The Next Generation of Cellular Therapies: Opportunities to Accelerate Development

Virtual Meeting
March 8, 2023

Background

Engineered cell therapies have emerged as a new treatment pillar poised to change the cancer therapy landscape for patients with serious or life-threatening malignancies. While current autologous cell-based immunotherapies approved by the U.S. Food and Drug Administration (FDA) have shown remarkable activity in hematologic malignancies, considerable scientific and operational obstacles remain to enable broader application of this novel therapeutic approach. This webinar will identify scientific and regulatory barriers to cell therapy development and discuss opportunities to enhance evidence generation through data extrapolation and mechanisms to enable regulatory flexibility. This can help facilitate optimal development, commercialization, and evolution of the next generation of safe and effective engineered cell therapies for oncology care.

Introduction

Drug developers often investigate multiple versions of an engineered cell therapy early in development to identify the most promising version to advance through later stages of clinical development. This is often accomplished by testing multiple iterations of a product, either as part of one trial or a series of trials. Recent FDA draft guidance outlines an approach to investigate several versions of a cell therapy product in an umbrella trial rather than initiating several trials.[1] This umbrella trial approach can streamline regulatory requirements and data collection to help expeditiously identify promising candidates while also enabling opportunities to leverage data across different product versions.

Data extrapolation to advance new versions of investigational products has occurred for several decades across therapeutic classes as our understanding of these drug classes improves (**Table 1**). For example, information and conclusions from one product can support inferences for the product in additional populations as well as new product versions, thus leveraging the totality of evidence and enabling targeted data collection to inform clinical trial strategies and support the approval of a new product. The FDA has on a case-by-case basis allowed Sponsors to extrapolate data from an earlier T-cell product to a second-generation product. To date, data extrapolation has been successful for chemistry, manufacturing, and controls (CMC) processes such as stability data, and clinical components, such as starting dose and safety data.

Following case study presentations about the successful data extrapolation in T-cell products to date, a panel discussion will outline considerations for data generation across different cell therapy product versions to efficiently develop safe and effective therapies for patients. This webinar will inform the development of a regulatory framework and policies to support flexible data generation and trial designs to be presented at a hybrid in-person event on May 22, 2023 (details forthcoming).

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[1] Studying Multiple Versions of a Cellular or Gene Therapy Product in an Early-Phase Clinical Trial. https://www.fda.gov/media/152536/download

Key Discussion Questions

- What learnings can be applied to support the design and execution of clinical development programs for the next generation of cell therapies?
- What are key considerations for developers when proposing to introduce modifications to cell therapy products?
- Can a risk-based approach be developed to assess the potential impact a modification might have on the safety and efficacy of the product?
- What are important regulatory considerations when leveraging learnings/data from first generation products to support second generation products?

Table 1. Examples of Data Extrapolation in Drug Development. A review of FDA summary documents publicly available on Drugs@FDA[2] includes examples where data extrapolation has been appropriately used in drug development.

Class	Data Type	Select Examples	Examples from Review Documents
Small molecule drugs	Clinical pharmacology and exposure-response data	Coreg/Coreg CR	**Clinical Pharmacology/Pharmacodynamics:** Based on equivalencies in pharmacokinetic (PK) and pharmacodynamic (PD) data in Coreg CR compared to Coreg IR the conclusion was drawn that the indications for which the immediate-release (IR) formulation had been approved can be inferred and claimed for the controlled-release (CR) formulation.
Peptide products (synthetic)	Pre-clinical and clinical for rDNA derived peptides	Liraglutide/future liraglutide ANDAs	**Pre-clinical Pharmacology/Toxicology**: Safety margins for toxicities calculated using steady state systemic exposure in healthy adults were similar based on plasma liraglutide area under the curve (AUC) supporting the basis for inclusion of boxed warning and REMS on the risk of thyroid C-cell tumors observed in rodents. **Clinical Pharmacology/Pharmacodynamics:** Exposure results Victoza in the thorough QTc trial were compared with exposures (Cmax) following Saxenda in weight management trials and found to be largely overlapping supporting extrapolation of results from Victoza's QTc trial to support approval of Saxenda for weight management.
Antibody-based biologic agents	Manufacturing/CMC and clinical data	Herceptin/ Herceptin Hylecta Rituxan/rituxan hycela	**Herceptin/Herceptin Hylecta** **Clinical Data:** Data extrapolation possible due to the same drug substance and only a formulation change and comparable PK profiles of IV trastuzumab across the neoadjuvant-adjuvant/adjuvant treatment settings in patients with early breast cancer (EBC) and metastatic breast cancer (EBC) **Manufacturing/CMC**: Due to same manufacturing processes and drug substances, cross referencing to the BLA was possible. **Rituxan/Rituxan Hycela** **Manufacturing/CMC:** Manufacturing processes cross referenced in product quality review **Pharmacology/Toxicology:** PK Bridging studies used as primary source to support approval/comparable benefit of Rituxan and Rituxan Hycela.
Vaccines	Manufacturing/CMC and clinical primary immunogenicity leverages parent profile as a control (PVN 13 vs PVN20)	Prevnar 13/ Pneumovax 23/ Prevnar 20	**Manufacturing/CMC:** PCV20 and PCV13 vaccines have nearly identical manufacturing processes for the 13 common serotypes **Clinical/Primary Immunogenicity:** Vaccine induced opsonophagocytic activity (OPA) activity was used in the licensure of Prevnar 13 (13vPnC) by comparing the OPA titers induced by 13vPnC with the licensed 7-valent pneumococcal conjugate vaccine.

[2] Drugs@FDA: FDA-Approved Drugs. https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm