What is the Role of Non-Profit Organizations in Clinical Trials?

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Ellen V. Sigal, PhD
Chair & Founder, Friends of Cancer Research

“Nothing About us Without Us”

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The Roles of the Patient Community In Drug Development Go Far Beyond Funding

• Patients are uniquely equipped to identify critical gaps and unmet needs in their disease areas, and to advocate for and develop collaborative solutions to meet those needs
  – Advocacy – advocate not only for appropriations but for a strong regulatory environment equipped with the resources and scientific expertise it needs to keep up with cutting edge technologies
  – Policy – speak to what patients need to accelerate new tools and treatments to market and contribute scientific expertise to policymaking process
  – Regulatory – the patient perspective is vital in the assessment of benefit/risk and development of FDA guidances to ensure that meaningful therapies are advanced
  – Science – patient groups can help develop resources, such as registries, that are vital for continued research
Non-profit Organizations and Foundations

- Lead the scientific and clinical agenda for the field
  - Focus funding for cutting-edge translational science on those projects that fill critical gaps in approaches to research and treatment
  - Force collaboration and accountability of the research community
- Priorities are driven by the needs of patient members, such as:
  - Development of biomarkers for diagnosis/assessment of therapeutic efficacy
  - Development of patient reported outcomes
- Provide/facilitate additional resources such as bio-banks and patient registries
- Examples:
  - Melanoma Research Alliance, The Leukemia & Lymphoma Society, Chordoma Foundation, Pancreatic Cancer Action Network, Castleman Disease Collaborative Network and many more...

Promoting Research through Legislation

- Prescription Drug User Fee Agreement (PDUFA) – originally passed in 1992; allows FDA to collect fees from drug manufacturers to fund the review of new drugs
  - Re-authorized every 5 years – each re-authorization represents an opportunity for the adoption of new legislation to improve or modernize components of the drug development and review process
  - 2012 re-authorization - the Food and Drug Administration Safety and Innovation Act (FDASIA) - included many provisions developed by advocacy groups
- Example: Kids V Cancer – founded in 2009 to overcome the barriers to pediatric cancer research and drug development
  - Authored and championed the Creating Hope Act, a component of FDASIA, which created a market-based incentive (transferrable priority review vouchers) to spur pediatric cancer drug development
21st Century Cures Act

- A landmark bi-partisan initiative by Rep. Fred Upton (R-MI) and Rep. Diana DeGette (D-CO) of the House Energy & Commerce Committee
- Aim to develop legislation that accelerates basic science discoveries, streamlines the drug and device development process, and facilitates the use of digital medicine and social media for treatment delivery
- Represents a unique opportunity for patient groups to weigh in on legislation affecting NIH and FDA policy
  - Held multiple committee meetings and roundtables across the country to hear expert testimony and solicit ideas and feedback from the patient community
- Some provisions included in draft bill released late January, 2015:
  - Optimize the collection of patient experience data by patient advocacy groups
  - Improve the expanded access process for investigational therapies
  - Streamline the review of supplemental indications for marketed therapies

Promoting Research by Contributing to the Science

- Example: Multiple Myeloma Research Foundation
  - Sequenced the entire MM genome in collaboration with the Broad Institute and TGen
  - Established the Multiple Myeloma Research Consortium to accelerate early phase clinical trials – a clinical network of 16 institutions which has advanced >20 compounds through trials
  - MMRC also established a tissue bank and IT system to facilitate collaboration
- Example: Stand Up to Cancer (SU2C)
  - Brings together brightest minds in different fields of cancer research in order to create “Dream Teams” - multi-institutional groups of scientists who work collaboratively, rather than competitively, to develop new treatments quickly. Innovative Research Grants support groundbreaking cancer research projects that are high-risk but could also be high-impact, and have the potential to significantly affect patient care.
Promoting Research through Regulatory Policy

- FDA’s Patient Focused Drug Development Program
  - a provision of FDASIA which aims to more systematically gather patients’ perspectives on their condition and available therapies to treat their condition
  - Series of disease-focused meetings being held that represent an opportunity for patients and advocacy groups representing patients to have their voices heard how FDA approaches review of new drugs in their disease area
- FDA Guidances
  - describe the agency’s interpretation of or policy on a regulatory issue
  - represent another opportunity for non-profit patient groups to effect regulatory change
  - Example: Parent Project Muscular Dystrophy – drafted guidance in 2014 to help accelerate development and review of potential therapies for Duchenne muscular dystrophy
  - encourages the FDA and trial sponsors to engage patients and their families at all stages of trial development and to take into account what they consider acceptable risk in clinical trials

