CTTI Patient Groups and Clinical Trials: Building the Value model

Matthew Harker
CTTI Associate Director, Projects
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Clinical trials in crisis
Addressing This Need

To identify and promote practices that will increase the quality and efficiency of clinical trials

Public-Private Partnership involving all stakeholders 60+ members
A New Rx for Medicine

Fed up with slow drug trials, cancer patients need faster treatments.

By RON WINSLOW

PERSONALIZED MEDICINE: How redesigning a clinical trial can speed drug development

Traditional clinical trial

Takes essentially all patients with a disease being studied and is typically intended to eliminate differences in patient characteristics that could bias measures of drug effectiveness.

New trial design

Uses genetic profiles to highlight "biomarker" differences among patients and to match drugs to patients with biomarkers that predict a benefit.

PHASE II

Randomized or non-randomized trials. In a randomized trial, about 60 patients are put in two groups: One receives the experimental drug and the other serves as a control group. In a non-randomized trial, about 40 patients receive the experimental drug.

PHASE III

If a drug graduates to phase II, it typically takes 3,000 patients and about three years to determine if it is safe and effective enough for approval.

HISTORIC SUCCESS RATE

30% to 40%

PHASE III

Researchers expect that drugs graduating from phase II can be tested with 300 patients selected according to genetic profiles found to respond to the drug in phase I. It is hoped that this will shorten the time to approval.

PROBABILITY OF SUCCESS

85%

Source: Donald Berry, M.D., Anderson Cancer Center

Goal: smaller, focused phase III
Moving risk and failure back = Value

Today: Bigger is better (closer to approval)

Need to move risk and failure back

Risk of Failure
Continuum of Patient Advocacy Organizations

Examples of Advocacy Outreach & Linkage

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<thead>
<tr>
<th>Patient Support:</th>
<th>Research:</th>
<th>Public Influence:</th>
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<tbody>
<tr>
<td>Provide medical, psychosocial support to patients &amp; families</td>
<td>Patient Decision Support</td>
<td>Trial Matching</td>
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<td>Caregiver Support</td>
<td>Trial Education</td>
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<td>Care Navigation</td>
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<td>Funding Patient Expenses</td>
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<td>Newsletter/Email</td>
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<tr>
<th>Education &amp; Information:</th>
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<tr>
<td>Inform &amp; Educate about risks, screening, disease &amp; treatment &amp; quality of life issues</td>
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<table>
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<th>Research:</th>
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<td>Involved in shaping the research agenda, oversight of the research process, &amp; starting new initiatives</td>
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<th>Political Activity:</th>
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<td>Influence elected/regulatory bodies about reimbursement, research funding, patient needs/access, legislative issues</td>
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<td>Legislation Development</td>
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PG Engagement Across the Research and Development Continuum

Building a model to evaluate impact

- Direct funding and fund raising for research or product development
- Natural history database/registry support
- Help define eligibility criteria within the study protocol
- Feedback on meaningful clinical endpoints
- Assist in creating the informed consent form
- Advise on study recruitment
- Accompany sponsor to FDA to advocate study design

- Direct funding and fund raising for trial operations support
- Network recruitment / outreach
- Serve on a Data Safety Monitoring Board
- Report on patient feedback regarding sites, investigators, and study participant experience

- Natural history database / registry support
- Provide feedback on how the patient community views results
- Help return study results to participants
- Write newsletter articles or blog about results
- Co-present results
- Serve on post-market surveillance initiatives

Pre-Discovery

- Interest of research question to patient community
- Provide data on unmet need and therapeutic burden
- Direct funding and fund raising for research or product development
- Understanding mechanisms of action relevant to disease and symptom burden

Pre-Clinical

- Network recruitment / outreach
- Direct funding and fund raising for research or product development
- Infrastructure support
- Provide input on study design (barriers to participation)
- Support trial awareness and recruitment
- Peer advocate during informed consent procedure

Phase 1

- Serve on FDA advisory committees
- Provide testimony at FDA hearings
- Feedback on meaningful clinical endpoints

Phase 2/3

- FDA review & approval

PAS/Outcomes

*Adapted from Parkinson's Disease Foundation materials for CTTI's Patient Groups & Clinical Trials Project*
### PG Engagement Across the Research and Development Continuum

**Building a model to evaluate impact**

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<th>Phase 2/3</th>
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<th>PAS/Outcomes</th>
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*Adapted from Parkinson’s Disease Foundation materials for CTTI’s Patient Groups & Clinical Trials Project*
Reports generated by Patient-focused meetings will help inform drug Benefit-Risk Assessments

Use of Benefit-Risk Assessment Framework in drug review
Meetings might stimulate longer-range development of new patient-focused outcome measures for a specified disease area.

Patients identify important dimensions of benefit not adequately captured in current studies; need for PRO tool(s).

