

T Cell Immunotherapy- Optimizing Trial Design

Session I

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

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Overview of TCR Trials Sponsored by Adaptimmune

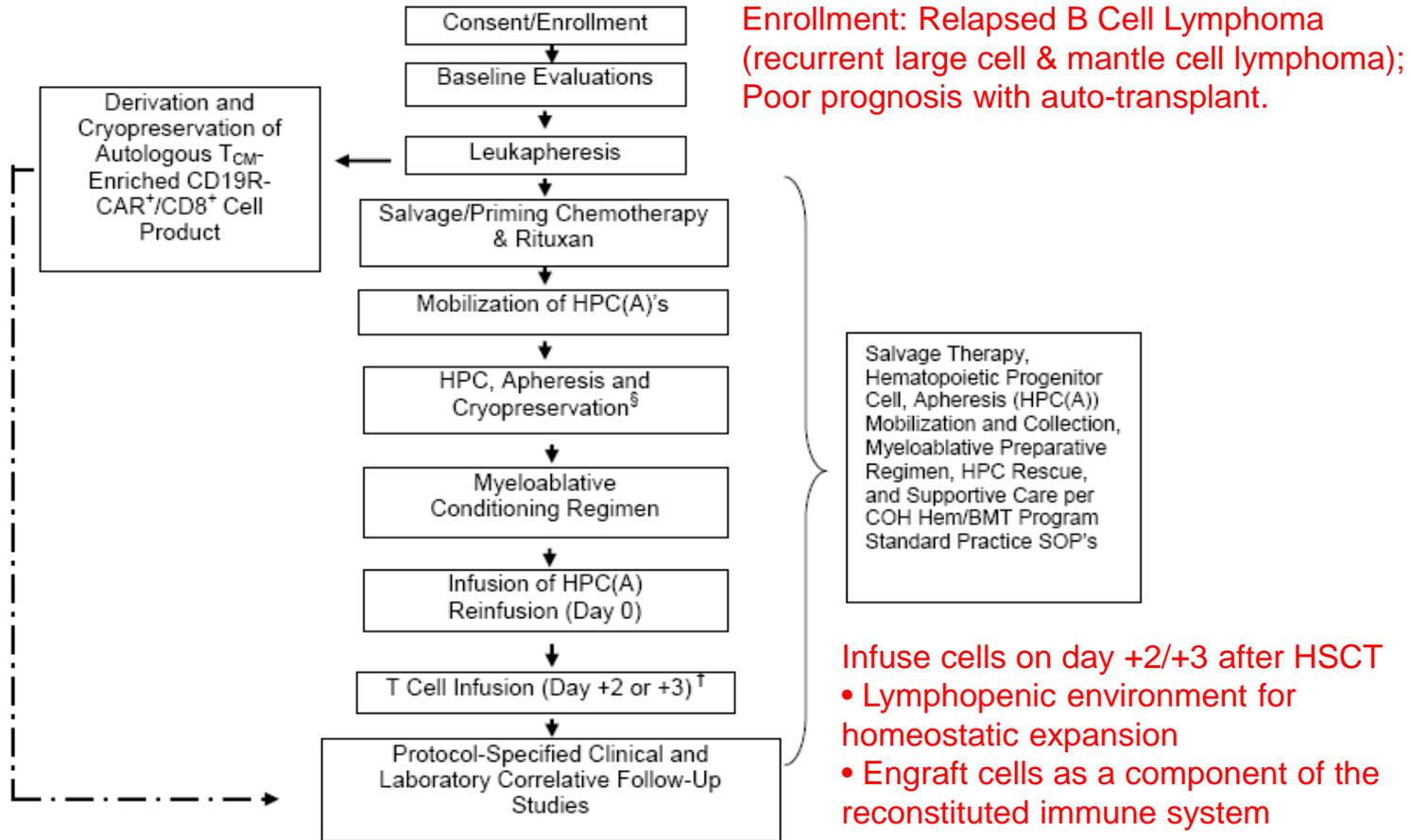
Protocol number/title	NIH-OBA#1177/BB-IND 14603 “Phase I/IIa Open Label, Multiple Site Clinical Trial Evaluating the Safety and Activity of Engineered Autologous T Cells Expressing an Affinity-Enhanced TCR Specific for NY-ESO-1 in Patients with Relapsed or Progressive Disease Following Prior Auto-HSCT”	NIH-OBA#1118/BB-IND 14603 “Phase I, Open Label, Dual Cohort, Triple Center Trial Evaluating the Safety and Efficacy of Autologous T Cells Expressing Enhanced TCRs Specific for NY-ESO-1 in Patients with Recurrent or Treatment Refractory Ovarian Cancer”
Disease indication/Research Participant population	Relapsed or progressive disease in multiple myeloma (HLA-A201+; NY-ESO-1+ tumor)	Recurrent or treatment refractory ovarian cancer (HLA-A201+; NY-ESO-1+ tumor)
TCR or CAR product (ex vivo cell/ vector/transgene) and Dose	TCR: NY-ESO-1 ^{c259} -specific Cells: autologous T cells Vector: Lentivirus Target Dose: 10 ⁹ to 10 ¹⁰ total cells	TCR: NY-ESO-1 ^{c259} -specific Cells: autologous T cells Vector: Lentivirus Target Dose: 10 ⁹ to 10 ¹⁰ total cells
Trial initiation date/status /enrollment	Initiated September 2013 Enrolling September 2013	Initiated June 2013 Currently Enrolling

