Getting to a Cure for Sickle Cell Disease

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Addressing Sickle Cell Disease: A Strategic Plan and Blueprint for Action
National Academy of Science and Medicine
April 16, 2019
Washington, D.C.
What Products Does CBER Regulate?

- Allergenics
- Blood Products
- Devices (subset including some IVDs)
- Gene Therapy Products
- Human Tissues and Cellular Products
- Vaccines (preventative and therapeutic)
- Xenotransplantation products
- Certain combination products
Sickle Cell Disease/CBER products

- Red Blood Cells for transfusion
- Hematopoietic Stem Cells for transplantation
- Gene therapy
  - Transgene expression
  - Gene editing
- Other products used for patient management such as vaccines for infectious disease prevention
New Gene Therapy Product IND Submissions (1990-2018)
Challenges in the Development of Gene Therapies

• Need novel approaches to clinical development
  – Limited patient populations for clinical trials argues for careful planning of development program
  – Potential use of appropriate surrogate endpoints
• Transition from pilot scale to commercial manufacturing can be challenging for gene therapies
  – Consider scalable manufacturing processes
• Limited methods for safety testing
Suite of Gene Therapy Draft Guidance Documents – July 2018

1. Chemistry, Manufacturing, and Control (CMC) Information for Human Gene Therapy Investigational New Drug Applications (INDs)
2. Testing of Retroviral Vector-Based Gene Therapy Products for Replication Competent Retrovirus (RCR) during Product Manufacture and Patient Follow-up
3. Long Term Follow-up After Administration of Human Gene Therapy Products
5. Human Gene Therapy for Retinal Disorders
6. Human Gene Therapy for Rare Diseases

Challenges for Gene Therapy for Sickle Cell Disease

• Variability in patient course of disease
  – Enrollment criteria
• Risk tolerance for gene therapy in sickle cell disease
• Selecting an appropriate outcome measure
  – Pain, organ function, surrogate...
• Need for ongoing long term patient follow up
SCD— Expedited Development Approaches

• Identify an unmet need population
  – Failed hydroxyurea, not eligible for HSCT and at risk of Vaso-occlusive episodes (VOEs)
  – Patients who have not responded to transfusions and at risk of stroke

• Identify potential surrogate endpoints
  – Transgene Hb effects on ↓VOEs
  – Transcranial Doppler (TCD) velocity in patients at high risk for stroke
SCD-Clinical Development Program Assistance (1)

- Early Phase
  - Characterizing the transgene Hb or gene edited product in-vitro and in-vivo
  - Manufacturing changes
  - Relationship between surrogate endpoints (novel) to preliminary clinical outcomes (reduction in VOE)
  - RMAT or BTD designation considerations
  - EOP2 meetings
SCD-Clinical Development Program Assistance (2)

• Later Phase
  – Single arm studies
  – Historical controls or Intra-patient controls
  – Quality of life indices (Patient Focused Drug Development Workshop 2014)
SCD – Challenges

• Partnering with patients to
  – Curative therapies – long term safety data
  – Ensure trial design capture improvement in symptoms/disease aspects that are of importance
  – Informative product labels
  – Enhance enrollment to clinical trials

• Need for historical control data/natural history in the unmet need space

• Develop/qualified biomarkers that are potential surrogate endpoints – imaging, hemoglobin, indicators of end-organ damage
Summary

FDA is committed to bringing the promise of innovative, safe and effective new therapies to those in need of them, as quickly as possible.
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