Patient input on effectiveness & tolerability of currently available therapy (unmet medical need).
Issues Around Engagement

Key sectors of the research community have identified a gap in knowledge and understanding about how and when to best interact with patient groups (PG) around clinical trials;

What is the defined value of engagement in economic terms that can resonate and be partnered with sponsors;

Industry based terms of expected Net Present Value, and Probability of Technical and Regulatory Success

Solution: CTTI project creating the value proposition and model – Initial conceptual model then possible plug-n-play tool
PGCT Workstream 2 Project Team Members

Team Leaders
- Eric Eisenstein (Duke)
- Ken Getz (Tufts CSDD)
- Bennett Levitan (J&J)

CTTI Staff
- Bray Patrick-Lake (project manager)
- Kimberley Smith (project assistant)
- Matthew Harker (former team lead Duke)

Team Members
- Joseph Dimasi (Tufts CSDD)
- Sharon Hesterlee (Formerly Parent Project Muscular Dystrophy, now Myotonic Dystrophy Foundation)
- Jim Kremidas (CenterWatch)
- David Leventhal (Pfizer)
PGCT Project Objectives (WS2)

1. Assess value proposition and impact of patient groups on clinical trials

2. Build model to quantify tools and metrics of PG engagement in the traditional medical product development life cycle
Methods

Using the “CTTI PG Engagement Lifecycle” conceptual model, financial models will be developed to illustrate possible impact on the probability of trial success with metrics.

Quantify ability to quantify impact and value of patient groups in CT development.

Outline and test best practices of determining clinical trial success in both regulatory and market metrics.
Timing of **Industry** Engagement with PG

*Choose all that apply*

- 80% at Phase III
- 62% at Phase IIA
- 35% at Phase I/Proof of concept
- 15% at Discovery/Pre-clinical
Top Barriers to Engagement Cited by Industry

- 40% Insufficient tools for identifying/engaging relevant PGs
- 40% Unsure how to engage with PGs
- 36% Internal resistance/lack of buy-in
- 33% Lack of Funding
- 21% Lack of sophistication of PGs
Building an Economic Model

Net Present Value (NPV)

Language of Business realities/constraints

Evaluation of opportunities/investment

\[ NPV = CF_0 + \sum_{i=1}^{n} \frac{CF_i}{(1 + r)^i} \]

Data Inputs:

Revenue Inputs:
- “Patient flow”
- Product adoption
- Price of therapy
- Length of therapy
- Number of episodes per year
- Reduced Discounting
- Sales time (Patent)
- 1st to market

Cost Inputs:
- Development
- Sales Force
- Pre-launch marketing
- Post-launch marketing
- Costs of goods sold
- NDA application
- Milestone payments

RISK

NPV decision making by industry and investment partners

Sharon Hesterlee provided, CTTI team additions
Possible Impact of Engaging PG’s Earlier on NPV

Increasing PG engagement reference points could

Decrease

- Launch time
- Cost of CTE

Leverage assets → De-risk investment

*Above graphic is based on “Considerations of net present value in policy making regarding diagnostic and therapeutic technologies” by Califf et al.*
Break apart the different paths towards success and failure

- Circles represent studies or other key risky events
  - Branches indicate success or failure of the event
- Success of one event brings the opportunity to attempt the next
  - Definition of success generally based on study protocol, target product profile, good clinical practices

Diagram:
- Phase 2: Succeed or Fail
  - Succeed leads to Phase 3
  - Fail leads to Development fails
- Phase 3: Succeed or Fail
  - Succeed leads to Regulatory Approval
    - Succeed leads to Treatment launched
    - Fail leads to Development fails
Including Technical and Regulatory Risk

- Characterize the technical uncertainty of each event with probabilities of success (POS or PTS)
- Several means to assess probabilities
  - Benchmarks
  - Company history
  - Subjective assessments
  - PK/PD modeling

Probability technical and regulatory success (PRTS)

Prob: 11%
Help finalize eligibility criteria within the study protocol; Assist in creating the informed consent form;

- **Impact on valuation**
  - Easier to obtain patients → increased rate of enrollment → shorter studies
  - Improves cost, timing, operational risk and intangibles (patients benefit earlier, reputation boost)

Need to talk with patient early

![Decision Tree Diagram]

- **Phase 2**
  - Succeed: 40%
  - Fail: 60%

- **Phase 3**
  - Succeed: 60%
  - Fail: 40%

- **Succeed**
  - Regulatory Approval: 90%
  - Fail: 10%

- **Prob NPV ($MM)**
  - 11%: 300
  - 1%: -45
  - 16%: -40
  - 60%: -3

DIA DEVELOP INNOVATE ADVANCE
PG Engagement Across the Research and Development Continuum

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# How Patient Group Engagement Impacts Value Drivers

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Main drivers of treatment valuation are cost, revenue, timing, risk and intangibles;
- Impact of PGs can be variable in each spectrum

Expected NPV modeling can account for most drivers in a clear and well-accepted summary metric to bridge sponsors and patient group interest;

Patient engagement activities impact on most drivers for treatment valuation;
- Create formal definitions
- Model tool for negotiations and partnership building

Characterize driver impact to support sponsor decisions to increase patient group engagement in trial development, especially in earlier phases.
Thank You

To identify and promote practices that will **increase the quality and efficiency** of clinical trials

Public-Private Partnership involving all stakeholders

60+ members

*Join the conversation #DIA2015*