Safety, tolerability and activity 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: a Phase 1b/2a randomised pilot study

Poster number: 1590TP

## Background

### Unmet need

- An unmet need exists for patients with advanced NSCLC who have failed prior pembrolizumab monotherapy and checkpoint inhibitor therapy, as well as for patients who have failed tyrosine kinase inhibitors targeted at genetic alterations such as EGFR mutation and ALK/ROS1 rearrangements.
- Only 10–20% of these patients receive any benefit from current treatments,1,2 and novel therapies are needed to improve outcomes.

### Clinical rationale

- Adaptive cell therapy using autologous engineered TCR-T against NY-ESO-1 is a promising treatment for metastatic melanoma and solid tumours.
- Preclinical testing using autologous T cells directed against NY-ESO-1/LAGE1 have shown objective response rates of 40% and 60%, in syngeneic sarcoma, metastatic melanoma and renal cell carcinoma.
- Unlike CART-T agents that primarily target cell surface proteins and have demonstrated clinical activity in haematological malignancies, engineered T2-T can be directed to target intracellular antigens and hence ideal for solid tumours.

### Genetic rationale

- Genetically engineered NY-ESO-1/LAGE1a-specific T cells (GSK3377794) are autologous and ST-TRa kits introduced with a self-inactivating lentiviral vector to express an enhanced NY-ESO-1 and LAGE1-directed TCR-T receptor.
- Preclinical testing has shown that the NY-ESO-1/LAGE1a-directed TCR-T can target intracellular antigens and have demonstrated substantial activity in haematological malignancies.
- Most patients with NSCLC have NY-ESO-1+ tumours.

### Objectives

- The primary objectives are to determine the clinical response to GSK3377794 alone or in combination with pembrolizumab, and assess the safety and tolerability of these regimens.
- The secondary objectives are to evaluate the duration of anti-tumour activity of GSK3377794 and to describe the pharmacokinetics of GSK3377794 over time.

## Study design (protocol amendment 2)

### Key inclusion:

- Advanced (IIIB/IV) NSCLC patients who are either:
  - Have received PD-1/PD-L1 therapy or are ineligible for SOC chemoradiotherapy, or
  - Have refused SOC
- Have terminated prior treatment due to disease progression per iRECIST criteria.

### Main inclusion criteria:

- Age ≥18 years
- Eastern Cooperative Oncology Group (ECOG) performance status of 0, 1
- Adequate organ function

### Main exclusion criteria:

- BRAF/any other actionable genetic alteration that can be treated with targeted SOC (GSK recommends),
- Other EGFR mutations or ALK/ROS1 translocations.

## Study design (protocol amendment 2)

### Treatment Arm A or B

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<thead>
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<th>Arm</th>
<th>Therapy</th>
<th>Key inclusion:</th>
</tr>
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<tr>
<td>A</td>
<td>GSK3377794 + pembrolizumab (Day 1)</td>
<td>Advanced (IIIB/IV) NSCLC patients who are either: have received PD-1/PD-L1 therapy or are ineligible for SOC chemoradiotherapy, or have refused SOC</td>
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### Treatment Arm C

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## Endpoints and Assessments

### Treatment pathway

1. Eligibility screening
2. Leukapheresis
3. Lymphodepletion
4. G-CSF
5. Day 0: pembrolizumab (single IV infusion) and GSK3377794 (single IV infusion)
6. Day 22: pembrolizumab (single IV infusion) and GSK3377794 (single IV infusion)
7. G-CSF

### Secondary objectives

- Frequency and severity of AEs
- Maximum tolerated dose and target of therapy.
- Duration of response.
- Best response
- Progression-free survival (PFS)
- Overall survival (OS)
- Objective response rate (ORR)
- Safety and tolerability
- Determination of PK/PD relationship
- Exploration of PK/PD relationship
- Quality of life

### Safety

- Safety will be continually assessed including: toxicity, frequency of AEs, quality of life.

## Statistical analysis

- All safety analyses will be performed in the ITT population.

## Acknowledgments

- The study is in a Rwanda-Decision framework for evaluating activity at interim and final analysis; this allows any arm to be halted due to futility at interim time points.

## References