U.S. Food and Drug Administration

Department of Health and Human Services

CENTER FOR BIOLOGICS EVALUATION AND RESEARCH

FDA Regulatory Updates: Related to Cancer Immunotherapy

Society for Immunotherapy of Cancer (SITC)

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Director, DCGT

Office of Cellular, Tissue and Gene Therapies, FDA, CBER

Date: November 8, 2013
Time: 12:15 PM to 12:30 PM
Location: National Harbor, MD

FDA Organization

- CBER (Center for Biologics Evaluation and Research): vaccines, blood and blood products, human tissue/tissue products for transplantation, cells, gene therapy
  - Office of Cellular, Tissue, and Gene Therapies
  - Office of Vaccines Research and Review
  - Office of Blood Research and Review

  } Product Offices
- CDER (Center for Drug Evaluation and Research): drugs, some biological products
- CDRH (Center for Devices and Radiological Health): devices for treatment, implants, diagnostic devices
- CVM
- CFSAN
- NCTR
- CTP
- ORA
- OC

FDA Regulation of Oncology Products

- Office of Hematology and Oncology Drug Products (OHOP), CDER
  - Drugs (small molecules)
  - Biologics, including Monoclonal Antibodies, Therapeutic Proteins, Cytokines
- Office of Cellular, Tissue and Gene Therapy, (OCTGT) CBER
  - Cell therapies
  - Gene Therapies
  - Oncolytic viruses
  - Therapeutic vaccines and immunotherapies
- Center for Device Radiological Health (CDRH):
  - Devices
    - Companion Diagnostics
    - Delivery devices

CBER Office of Cellular, Tissue, and Gene Therapies (OCTGT)

Office of the Director

Celia M.Witten, Ph.D., M.D., Director
Stephanie Simek, Ph.D. Deputy Director
Suzanne Epstein, Ph.D. Associate Director of Research
Richard McFarland, M.D., Ph.D., Associate Director of Policy

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Kimberly Benton, Ph.D., Deputy Director

Division of Human Tissues

Ellen Lazarus, M.D., Director

Division of Clinical Evaluation and Pharmacology/Toxicology

Wilson Bryan, M.D., Director

CDER Office of Hematology and Oncology Products (OHOP)

Office of the Director
Richard Pazdur, M.D. Director

Division of Hematology Oncology Toxicology
John Leighton, Ph.D., Director

Division of Oncology Products 1
Anthony Murgo, M.D., M.S., FACP, Acting Director

Division of Oncology Products 2
Patricia Keegan, M.D, Director

Division of Hematology Products
Ann Farrell, M.D., Director

Oncology Product Approvals by OCTGT

- Provenge (sipuleucel-T) – Dendreon
  - ARPC
- BCG Live (Intravesical) - TheraCys, Sanofi Pasteur Limited
- HEMACORD (HPC, Cord Blood) – NY Blood Center
- HPC, Cord Blood – Clinimmune labs, University of Colorado Cord Blood Bank
- DUCORD (HPC, Cord Blood) – Duke University
- HPC, Cord Blood - LifeSouth Community Blood Centers, Inc.
- Allocord, HPC Cord Blood - SSM Cardinal Glennon Children's Medical Center
- *Indication:* HPC, Cord Blood is an allogeneic cord blood hematopoietic progenitor cell therapy indicated for use in unrelated donor hematopoietic progenitor cell transplantation procedures in conjunction with an appropriate preparative regimen for hematopoietic and immunologic reconstitution in patients with disorders affecting the hematopoietic system that are inherited, acquired, or result from myeloablative treatment.

Recent Guidances (OCTGT)

- Draft Guidance for Industry: Considerations for the Design of Early Phase Clinical Trials of Cellular and Gene Therapy Products 7/2013
- Draft Guidance for Industry and FDA Staff: Investigational New Drug Applications for Minimally Manipulated, Unrelated Allogeneic Placental/Umbilical Cord Blood Intended for Hematopoietic and Immunologic Reconstitution in Patients with Disorders Affecting the Hematopoietic System 6/2013
- Draft Guidance for Industry: Biologics License Applications for Minimally Manipulated, Unrelated Allogeneic Placental/Umbilical Cord Blood Intended for Hematopoietic and Immunologic Reconstitution in Patients with Disorders Affecting the Hematopoietic System 6/2013
- Draft Guidance for Industry: Preclinical Assessment of Investigational Cellular and Gene Therapy Products 11/2012.

