Autologous T cells with NY-ESO-1–specific T-cell receptor (GSK3377794) in HLA-A*02+ previously treated and untreated advanced metastatic/unresectable synovial sarcoma: A master protocol study design (IGNYTE-ESO)

Background

NY-ESO-1 is a member of the cytoplasmic cancer/testis family of tumor antigens detectable in many cancer types, including:

- SS
- Melanomas
- Breast cancers

Previous clinical studies using adoptively transferred T cells against NY-ESO-1 have reported objective responses in 40%–50% of patients with HLA-A*02+ tumors having NY-ESO-1+ SS. Genetically engineered NY-ESO-1–specific T cells (GSK3377794) and TCR engineered to specifically and optimally express NY-ESO-1 and HLA-A*02:06 have therefore been developed for the treatment of metastatic/unresectable synovial sarcoma (SS), which is a rare pediatric and adolescent solid tumor.

Study rationale

- SS is a heterogeneous disease, often with a high incidence of recurrent disease.
- NY-ESO-1+ SS is a rare pediatric and adolescent disease, and its treatment is challenging.
- This innovative Master Protocol study design permits evaluation of NY-ESO-1 T cells in various tumor types and settings, including:
  - NY-ESO-1+ metastatic SS
  - NY-ESO-1+ hematologic malignancies
  - NY-ESO-1+ solid tumors

Mechanism of action

NY-ESO-1 is expressed in various malignancies but is absent in healthy, normal, adult tissues, except for germ cells of the adult testis.

- Due to its expression in malignant tumors but not normal tissues, NY-ESO-1–specific T cells have the potential to be selectively cytotoxic to NY-ESO-1+ tumors.
- NY-ESO-1+ SS is one of the most immunogenic proteins identified in human cancer, based on its capacity to elicit strong immunity and GSK3377794–specific T cell responses in vivo.

Substudy design

- This master protocol (IGNYTE-ESO) has a Master Protocol design consisting of a core protocol and multiple substudies to investigate the efficacy of NY-ESO-1–specific T cells in various tumor types. The first 2 substudies are non-randomized, single-arm investigations of GSK3377794 in patients with metastatic SS.

- The protocol may be amended to include additional substudies to investigate other NY-ESO-1+ tumor types in HLA-A*02:01, HLA-A*02:05, and HLA-A*02.*

- The study is designed to evaluate the efficacy and safety of GSK3377794 in a variety of clinical settings, including:
  - NY-ESO-1+ hematologic malignancies
  - NY-ESO-1+ solid tumors

Summary

- GSK3377794 has shown encouraging clinical activity in earlier clinical trials.
- This innovative Master Protocol study design permits evaluation of NY-ESO-1–specific T cells in other NY-ESO-1+ tumor types in HLA-A*02+ patients, potentially expanding the indications for NY-ESO-1–specific T cells.

Ethics approval statement

This Master Protocol (IGNYTE-ESO) will be conducted under approval by the appropriate institutional review boards and independent ethics committees.