

T Cell Immunotherapy- Optimizing Trial Design

Session I

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

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Overview of Trials

Protocol number/title	PROTOCOL # 969: Administration of HER2 Chimeric Antigen Receptor Expressing T Cells for Subjects with Advanced Sarcoma
Disease indication/Research Participant population	Recurrent/refractory patients with HER2+ sarcomas
TCR or CAR product (ex vivo cell/vector/transgene) and Dose	HER2 (FRP5scFv).CD28.ζ CAR Retrovirus; CD3/CD28-act T cells $1 \times 10^4 - 10^8/m^2$
Trial initiation date/status/enrollment	8/2010 – 3/2013 19 Patients infused Met accrual

Overview of Trials (continued)

Protocol number/title	PROTOCOL # 970: Administration of HER2 Chimeric Antigen Receptor Expressing CMV-Specific Cytotoxic T Cells in Patients with GBM
Disease indication/Research Participant population	Recurrent/refractory patients with HER2+ GBM
TCR or CAR product (ex vivo cell/vector/transgene) and Dose	HER2 (FRP5scFv).CD28.ζ CAR Retrovirus; CMV-specific T cells $1 \times 10^6 - 10^8/m^2$
Trial initiation date/status/enrollment	7/2011 – present 14 Patients infused

Overview of Trials (continued)

Protocol number/title	PROTOCOL # 971: Administration of HER2 Chimeric Receptor and TGFβ Dominant Negative Receptor (DNR) Expressing EBV Specific Lymphocytes for Subjects with Advanced HER2+ Cancer
Disease indication/Research Participant population	Recurrent/refractory patients with HER2+ Cancer
TCR or CAR product (ex vivo cell/vector/transgene) and Dose	HER2 (FRP5scFv).CD28. ζ CAR DNR TGF β receptor Retrovirus; EBV-specific T cells $1 \times 10^4 - 10^8/m^2$
Trial initiation date/status/enrollment	8/2010 – present 5 Patients infused

Lessons Learned

- **Infusion of up to $1 \times 10^8 / m^2$ HER2-CAR T cells**
 - Safe, no dose limiting toxicity
- **CAR T cells**
 - No significant expansion
 - Detectable for 6 weeks to 3 months
 - Home to tumor sites (*including CNS*)
- **Plasma cytokines**
 - Transient increase in IL8

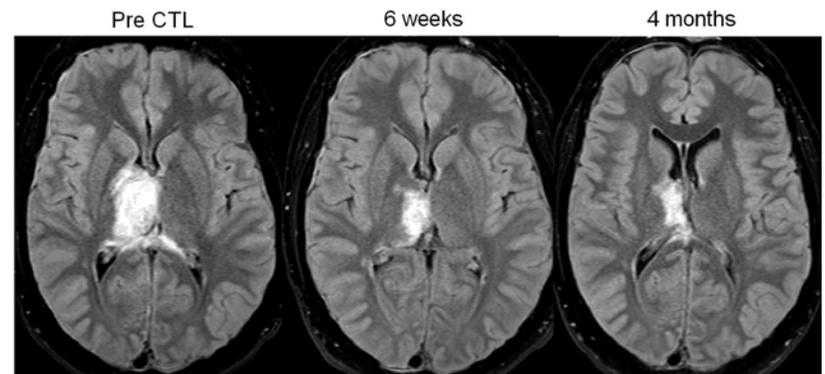
Lessons Learned

- **Clinical Outcome: *Sarcoma***

- 5 stable disease (6 weeks to 14 months)
 - 1 patient: tumor resected (>90% necrosis)
- 14 progressive disease
- Median OS: ~10 months

- **Clinical Outcome: *GBM***

- 1 partial response
- 4 stable disease
 - 6 wks (ongoing), 2 mths, 4 ½ mths, 6 mths (ongoing)
- 8 patients progressive disease



Lessons Learned

- **Clinical Outcome: *Lung cancer and other solid tumors***
 - 3 stable disease (12 wks, 12wks, 15 mths)
 - 1 progressive disease
- **Future**
 - Lymphodepletion
 - Improve CAR