Recent Guidances (CDER/CBER)

- Draft Guidance for Industry: Expedited Programs for Serious Conditions—Drugs and Biologics. 6/2013. http://www.fda.gov/Drugs/ucm362706.htm
- Draft Guidance for Industry: Expanded Access to Investigational Drugs for Treatment Use—Qs & As. 5/2013
- Draft Guidance for Industry: Charging for Investigational Drugs Under an IND—Qs & As. 5/2013
- Guidance for Industry: Codevelopment of Two or More New Investigational Drugs for Use in Combination.
  6/2013 [CDER]
- Guidance for Industry: Enrichment Strategies for Clinical Trials to Support Approval of Human Drugs and Biological Products.
  12/2012 [CBER, CDER, CDRH]
- Draft Guidance for Industry: Pathologic Complete Response in Neoadjuvant Treatment of High-Risk Early-Stage Breast Cancer: Use as an Endpoint to Support Accelerated Approval 5/2012 [CDER]
- Draft Guidance for Industry: Determining the Extent of Safety Data Collection Needed in Late Stage Premarket and Postapproval Clinical Investigations 2/2012 [CDER/CBER]

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Workshops

- May 6, 2013. FDA Public Workshop: Clinical Trial Design Issues - Development of New Therapies for Non-Muscle Invasive Bladder Cancer.
- May 5, 2013. FDA Public Workshop: Clinical Trial Design Issues - Drug & Device Development for Localized Prostate Cancer.
- FDA Public Workshop, Innovations in Breast Cancer Drug Development – Neoadjuvant Breast Cancer Workshop, March 22, 2013.
- Public Workshop on Minimal Residual Disease (MRD) as a Surrogate Endpoint in Acute Myeloid Leukemia (AML), March 4, 2013.
- Public Workshop on Minimal Residual Disease (MRD) as a Surrogate Endpoint in Chronic Lymphocytic Leukemia (CLL), February 27, 2013.
- FDA/ASCO Public Workshop on Minimal Residual Disease, April 18, 2012.

International Activities

- FDA-European Medicines Agency (EMA)-Health Canada ATMP Cluster
- FDA-EMA Parallel Scientific Advice
- International Pharmaceutical Regulators Forum
  - Cell Therapy Group
    - 6 teleconferences since 2011
    - New Zealand meeting 2013
  - Gene Therapy Discussion Group
    - 3 teleconference since 2012

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Food and Drug Administration Safety and Innovation Act (FDASIA)

- Signed into law July 9, 2012
- Fifth reauthorization of PDUFA
- Section 901: Enhancement of Accelerated Patient Access To New Medical Treatments
  - Clarifies provisions and encourages expanded use and scope, listing types of evidence FDA can rely upon
- Section 902: Breakthrough Therapies
  - New designation with goal of expediting development of drugs that offer substantial improvement over existing therapies

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Fast Track Designation

- Criteria
  - Serious Condition
  - Nonclinical or clinical data demonstrate the potential to address unmet medical need
- Features
  - Actions to expedite development and review
  - Rolling Review

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Breakthrough Therapy Designation

- New designation created by FDASIA
- Criteria
  - Serious condition
  - Preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over available therapy on one or more clinically significant endpoints
- Features
  - All of FT features
  - Intensive guidance on efficient drug development
  - Organizational commitment

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Breakthrough Therapy Designation

- As of May 31, 2013, FDA received 59 BT designation requests*
  - 20 requests granted
  - 20 requests denied

  *Includes requests received but pending a decision at the time of the update

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Accelerated Approval Pathway

- Existing regulations-21CFR part 314, subpart H, and part 601, subpart E
- No prior guidance
- FDASIA provides additional flexibility and clarity to the accelerated approval pathway
  - Flexibility: Approval takes into account the availability or lack of alternative treatments
  - Clarity: Approval can be based on clinical endpoint that can be measured earlier than irreversible morbidity or mortality (IMM) that is reasonably likely to predict an effect on IMM or other clinical benefit.

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Priority Review Designation

- Criteria
  - Serious Condition
  - Demonstrates potential to be significant improvement in safety or effectiveness
- Features
  - Marketing application reviewed in 6 months (compared to 10 months for standard review)
- Includes special criteria which qualifies products for PR (e.g., qualified infectious disease product, priority review vouchers)

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Expanding Access to Investigational Drugs

- Use of an investigational drug outside of a clinical trial, for the sole purpose of treating a patient or patients with a serious or life-threatening disease who have no acceptable medical options
- Levels of expanded access are based on the number of patients to be treated and how much is already known about the drug:
  - Individual or intermediate size group access
  - Treatment IND

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Useful FDA Information

- References for the Regulatory Process for the Office of Cellular, Tissue, and Gene Therapies (OCTGT) http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/OtherRecommendationsforManufacturers/ucm094338.htm
- OCTGT Learn Webinar Series: http://www.fda.gov/BiologicsBloodVaccines/NewsEvents/ucm232821.htm
- FDA Clinical Investigator Training course (Nov 12-14 2013): http://continuingeducation.dcri.duke.edu/fda-clinical-investigators-training-course-registration

Public Access to CBER

CBER website:
http://www.fda.gov/BiologicsBloodVaccines/default.htm

Phone: 1-800-835-4709 or 301-827-1800

Consumer Affairs Branch (CAB)
Email: ocod@fda.hhs.gov
Phone: 301-827-3821

Manufacturers Assistance and Technical Training Branch (MATTB)
Email: industry.biologics@fda.gov
Phone: 301-827-4081

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Contact Information

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