Promoting Research through Venture Philanthropy

- Disease-focused non-profits can provide financial, intellectual, and human capital to for-profit biotechnology firms to help enable, de-risk, and ultimately accelerate the development of new therapies, particularly targeted therapies for rare diseases.
- Re-invest resulting funds into further research
- High involvement by donors with their grantees
- Examples:
  - Cystic Fibrosis Foundation - work with Vertex Pharmaceuticals led to discovery and approval of Kalydeco for rare subsets of cystic fibrosis
  - Alzheimer’s Drug Discovery Foundation - partners with Merck, Pfizer, and others. Funded early research that led to the FDA approval of Amyvid, a diagnostic test for Alzheimer’s disease.
  - Michael J. Fox Foundation for Parkinson’s Research - has provided funding, research tools, networking, and clinical trial recruitment assistance to nearly 225 pharmaceutical-industry projects.
Promoting Research through Public-Private Partnerships

- Non-profit organizations funded and operated through a partnership of government and the private sector
- Foster goal-oriented collaboration and bring an array of resources and perspectives to bear on high priority research projects.
- Examples:
  - Reagan-Udall Foundation – mission is to help FDA to modernize medical product development, accelerate innovation, and enhance product safety
  - Critical Path Institute – aim to develop pre-competitive drug development tools to accelerate the pace and reduce the cost of drug development
  - Foundation for the NIH – identifies and develops opportunities for innovative collaborations between industry, academia, and the philanthropic community to support the mission of the NIH
  - CDC Foundation - helps CDC pursue innovative solutions to priority public heath challenges by providing funding, expertise, and connections, so that CDC experts have the flexibility to quickly and effectively connect with the right partners, information and technology

Reagan-Udall Foundation Projects

- Innovation in Medical Evidence and Surveillance (IMEDS) Program
  - Developing tools, methodology, and a robust electronic healthcare data platform to support post-market evidence generation on regulated products
- PredicTox
  - Building a pilot study with a multitude of partners to use systems pharmacology models to predict and better understand the mechanisms of cardiotoxicity resulting from specific classes of cancer drugs
- Critical Path to Tuberculosis Drug Regimens
  - A global initiative launched by the Bill and Melinda Gates Foundation, the Critical Path Institute, and the TB Alliance to accelerate the development of new tuberculosis (TB) multidrug regimens.
  - RUF’s role is to aid in the development and qualification of new regulatory science tools and pathways that improve and facilitate TB drug regimen development.
Examples of Critical Path Institute Projects

- **Predictive Safety Testing Consortium**
  - brings together pharmaceutical companies to share and validate innovative safety testing methods under advisement of the FDA and its counterparts, the EMA (European Medicines Agency), and PMDA (Japanese Pharmaceutical and Medical Devices Agency)

- **Patient-Reported Outcome Consortium**
  - collaborative framework that develops qualified and publicly available PRO instruments for use in clinical trials in order to support labeling claims

- **Multiple Sclerosis Outcome Assessments Consortium**
  - Created jointly with the National Multiple Sclerosis Society, MSOAC will collect, standardize, and analyze data about MS with the goal of qualifying a new measure of disability as a primary or secondary endpoint for future trials of MS therapies.

Examples of Foundation for the NIH Projects

- **Alzheimer's Disease Neuroimaging Initiative (ADNI)**
  - tracks normal, mildly cognitively impaired, and Alzheimer’s disease brain changes to measure the progression of Alzheimer’s and identify prognostic biomarkers (with National Institute on Aging)

- **I-SPY2**
  - a groundbreaking phase 2 screening clinical trial in breast cancer that used an adaptive trial design in which early patient outcomes inform treatment assignments for subsequent trial participants (with FDA, NCI, many cancer centers)

- **Biomarkers Consortium**
  - endeavors to discover, develop, and qualify biomarkers to support new drug development, preventive medicine, and medical diagnostics (with NIH, FDA, PhRMA, BIO)

- **Lung-MAP**
  - A multi-drug, multi-arm, biomarker-driven registrational clinical trial for patients with advanced squamous cell lung cancer (with FDA, NCI, SWOG Cancer Research, Friends of Cancer Research, several pharmaceutical companies)
CDC Foundation

• Global Disaster Response Fund
  – Support CDC’s Response to the West African Ebola Outbreak

• Viral Hepatitis Action Coalition
  – A collaborative initiative aimed at improving prevention, screening and treatment of viral hepatitis

• Global Tobacco Surveillance System
  – CDC Foundation supports the work of CDC, the World Health Organization (WHO), and other international partners in implementing select components of GTSS.
  – GTSS is comprised of several surveys on tobacco usage and provides globally standardized data to track adult and youth tobacco use prevalence and trends across the world.

