FDA/CDER Office of Clinical Pharmacology and International Society of Pharmacometrics (ISoP)

Public Workshop

Optimizing Dosages for Oncology Drug Products:

Using Modeling and Simulation to Evaluate Effects of Intrinsic and Extrinsic Factors

October 16, 2023

Food and Drug Administration White Oak Campus or Virtual

10:00 AM **Welcome & Housekeeping** – Stacy Shord, FDA

10:05 AM **Identifying Optimal Dosages for Specific Populations** – Stacy Shord, FDA

- Highlight the need to select dosages for specific populations earlier in development
- Discuss the current regulatory framework, including guidance documents, projects, plans, and best practices, that support broadening eligibility criteria
- State how model-informed and model-based approaches can be used to select dosages for specific populations to be investigated in clinical trials

10:15 AM **Session 1: Using Model-Informed Approaches to Develop Oncology Drugs for Pediatric Patients and Older Adults**

Moderator: CJ Musante, Pfizer (ISoP)

10:20 AM *Understanding the Regulations and Recommendations for Drug Development in Pediatrics and Older Adults with Cancer – Youwei Bi, FDA*

- Discuss regulatory framework for developing oncology drugs for pediatrics and older adults
- Describe how model-informed and model-based approaches have supported oncology drug approvals in pediatrics and older adults

10:30 AM *Understanding the Effects of Chronological and Functional Age on Dosage Selection in Older Adults– Ginah Nightingale, Abbvie*

- Compare and contrast functional and chronological age
- Identify physiologic changes and clinical pharmacology considerations for older adults when selecting treatments and dosing regimens
- Describe how the geriatric assessment can be used to identify vulnerabilities when selecting treatment options for older adults with cancer

10:50 AM *Model-informed Approaches to Support Dosage Selection in Pediatric Patients – Tomoyuki Mizuno, University of Cincinnati*

- Identify unique challenges to developing a model suited for all pediatric age groups
- Highlight efficient approaches for designing and expediting oncology drug development in pediatrics
- Describe model-informed drug approaches used to support the dosage selection for drugs or biological products in pediatric patients with cancer

11:10 AM *Panel Discussion*

- Youwei Bi, FDA

- Qi Liu, FDA
- Harpreet Singh, FDA
- Tomoyuki Mizuno, University of Cincinnati
- Ginah Nightingale, Abbvie

11:40 AM **Lunch (Kiosk)**

12:45 PM **Session 2: Evaluating How Race, Ethnicity, Geography & Ancestry Influence Dosage Optimization for Oncology Drug Development**

Moderator: Jiang Liu, FDA

12:50 PM *Expanding Clinical Trial Eligibility to Include Relevant Populations – Olanrewaju Okusanya, FDA*

- Articulate importance of enrolling patient populations reflective of US population with the disease of interest and understanding the effects of race, ethnicity, geography and ancestry during drug development
- Highlight impact of discrepancies between clinical trial enrollment and US population on marketing application

1:00 PM *Clinical Pharmacology Considerations for Evaluation of Race, Ethnicity, Geography, and Ancestry During Drug Development and Regulatory Review – Anuradha Ramamoorthy, FDA*

- Highlight examples, causes, and consequences of differences in exposure or response among racial, ethnic, geographic, and ancestral subpopulations
- Discuss the role of clinical pharmacology in understanding drug response variability

1:20 PM *The Role of Clinical Pharmacology in Dosage Selection* and *Design of Multi-Regional Clinical Trials– Karthik Venkatakrishnan, EMD Serono*

- Discuss opportunities for clinical pharmacology and model-informed approaches in dosage selection and design of multi-regional oncology clinical trials aligned with ICH E17 principles
- Illustrate the assessment of cross-population conservation in drug- and disease-related intrinsic and extrinsic factors leveraging population PK, PK/PD and disease progression models

1:40 PM *PMDA Experience with Dosage Selection - Shinichi Kijima, Pharmaceuticals and Medical Devices Agency*

- Compare and contrast regulatory framework and current approaches implemented to select dosages in Japan, Europe and USA
- Discuss how model-informed approaches is used to select dosages in Japan

2:00 PM *Panel Discussion*

- Anu Ramamoorthy, FDA
- Olanrewaju Okusanya, FDA
- Karthik Venkatakrishnan, EMD Serono
- Shinichi Kijima, Pharmaceuticals and Medical Devices Agency

2:30 PM **Break**

2:45 PM **Session 3: Understanding the Effects of Food and Drug-Drug Interactions on Dosage Optimization**

Moderator: Vijay Ivaturi, University of Maryland School of Pharmacy (ISoP)

2:50 PM *Impossible Recommendations Regarding Administration with Food and Use of Concomitant Medications – Brian Booth, FDA*

- Discuss the importance of understanding potential effect of food and concomitant medications on recommended dosage, tolerability and adherence early in development
- Describe how patients with cancer may be receiving concomitant medications, such as anti-seizures or anti-infectives, to manage disease- or treatment-related signs or symptoms that could interact with the investigational new drug

3:00 PM *Leveraging Modeling to Understand the Effects of Food on Dosage Selection– Xinyuan (Susie) Zhang, Daiichi Sankyo*

- Describe using model-informed approaches to predict food interactions to inform dosing relative to food in the registration trial
- Discuss model-informed approaches that have been used to support dosage recommendations that accounts for food interactions before registration trial

3:20 PM *Leveraging Modeling to Understand the Effects of Concomitant Medications on Dosage Selection– Ping Zhao, Bill & Melinda Gates Foundation*

- Describe using model-informed approaches to predict drug-drug interactions to inform dosing relative to common concomitant medications
- Discuss model-informed approaches that have been used to support dosage recommendations that accounts for interactions before registration trial

3:40 PM *Panel Discussion*

- Yuching Yang, FDA
- Rebecca Moody, FDA
- Brian Booth, FDA
- Xinyuan (Susie) Zhang, Daiichi Sankyo
- Ping Zhao, Bill & Melinda Gates Foundation

4:10 PM **Summary and Closing Remarks** – Wei Gao, EMD Serono (ISoP)

4:30 PM End