American Association for Cancer Research Annual Meeting 2016

Early-Phase Expansion Cohort Trial Design in the Development of Future Oncology Products

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Disclosure Information

- I have no financial relationships to disclose
- I will not discuss off label use and/or investigational use in my presentation

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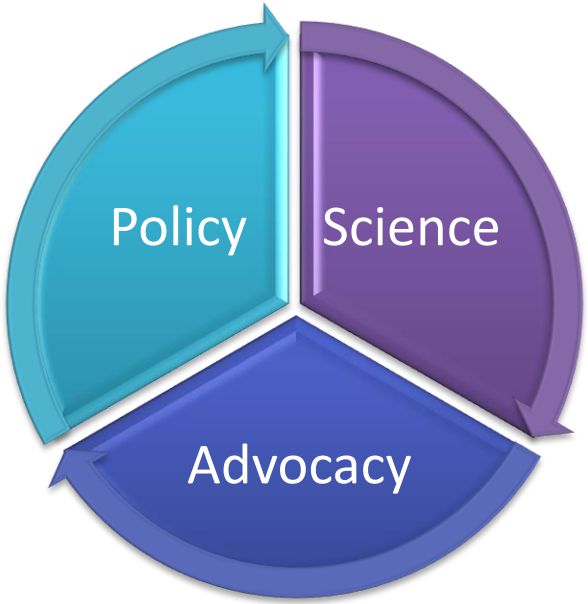
Accelerating the Pace of Innovation

Washington, DC-based Think Tank & Advocacy Organization

A unique model to create a path to better drug development and approval through **scientific**, **regulatory**, and **legislative solutions**.

Develops groundbreaking partnerships:

- Federal Agencies (FDA, NIH, NCI)
- Academic Research Centers
- Professional Societies
- Industry
- Advocacy Organizations



Demand for Accelerated Progress

Better drugs + continued unmet need = desire for more efficient drug development and increased patient demand for access to new therapies.

- Breakthrough Therapies
- Increased pressure for access to clinical trials
- “Seamless” drug development

Seamless Drug Development - Opportunities

- Speed and efficiency:
  - Pembrolizumab development through expansion cohorts let to approval less than 4 years after FIH studies – win for patients.
- Ability to ask very specific, discrete questions:
  - Dose comparison
  - Biomarker development
  - Study patient populations that are typically excluded from adult cancer clinical trials

Modernizing Eligibility Criteria

- Joint Friends-ASCO-FDA Workshop May 12 at ASCO headquarters
- Identify scientifically and medically appropriate opportunities to expand eligibility criteria in cancer clinical trials
- Four working groups focused on specific traditional exclusion criteria:
  - Organ dysfunction
  - HIV/AIDS
  - Brain metastases
  - Pediatric populations
- Expansion cohorts are an under-utilized opportunity to study these patients

Seamless Drug Development - Concerns

- Are there adequate patient safety protections?
- Are the objectives clear and supported by a strong rationale?
- When is this type of approach appropriate?
- What kind of oversight is needed?

ISSUE BRIEF

Conference on Clinical Cancer Research
November 2015

The Blurring of Phase 1, 2, and 3 Trials in Oncology: Expansion Cohorts in Phase 1 Trials

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Aman Buzdar, MD Anderson Cancer Center
Keith Flaherty, Massachusetts General Hospital Cancer Center
Elizabeth Garrett-Mayer, Medical University of South Carolina
Percy Ivy, National Cancer Institute
Geoffrey Kim, FDA Office of Hematology and Oncology Products
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Introduction

With the advent of more effective drugs to treat some forms of cancer has come a desire for greater efficiency in drug development. Particularly in situations where clear benefit is being observed for conditions that otherwise lack satisfactory treatment options, the traditional stepwise approach to drug development may not always be appropriate. The potential benefits of moving away from this paradigm

- When does a trial move beyond “Phase 1”?
- What are the study plan expectations?
- What is the appropriate form of oversight?
- How can FDA-Sponsor interactions be improved?

What is meaningful oversight?

- At what point is additional oversight needed?
  - When is a “Phase 1” trial no longer really a phase 1 trial?
- Who is responsible for this oversight?
  - DSMB/DMC – external, unbiased – but takes time to assemble
  - Steering committee – includes study investigators
- What do they review?
  - Safety – can coordinate response to safety signals across cohorts
  - Should efficacy data also be monitored?

Thoughtful Drug Development

- Find the right balance between speed and caution
- Not every drug is a breakthrough, and not every product with a breakthrough designation will prove to be a clinical advance
- Keep the needs of both current and future patients in mind