the ambition of VISION-DMD has been to conduct further clinical studies (Phase 2) in order to determine the safety and tolerability of

[1] https://www.ncbi.nlm.nih.gov/pubmed/31501599

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increasing doses of vamorolone and to demonstrate the efficacy and safety of two doses of vamorolone in young ambulant DMD boys. VISION-DMD links the leading networks Treat NeuroMuscular Disease[2] (TREAT-NMD) and the Cooperative International Neuromuscular Research Group[3](CINRG) with the European Clinical Research Infrastructure Network-European Research Infrastructure Consortium[4] (ECRIN-ERIC), for carrying out clinical trials and obtaining regulatory approval in Europe and the USA.

Since the project started in 2016, part of the clinical studies were successfully completed, whereas other part of international clinical studies are ongoing to advance the development of this innovative drug in the EU and the rest of the world. VISION-DMD has demonstrated a reduction in side effects compared to the current standard treatment. The vamorolone trial in DMD showed a dose-related improvement of muscle function[5]. The project has developed and is using an innovative tool – a simple narrated animation in five European languages (English, Swedish, Dutch, Spanish and Czech) to explain the VISION-DMD project to young children participating in the studies[6]. To advance research and innovation in vamorolone programme, the project is combining the EC funding with a patient-led venture philanthropy funding model and NIH funding[7]. As such, venture philanthropy is a novel approach towards a research funding where non-profit sector comes together with industry in order to increase a social impact, which is a particularly valuable model in rare diseases drug development also bringing patients very closely onboard. The longer-term impact of this project will be to provide Duchenne patients with a better, safer treatment through the use of vamorolone. This will meet the need for better treatment for DMD, with widespread acceptance and potentially to be used in combination with further therapies as they are developed.

VISION-DMD

Phase 2 Clinical Trials of VBP15: an innovative steroid-like intervention on Duchenne Muscular Dystrophy

Led by: University of Newcastle upon Tyne, United Kingdom
EU grant: €6 million - funded under **Horizon 2020** topic **New Therapies for rare diseases**
Duration: January 2016 to June 2021
CORDIS: https://cordis.europa.eu/project/id/667078
Project website: www.vision-dmd.info

[2] https://treat-nmd.org/
[3] https://cinrgresearch.org/
[4] https://www.ecrin.org/
[5] https://vision-dmd.info/vbp15-publications/
[6] https://vision-dmd.info/vamorolone-study-app-for-boys/
[7] https://vision-dmd.info/vision1/wp-content/uploads/2018/10/VP-poster-ECRD-18-Vision-DMD-v4.jpg