

# FIAMMA (CHIMERIC ANTIGEN RECEPTOR T CELL THERAPY FOR CHILDREN AND ADULTS WITH RELAPSED ACUTE MYELOID LEUKEMIA)

Project

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## Introduction

The FIAMMA project (CHIMERIC ANTIGEN RECEPTOR T CELL THERAPY FOR CHILDREN AND ADULTS WITH RELAPSED ACUTE MYELOID LEUKEMIA), supported by a 2.8 million CHF private donation and coordinated by the ISREC Foundation, targets pediatric and adult patients who have relapsed after standard treatment.

Conducted in close collaboration by PD Dr. Francesco Ceppi, senior physician in the pediatric hemato-oncology unit at the CHUV, and Prof. Caroline Arber, senior physician in the oncology department UNIL CHUV (immuno-oncology and hematology wards), the "FIAMMA" research project aims to develop a novel therapy for pediatric and adult patients who have relapsed after standard treatment.

This project is in line with the translational research vision of the Centre Hospitalier Universitaire Vaudois (CHUV), the University of Lausanne (UNIL) and the Ludwig Institute for Cancer Research (LICR). It reflects the close collaboration that has been established between various institutions in the Lake of Geneva area, united within the Swiss Cancer Center Léman (SCCL). The study is fortunate to benefit from the resources made available by the UNIL CHUV oncology department platform, which has already conducted several promising clinical studies on immunotherapies for various types of cancer and enjoys worldwide recognition in its field. Additionally, the project combines the complementary expertise of two immunotherapy specialists who have already carried out several studies in this area.

The FIAMMA project is funded through donations amounting to 2.8 million CHF. It benefits from the generous support of two private foundations based in Lausanne, namely the Jacqueline de Cérenville Foundation and the Jan Baron Mladota Foundation. Each has donated 1.25 million CHF via the ISREC Foundation, which itself has contributed a further 300'000 CHF to the project. With the assistance of its Scientific Board, chaired by Prof. Michael Hall, and its Scientific Director, Prof. Susan Gasser, the ISREC Foundation will supervise the project and coordinate the funding stages spread across five years (from 2023 to 2027).

## Acute myeloid leukemia (AML)

With an incidence of 7 cases per million children under the age of 15, acute myeloid leukemia (AML) is the most aggressive subtype of pediatric acute leukemia.

Despite remarkable advances in the past 40 years, recent data suggests that standard treatment, including conventional chemotherapy and, in more than half of the cases, hematopoietic stem cell (HSC) transplant, fails in 30 to 40% of all newly diagnosed patients.

In adults, AML is the most frequent acute leukemia type, with an average of 5 new cases per year per 100'000 inhabitants in Europe. The outcomes of standard treatments (intensive chemotherapy, where feasible in combination with targeted, personalized drugs and an HSC transplantation) are similar to those obtained in children. The prognosis for relapsing AML patients after an HSC transplantation and for those refractory to intensive chemotherapies remains extremely poor, and the development of novel therapies for this group of patients is a yet unmet medical need.

“Our FIAMMA project targets this population of pediatric and adult patients, often neglected in medical research. We propose to evaluate a novel immunotherapeutic approach, based on T lymphocytes that have been equipped with a chimeric antigen receptor (CAR). The CAR grants lymphocytes the capacity to recognize leukemic cells and to destroy them. This novel treatment is potentially curative”, comments Prof. Caroline Arber.

## How does CAR-T lymphocyte immunotherapy work?

CAR-T lymphocyte immunotherapy constitutes an innovative therapeutic approach and a new source of hope for the treatment of certain types of cancer. At the CHUV, commercial CAR-T treatments have already been introduced by the immuno-oncology department for acute lymphoblastic leukemia (ALL), certain types of aggressive lymphoma and multiple myeloma. A CAR-T therapy makes use of the patient's immune system to fight the disease. It is characterized by a spectrum of short-term side effects, as opposed to standard treatments which can cause longer-term complications.

“In Switzerland, no clinical studies are currently being performed in this field, and commercial products based on CAR-T cells are not available for acute myeloid leukemia. On an international level, studies in the United States and in China are in a very early stage. If we do not develop our own academic study, we will not have a similar approach available in Switzerland for the treatment of relapsed AML in the medium term”, explains Dr. Francesco Ceppi.

The CHUV offers the infrastructure needed to produce CAR-T products for use in an academic clinical trial. Patients for the FIAMMA study – 6 adults and 6 children – will be recruited in Switzerland as well as abroad, given the unique nature of the project.

## Project phases

The first step will be to finalize the preclinical studies in Prof. Arber's lab, in order to document the proper functioning of the new CAR-T products against AML. The second stage of the project, to be conducted in close collaboration with the Center of Experimental Therapeutics in the oncology department UNIL CHUV, will serve to optimize the manufacturing process and the production of the viral vector required to express the CAR on the surface of the T lymphocytes.

A next important step in the project will be the development of the clinical trial protocol, which will then be submitted for approval to the Swiss Agency for Therapeutic Products (Swissmedic) and the Commission cantonale d'éthique de la recherche sur l'être humain (CER-VD, cantonal ethics commission). Once both authorities have given their go-ahead, the phase I clinical trial can begin at the CHUV, ideally somewhere between late 2024 and early 2025.

Patients will be recruited mainly in Switzerland, but also in neighboring countries where similar trials are not available. The researchers estimate that the recruitment process and the administration of the treatment will take approximately 24 months. In-depth analyses of the

performance of this novel treatment, with correlative studies on samples taken from each patient during and after treatment, will also be carried out. These studies will help understand the biological parameters associated with this novel therapeutic strategy.