

T Cell Immunotherapy- Optimizing Trial Design

Session I

Current Status of Cancer Immunotherapy: Trials, Results, and Challenges



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 NOVARTIS

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National Institutes of Health



Overview of Trials - I

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
Disease indication/Research Participant population	r/r CLL	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 <2 year survival) with currently available therapies.
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: 1.6×10^8
Trial initiation date/status /enrollment	July, 2010	14 CLL patients infused and evaluable

Overview of Trials - II

Protocol number/title	<p>03712 Dose optimization trial of autologous T Cells engineered to express anti-CD19 chimeric antigen receptor (CAR-T19) in patients with relapsed or refractory CD19+ chronic lymphocytic leukemia</p>	<p>Phase II CLL dose optimization study NCT01747486</p>
Disease indication/Research Participant population	<p>r/r CLL</p>	<p>Two arm trial. Randomization between 5×10^8 and 5×10^9 cells</p>
TCR or CAR product (ex vivo cell/ vector/transgene) and Dose	<p>CART19 Infusion schedule Day 0, 100%</p>	<p>CD19 scFv 4-1BB:zeta signaling domains Lentiviral vector</p>
Trial initiation date/status /enrollment	<p>December, 2012</p>	<p>31 patients enrolled 14 patients infused</p>

Overview of Trials - III

Protocol number/title	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	Phase 1 NCT01626495
Disease indication/Research Participant population	r/r pre-B cell ALL	Pediatric patients aged 1-24 years with CD19+ B cell malignancies with no available curative treatment options
TCR or CAR product (ex vivo cell/ vector/transgene) and Dose	CART19 Split dose infusion: Day 0, 10% Later amended to: Day 0, 10% Day 1, 30%	CD19 scFv 4-1BB:zeta signaling domains Lentiviral vector Median CART19 dose: 3.6 x10 ⁶ /kg
Trial initiation date/status /enrollment	April, 2012	25 patients enrolled 17 patients infused, 16 evaluable

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
Disease indication/Research Participant population	r/r ALL	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 <2 year survival) with currently available therapies.
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

Overview of Trials - V

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
Disease indication/Research Participant population	Malignant Pleural Mesothelioma	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.
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 1×10^7 to 1×10^9 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**