

FDA/HESI-ITC Workshop on Safety Assessment of Engineered T cell Therapies

The mission of HESI, is to collaboratively identify and help to resolve global health and environmental challenges. The Immuno-safety Technical Committee (ITC) is one of the HESI Scientific Technical Committees and is composed of Scientists from Industry, Academia and Government (<http://hesiglobal.org/immunotoxicology/>). The HESI-ITC identifies and addresses scientific issues related to immune safety and translation to human health risk assessment. It addresses this mission by leveraging technical and scientific expertise from industry, academic and regulatory organizations to advance immuno-safety science, contributing to the scientific decision-making processes relative to the development of guidelines and regulations for immune safety testing, and educating stakeholders in safety sciences and promote the understanding and appropriate use of immune safety data.

Workshop Dates and Location: 24-25 Sept 2019 at US FDA Silver Spring, MD (The great room) 8:15am – 5:00pm

Goal: The goal of this workshop is to discuss the preclinical and translational safety assessment of engineered T cell therapies, focusing on topics as described based on sessions below. The intent is to have multiple short talks (~10-20 min each) followed by longer in-depth discussion within each session. To this end, key stakeholders will come from institutions working actively in the area of T cell therapeutics or areas with overlapping safety concerns.

Output: This symposium is intended to provide an interdisciplinary forum for industry, academia and regulatory scientists to discuss:

- 1) how current nonclinical immune safety evaluation is carried out for engineered T cell therapies
- 2) understanding both the usefulness and limitations to in vivo and in vitro methodologies currently employed
- 3) what the clinical data is demonstrating, and how it can be used to design more informative nonclinical studies
- 4) global regulatory considerations.

Agenda: Day 1, Tuesday, September 24, 2019

*Denotes presenters who will participate remotely

8:15 AM – 8:30 AM		Welcome Address – Hervé Lebrec (Amgen)
8:30AM – 9:15 AM	1	Keynote: Review of safety issues related to engineered T cell therapies – experience with JCAR015 as a case study - Stan Frankel (Celgene)
9:15 AM – 11:40 AM	2	Designing engineered T cells for optimal activity and safety Moderator: Rafael Ponce –(Shapetx)
9:15 AM – 9:45 AM		Terry Fry (University of Colorado) - <i>The Immune Biology of T cells Redirected Using Synthetic Receptors</i>
9:45 AM – 10:05 AM		Saul Priceman (City of Hope) - <i>Designing an Effective CAR T Cell Therapy</i>
10:05 AM – 10:25 AM		Nathan Singh (University of Pennsylvania) - <i>From bedside-to-bench and back: the role of CAR structure on clinical efficacy</i>
10:25 AM – 10:45 AM		David Miklos (Stanford University)- <i>CAR-T Antigen Evasion: The Emerging Role for Multi-targeted CAR Therapy</i>
10:45 AM – 11:00 AM		Break
11:00 AM – 11:20 AM		Olivia Finney (Bluebird Bio)- <i>Manufacturing the right CAR T cell: the importance of T cell memory</i>
11:20 AM – 11:40 AM		Iulia Diaconu (Elevate Bio)- <i>The characteristics of various platforms in use clinically (CAR/TCR) and their impact on activity and safety</i>
11:45 AM – 12:30 PM		Lunch
12:30 PM -3:00 PM	3	Target expression and associated liability assessment Moderators: Herve Lebrec (Amgen), Shon Green (Altius)
12:30 PM – 12:45 PM		Hervé Lebrec (Amgen)– Overview of the session
12:45 PM – 1:00 PM		Jim Rottman (Bluebird Bio) - <i>A General Approach To Cellular Immunotherapy Target Discovery</i>
1:15 PM – 1:30 PM		Tara Arvedson/ Christine Karbowski (Amgen) - <i>FLT3 expression characterization and lessons learned</i>
1:30 PM – 1:45 PM		Vladimir Ponomarev (Memorial Sloan Kettering Cancer Center) - <i>Non-invasive imaging of CAR-T cells</i>
1:45 PM – 2:00 PM		Keith Mansfield (Novartis) - <i>Assessment of off-tumor on-target effects of CAR-engineered human T cells in NSG mice</i>
2:00 PM – 2:15 PM		Martina Canestraro (Bluebird Bio) - <i>Transgenic TCR T cells: approaches for target selection and off-target identification & derisking</i>
2:15 PM – 2:30 PM		*Andrew Gerry (Adaptimmune) - <i>Safety Assessment of Engineered T cell Therapies - Experience and lessons from the engineered TCR field</i>
2:30 PM – 2:45 PM		Break
2:45PM – 3:00PM		Discussion/Q&A
3:00 – 5:00 PM	4	In vivo models informing safety and activity Moderators: Jenny Marlowe (Bluebird Bio) and Kathryn Packman (Janssen) Speakers:
3:00 – 3:20 PM		Kathryn Packman (Janssen) - <i>Evaluation of Efficacy, Biodistribution, Persistence and Safety of Human CAR-T Therapies in Mouse Models</i>
3:20 – 3:40 PM		Jule Gust (Seattle Children’s Hospital) - <i>The unpredictable brain: modeling CAR T cell neurotoxicity</i>
3:40– 4:00 PM		Herve Lebrec (Amgen) - <i>Experience of challenges and limitations associated with in vivo CART studies in nonhuman primates</i>
4:00 – 4:20 PM		Christine Karbowski (Amgen) - <i>Nonclinical Safety Assessment of an Investigational CAR-T</i>
4:20 – 4:40 PM		Chelsea Xue (Takeda) - <i>In vivo product characterization for process change control in Cell Therapies</i>
4:40 – 5:00PM		General Discussion
5:00 PM		Adjourn Day 1

