FDA-American Society of Clinical Oncology-Friends of Cancer Research
Workshop on Development of Tissue-Agnostic, Biomarker-Based Indications
Co-Sponsored by the:
U.S. Food & Drug Administration (FDA), American Society of Clinical Oncology (ASCO), and Friends of Cancer Research (Friends); Twitter: #FDATissueAgnostic19
April 26, 2019 – 8:30 am – 4:00 pm (Eastern)

Questions for Multi-Stakeholder Panels

Multi-Stakeholder Panel – Early Research and Development Considerations
Questions for Panel Discussion:

- What considerations could be employed when moving from pre-clinical or early-clinical studies across multiple tumors to a tissue- and age-agnostic approach in phase 1B or 2a?
- What are key indicators that might occur early in development to signal a potentially successful tissue- and age-agnostic approach?
- What statistical methods could be used to analyze tissue-agnostic data, including potentially borrowing information across tissue types?
- What types of strategies might be effective to engage patient advocates in trial design and operations planning to ensure engagement across multiple disease types?
- What strategies could be employed to isolate individual drug effects in a combination regimen across multiple tumor types?
- What role does the underlying biology play in consideration of a tissue-agnostic approach? What strategies could help assess a biomarker's contribution to cancer development and/or immune system response across tumor types?
- Aside from a companion diagnostic approach, what strategies could be used to ensure consistent identification of the biomarker? When should the biomarker parameters be locked down to identify patients for enrollment into a basket study?
- Are there efficient strategies for examining performance of assays across multiple tissue types and accounting for potential tissue heterogeneity?

Multi-Stakeholder Panel – Registration Research and Development Considerations
Questions for Panel Discussion:

- What is the optimal number of tissue types for a tissue-agnostic approach?
    - What tumor types should sponsors prioritize for inclusion in the registration studies?
    - What considerations could assist in situations involving low-incidence biomarkers and which tissue types to include in the registration studies?
    - How should we approach a lack of observed activity in a single tissue type for a drug that demonstrates activity in multiple tissue types with a shared biomarker?
    - Under what circumstances should common tumors (e.g. lung, breast, colorectal, prostate) be included in a tissue-agnostic indication?
- What strategies could one consider for approaches that involve drug combinations?
- What types of strategies could be employed prior to drug approval to maximize data collection across disease-specific patient advocacy organizations and provider communities?
- How feasible is it to get the trial to the patient vs. patient to the trial?
- How do we approach contemporaneous approval of test and drug?
- Are there additional considerations for drug sponsors that seek traditional, tissue-based development programs for a drug that has received a tissue agnostic approval?

Multi-Stakeholder Panel – Post-Market Research and Development Considerations

Questions for Panel Discussion:

- How could disease-based patient advocacy groups and disease-focused clinician groups think about developing awareness and education about tissue-agnostic indications?
- If a drug is initially approved as a tissue-specific indication, when are the number of tumor types sufficient to change to a tissue-agnostic supplemental indication?
- Is it enough to only rely on clinical evidence or can we collect this tissue agnostic data in a more registry-like format or through testing of patient tissue specimens?
- What examples does the TAPUR Study provide that lend some insight?
- What types of controls (e.g., synthetic control arms, external control, etc.) can be appropriate for real-world data analysis either 1) to conduct a confirmatory study in support of a tissue-agnostic indication or 2) to generate evidence for a supplemental tissue-agnostic indication?
- When the biomarker defines the disease (e.g., microsatellite instability-high), how do we extract data from the controlled trials? Can this be replicated in real-world cases?
- If the initial indication is tissue agnostic, what level of post-market evidence would be necessary to modify or omit the indication for a specific histology?
- If clinicians aren't using the drug for a certain subtype that would have important research and development implications, what type of data could prompt modification or removal of a tumor type from the tissue-agnostic indication?