HOW BIOMARKERS CAN IMPROVE THE DRUG DEVELOPMENT PROCESS

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BIOMARKERS IN HEALTH CARE AND RESEARCH

Health Care
- Blood pressure
- Blood glucose

Research
- Tumor markers in cancer research
- Interleukins in inflammation research
Biomarkers can:

- Monitor the safety of a therapy
- Determine if a treatment is having the desired effect on the body
- Predict patients who might respond better to a drug from a safety or efficacy perspective
- Potentially enable time and cost savings in clinical trials
BIOMARKERS: DRUG DEVELOPMENT

- **Mechanism of Action**
  - Drug Target Selection
- **Stratification**
  - Patient Selection
  - Dose Selection
- **Enrichment**
  - Safety Assessment
  - Efficacy Assessment

**Basic Research**
- Molecular Pathways Leading to Disease
  - Preclinical Safety Assessment
  - Mechanism of Action
  - Dose Selection

**Prototype Design or Discovery**
- Preclinical Development

**Preclinical Development**
- Clinical Development
  - Phase 1
  - Phase 2
  - Phase 3

**Clinical Development**
- FDA Filing/Approval and Launch

- **Selection**: Galactomannan
- **Safety**: Hepatic aminotransferases
- **Response/Efficacy**: HIV viral load
- **Monitoring**: Hepatitis C virus ribonucleic acid (HCV-RNA)

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BIOMARKERS USED AS OUTCOMES

Conventional approach:

• Measures performance of novel therapies using clinical outcomes, such as mortality or disease progression.
• Accruing enough information for clinical endpoints may take many years.

Biomarker-driven approach:

• Biomarkers can sometimes predict drug efficacy more quickly than conventional clinical endpoints.
• Potential to accelerate product development in certain disease areas.
Examples of Biomarkers Used as Outcomes in Development of FDA-Approved New Molecular Entities (NMEs) and New Biological Therapeutics (October 2007 to December 2015)

<table>
<thead>
<tr>
<th>Therapeutic Area</th>
<th>Biomarker</th>
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<tbody>
<tr>
<td>Anesthesiology</td>
<td>T1*; magnitude of T4/T1* ratio by acceleromyography</td>
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<tr>
<td>Cardiology</td>
<td>Blood pressure</td>
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<td>Serum low-density lipoprotein (LDL-C)</td>
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<td>Hematology</td>
<td>Hemoglobin</td>
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<td>Platelet count</td>
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<td>Ecarin clotting time; activated partial thromboplastin time; thrombin time; activated clotting time; plasma diluted thrombin time</td>
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<td>Serum ferritin</td>
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<td>Infectious Disease</td>
<td>Hepatitis C virus (HCV) RNA*</td>
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<td>Human immunodeficiency virus (HIV)-1 RNA</td>
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<td>Sputum culture conversion to negative</td>
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<td>Parasite count resolution</td>
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BIOMARKER QUALIFICATION PROGRAM

• **Concept:** CDER developed the Biomarker Qualification Program to make biomarker data publicly available by establishing a biomarker’s value for a particular context of use in drug development and regulatory review.

• **Regulatory implication:** No need to resubmit extensive data and request that the CDER review group reconsider or reconfirm the biomarker.