## Overview of Trials

<table>
<thead>
<tr>
<th>Protocol number/title</th>
<th>FHCRC 1503 – “1&lt;sup&gt;st&lt;/sup&gt; generation” anti-CD20 CAR</th>
<th>FHCRC 2154 – “3&lt;sup&gt;rd&lt;/sup&gt; generation” anti-CD20 CAR</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Disease indication/Research Participant population</strong></td>
<td>Relapsed/refractory indolent CD20+ lymphoma and mantle cell lymphoma</td>
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</tbody>
</table>
| **TCR or CAR product (ex vivo cell/ vector/transgene) and Dose** | • αCD20-ζ  
  • Naked DNA plasmid (electroporation with G418 selection)  
  • 3 infusions 2-5 days apart at 10<sup>8</sup>, 10<sup>9</sup>, and 3.3 x 10<sup>9</sup> cells/m<sup>2</sup>  
  • Low-dose IL-2 | • αCD20-CD28-41BB-ζ  
  • Naked DNA plasmid (electroporation with G418 selection)  
  • 3 infusions 2-5 days apart at 10<sup>8</sup>, 10<sup>9</sup>, and 3.3 x 10<sup>9</sup> cells/m<sup>2</sup>  
  • 1 g/m<sup>2</sup> CY + low-dose IL-2 |
| **Trial initiation date/status /enrollment** | Study closed in 2008  
Accrued 10 patients, treated 7 | Study closed in 2012  
Accrued 4 patients, treated 3 |
## Clinical Responses

<table>
<thead>
<tr>
<th>Patient</th>
<th>Response</th>
<th>Duration (mo.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>NED</td>
<td>13</td>
</tr>
<tr>
<td>B</td>
<td>SD</td>
<td>3</td>
</tr>
<tr>
<td>D</td>
<td>SD</td>
<td>12</td>
</tr>
<tr>
<td>F</td>
<td>NED</td>
<td>3</td>
</tr>
<tr>
<td>G</td>
<td>SD (PET)</td>
<td>5</td>
</tr>
<tr>
<td>H</td>
<td>PR</td>
<td>3</td>
</tr>
<tr>
<td>I</td>
<td>SD</td>
<td>48</td>
</tr>
</tbody>
</table>
Summary of Trial #1

- No T cell-related AEs
- Bulk cultures more efficient than cloning
- *In vivo* persistence was modest but better with bulk culture cells + IL-2 (9 weeks)
- Modest clinical responses
- No cellular immune responses (but 2 pts HAMA+)
## Clinical Responses

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<thead>
<tr>
<th>Patient</th>
<th>Response</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>UPN-02</td>
<td>NED</td>
<td>2 years</td>
</tr>
<tr>
<td>UPN-03</td>
<td>NED</td>
<td>1 year</td>
</tr>
<tr>
<td>UPN-04</td>
<td>PR</td>
<td>1 year</td>
</tr>
</tbody>
</table>
Partial Response (UPN-04)

Cumulative Tumor Area

Baseline 3 months

SPD (cm²)

0 10 20 30 40

0 5 10 15 20

Partial remission (50% reduction)

Months after T cell infusions
Summary of Trial #2

1) 3 of 4 patients treated, generally tolerated well
2) Fever and hypoxemia after infusions in 1 pt
3) 1 partial remission, 2 pts NED for 1-2 years
4) T cells tracked to LN/BM, persisted 9-12 mo
5) CY 1 g/m² led to lymphodepletion
6) IL-2 led to increased Tregs
7) No evidence of immunogenicity
Lessons Learned

- Linearized plasmid vector was inefficient
- Only 1 of 10 pts with AEs: immediate and transient
- Longer *in vivo* persistence with IL-2 but increased Tregs
- T cells detectable to 1 year with 3rd generation CAR
- Intermediate dose CY well tolerated, led to effective lymphodepletion
Planned Trial

- Lentiviral vector encoding iCasp9 + αCD20-28-41BB-ζ CAR + truncated hCD19
- Use central memory T cells (CD14-/CD45RA-/CD62L+)
- Intermediate-dose CY (1 g/m²)
- Single T cell infusion in 4-pt dose-escalation cohorts
  - $2 \times 10^5$, $2 \times 10^6$, $2 \times 10^7$ CAR+ cells/kg
- 12 patients with relapsed/refractory indolent CD20+ indolent NHL or mantle cell lymphoma