OVERVIEW OF RECENT CBER CANCER PRODUCT APPROVALS

Najat Bouchkouj, MD
Medical Officer
Office of Tissues and Advanced Therapies
Center for Biologics Evaluation and Research
FDA Regulation of Oncology Products

**Oncology Center of Excellence (OCE)**

<table>
<thead>
<tr>
<th>CDER</th>
<th>CBER</th>
<th>CDRH</th>
</tr>
</thead>
</table>
| Office of Hematology and Oncology Drug Products (OHOP)  
- Drugs (small molecules)  
- Biologics  
  - Monoclonal Antibodies  
  - T cell engagers  
  - Therapeutic Proteins  
  - Cytokines  | Office of Tissues and Advanced Therapies (OTAT)  
- **Cell therapies**  
- **Gene Therapies**  
  - Oncolytic viruses  
  - Therapeutic vaccines and immunotherapies  | Office of In Vitro Diagnostics and Radiological Health (OIR)  
- Devices  
- Companion Diagnostics  |
The New York Times (OCT. 15, 2014)
Cell Therapy Puts Leukemia Patients in Extended Remission

The Washington Post
Aug 30, 2017
FDA clears first gene-altering therapy — ‘a living drug’ — for childhood leukemia
Oct 18, 2017
US regulators approve 2nd gene therapy for blood cancer
What is Chimeric Antigen Receptor (CAR) T Cell Therapy?

- Novel type of cancer immunotherapy
- Involves training patients’ own immune cells (T cells) to attack cancer cells

Emily Whitehead, shown with her parents, was the first child treated with CAR T cell therapy
CAR T Cell Therapy

Source: National Cancer Institute at the National Institutes of Health
CAR T Cell Therapy Approvals:

Developed under FDA’s expedited programs

- **Kymriah** (tisagenlecleucel)
  - CAR T cells (target – CD19)
  - Refractory/relapsed childhood acute lymphoblastic B cell leukemia (2017)
  - Adult patients with relapsed or refractory large B cell lymphoma (2018)
  - Oncology Drugs Advisory Committee meeting
  - Novartis

- **Yescarta** (axicabtagene ciloleucel)
  - CAR T cells (target – CD19)
  - Adult patients with relapsed or refractory large B cell lymphoma (2017)
  - Gilead (Kite)
Efficacy:

• Single arm studies

• Approval was based on:
  – Overall Response Rate (ORR) = Complete Response (CR) + Partial Response (CR)
  – Duration of response

• Pediatric and young adult leukemia
  – CR = 63%

• Adult large B cell lymphoma
  – CR = 32-52%
  – ORR = 50-72%
CAR T Cell Therapy Can Cause Severe Side Effects

• Side effects can be fatal or life-threatening

• Majority of patients experienced:
  – Cytokine Release Syndrome (CRS):
    • Systemic response to T-cell activation: flu-like symptoms, difficulty breathing, body organ toxicities
    • FDA expanded the approval of Actemra (tocilizumab) to treat CRS
  – Neurologic toxicities:
    • Confusion, inability to talk, seizures, brain swelling
FDA’s Measures To Reduce The Risks of CAR T Cell Products

• Boxed warning for CRS and neurologic toxicities
• Approval with a Risk Evaluation and Mitigation Strategy (REMS)
  – To ensure the benefits of the drug outweigh the risks
  – Protective measures in place to ensure patients’ safety:
    • Hospitals must be certified
    • Education of physicians, hospital staff and patients about the recognition and management of CRS and neurologic toxicity

www.fda.gov
Long-Term Safety Concerns

• Theoretical risk:
  – Secondary malignancies

• Post-marketing requirement (PMR)*:
  – Observational study to collect safety and survival information
  – 15 year follow-up for known and anticipated adverse reactions

*Note: post marketing requirements (PMRs) are distinct from REMS programs
Summary

Tisagenlecleucel (Kymriah)
Axicabtagene ciloleucel (Yescarta)

• Compelling efficacy in highly refractory or resistant population

• Major safety issues: fatal and life-threatening CRS, neurologic toxicity
  – Black box warning
  – Approval with REMS

• Concern for long-term safety issues and secondary malignancies
  – Approval with post-marketing studies
Acknowledgements

• Kristin Baird
• Bindu George
• Poornima Sharma
• OTAT and OCE
Questions?
Contact Information

• Najat Bouchkouj, MD
  Najat.bouchkouj@fda.hhs.gov
• Regulatory Questions:
  OTAT Main Line – 240 402 8190
  Email: OTATRPMS@fda.hhs.gov and
  Lori.Tull@fda.hhs.gov
• OTAT Learn Webinar Series:
  http://www.fda.gov/BiologicsBloodVaccines/NewsEvents/ucm232821.htm
• CBER website: www.fda.gov/BiologicsBloodVaccines/default.htm
• Phone: 1-800-835-4709 or 240-402-8010
• Consumer Affairs Branch: ocod@fda.hhs.gov
• Manufacturers Assistance and Technical Training Branch: industry.biologics@fda.hhs.gov
• Follow us on Twitter: https://www.twitter.com/fdacber
Useful FDA Information

- References for the Regulatory Process for the Office of Tissues and Advanced Therapies

- OTAT Learn Webinar Series:

- Cell and Gene Therapy Guidances

- Expedited Programs Guidance: