Seamless Cancer Drug Development Paradigm

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The Historic Paradigm – Can it be Enhanced?

Drug Discovery and Development Timeline

- **Drug Discovery**
  - ~ 5,000 – 10,000 Compounds
  - 3 – 6 Years
  - IND Submitted

- **Preclinical**
  - 250

- **Clinical Trials**
  - Phase 1
    - 5
    - 20–100
    - 6 – 7 Years
  - Phase 2
    - 100–500
    - 6 – 7 Years
  - Phase 3
    - 1,000–5,000
    - 6 – 7 Years

- **FDA Review**
  - NDA Submitted
  - 0.5 – 2 Years

- **Scale-Up to Mfg.**
  - ONE FDA-APPROVED DRUG

- **Post-Marketing Surveillance**
  - INDEFINITELY

Courtesy of the American Association of Cancer Research 2011 Cancer Progress Report
3 Ways to Add Efficiencies to Drug Development

1) Innovative Trial Designs & Operation
2) Development & Regulatory Coordination
3) Enhanced Public Policy
Innovative Trial Designs & Operation

• Several novel clinical trials have employed methodologies designed to make transition between phases of research less distinct (Adaptive designs, Phase 2/3 trials)

• Standing trial networks can make the conduct of trials more seamless by not having to launch each new study from scratch

• In order for research networks to be successful, they need to access community sites and have trials that are actually interesting to patients

• Examples:
  • Lung-MAP: Incorporates genetic screening into a master protocol to identify patients that match to different sub-studies based on biomarker expression
  • I-SPY2: Utilizes an adaptive randomization design to identify active investigational drugs, potentially paired with biomarkers predictive of response
  • GBM-AGILE: Research network to create standards-based end-to-end systems solutions for biomarker discovery, development and delivery
Enhanced coordination can help make development processes and regulatory review more seamless particularly for treatment regimens that involve different products from different FDA Centers.

FDA Oncology Center of Excellence included in the Cancer Moonshot and included in 21st Century Cures Initiatives.

Intended to reflect the current state of multi-modal interventions in cancer treatment.

Organize clinical aspects in a more patient-oriented approach rather than a product-oriented approach.
Development & Regulatory Coordination (Cont.)

• Validation & Utilization of Common Tools
  • Patient Reported Outcomes
    • Development and validation of a PRO adds a layer of complexity to any development program
    • Use of a previously validated tool that can be applied in multiple settings can provide valuable information with less logistical burden (i.e. NCI PRO-CTCAE)

• Proactive Trial Planning – Exploratory Randomized Trials
  • Randomized Phase 2 studies can be used to make “go/no-go” decisions
  • If a notable effect is seen in a small study, questions arise about the need for additional studies
  • Pre-specifying thresholds and plans to expand the patient cohort when unanticipated activity is seen can help ensure confidence in the result without necessarily requiring a brand new trial.
Enhanced Public Policy

• Successful policy needs to be reflective of current science

• This was the premise behind the Breakthrough Therapy Designation
  • When large treatment effects early in development are observed, a new approach is needed
  • The Breakthrough Program is public policy that is operationalizing seamless development
  • 441 total requests for Designation
  • 145 requests granted
  • 46 Breakthrough Therapies approved
Enhanced Public Policy (cont.)

• 21st Century Cures Initiative
  • Recently passed the House and the Senate and funding for Year 1 has been provided through the Continuing Resolution
  • Contains Several provisions that will enhance more streamlined development
    • Accelerate Approval Development Plans – Enhanced communication for use of surrogate endpoints
    • Biomarker Qualification – Process for validating new biomarkers
    • Hiring and Retention – Improved mechanisms to help FDA attract top talent

• PDUFA
  • Renews FDA authority to collect user fees – needs passed by Sept 30, 2017
  • Will provide funding for several projects related to 21st Century Cures
  • Will provide specific funding to support use of the Breakthrough Designation