Clinical trial to evaluate safety and activity of autologous T cells with enhanced NY-ESO-1–specific T-cell receptor (GSK3377794) in HLA-A*02+ previously treated and previously untreated patients with advanced metastatic or unresectable synovial sarcoma as part of a master protocol design (IGNYTE-ESO)

Abstract number: 326481


Background

Response rates to anthracycline-based chemotherapy, a first-line treatment in advanced metastatic/unresectable synovial sarcoma (SS), are low (30%) and often not durable.

Study rationale

NY-ESO-1 is a member of the cytotoxic T-lymphocyte antigen family of tumor antigens detectable in many cancer types, including SS. NY-ESO-1-specific T cells are detectable in many cancer types, including SS.

Previously untreated patients who:

- NY-ESO-1+ (NCT03967223) was funded by GSK.

Previously treated patients who:

- Previous clinical studies using adoptively transferred T cells against NY-ESO-1 have reported clinical responses in 45%–60% of patients with HLA-A*02+ bearing NY-ESO-1+ SS.

Genetically engineered NY-ESO-1–specific T cells (NY-ESO-1+ T cells, GSK3377794) are autologous CARs and CAR-T cells transfected with a self-targeting bioluminescent vector to express an affinity-enhanced NY-ESO-1–specific TCR.

This innovative Master Protocol study design permits evaluation of NY-ESO-1–specific T cells in multiple tumor types, overall response rate is not fixed. The first 2 substudies are non-randomized, single-arm investigations of GSK3377794 in patients with metastatic SS.

Key inclusion criteria

- ≥18 years of age
- Measurable disease
- Positive for HLA-A*02:01, HLA-A*02:05, HLA-A*02:06
- Adequate organ function
- Tumor expression of NY-ESO-1
- Positive for HLA-A*02+ allele
- Low HLA-ABC expression
- NY-ESO-1+ metastatic or unresectable SS
- Adequate white blood cell and platelet counts
- Adequate liver function (ALT ≤ 2.5 upper limit of normal (ULN), AST ≤ 2.5 ULN)
- ECOG performance status 0–1

Key exclusion criteria

- Central nervous system metastases
- Clinically significant systemic disease
- Prior gene therapy with integrating vectors in NY-ESO-1–specific T cells
- Prior allogeneic hematopoietic stem-cell transplant
- Prior immunotherapies or small molecule inhibitors targeting NY-ESO-1

Primary endpoints

Substudy 1:
- Overall response rate per RECIST v1.1 assessed by investigators

Substudy 2:
- Overall response rate per RECIST v1.1 assessed by independent central review

Key secondary endpoints for Substudy 1 and Substudy 2:
- Time to and duration of response
- Disease control rate
- Progression-free survival
- Overall survival
- Adverse events, including serious adverse events
- Potential immune response to GSK3377794 studied over time

Key exploratory objectives for Substudy 1 and Substudy 2:
- Correlation of T-cell persistence with safety, clinical response and phenotype of infused T cells
- Relationship between antigen expression and treatment responses
- Relationship between antigen expression and CD8+ T-cell responses
- Relationship between antigen expression and circulating NY-ESO-1 antigen levels

Study design

This trial (IGNYTE-ESO; NCT03967223) has a Master Protocol design consisting of a core protocol (Study 208750) with the potential to be amended to include additional substudies to investigate other NY-ESO-1+ or LAGE-1+ positive tumor types and other NY-ESO-1–specific T cells, potentially in combination with other agents

Potential additional substudy

- NY-ESO-1–specific T cells in non-SS tumor types
- NY-ESO-1+ T cells in combination with other agents

NY-ESO-1+ is expressed in various malignancies, and is absent in healthy, normal, adult tissue, with the exception of germ cells of the adult testis. NY-ESO-1+ T cells have low HLA expression, and if high side effects would be expected to be limited when targeting NY-ESO-1.

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

Disclosures

- All authors participated in the design of this study.
- All authors had access to the data, analyzed the data, and wrote the manuscript.
- All authors have no personal, financial, or other conflicts of interest.
- All authors are employees of GSK; have nothing to disclose.
- YW, CS, WC, MC, CJC, GD, WR, PS, MB, SW, LW have personal, financial, or other conflicts of interest.

Ethics approval statement

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

References