Myth Busters

What you think you know about the FDA may not be true

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Audience Participation

• Please respond to the questions that follow using the Slido Application on your cell phone (or computer)

• Audience responses (from in the room and remotely participating) will be displayed after each question.
Question #1

FDA’s OHOP requires two randomized trials for approval of a new product.

1 OR 2?
Question #1: Two Trials

- Two trial requirement
  - One trial may be allowed in the following settings*:
    - High unmet medical need
    - Serious, life-threatening illnesses
    - Difficult to repeat a positive trial

* FDAMA 1997
Question #2

FDA’s OHOP requires that trials use overall survival as the primary endpoint for approval of a new product
### Question # 2: Endpoints

<table>
<thead>
<tr>
<th>Endpoint Used for First Approval (in OHOP)</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Response Rate</td>
<td>60%</td>
</tr>
<tr>
<td>Progression Free Survival</td>
<td>20%</td>
</tr>
<tr>
<td>Overall Survival</td>
<td>13%</td>
</tr>
<tr>
<td>Other</td>
<td>7%</td>
</tr>
</tbody>
</table>
Question #3

• FDA’s OHOP requires that trials to support approvals only enroll patient in the U.S.
Question # 3: U.S. Enrollment

- Trials are not required to be limited to the U.S. population, or even mostly in a U.S. population...
- However, the results should be relevant to the U.S. population:
  - Patient population
  - Control arm
  - Biomarker data
  - Supportive care measures
  - Available prior/subsequent therapy
Question # 4

FDA’s OHOP permits crossover in trials
Question # 4: Crossover

• Recent approvals where crossover was permitted at time of progression
  – Dabrafenib and trametinib in metastatic melanoma
  – Erlotinib in non-small cell lung cancer
  – Afatinib in non-small cell lung cancer
  – Crizotinib in non-small cell lung cancer
Question # 5

FDA advisory committees, such as the ODAC (Oncologic Drug Advisory Committee), are the final decision makers in drug approval.
Question # 5: Advisory Committee

• Advisory committees provide opinions based upon their clinical and scientific expertise.

• FDA generally follows an AC’s recommendation, but is not bound to do so.
Question # 6

FDA staff lack scientific and clinical expertise.
Question # 6: Expertise

• FDA Review Multidisciplinary Team
  – Clinical
  – Biostatistics
  – Clinical Pharmacology
  – Chemistry and Manufacturing
  – Pharmacology/Toxicology

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Question # 7

• FDA permits access to investigational drugs (e.g., compassionate use)
Question # 7: Compassionate Use

- FDA has an expanded access program for clinicians to obtain access to investigational drugs for individual patients.

Stay tuned for more on this later from Aviva Krauss.
Question # 8

• FDA determines the cost of drugs/biological products
Question # 8: Drug Cost

• No legal authority over drug costs
• Cost savings with generics and biosimilar products
• Reduced drug development expenses
• Sources of assistance:
  – Drug manufacturer patient assistance programs
  – Ask your health-care provider if your drugs are available in a generic form
Question # 9

FDA takes the patient experience into account in approval decisions and encourages the assessment of clinical outcomes such as symptoms and physical function in clinical trials.
Question # 9: Patient Experience

• Advisory Committee: Patient Representative
• 2009 Patient-Reported Outcomes (PRO) Guidance
• Patient Representative Program
• PROs in Labeling: Hycela and Imbruvica
• Patient Focused Drug Development Meetings
Question # 10

FDA may publish its reasons for non-approval of a drug
Question # 10: Negative Reviews

• By law, FDA is NOT permitted to post reviews or letters to the Applicant for products that do not receive approval

• Reviews and approval letters for approvals ARE posted.
Acknowledgments

• Amy McKee
• Paul Kluetz