Personalised tumour trained lymphocytes derived from regional lymph nodes for treatment of colorectal cancer


Highlights

We present a novel personalised tumour trained lymphocytes (pTTL) therapy.
- pTTLs can be applied in any cancer expressing targetable neoantigens by the use of PIOR Manufacturing®.
- Personalised therapy takes advantage of the patient’s own immune system.
- The EpiTcer® technology offers a novel approach for efficient antigen delivery and specific T cell activation. Also applicable to the use of alternative starting materials.
- Despite individuals singularities, pTTLs are produced in a reproducible manufacturing process.
- pTTLs are part of a virtuous cycle: every production linked to patient’s tumour characteristics provides information to develop both process and product further.

Background

We aim to develop a novel adoptive T cell therapy. pTTL therapy intends to re-educate immune cells to eradicate tumour cells regardless of cancer type.

pTTLs consist of regional lymph node (RLN) tumour-antigen selected expanded T cells.

pTTL characterisation of n=12 development batches derived from urinary bladder cancer (UBC) or colorectal cancer (CRC) is presented.

pTTL identity

- Patient’s individual variation confers pTTL’s phenotypic diversity (CD4+ and CD8+ T-cells).
- pTTLs are mainly composed of Tcm or Tem cells. Only a small proportion display a phenotype indicative of a limited in vivo functionality.
- pTTLs are oligoclonal and partly derive from clones enriched in the starting material.

Expansion data

- Patient’s individual variations confer growth kinetic diversity.
- pTTLs derived from UBC or CRC patient materials show comparability.
- EpiTcer® bead stimulation does not favour regulatory T cell expansion.

A First-in-human trial is underway

- Up to 16 adult patients with colorectal cancer Stage IV
- Primary endpoint - Safety
- Secondary endpoints - Standard clinical measurements: Response, OS, PFS, Disease-specific survival, Time to progression.

pTTL production process overview

1. collection of tumour material and peripheral blood samples for next generation sequencing
2. analysis of NGS data by in house software system PIOR Manufacturing® for neoantigen identification, selection and ranking
3. production of EpiTcer® beads, including coupling of neoantigens to super-paramagnetic beads
4. surgical collection of RLNs (starting material) and in vitro stimulation with EpiTcer® beads for pTTL expansion
5. harvest and formulation. pTTL product is infused to the patient.