Roles of Non-Profit Groups May Evolve Over Time

• Friends of Cancer Research
  – Founded in 1996 to increase public awareness and support for cancer research and for increased scientific capacity across all federal health agencies
  – Began by holding educational “town halls” across the US, with leaders from science, industry, academia and key members of Congress in order to educate lawmakers and create new champions for biomedical research
  – Work with all sectors and hold public policy forums to develop collaborative approaches to accelerate the translation of research into treatments for patients
  – Worked with Congress and Federal agencies to establish the Office of Oncology Drug Products at FDA – focusing reviewers by disease type rather than molecule type

• Where are we today?
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

Friends - Regulatory Guidance Development

- How can two novel drugs intended for use in combination be developed?
  - Cancer cells may have numerous molecular alterations resulting in uncontrolled growth and the ability to evade normal death signals
  - Combinations of 2 or more drugs that target different pathways may be more effective than single agents alone
- 2009 Conference on Clinical Cancer Research, with the Center for Healthcare Reform at the Brookings Institution, brought key experts together to discuss:
  - What information should regulatory authorities require about the contribution of each agent?
  - What trial designs are appropriate for testing of new drugs in combination
- Strategies proposed in this meeting led directly to the development of an FDA Guidance for Industry
The 2011 Conference included a panel entitled: Development Paths for New Drugs with Large Treatment Effects Seen Early.

This panel proposed scientific strategies to ultimately expedite FDA approval for a drug showing dramatic responses in the early stages of development while maintaining drug safety and efficacy standards.

This led to the Breakthrough Therapy Designation

- Goal 1: Expedite drug development process for products that show remarkable clinical activity early
- Goal 2: Minimize the number of patients exposed to a potentially less efficacious treatment
**Distinguishing Features of Breakthrough Designation**

- **Expedited Development Program**
  - Shortened Review; Rolling Submission
  - Full or Conditional Approval

“All hands on deck” mindset – collaborative effort by senior FDA staff

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**Getting Breakthrough Therapies to Patients**


  - “Breakthrough Therapy” designation received public endorsement from FDA, industry and academia.

- In the spring of 2012, the bipartisan *Advancing Breakthrough Therapies for Patients Act* was introduced by Senators Michael Bennet (D-CO), Orrin Hatch (R-UT) and Richard Burr (R-NC) and Representatives Diana DeGette (D-CO) and Brian Bilbray (R-CA).
Friends – Integrating Modern Science into Clinical Trial Designs

- 2012 Conference evaluated the feasibility of developing a Master Protocol registration trial for non-small cell lung cancer

- **Challenges in traditional clinical trials:**
  - Each potential new therapy is typically tested independently from other therapies seeking to treat the same condition
  - For every new trial, the protocol must be reviewed by a number of oversight entities
    - New phase III trials requires an average of 36 administrative or regulatory approvals and averages more than 2 years
    - Approximately 4% of adult cancer patients enroll in clinical trials
      - Inability to meet accrual goals is a frequent factor causing trials to close - wasting time, money, and limited patient resources
  - New therapies molecularly targeted against specific mutations may be present in only a fraction of the patient population
Benefits of a Master Protocol

- **Enrollment Efficiency**: Grouping these studies under a single trial reduces the overall screen failure rate.
- **Operational Efficiency**: single master protocol can be amended as needed as drugs enter and exit the study.
- **Consistency**: every drug entered into the trial would be tested in the identical manner.
- **Predictability**: if pre-specified efficacy and safety criteria are met, the drug and accompanying companion diagnostic will be approved.
- **Patient Benefit**: offers the advantage of bringing safe and effective drugs to patients sooner than they might otherwise be available.

Design of a Disease-Specific Master Protocol

2012 Friends/Brookings Conference on Clinical Cancer Research
http://www.focr.org/events/design-lung-cancer-master-protocol
S1400 Master Protocol
Unique Private-Public Partnerships with the NCTN

S1400 Master Lung-1 Protocol

Common Broad Platform
CLIA Biomarker Profiling*

Target: PI3K
Target: CDK4/6
Target: HGF
Non-match

PI3Ki CT* Cdk4/6i CT* HGFi+E E* Anti-CTLA-4 CT*

Endpoint (Interim PFS)
PFS/OS

TT=Targeted therapy, CT=chemotherapy (docetaxel or gemcitabine), E=erlotinib
*Archival FFPE tumor, fresh CNB if needed
Conclusion:
Non-profit patient groups are no longer just funders for, but partners in research

- Keeps the patient voice in translational and clinical research to ensure that meaningful studies are designed to meet patient needs
- Partnership is essential: only by working together can the promise of biomedical research be fully realized in the form of safe and effective treatments for patients