PERSONALISED TUMOUR-TRAINED LYMPHOCYTES DERIVED FROM REGIONAL LYMPH NODES FOR TREATMENT OF COLORECTAL CANCER


Background Adoptive T cell therapy as a treatment for solid tumours is gaining increasing interest. Cancer neoantigens as targets for such therapy is also gaining recognition. Personalised tumour trained lymphocytes (pTTL) is a novel autologous T cell therapy targeting patient-specific neoantigens. A phase I/II First in Human (FIH) clinical trial of pTTL in Stage IV colorectal cancer (CRC) patients will be initiated in the near future.

Methods pTTL is produced through in vitro expansion of T cells derived from regional lymph nodes (RLNs). The T cells derived from RLNs, nodes in anatomical proximity of the tumour, contain a pool of naive and antigen-experienced T cells enriched for tumour-antigen specificity. This enriched population is stimulated during pTTL production with an array of neoantigen epitopes individually designed using PIOR®, an in house-developed software for neoantigen detection and selection. Selected neoantigens are linked to paramagnetic particles using EpiTCer® technology. The resulting EpiTCer® particles are used to stimulate the RLN T cells via phagocytosis and presentation of the neoantigen epitopes by antigen-presenting cells. This process is HLA-independent. Each pTTL product is unique due to the personalised nature of cellular and molecular players (cancer characteristics, immune cell properties and neoantigens are specific to one single individual).

In the planned FIH trial patients with Stage IV CRC which have either no remaining relevant standard care therapies or which are in a scheduled break in such therapy can be included. pTTL will be administered as a single dose monotherapy after chemotherapy-based preconditioning with cyclophosphamide and fludarabine. The primary endpoint of the trial is safety of pTTL. Biomarker analysis of pTTL persistence and characteristics will also be central in trial assessments, and clinical outcome and response will be evaluated.

Results Clinical results are not yet available. We here present central pTTL product characteristics. We have found that pTTL can be manufactured with a high rate of success despite the patient-specific nature of each product. The majority of the cells in pTTL are T cells, with small proportions of remaining NK and B cells originating from the RLN. The CD4 and CD8 T cell ratio are variable. Main pTTL characteristics include a significant proportion of memory T cells and phenotypic markers indicating maintained functionality such as limited levels of Temra (late stage memory cells re-expressing CD45RA) and CD57+ T cells, and maintained expression of CD28. TCR-seq data have shown increased clonality in pTTL compared to RLNs, indicating antigen-specific expansion.

Trial Registration EUDRA CT #2022-000394-96
Ethics Approval The trial have been approved by the Swedish Ethical Review Authority, Approval #2022-01842-01
Consent Written informed consent will be requested from study participants in future, but no study subjects have yet been included.