### Protocol number/title
04409
**PILOT STUDY OF REDIRECTED AUTOLOGOUS T CELLS ENGINEERED TO CONTAIN ANTI-CD19 ATTACHED TO TCRζ AND 4-1BB OR CD28 SIGNALING DOMAINS IN PATIENTS WITH CHEMOTHERAPY RESISTANT OR REFRACTORY CD19+ LEUKEMIA AND LYMPHOMA**

### Disease indication/Research Participant population
- r/r CLL

### TCR or CAR product (ex vivo cell/ vector/transgene) and Dose
- **CART19**
  - Split infusion schedule
  - Day 0, 10%
  - Day 1, 30%
  - Day 2, 60%
- **CD19 scFv**
- **4-1BB:zeta signaling domains**
- **Lentiviral vector**
- Median cell dose: \(1.6 \times 10^8\)

### Trial initiation date/status /enrollment
- July, 2010
- 14 CLL patients infused and evaluable
| Protocol number/title | 03712  
Dose optimization trial of autologous T Cells engineered to express anti-CD19 chimeric antigen receptor (CART-19) in patients with relapsed or refractory CD19+ chronic lymphocytic leukemia | Phase II CLL dose optimization study NCT01747486 |
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease indication/Research Participant population</td>
<td>r/r CLL</td>
<td>Two arm trial. Randomization between 5 x 10^8 and 5 x 10^9 cells</td>
</tr>
</tbody>
</table>
| TCR or CAR product (ex vivo cell/ vector/transgene) and Dose | CART19  
Infusion schedule  
Day 0, 100%                                                                 | CD19 scFv  
4-1BB;ζeta signaling domains  
Lentiviral vector |
| Trial initiation date/status /enrollment | December, 2012                                                                                   | 31 patients enrolled  
14 patients infused |
# Overview of Trials - III

<table>
<thead>
<tr>
<th>Protocol number/title</th>
<th>CHP959 PILOT STUDY OF REDIRECTED AUTOLOGOUS T CELLS ENGINEERED TO CONTAIN ANTI-CD19 ATTACHED TO TCRζ AND 4-1BB OR CD28 SIGNALING DOMAINS IN PATIENTS WITH CHEMOTHERAPY RESISTANT OR REFRACTORY CD19+ LEUKEMIA AND LYMPHOMA</th>
<th>Phase 1 NCT01626495</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease indication/Research Participant population</td>
<td>r/r pre-B cell ALL</td>
<td>Pediatric patients aged 1-24 years with CD19+ B cell malignancies with no available curative treatment options</td>
</tr>
<tr>
<td>TCR or CAR product (ex vivo cell/ vector/transgene) and Dose</td>
<td>CART19 Split dose infusion: Day 0, 10% Later amedned to: Day 0, 10% Day 1, 30%</td>
<td>CD19 scFv 4-1BB:zeta signaling domains Lentiviral vector Median CART19 dose: 3.6 x10^6/kg</td>
</tr>
<tr>
<td>Trial initiation date/status /enrollment</td>
<td>April, 2012</td>
<td>25 patients enrolled 17 patients infused, 16 evaluable</td>
</tr>
</tbody>
</table>
# Overview of Trials - IV

| Protocol number/title | 04409  
PILOT STUDY OF REDIRECTED AUTOLOGOUS T CELLS ENGINEERED TO CONTAIN ANTI-CD19 ATTACHED TO TCRζ AND 4-1BB OR CD28 SIGNALING DOMAINS IN PATIENTS WITH CHEMOTHERAPY RESISTANT OR REFRACTORY CD19+ LEUKEMIA AND LYMPHOMA | Phase 1  
NCT01029366  
Cohort 2: Adult ALL |
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease indication/Research Participant population</td>
<td>r/r ALL</td>
<td>CD19+ B cell malignancies with no available curative treatment options (such as autologous or allogeneic stem cell transplantation) who have limited prognosis (several months to &lt;2 year survival) with currently available therapies.</td>
</tr>
</tbody>
</table>
| TCR or CAR product (ex vivo cell/ vector/transgene) and Dose | CART19  
Split infusion schedule  
Day 0, 10%  
Day 1, 30%  
Day 2, 60% | CD19 scFv  
4-1BB:zeta signaling domains  
Lentiviral vector |
| Trial initiation date/status /enrollment | January, 2013 | 9 ALL patients enrolled  
5 patients infused and evaluable |
| Protocol number/title | 17510
PHASE I CLINICAL TRIAL OF AUTOLOGOUS MESOTHELIN RE-DIRECTED T CELLS ADMINISTERED INTRAVENOUSLY IN PATIENTS WITH MALIGNANT PLEURAL MESOTHELIOMA | Phase 1
NCT01355965 |
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease indication/Research Participant population</td>
<td>Malignant Pleural Mesothelioma</td>
<td>Subjects must have completed standard first line therapy with a platinum-based double regimen and had PD or they must have chosen not to pursue primary standard of care therapy.</td>
</tr>
</tbody>
</table>
| TCR or CAR product (ex vivo cell/ vector/transgene) and Dose | CARTmeso
Schedules tested:
Infusions 1x per week
Infusions 3x per week | SS1 scFv
4-1BB:zeta signaling domains
mRNA electroporation
Doses tested at 1x10^7 to 1x10^9 cells |
| Trial initiation date/status/enrollment | May, 2012 | 7 patients enrolled
4 patients infused and evaluable |
Lessons Learned

- Have treated 49 adult and pediatric B cell malignancy patients to date: potent responses observed in all age groups
- CLL: ~50% overall response rate in patients with bulky relapsed and refractory disease. Patients who achieve CR have not relapsed. Longest duration of response is > 3 years.
- ALL: >80% complete remission rate in pediatric (13 of 16) and adult (4 of 4) patients.
- CART19 cells traffic to CSF in pediatric ALL
- On target cytokine release syndrome and macrophage activation syndrome in responding patients
- Infusions of mRNA electroporated, mesothelin-redirected CARTmeso T cells are safe to date