Day 2, Wednesday, September 25, 2019

*Denotes presenters who will participate remotely

8:30AM – 10:15 AM	5	<p>Safety of viral and non-viral gene delivery systems – utility, risk of genomic injury Moderators: Shon Green (Altius), Jenny Marlowe (Bluebird Bio) Speakers: 8:30 AM – 8:45 AM Shon Green (Altius) - <i>Introduction: viral delivery vs targeted integration and the unique risks associated with gene-editing</i> 8:45 AM – 9:00 AM Sarah Voytek (Bluebird Bio) - <i>Considerations for the Nonclinical Development of Gene-Edited CAR T Cell Products using megaTALs</i> 9:00 AM – 9:15 AM Laura Serwer (Crisprtx) - <i>Case Study: Nonclinical Studies Supporting the Development of a CRISPR/Cas9-edited Allogeneic CAR T-cell</i> 9:15 AM – 9:30 AM Roman Galetto (Cellecris) - <i>TALEN-mediated multiplex gene edited CAR T-cells: preclinical evaluation of allogeneic cell therapy products</i> 9:30 AM – 10:15 AM Discussion/Q&A</p>
10:15 AM – 10:30 AM		Break
10:30 AM – 12:15 PM	6	<p>Linking preclinical development with the clinical experience Moderators: Rafael Ponce (Shapetx) and Shon Green (Altius) Speakers: 10:30 AM – 10:35 AM Shon Green (Altius) - Overview of the session 10:35 AM – 10:50 AM Indrajeet Singh (Janssen) - <i>Clinical Pharmacology Strategies to Support Efficient Development of CAR-T Cell Therapy: From FIH Starting dose to RP2D</i> 10:50 AM – 11:05 AM Krishna Komanduri (University of Miami Health System) - <i>Consensus efforts to standardize the grading, reporting and management of immune effector cell toxicities</i> 11:05 AM – 11:20 AM Rimas Orentas (Seattle Children’s Hospital) - <i>CAR-T development: a rapid and risky transition from pre-clinical to clinical application greatly benefitted our patients</i> 11:20 AM – 11:35 AM Jos Melenhorst (University of Pennsylvania) - <i>Translational Studies in Support of Immunogene Therapies at the University of Pennsylvania</i> 11:35 AM – 12:15 PM Discussion/Q&A</p>
12:15 PM – 1:00 PM		Lunch
1:00-4:00PM	7	<p>Regulatory Perspectives Considerations Moderators: Allen Wensky (US FDA) and Jacintha Shenton (Janssen) Speakers: 1:00 PM – 1:20 PM Snehal Naik (Janssen) - <i>The Evolving Global Regulatory Landscape for Engineered Cell Therapies</i> 1:20 PM – 1:35 PM Allen Wensky (US FDA) - <i>Preclinical considerations for engineered T cell products at FDA</i> 1:35 PM – 1:50 PM *James McBlane (Medicines and Healthcare products Regulatory Agency) - <i>Preclinical assessment of CAR T cell therapies – a view from Europe</i> 1:50 PM – 2:05 PM Kazushige Maki (PMDA) - <i>Preclinical safety evaluation of engineered T cell products at PMDA</i> 2:05 PM – 2:25 PM Peter Bross (US FDA) - <i>Development of Engineered T cell Therapies – FDA clinical regulatory perspective</i> 2:25 PM – 2:40 PM Kim Schultz (US FDA) - <i>FDA CAR T cell Safety Database</i> 2:40 PM – 2:55 PM Break 2:55 PM – 3:45 PM Discussion/Q&A/ Panel Discussion</p>
3:45 PM – 4:00 PM		Final thoughts/ Discussion
4:00 PM		Adjourn