ATECT (602239)
Advanced T-cell Engineered for Cancer Therapy

PUBLISHABLE SUMMARY

Introduction: Chimeric Antigen Receptors (CARs), generated by fusing the antigen-binding region of a monoclonal antibody (mAb) to intracellular T-cell signalling domains\(^1\), hold the promise to revolutionize cancer treatment. Introduction of genes coding for CARs into T-cells using integrating vectors endow antigen recognition independent of MHC restriction. Recent clinical data leave no doubt that this new form of cancer therapy can be remarkably effective, engendering long-lived remissions in patients with refractory disease.

There are, however, considerable barriers to be overcome to take this new form of therapy. Some of these barriers are practical – for instance can we develop ways of making such products cheaper and easier. Other barriers relate to engraftment of engineered T-cells in the face of hostile microenvironment.

Technological background: The ATECT consortium proposes to address these limitations through advanced cellular engineering. The central technological theme of this consortium is the application of gene editing strategies alongside advanced standard methods of genetic modification with insertional vectors, which we describe as a combination of advanced “positive” and “negative” engineering (figure 1).

Figure 1. Concept of CAR therapy: T-cells are subjected to “positive” engineering with a lentiviral vector or with “negative” engineering by transient expression of a gene-specific endonuclease. The T-cells are then administered to the patient as treatment.
Commercial and intellectual considerations limit this public report but the achievements so far can be summarized as follows:

- Cell processing development has proceeded well.
- Important targeting components for targeting brain tumours, lung cancer and paediatric cancers such as Neuroblastoma have been generated.
- Other components including a high-sensitivity transcriptional switch for clean payload release has been successfully developed.
- Other components to target the tumour microvasculature have also been developed.
- Models of human cancers where therapeutics which may work in humans have been developed ready for testing these new approaches.
- Advanced engineering approach to disruption checkpoint blockade has been developed and tested.

**Potential impact of ATECT research output**

Clinical and research output from the ATECT consortium has the potential to develop new treatments to treat cancers which are currently very difficult to treat. Currently many cancers which have spread from their primary site are incurable with conventional treatment. Increasingly, using the immune system to treat such cancers (immuno-oncology) is being recognized was one of the most promising approaches to treat otherwise resistant tumours. Some aspects of this consortium also may in future increase access of new immunotherapies to cancer patients by making the manufacturing process more practical and scalable. Further this work provides support for European academia and industry in developing novel treatments with concomitant employment, training and financial benefit.

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Logo(s):

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