A Phase 1b/2a Randomized Pilot Study to Investigate the Safety and Tolerability of Autologous T Cells With Enhanced T-Cell Receptors Specific to NY-ESO-1/LAGE-1a (GSK3377794) Alone, or in Combination With Pembrolizumab, in Advanced Non-small Cell Lung Cancer

Objectives

The primary objective is to evaluate the safety and tolerability of GSK3377794 alone, or in combination with pembrolizumab, in patients with NY-ESO-1/LAGE-1a positive advanced NSCLC.

Methods

Study Design (Protocol Amendments)

This will be a Phase I/II randomized, multi-arm, open-label pilot study (NCT03709706) of GSK3377794 in combination with pembrolizumab. Patients will be randomized to one of three treatment arms:

- **Arm A**: pembrolizumab alone
- **Arm B**: pembrolizumab plus GSK3377794
- **Arm C**: pembrolizumab plus GSK3377794 followed by allogeneic hematopoietic stem cell transplantation (HSCT)

Eligibility Criteria

Inclusion Criteria:

- Patients with histologically or cytologically confirmed advanced or metastatic squamous cell or non-squamous (adenocarcinoma or large cell) NSCLC.
- Patients must have at least one NY-ESO-1/LAGE-1a positive measurable or evaluable lesion.
- Patients must have a NY-ESO-1/LAGE-1a positive pretreatment biopsy.
- Patients must have an Eastern Cooperative Oncology Group (ECOG) performance status of 0-1.
- Patients must have adequate organ function and normal bone marrow function.

Exclusion Criteria:

- Patients with active central nervous system metastases.
- Patients with prior treatment with any investigational agent or therapy for NSCLC.
- Patients with a history of another malignancy within the past 3 years.

Randomization or Assignment

Patients will be randomized to one of the three treatment arms: Arm A, Arm B, or Arm C. The randomization will be stratified by tumor type and EGFR status.

Study Treatment

- **Arm A**: pembrolizumab alone at a dose of 200 mg every 3 weeks until disease progression or unacceptable toxicity.
- **Arm B**: pembrolizumab plus GSK3377794 at a dose of 1 mg/kg every 3 weeks until disease progression or unacceptable toxicity.
- **Arm C**: pembrolizumab plus GSK3377794 at a dose of 1 mg/kg every 3 weeks until disease progression or unacceptable toxicity, followed by HSCT.

Supportive Care

- Patients in all arms will receive supportive care including antihistamines and acetaminophen.
- Patients in Arm C will receive HSCT at a dose of 2x10^6 CD34+ cells/kg on Day 30.

Live-virus vaccination

- Patients in all arms will receive live-virus vaccination 4 weeks after the first pembrolizumab dose.

Concurrent Anticancer Treatments

- Patients in all arms are not permitted to receive any other systemic treatments that are known to interact with pembrolizumab or GSK3377794.

Table 1: Concomitant Interventions and Concomitant Medications

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Table 2: Follow-up Intervals

- **Arm A**: every 6 weeks for 1 year, then every 12 weeks until disease progression or unacceptable toxicity.
- **Arm B**: every 6 weeks for 1 year, then every 12 weeks until disease progression or unacceptable toxicity.
- **Arm C**: every 6 weeks for 1 year, then every 12 weeks until disease progression or unacceptable toxicity.

Table 3: Follow-up Intervals and Concomitant Medications

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References


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