

# **T Cell Immunotherapy- Optimizing Trial Design**

## **Session I**

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

**Powell/Coukos  
University of Pennsylvania**

**September 10, 2013**



# Overview of Trials

<p><b>Protocol number/title</b></p>	<p><b>UPCC 20811</b>  Phase I Clinical Trial of Autologous Alpha-Folate Receptor Redirected T Cells Administered Intravenously in Ovarian Cancer Patients</p>
<p><b>Disease indication/Research Participant population</b></p>	<p>Subjects with ovarian, primary peritoneal or fallopian tube cancer that expresses a-FR as assessed by immunohistochemistry.</p> <p>Inclusion criteria are designed to include subjects that are 18 years old or older diagnosed with advanced ovarian cancer that is incurable by presently available therapy, who have failed two or more prior chemotherapy regimens, with ECOG <math>\leq 2</math> performance status and <math>&gt;3</math> month expected survival.</p>
<p><b>TCR or CAR product (ex vivo cell/ vector/transgene) and Dose</b></p>	<p>CAR (anti-CD3/28 bead activated auto T cell/Lentivirus/pELNS-Mov19-BBz) + Lymphodepletion (cy/Flu)</p> <p>CAR T cells dosed by intravenous infusion using a “split dose” approach to dosing: 10% on Day 0, 30% on Day 1 and 60% on Day 2. Three dose levels:</p> <p><b>Cohort 1</b> 3 x10<sup>7</sup> CAR T cells/m<sup>2</sup></p> <p><b>Cohort 2</b> 1 x10<sup>8</sup> CAR T cells/m<sup>2</sup></p> <p><b>Cohort 3</b> 3 x10<sup>8</sup> CAR T cells/m<sup>2</sup></p> <p><b>Cohort 4</b> 3 x10<sup>8</sup> CAR T cells/m<sup>2</sup> + rhIL--7 (CYT--107)</p>
<p><b>Trial initiation date/status /enrollment</b></p>	<p>Trial has yet to enroll subjects</p> <p>New PI needs to be identified following the departure of Dr. Coukos’ from PENN</p>

# Lessons Learned

- **CAR T cells with 4-1BB costimulatory domains can undergo robust and delayed numerical expansion following infusion**

(Kalos et al. Sci Transl Med. 2011 August 10; 3(95): 95ra73.)

<b>Protocol number/title</b>	<b><i>Proposed amendment:</i></b> UPCC 20811 Phase I Clinical Trial of Autologous Alpha-Folate Receptor Redirected T Cells Administered Intravenously in Ovarian Cancer Patients
<b>TCR or CAR product (ex vivo cell/ vector/transgene) and Dose</b>	<b>Accelerated Escalation Phase:</b> 1 cohort of 3 subcohorts of 1 subject per dose level. Single dose on Day 0: <b>Cohort 1A:</b> 3 million CAR T cells + 1 billion PBL on Day 2 <b>Cohort 1B:</b> 10 million CAR T cells + 1 billion PBL on Day 2 <b>Cohort 1C:</b> 30 million CAR T cells + 1 billion PBL on Day 2  <b>Standard Escalation Phase:</b> 4 cohorts of 3 subject per dose level using a “split dose” approach to dosing: 10% on Day 0, 30% on Day 1 and 60% on Day 2.  <b>Cohort 2:</b> 100 million CAR T cells + 1 billion PBL on Day 2 <b>Cohort 3:</b> 300 million CAR T cells + 1 billion PBL on Day 2 <b>Cohort 4:</b> 300 million CAR T cells <b>Cohort 5:</b> 300 million CAR T cells  (Kandalaft et al. J Transl Med. 2012 Aug 3;10:157.)