Scope of the contract

Erasmus MC is planning to conduct a Phase I/II clinical trial (N=10 patients) to evaluate Neoantigen peptide-based cancer vaccines for the treatment of pancreatic ductal adenocarcinoma (PDAC). To this end, we require clinical-grade peptides that can be used to formulate personalised investigational drug products in our institute.

PDAC remains one of the most formidable malignancies, characterised by a poor prognosis and limited therapeutic options. With an annually increasing incidence rate of 1.3%, PDAC is projected to become the second-leading cause of cancer-related death by 2030. Despite significant advancements in cancer therapies over the past decade, the overall survival (OS) rate for pancreatic cancer patients remains dismally low, with a 5-year OS of approximately 12%. Hence, developing more effective treatment options for PDAC is of critical importance.

Current treatment options for PDAC are limited and often ineffective in significantly improving long-term survival. The primary treatment approach for patients with resectable or borderline resectable PDAC is surgical resection, which is typically followed by adjuvant chemotherapy. For advanced or metastatic cases, systemic chemotherapy regimens such as FOLFIRINOX or gemcitabine with nab-paclitaxel remain the standard of care. However, these treatments are associated with significant toxicity and only marginal survival benefits. Emerging modalities, including targeted therapies and combination approaches, have yet to demonstrate substantial efficacy in PDAC.

Immunotherapy, which has transformed the treatment landscape for several cancers, has historically shown limited efficacy in PDAC. This is attributed to PDAC's highly immunosuppressive tumour microenvironment characteristic, which hinders immune system activation. Recent studies have highlighted the unique challenges in targeting PDAC with immune checkpoint inhibitors, such as PD-1/PD-L1 or CTLA-4 inhibitors, due to low tumour mutational burden and T-cell exclusion. However, advances in neoantigen-based immunotherapy offer a new avenue to overcome these barriers, holding potential where conventional immunotherapy has failed.

Neoantigens are mutated self-proteins which arise from genomic mutations during tumour cell development. The genomic mutations are often unique and, therefore, specific for each patient. They can even differ between tumour cells present in the same tumour. This, in turn, creates a unique, fingerprint-like, neoantigen landscape for each tumour. Their origin ensures that neoantigens are solely expressed in tumour cells and are completely absent in healthy cells. This trait renders neoantigens a very promising candidate for immunotherapy, as targeting these would not target healthy cells, preventing the risk of off-target effects of the therapy.

Our Personalised Neoantigen Cancer Vaccine

We are developing a patient-tailored, personalised cancer vaccine which utilises neoantigens identified from the patient's tumour. The neoantigens are identified using

advanced bioinformatic tools and verified for high immunogenicity. From the identified neoantigens, both short-sized (9-11 Amino Acids (AA)) and long-sized peptide (13-25 AA) sequences are designed and used as therapeutics. Hereby, this vaccine aims to elicit a robust and highly specific immune response, activating tumour-specific T cells to combat malignancy effectively.

What we require

The trial will encompass 10 patients, with each receiving up to 24 neoantigen peptides in their treatment. The sequences will range from 8 to 30 amino acids in length. It's important to note that it could occur, in case of a lower Tumour Mutational Burden (TMB) in an individual patient, fewer neoantigen peptides are identified from their neoantigen landscape, resulting in the identification of less than 24 neoantigen peptides. Consequently, a maximum of 240 neoantigen peptides will need to be prepared for this trial. Each patient's peptides need to be produced individually and then pooled into no more than 4 pools, each containing up to 6 peptides. These pools must be sterile filtered and lyophilized and are considered the Drug Substance (API) for our product. For additional acceptance criteria on the API, please refer to the PvE/PvW documentation. Turn-Around Times (TAT) are crucial for our product since they relate to personalised medicine, which must be administered to patients promptly to maximise the likelihood of a positive clinical response. By preference, the API manufacturer additionally has the abilities/facilities to prepare the final Drug Product (DP, concerns sterile fill finish of the API in 2R glass vials) as our intent is to outsource these activities also.

We expect to include the 10 patients in the trial in 18 months.