Clinical Trials and YOU

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Disclosure

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   Future Pipeline Discovery
   Research & Development

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   Board of Directors

The content of this talk and the views expressed are those of JC and do not necessarily reflect the views or position of my employer GSK. This talk is about clinical trials and will not discuss GSK products or specific clinical research projects.
Introduction

• Thanks to the PBCers organization

• My objectives for this talk
  • Broad topic
  • Selected aspects with a patient focus

• Understanding clinical trials
  • The process of determining if a candidate medicine is safe and effective for the disease being treated
  • In many ways trials are the end-game

• Personal perspective
  • HUGE responsibility to many stakeholders
    • Patients waiting for a cure
    • Patients considering or have participated in earlier trials
    • Researchers who have worked tirelessly to advance candidate
Drug development is not for the faint of heart

<table>
<thead>
<tr>
<th>Metric</th>
<th>Estimates*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avg. time to develop a drug</td>
<td>10-15 years</td>
</tr>
<tr>
<td>Avg. cost to develop a new drug</td>
<td>1.2 to 2.6 billion USD</td>
</tr>
<tr>
<td>Est. success from discovery to human CTs</td>
<td>~1 in 5000 (~10%)</td>
</tr>
<tr>
<td>Est. success from early trials to approval</td>
<td>~1 out of 5 (~20%)</td>
</tr>
</tbody>
</table>

*Cost and times depend on many variables

Phase 3/submission Failures 2007-2010 (120 drugs)

- Efficacy 64%
- Safety 27%
- Other 9%
- Unknown 4%

U. Nitin Kashyap et al *J Pharm. Sci. & Res.* 5(6), 2013, 131 – 136; *Pharma Profile 2013 Tufts center for the study of drug development, 2014*
Cost of Drug Development
The drug discovery moon-shot

We can fund 20 space missions for the cost of developing a single drug.
Clinical trials (CT)

- Human research that determines if a drug is both safe and effective for its intended use

- A clinical trial almost never stands alone
  - Part of a clinical development program
  - Detailed pre-defined plan
  - Regulatory checks along the way

- Goal is to estimate Risk/Benefit
  - Risk/benefit is assessment of safety and efficacy
  - Other currently available treatments
  - Severity of the condition for treatment

- Rare disease presents special considerations that can impact risk/benefit

- It’s (still) all about the data
Phases of CTs

Phase 1
• Safety focused; usually in healthy volunteers (without disease)
• Small # participants, dose-finding, first-time in human

Phase 2
• Safety and effectiveness in patient population
• Larger, dose-ranging and vs. comparator (placebo)

Phase 3
• Efficacy and safety in intended population
• Larger than Ph2, comparator (Standard of care and/or placebo)
• Pivotal

Phase 4
• Testing an approved drug for a different disease, population or dose, etc.
Key roles in a CT

- Patient/Participant/Subject/Volunteer
- Sponsor – commonly pharma
  - Multiple functions in concert
  - Sponsor is defined as ‘holder’ of the Investigational New Drug Application (IND)
- Principal Investigator (PI) – leads site team & medical oversight
  - Study Coordinator
  - Pharmacy
- Institutional Review Board (IRB)
- Regulatory Authority- FDA
- Personal Health Care providers
- Patient advocates
- Caregiver
Key CT elements

- Informed consent (ICF)
- Clinical protocol
  - Pre-specified instructions for clinical trial
  - Comprehensive
  - Part of a Clinical Development Plan (CDP)
- Investigational New Drug Application (IND)
  - Pre-IND meeting with FDA
  - End of Phase 2 meeting
- New Drug Application (NDA)
- Publication (Paper, Manuscript or other dissemination)
Informed consent (IC)

• Purpose and elements
  • Explain the **reason** for the trial
  • Investigational medicine being studied
  • The **time commitment** involved (# of visits and duration)
  • Procedures that will be done at each visit
  • Chances of receiving the Investigational drug or comparator
  • Who may see your data and how it will be used
  • Potential risks and/or benefits of participation
  • Your rights pertaining to your participation and your data

• Important document to understand
  • PI or designee is required to make sure it is fully understood
  • The IC is also an agreement to participate and comply
Special topics

• Clinical trial controls – comparison?
  • Demonstrate Investigational Drug works as intended
  • Need to compare to something (Risk/Benefit)
  • FDA expectation

• Randomization & blinding – minimize bias & confounders
  • Single vs. double-blind

• Rare disease clinical trials
  • Differences – mostly on sponsor side
  • How they are not different

• Can a clinical trial be stopped?
  • Safety Monitoring Committee or Data Safety Monitoring Board
  • Interim analysis - futility

• Compensation
  • Personal expenses
  • Injury

• Dissemination of results
  • Regulatory, professional & public
Risk/Benefit

The risk/benefit equation differs

1. Regulators - FDA
2. Provider – patient welfare
3. Patient – quality of life
   • Especially true in rare disease
   • Emphasis on the patient perspective
   • Endpoints that are clinically meaningful
   • Endpoints that improve functional outcomes, reduce disease burden or improve quality of life
# Online information sources

<table>
<thead>
<tr>
<th>Source</th>
<th>Sponsor</th>
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</thead>
<tbody>
<tr>
<td>Clinical trials.gov</td>
<td>FDA/NIH</td>
</tr>
<tr>
<td>CenterWatch</td>
<td>Corporate</td>
</tr>
<tr>
<td>FDA Websites</td>
<td>FDA</td>
</tr>
<tr>
<td>Patient Advocacy Groups</td>
<td>Private</td>
</tr>
<tr>
<td>Pharma websites</td>
<td>Corporate</td>
</tr>
<tr>
<td>NORD</td>
<td>National</td>
</tr>
</tbody>
</table>

- Critically read & compare
- Know source of information
- Access multiple sources
  - Look for differences
- Discuss with trusted family, friends & colleagues
- Talk with others who have participated
- Consult your PCP and specialist
- Research development drug and other options

*Very important to consult your own physician(s) to discuss the risks and benefits of YOUR clinical trial participation*
Key online resources

ClinicalTrials.gov - Official Site
https://clinicaltrials.gov
ClinicalTrials.gov is a registry and results database of publicly and privately supported clinical studies of human participants conducted around the world.

