IGNYTE-ESO: a master protocol to assess safety and activity of letetrutse autoleucel (lete-cell; GSK3377974) in HLA-A*02+ patients with squamous cell carcinoma (Substudies 1 and 2)

**Background**

There is an unmet need for effective therapies in many metastatic or advanced stage solid tumor types, including soft tissue sarcomas (STS) for which novel immunotherapies present a promising therapeutic option.

- Squamous cell carcinoma (SCS) and mesothelial sarcoma (MRLCS), both of which harbor chromosomal alterations, each represent an unmet need.
- Objective response rates to standard therapies among patients with metastatic, recurrent, or unresectable SCS and MRLCS are poor, particularly after failure of frontline chemotherapies.
- For second-line treatment, a recent multicenter study identified a 15% response rate among 24S patients with advanced SCS.
- Although response rates in individual studies can be high, data among a larger cohort (n=67) indicated 28% responses with pembrolizumab and second-line treatment in patients with advanced MRLCS.

**Objectives**

- Evaluate safety and antitumor activity of letetrutse autoleucel in advanced SCS or MRLCS.

**Study design**

**Ignyte-eso (NCT01670728)** is a master protocol that enables evaluation of multiple cell therapies in multiple tumor types and treatment regimens across separate substudies.

- **Substudy 1:** Previously untreated patients
- **Substudy 2:** Patients with disease progression following prior treatment with an anti-PD-1/anti-PD-L1 therapy.

The protocol may be amended in the future to add additional substudies for different patient populations or tumor types.

**Study objectives and endpoints**

Table 2 describes the endpoints for each substudy.

**Primary endpoint**

- **Substudy 1:** ORR by RECIST v1.1; primary endpoint: ORR using investigator-assessed PET/CT.
- **Substudy 2:** ORR per RECIST v1.1, assesses the goal of the trial.

**Secondary endpoints**

- **Substudy 1:** Safety, progression-free survival (PFS), and overall survival (OS).
- **Substudy 2:** OS, safety, and progression-free survival (PFS).

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