Case studies of synovial sarcoma and MRCLS following treatment with NY-ESO-1 TCR T cells (GSK3377794): correlates of predictable response characteristics

### Introduction
- Genetically engineered NY-ESO-1-specific T cells (NY-ESO-1 T cells; GSK3377794) were autologous CD8+ and CD4+ T cells transduced with a self-modulating immobilized receptor vector and evaluated in two ongoing Phase I/II trials.

### Methods
- Patients with SS or MRCLS who were progression free were selected.
- We reviewed the biomarker data of eight patients from two ongoing Phase I/II pilot studies (five patients with SS and three patients with MRCLS) to evaluate the durability of response and potential biomarkers for response prediction.

### Results
- **Patient Characteristics**
  - Following the first infusion, five of seven patients with SS had stable disease and two had partial responses.
  - The duration of stable disease ranged from 25.3 to 47.3 weeks in the five patients with SS who had stable disease (Figure 1).
  - The duration of response for two patients with SS was 14.3 and 93.6 weeks, respectively.

- **Transduced CD8+ T cells**
  - In two patients (Patients 2 and 6), transduced CD8+ cells primarily had a TEMRA (25%) phenotype.
  - The remainder more evenly distributed over TEMRA (25%), TEM, and TCM.

- **Transduced CD4+ T cells**
  - In four patients with SS (Patients 1, 3, 4, and 8), 20% to 30% at 3+ and 20% at 1+ transduced CD4+ T cells were observed.

### Conclusions
- SS and MRCLS tumors showed an immunoablation reaction in the first 3 to 6 months of treatment followed by NY-ESO-1 T cell recognition and persistence for at least 9 to 12 months.

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### Table: Frequency and Percentage of T-cell Phenotypes

<table>
<thead>
<tr>
<th>Patient</th>
<th>CD8+ T Cell Phenotype</th>
<th>CD4+ T Cell Phenotype</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 1</td>
<td>TEMRA: 25%</td>
<td>TEMRA: 20%</td>
</tr>
<tr>
<td>Patient 2</td>
<td>TEMRA: 25%</td>
<td>TEMRA: 20%</td>
</tr>
<tr>
<td>Patient 3</td>
<td>TEMRA: 25%</td>
<td>TEMRA: 20%</td>
</tr>
<tr>
<td>Patient 4</td>
<td>TEMRA: 25%</td>
<td>TEMRA: 20%</td>
</tr>
<tr>
<td>Patient 5</td>
<td>TEMRA: 25%</td>
<td>TEMRA: 20%</td>
</tr>
<tr>
<td>Patient 6</td>
<td>TEMRA: 25%</td>
<td>TEMRA: 20%</td>
</tr>
<tr>
<td>Patient 7</td>
<td>TEMRA: 25%</td>
<td>TEMRA: 20%</td>
</tr>
</tbody>
</table>

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**Figure 1: Cytokine fold changes in a patient with SS who received 2 infusions (left) and a patient with MRCLS who received a single infusion of GSK3377794 (right)**

**Figure 2: T-cell phenotypes of transduced CD8+ pentamer+ cells, as determined by flow cytometry**

**Figure 3: Peak persistence in Patients 2 (left), 6 (middle), and 7 (right)**

**Figure 4: Tumor persistence in Patients (left) who had a complete response and (right) who had a partial response**

**Figure 5: T-cell phenotypes of transduced CD8+ pentamer+ cells, as determined by flow cytometry**

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**References**
- Cancer 2009; 118(18): 4564–70.
- Rare Tumours; 2018; 11(3): 198.
- GSK. 2019. GSK3377794: NY-ESO-1 T Cell for Synovial Sarcoma and MRCLS. Available from: [GSK website].

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