Overview of CD19-CAR Trials for Lymphoma Following HSCT

Protocol number/title	NIH-OBA#1062/BB-IND 14645 “Phase I/II Study of Cellular Immunotherapy Using Central Memory-Enriched CD8+ T Cells Lentivirally Transduced to Express a CD19CAR Following HSCT for patients with High Risk Intermediate Grade, B-lineage NHL.” NHL-1	NIH-OBA#1183/BB-IND 15490 “Phase I Study of Cellular Immunotherapy Using Central Memory Enriched T Cells Lentivirally Transduced to Express a CD19-Specific, CD28-Costimulatory CAR and a Truncated EGFR Following HSCT for Patients with High-Risk Intermediate Grade B-Lineage NHL.” NHL-2
Disease indication/Research Participant population	Relapsed B cell lymphoma (Diffuse large B cell and recurrent mantle cell lymphoma)	Relapsed B cell lymphoma (Diffuse large B cell, transformed B cell and recurrent mantle cell lymphoma)
TCR or CAR product (ex vivo cell/ vector/transgene) and Dose	CAR: CD19-specific, CD3 ζ (1 st Gen) Cells: Autologous CD8+ Tcm Vector: Lentivirus, epHIV7 Dose escalation: 5x10 ⁷ to 10 ⁹ CAR+	CAR: CD19-specific, CD28 , CD3 ζ (2 nd Gen) Additional Transgene: EGFRt Cells: Autologous CD4+CD8+Tcm Vector: Lentivirus, epHIV7 Dose escalation: 5x10 ⁷ to 8x10 ⁸ CAR+
Trial initiation date/status /enrollment	Initiated June 2012 11 Enrolled 6 treated (2 pending) 5 of 6 w/ active disease at time of HSCT	Initiated June 2013 Enrolling Oct 2013

NIH-OBA#1062 (NHL-1)

Phase I/II Study of Cellular Immunotherapy Using Central Memory-Enriched CD8+ T Cells Lentivirally Transduced to Express a CD19CAR Following HSCT for patients with High Risk Intermediate Grade, B-lineage NHL.”



Dose Schedule				
CAR+ Dose	≤ 50M	100M	500M	1000M
Treated Patients	5	1		

Lessons Learned

- **NIH-OBA#1062/NHL-1**
 - **Feasibility of manufacturing CD8+ CD19R ζ + Tcm**
[Wang *et al* J Immunother 2012]
 - **No infusional toxicities (T cells D+2 after HSCT)**
 - **No interference with HSC engraftment**
 - **Low levels of T cells detected by flow cytometry/qPCR in a subset of patients**
 - **B cell aplasia observed (up to 6 mos)**
 - **4/5 currently in remission (6-13 mos); 1/6 too early to evaluate.**