Phase I trial of NY-ESO-1-specific adoptive T-cell therapy with GSK3377794 in patients with advanced synovial sarcoma: report of Cohorts 2 and 4

Abstract A256364

Background

Adoptive T-cell receptor (TCR) therapy is a promising treatment for recurrent or metastatic solid and hematologic malignancies with encouraging activity demonstrated in patients with synovial sarcoma, metastasis, and multiple myeloma.

New York synovial antigen-1 (NY-ESO-1)-specific TCRs. A member of the cancer-testis family of tumor antigens that generates a GSK3377794-specific TCR was generated.

GSK3377794 is a fully human, IgG1 monoclonal antibody that recognizes the GSK3377794 antigen.

Further details regarding the phase I trial are provided elsewhere.

Methods

Key eligibility criteria

- Age: up to 70 years old
- Histologically confirmed, metastatic, progressive, persistent, or recurrent disease
- At least one prior systemic therapy regimen
- At least one measurable lesion
- No prior treatment with checkpoint inhibitors or CAR T-cells
- Adequate organ function
- Enrolled in the phase I trial through institutional review board approval
- Written informed consent

Patients who met the criteria were enrolled in one of four cohorts based on NY-ESO-1 expression by IHC (Table 2). Patients were assessed for clinical benefit at 2-month intervals and efficacy assessment was done at the 2-month assessment and every 3 months thereafter.

Objectives

- To report efficacy and safety parameters of GSK3377794 in Cohorts 2 and 4 patients with NY-ESO-1 expression who received high-dose lymphodepletion and Cohort 4 patients with NY-ESO-1 expression who received low-dose lymphodepletion of the Phase I study and evaluate the feasibility of these two approaches.

Results

- As of April 2019, 62 patients were enrolled in the study, of whom 16 patients enrolled in Cohorts 2 and 4, respectively.
- 13 patients in Cohorts 2 and 15 patients in Cohort 4 received GSK3377794 injection and were enrolled in the study.
- The median time to study in Cohort 2 was 107 days (range, 5–242 days) for patients in Cohort 2 and 202 days (range, 70–595) for patients in Cohort 4.
- All patients were eligible for NY-ESO-1 positive and 2 patients were NY-ESO-1 negative.
- Median treatment duration was 70.4 days for patients in Cohort 2 and 202 days for patients in Cohort 4.
- All patients in Cohort 2 and 4 received a second administration.

GSK3377794 immunogenicity

- Persistence of GSK3377794 was measured in serial serum samples from NY-ESO-1 positive patients who received high-dose lymphodepletion and Cohort 4 patients who received low-dose lymphodepletion of the Phase I study and evaluated the feasibility of these two approaches.

Safety

- Treatment-related adverse events (TRAEs) that occurred in ≥10% of patients across all cohorts (n = 46) were: fatigue (n = 13, 28%), neutrophilic leukocytosis (n = 12, 26%), and neutropenia (n = 10, 21%).
- No patients in Cohort 2 and 4 had grade 3 or higher neutropenia.

Efficacy

- Objective response rates were 1 (7.7%) in Cohort 2 and 1 (6.7%) in Cohort 4.
- Complete response was observed in 1 (7.7%) patient in Cohort 2 and 1 (6.7%) patient in Cohort 4.
- Safety was monitored throughout and evaluated using Common Terminology Criteria for Adverse Events v6.0.

Conclusions

- The Phase I trial met the primary objective and was used to describe patient demographics and clinical characteristics.
- Safety and efficacy were evaluated in all patients who received at least one dose of study drug (ITT / treated population).
- All efficacy parameters are summarized based on first-line.
- The study was not designed to show clinical benefit.
- The data cut-off for the current analysis was March 4, 2019, except for OS data, which was January 8, 2019, last follow-up.

Figure 2. Study design

Figure 3. Median/maximum in each of the dimensions of target lesions based on baseline / treatment response (A) and overall response (B) and prior treatments (C) and untreated (D) patients in Cohort 2 and 4.

Figure 4. (A) GSK3377794 peak antigen and (B) NY-ESO-1-bound GSK3377794 levels in serum samples (including complete and partial response).

Figure 5. Outcomes of CR in Cohorts 2 and 4 in both the "treated" and "untreated" populations

Table 1: Patient demographics and baseline characteristics (ITT population)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Cohort 2</th>
<th>Cohort 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age, years (range)</td>
<td>60 (16–70)</td>
<td>59 (20–75)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>9 (60)</td>
<td>10 (67)</td>
</tr>
<tr>
<td>Open-label</td>
<td>3 (20)</td>
<td>2 (13)</td>
</tr>
</tbody>
</table>

Table 2: Summary of response in patients assessed by investigator (ITT population)

<table>
<thead>
<tr>
<th>Response</th>
<th>Cohort 2</th>
<th>Cohort 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete response</td>
<td>1 (7.7%)</td>
<td>1 (6.7%)</td>
</tr>
<tr>
<td>Partial response</td>
<td>1 (7.7%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Stable disease</td>
<td>10 (63)</td>
<td>18 (121)</td>
</tr>
<tr>
<td>Progression</td>
<td>2 (13)</td>
<td>1 (7)</td>
</tr>
</tbody>
</table>

Table 3: Summary of benefit assessment in patients treated with GSK3377794 (ITT population)

<table>
<thead>
<tr>
<th>Benefit Assessment</th>
<th>Cohort 2</th>
<th>Cohort 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Objective response</td>
<td>2 (13)</td>
<td>2 (13)</td>
</tr>
<tr>
<td>Clinical benefit</td>
<td>1 (13)</td>
<td>0 (0.0%)</td>
</tr>
</tbody>
</table>