Long-term efficacy and safety of lifileucel tumor-infiltrating lymphocyte (TIL) cell therapy in patients with advanced melanoma: A 4-year analysis of the C-144-01 study


Background
- Includes checkpoint inhibitors (CPI) have improved outcomes for patients with metastatic melanoma – Nevertheless, responses are in context and subsequent treatment options are limited
- Autologous tumor-infiltrating lymphocyte (TIL) cell therapy recognizes and targets a multitude of patientspecific neoantigens in metastatic cancer cells

C-144-01 (NCT02290183) is a phase 2, multicenter, multicenter study of lifileucel autologous TIL cell therapy in patients with unrefractory metastatic or unresectable melanoma who progressed on or after anti–PD-1/PD-L1 therapy (Figure 1).

Objective
- The study was not designed to update on durable responses from C-144-01, as long as the longest follow-up of the population of patients with anti–PD-1/PD-L1 advanced melanomas treated with TIL therapy is reached.
- We report independent review committee (IRC)-assessed response data, investigator-assessed data and updated long-term survival data.

Methods

Key Evaluation
- Primary: Objective response rate (ORR) (IRC)-assessed using Response Evaluation Criteria in Solid Tumors (RECIST) 1.1
- Secondary: Duration of response (DOR), progression-free survival (PFS), safety assessments

Key Eligibility Criteria
- Documented metastatic disease progression
- In tumor lesion resolvable for TIL generation (≥1.5 cm in diameter) and ≥1 target tumor lesion for therapy in patients with unresectable metastatic or unresectable melanoma who progressed on or after anti–PD-1/PD-L1 therapy (Figure 1).

Eligibility, TIL manufacturing process, and monitored were identical for Cohorts 2 and 4

Results
- As of the data cut-off date (June 30, 2020), median follow-up was 46.9 months
- 153 patients were included in the Full Analysis Set
- Among the 153 patients, 23 (15.0%) patients were ongoing in study follow-up, and 7 (4.6%) patients completed the study with 5-year follow-up
- Overall, all patients had either tumor lesions as measured by lower tumor lesions, lower DLBCL, and lower liver and/or brain metastases relative to the total population (Table 1).
- Median duration of disease-free survival was consistent between all responders and responders with DOR ≥3 months (Table 1).
- IRC-assessed ORR was 21.4% (n=14) (Figure 2).
- The median duration of DOR was not reached (NR) (Figure 3).
- Median time to best response was ongoing at 55.8 months (Figure 4).
- Patient responses to lifileucel treatment deepened over time (Figure 4).
- The median OS was not reached (NR) (Figure 5).
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Table 1: Baseline Patient and Disease Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Responders with DOR ≥3 months (n=26)</th>
<th>Responders with DOR &gt;6 months (n=10)</th>
<th>Responders with DOR ≥12 months (n=6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age, years</td>
<td>61 (37, 77)</td>
<td>58 (26, 77)</td>
<td>56 (30, 78)</td>
</tr>
<tr>
<td>Follow-up time, months</td>
<td>24 (18, 28)</td>
<td>36 (24, 51)</td>
<td>48 (42, 58)</td>
</tr>
<tr>
<td>Overall survival (%), 95% CI</td>
<td>79.3% (111/140)</td>
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Conclusions
- This is the largest analysis representing the longest follow-up to date of patients treated with lifileucel TIL cell therapy in the post–PD-1/PD-L1 setting for advanced melanoma
- In patients with advanced melanoma who progressed on or after anti–PD-1/PD-L1 therapy and targeted therapy (carboplatin, gemcitabine, nivolumab), one-time lifileucel TIL cell therapy demonstrated durable efficacy and a long-term survival benefit compared with the 19.5% standard-of-care 12-month progression-free survival rate reported by the CheckMate 030 trial (26% vs 19.5% at 12 months and 36% vs 25% at 24 months).