The Drug Development Paradigm in Oncology: Concluding Remarks

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Historical Context and Rationale for Change

- Traditional phased drug development paradigm
  - Primarily cytotoxic cancer therapies

- What is different now?
  - Rapid progress in cancer research has led to better biological understanding of disease, more and better characterized drug targets, new drug classes with better therapeutic indexes
  - Biomarkers to better characterize patient populations
  - New sources of data and analytical methods (RWE)
  - Supportive regulatory environment with broader authority
  - Recognition of the importance and urgency of addressing cancer among many stakeholders

- How can we capitalize on these changes moving forward to improve the drug development process?

Goals of a New Oncology Drug Development Paradigm

- Features of a new paradigm
  - Patients at the center of the paradigm
    - Clinically meaningful endpoints, PROs
  - Learning throughout the entire continuum of the drug development process, not just individual trials
  - Focus on learning and confirming (sequentially and/or in parallel) rather than artificial phases
  - Efficiency (rather than speed) in drug development
    - Avoid waste (failing late, me-too drugs)
    - Recognition that there is risk both in moving too fast and too slow
  - Fit-for-purpose
    - Utilize the right study at the right time with the right data sources to address the question at hand
    - Balance rigor in study design with flexibility to adapt to new information
  - Improved collaboration and information sharing among all parties

Challenges

- Aligning culture and science
  - Culture within a company (early/late development teams), within industry, within academia, within government, and across all stakeholders typically driven by clinical/business opportunity, competitive landscape, risk-tolerance

- Zeal to move quickly, but cannot forget first principles of drug development
  - Understanding basic science (biology and target) as well as the drug (pharmacology, formulation, structure/function relationship, dosing, PK and PD)

- Determining the level of confidence in information about a drug to make key decisions across drug development process

- Biomarker/diagnostic development lags behind therapeutic development

- Numerous endpoints in oncology, each with challenges

- Conducting post-marketing research difficult in U.S. health care system

Strategies to Advance Oncology Drug Development

- Regulatory approaches aligned with a new paradigm (flexibility, enhanced communication, adaptations, consideration of unmet need, striking signals, etc)

- Incentives for investigators & sponsors to spend more time at earlier phases of drug development; will improve both safety and effectiveness in intended use population

- Modeling for dose finding, combination strategies may improve efficiency and precision

- New imaging approaches for in vivo assessment of drug-target interactions and anti-tumor effects

- Use of real world data and evidence as appropriate to clinical question and regulatory need

- Broaden eligibility criteria and consider how to learn from expanded access experiences

- Clinical trial design considerations
    - Invest up-front time in determining the appropriate design
    - Minimize waste (common control arm designs)
    - Leverage innovations (master protocols, adaptive features, expansions)
    - Recognize randomized designs are usually the most informative but not always required

Next Steps

- Ongoing analysis of the impact of current policies on oncology drug development (21st Century Cures, Moonshot, PDUFA, PMI, etc)

- More emphasis on data standardization, quality (biomarkers/diagnostics, RWE)

- Focus on the disease context (role of RT, surgery, combinations in treatment)

- Opportunities to better align culture and science of drug development

- Reducing silos across the learning lifecycle

- Consider appropriate design and timing (pre- vs post-market) of confirmatory studies

- Drug development is inherently risky and the drug development paradigm is essentially about managing uncertainty in the context of unmet medical need and business opportunity.