



## RECOMBINANT DNA ADVISORY COMMITTEE

Office of Biotechnology Activities - Office of Science Policy  
National Institutes of Health  
Natcher Conference Center (Building 45)  
Bethesda, MD



### **Cytokine Release Syndrome after T Cell Immunotherapy** *Establishing Definitions, Developing Criteria, and Optimizing Management*

#### AGENDA - JUNE 10, 2015

- 8:30 AM**      **Welcome and Introductory Remarks**  
*Chair:* Donald Kohn, MD – University of California, Los Angeles
- 8:45 AM**      **Overview of T Cell Immunotherapy and Cytokine Release Syndrome (CRS)**  
Donald Kohn, MD – University of California, Los Angeles

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#### **SESSION I: PROTOCOL UPDATES AND CRS EXPERIENCES**

- 9:15 AM**      **Chimeric Antigen Receptor (CAR) T Cell Immunotherapy Trials Targeting Hematologic Malignancies**
- **CRS Events: OBA Data Analysis**  
Morad Hassani, MD, PhD – National Institutes of Health
  - **Panel Discussion**  
*Moderator:* Michel Sadelain, MD, PhD – Memorial Sloan Kettering Cancer Center  
*Panelists:*
    - Noelle Frey, MD – University of Pennsylvania
    - Jae Park, MD – Memorial Sloan Kettering Cancer Center
    - Helen Heslop, MD – Baylor College of Medicine
    - Richard Champlin, MD – MD Anderson Cancer Center
    - Brian Till, MD – Fred Hutchinson Cancer Research Center
    - Michael Jensen, MD – University of Washington
    - Renier Brentjens, MD, PhD – Memorial Sloan Kettering Cancer Center
    - Daniel Lee, MD – National Institutes of Health
    - David Porter, MD – University of Pennsylvania
    - Cameron Turtle, MBBS, PhD – Fred Hutchinson Cancer Research Center
    - L. Elizabeth Budde, MD – City of Hope National Medical Center
    - Catherine Bollard, MD – Children's National Health System
    - David Maloney, MD, PhD – Fred Hutchinson Cancer Research Center

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*Discussion Questions:*

1. *What are the potential contributing factors for severe CRS?*
  - a. *Patient specific factors- Target disease, predisposing conditions, age, host genetics, etc.*
  - b. *Tumor burden*
  - c. *Construct specific factors- signaling domains, tumor antigen targets, etc.*
  - d. *Others: chemotherapy, lymphodepletion, conditioning cytokines (e.g., IL-2)*
2. *Are neurological symptoms and/or toxicities components of CRS or part of a distinct syndrome?*

**11:15 AM      BREAK**

**11:30 AM      CAR T Cell Immunotherapy Trials Targeting Solid Tumors**

- **CRS Events: OBA Data Analysis**  
Morad Hassani, MD, PhD – National Institutes of Health
- **Panel Discussion**  
*Moderator:* Howard Kaufman, MD – Rutgers Cancer Institute of New Jersey

*Panelists:*

- Helen Heslop, MD – Baylor College of Medicine
- Stephen Gottschalk, MD – Texas Children’s Cancer and Hematology Centers
- Michael Jensen, MD – University of Washington
- Nabil Ahmed, MD – Baylor College of Medicine
- Daniel Powell, PhD -University of Pennsylvania

**12:00 PM      Engineered T Cell Receptor (TCR) Immunotherapy Trials Targeting Human Cancers**

- **CRS Events: OBA Data Analysis**  
Morad Hassani, MD, PhD – National Institutes of Health
- **Panel Discussion**  
*Moderator:* Howard Kaufman, MD – Rutgers Cancer Institute of New Jersey

*Panelists:*

- Antoni Ribas, MD, PhD – University of California, Los Angeles
- Philip Greenberg, MD – University of Washington
- James Yang, MD – National Institutes of Health

**12:30 PM      Public Comment**

**12:45 PM      LUNCH**

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**SESSION II: ESTABLISHING A UNIFORM DEFINITION AND GRADING SYSTEM FOR CRS**

**1:30 PM Discussion Session**

*Moderator:* Donald Kohn, MD – University of California, Los Angeles

*Discussion Questions:*

1. *What should be the clinical criteria for a common definition of CRS?*
2. *What grading systems currently exist? What should be the common grading criteria for CRS?*
3. *How do CRS events differ in CAR immunotherapy trials against solid tumors vs. hematologic malignancies? Are CRS events in engineered TCR trials different?*
4. *What cytokines are most useful in identifying CRS? What are the optimum methods and timing for collection of cytokines for monitoring CRS? Are there other available or potential biomarkers for diagnosis and monitoring of severe CRS? Can cytokine or other biomarker data be expected to be available in time to inform therapeutic decisions?*
5. *How does one best distinguish CRS from infection/sepsis?*

**3:00 PM BREAK**

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**SESSION III: OPTIMIZING THE MANAGEMENT OF CRS**

**3:15 PM Discussion Session**

*Moderator:* Michael Atkins, MD – Georgetown University School of Medicine

*Discussion Questions:*

1. *Are there common treatment strategies that could be elements of a CRS management algorithm?*
  - a. *What are the roles of corticosteroids and monoclonal antibodies (e.g., tocilizumab, siltuximab) in the management of severe CRS? Is there an optimum dose/frequency/timing of administration? Should there be concerns about anti-tumor effects?*
  - b. *What other strategies or agents are being successfully employed?*
2. *What is the role of suicide genes and has one been successfully used to abort CRS? For the different suicide genes, when is the expected onset of action compared to the pathogenic course of CRS?*
3. *What are the contributing factors to neurologic toxicity and how are these being managed?*
4. *What data sharing mechanisms would facilitate optimization of CRS management?*

**4:15 PM Public Comment**

**4:30 PM Discussion Wrap-up**

Donald Kohn, MD – University of California, Los Angeles

**5:00 PM ADJOURN**