Search
Search Tips and Examples: You can enter a word or a phrase, such as the name of a ...

For Researchers
For Researchers. ClinicalTrials.gov is a registry and results database of publicly and ...

Home
ClinicalTrials.gov is a registry and results database of publicly and privately supported clinical studies of human participants conducted around the world.

How to Search - Selected Publications

Find Studies
Find Studies. The Find Studies section of this site describes the options for finding studies ...

For Patients & Families
For Patients and Families. The ClinicalTrials.gov Web site provides current ...

Study Record Managers
For Study Record Managers. Clinical studies are registered on ClinicalTrials.gov via a ...

Why Register
Why Should I Register and Submit Results? Contents. What Is the Purpose of Trial ...

Learn About Studies
Learn About Clinical Studies Contents. What Is a Clinical Study? Clinical Trials; ...
Patient Advocacy Resources

Home - PBCers.org

The PBCers Organization is a wonderful source of education and support for those who suffer from Primary Biliary Cholangitis (originally Primary Biliary Cirrhosis) and other autoimmune liver diseases. Formed December 1, 1996, the PBCers is the largest PBC online support group worldwide.

We offer our members:

• PBC E-mail Daily Digest
• Facebook & Twitter
• Family & Friends E-mail Group
• Find a Doctor
• Local PBC Groups
• Partners & Other Links
• Patient Registry

2018 Clinical Trials
ClinicalTrials.gov (Search) ClinicalTrials PBC
Arena Pharmaceuticals
Genefit Corp
Target Pharma Solutions

Clinical Trials PBC
CymaBay Therapeutics
Genkyotex
Zydus Healthcare
Thank you

Acknowledgements
  • PBCers
  • GlaxoSmithKline
  • Patients

Questions & answers
Back-up
<table>
<thead>
<tr>
<th>Key terms</th>
<th>Definition</th>
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<tr>
<td>Protocol</td>
<td>Comprehensive and detailed instructions for a clinical trial</td>
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<tr>
<td>Randomized</td>
<td>A way of removing bias in a trial by randomly assigning treatments and entry</td>
</tr>
<tr>
<td>Blinded vs. open-label</td>
<td>Double vs. Single-blind</td>
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<tr>
<td>Control (placebo vs. comparator)</td>
<td>RCT</td>
</tr>
<tr>
<td>Informed consent</td>
<td>Patient document that explains trial and agreement to participate</td>
</tr>
<tr>
<td>Phase</td>
<td>Pre-defined in protocol</td>
</tr>
<tr>
<td>Primary endpoint</td>
<td></td>
</tr>
<tr>
<td>Sponsor</td>
<td>Medical oversight and responsible for conduct</td>
</tr>
<tr>
<td>Investigator (PI)</td>
<td></td>
</tr>
<tr>
<td>Patient, participant, subject</td>
<td></td>
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<tr>
<td>Investigational drug</td>
<td></td>
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<tr>
<td>Investigational New Drug Application (IND)</td>
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<tr>
<td>Regulatory Authority (In US –FDA)</td>
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<tr>
<td>Biomarker</td>
<td></td>
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<tr>
<td>Natural History</td>
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<tr>
<td>New Drug Application (NDA)</td>
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<tr>
<td>Standard of Care</td>
<td>The current best medical practice for treatment</td>
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<tr>
<td>Pivotal trial</td>
<td>A trial intended to support regulatory approval</td>
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<tr>
<td>Good Clinical Practice (GCP)</td>
<td>quality standard that is provided by ICH that govt.’s use to set clinical research standards</td>
</tr>
<tr>
<td>International Conference on Harmonization (ICH)</td>
<td>International harmonized guidelines for global drug development</td>
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Drug development takes a long time and is a process of attrition.

<table>
<thead>
<tr>
<th>Stage</th>
<th>Number of Volunteers</th>
<th>Duration</th>
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<tbody>
<tr>
<td>Pre-Discovery</td>
<td>5,000 - 10,000</td>
<td>3-6 Years</td>
</tr>
<tr>
<td>Drug Discovery</td>
<td>250</td>
<td>6-7 Years</td>
</tr>
<tr>
<td>Clinical Trials</td>
<td>5</td>
<td>6-7 Years</td>
</tr>
<tr>
<td>FDA Review</td>
<td></td>
<td>0.5-2 Years</td>
</tr>
<tr>
<td>LG Scale MFG</td>
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<tr>
<td>Phase IV: Post-Mark</td>
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</tbody>
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Topics

• Clinical trials – nuts and bolts
  • The drug development journey
  • Types and phases of clinical trials
  • It’s all about the data

• It takes a village
  • Pharma perspective
  • Patient perspective
  • Risk vs. Benefit

• Limitations and challenges

• Importance and benefits

• So you want to be in a clinical trial?
  • Consentig process
  • What to know & what to ask

• Information resources
  • Know the source
  • Prioritize
  • Consult your physician