Long-term follow-up after adoptive transfer of CD19-specific CAR T cells genetically modified via non-viral Sleeping Beauty system following hematopoietic stem-cell transplantation (HSCT)


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**Background**

- Current gene transfer – Sleeping Beauty (SB) transposon/transposase system – used to stably express a CD19-specific chimeric antigen receptor (CAR), designated CD19C18D20, that signals via chimeric CD19 and CD20.
- CD19 and CD20 are cell-surface glycoproteins and are involved in the activation, proliferation, and survival of B cells.
- CD19 is specifically expressed on B cells, follicular dendritic cells, and other B-cell malignancies; CD20 is involved in the function of normal and neoplastic lymphoid cells.
- CD19 and CD20 do not possess endodomains.
- Sleeping Beauty (SB) transposase, a bacterial enzyme, has been engineered with C18 and D20 endodomains.

**Study Design**

- Study: Twenty patients with advanced non-Hodgkin lymphoma (NHL) or acute lymphoblastic leukemia (ALL) genetic modified to co-express CAR and SB transposase using SB-1 or SB-10 (SB-10) and autologous hematopoietic stem cell transplantation (HSCT) with CD19-specific SB CAR-self-inactivating lentiviral vector

**Patient Summary**

- **CD19-specific CAR structure and patient dose levels**
- **Patient Summary**
- **Overall Survival (OS) and Progression-Free Survival (PFS)**

**Disclosures**


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**Figure 1: Implementing Sleeping Beauty-Modified Cells, a Non-Viral Approach**

- **1st generation SB complete: CAR T cells**
  - Patients in remission show long-term T cell persistence
- **2nd generation SB ongoing: CAR T cells**
  - Safety, feasibility & efficacy of SB system
- **3rd generation planned 2018: CAR miRNA switch T cells**
  - Very rapid (<2 days) manufacture without need for feeder cells, administer fresh T cells

**Table 1: T-cell dose levels (No. Autologous pts/No. Haploidentical pts)**

<table>
<thead>
<tr>
<th>T-cell Dose Level</th>
<th>No. Autologous pts (Haploidentical subset)</th>
<th>No. Autologous pts dosed</th>
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</thead>
<tbody>
<tr>
<td>10^7/kg</td>
<td>3 (2)</td>
<td></td>
</tr>
<tr>
<td>10^8/kg</td>
<td>6 (3)</td>
<td></td>
</tr>
<tr>
<td>10^9/kg</td>
<td>5 (1)</td>
<td></td>
</tr>
<tr>
<td>10^10/kg</td>
<td>3 (2)</td>
<td></td>
</tr>
<tr>
<td>10^11/kg</td>
<td>1</td>
<td></td>
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</tbody>
</table>

**Table 2: Patient summary characteristics for patients dosed with CD19C18D20 and CD19C20D18**

- **Hematology**
- **Histology**
- **Age (years):**
- **Sex:**
- **Proliferation Rates of AK:**

<table>
<thead>
<tr>
<th>HCT</th>
<th>N</th>
<th>Histology</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Proliferation Rates of AK</th>
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</thead>
<tbody>
<tr>
<td>Autologous</td>
<td>7</td>
<td>ALL</td>
<td>18</td>
<td>50</td>
<td>63</td>
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<tr>
<td>All</td>
<td>19</td>
<td>ALL</td>
<td>17</td>
<td>31</td>
<td>21</td>
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<tr>
<td>Haploidentical subset</td>
<td>8</td>
<td>ALL</td>
<td>7</td>
<td>34</td>
<td>21</td>
</tr>
</tbody>
</table>

**References**


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**Figure 2: Probability of Survival**

- **Probability of Survival**
- **Survival Time Since Infusion (Months)**
- **Survival for recipients of autologous CAR T cells**
- **Survival for recipients of allogeneic CAR T cells**

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**Summary and Conclusions**

- **Progression-free and overall survival of patients receiving CD19-specific CAR T cells following autologous and allogeneic HCT continue to show significant benefits over historical controls of HCT recipients.
- **CAR T cells are detected by ddPCR and flow cytometry as long as 6 months after infusion in autologous HCT recipients and 2 years after allogeneic HCT recipients.
- **Persistence of T cells is noted, even in such patients who have reconstituted their T-cell compartment.
- **Further follow-up will evaluate continued persistence of CAR T cells and B cells.
- Patients can remain in CR for 5 years after recovery of normal B-cell counts.
- **Approximately 46% of cumulative follow-up in surviving recipients support the safety of infusing CAR T cells modified with the SB system.
- **SB-modified CAR T cells demonstrated to be safe, further supporting non-viral gene transfer in future clinical studies, including the 2018 planned 2nd generation panel of CARs to very rapidly manufacture (<2 days) CD19-specific T-Cells.