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	IND 13859, RAC 0802-901 MART-1 F5 ACT	IND 15167, RAC 1203-1157 NY ESO TCR ACT
Disease indication/Research Participant population	Metastatic melanoma HLA-A2.1 positive MART-1 positive	Metastatic cancer HLA-A2.1 positive NY ESO-1 positive
TCR or CAR product (ex vivo cell/ vector/transgene) and Dose	F5 TCR 1×10^9 to up to 1×10^{10}	NY ESO-1 TCR 1×10^9
Trial initiation date/status /enrollment	July 2009 14 patients enrolled	January 2013 2 patients enrolled

Lessons Learned

- **F5 TCR clinical trial:**
  - **High frequency of tumor responses**
  - **All non-durable**
  - **TCR transgenic cells can be made in 6 days**
  - **Fresh TCR transgenic cells may have higher functionality than cryopreserved TCR transgenic cells**
  - **F5 TCR transgenic cells lose polyfunctionality after ACT**

Lessons Learned

- **Summary of unexpected results**

Subject ID#	SAE Description	Related to
F5 trial		
F5-6	Seizures	Disease progression with brain metastases
F5-10	Bone marrow aplasia	Disease progression with bone marrow involvement
F5-12	Respiratory distress, respiratory acidosis, renal insufficiency, and hypotension, anemia	Pneumonia due to Klepsiella with ARS
F5-14	Acute respiratory distress, renal insufficiency, hypotension, supraventricular tachycardia, pancytopenia	Required corticosteroid therapy and recovered
F5-15	DVT left subclavian, cardiopulmonary arrest, rapid drop in hemoglobin level, death	Massive retroperitoneal bleed from a melanoma lesion while on anticoagulant therapy
NY ESO TCR trial		
ESO-2	Pancytopenia, vision loss	No recovery of pancytopenia after Cy-Flu, and fludarabine-induced vision loss