GBS | CIDP Foundation International

Speaker Series Summary Episode 14: How New Treatments are Found: What is Drug development?

Overview

In this Speaker Series episode, we talked with Rebecca Aune, Director of Education Programs, and Hayley Mason, Policy Analyst, at the National Organization for Rare Disorders (NORD). This Speaker Series Summary will dive into the drug development process along with the factors and people that influence it.

Summary

What is Drug Development?	**The process of creating a drug to cure or greatly reduce the effects or symptoms of a condition** **5 Stages of Drug Development** 1. Discovery and Development: understanding a disease 2. Pre-Clinical Research: testing, including animal testing 3. Clinical Research: human testing 4. FDA Review Process: evaluating a drug's safety, effectiveness, and if the benefits outweigh its risk 5. Post-Market Safety Monitoring • About 1 in 5,000 treatment candidates will be approved while only 14% of drugs in the clinical trial step will be FDA-Approved. • It takes about 314 million to 2.8 billion dollars for a drug to be approved
Discovery and Development Stage	In this stage, researchers first identify "targets", such as a specific protein or gene that could be changed in order to improve a person's wellbeing. Then they will work with substances like chemicals or compounds that impact this "target". If there isn't a substance that can impact this "target", scientist will work to create a new substance or change the "targets" they are trying to impact. **Risk-Benefit Ratio:** Even if a new treatment is promising, the risks and tradeoffs cannot outweigh its benefits.

What makes rare disease drug development different?	• Narrow patient population that researchers have to connect to • Limited research in rare disease overall • Funding for rare disease research can be more limited • Limited pre-existing understanding of a disease or the pathways in the body that is impacted by the disease • Some rare diseases do not have biomarkers making the diagnosis process harder • Researchers sometimes have to start from scratch because of the limited funding, small population, cost to research, lack of pre-existing data, etc. • Many clinical trials need original designs

The Beginning Steps to Developing a New Drug	Understanding the biology of the disease is typically accomplished by two types of studies:
	• Natural History Studies
	  ◦ A research study that tracks a group of people with the same disease over time to understand how a disease develops. The ultimate goal of a Natural History Study is to assist current research that can determine the best avenue of treatment of the disease.
	• Patient Registry Data
	  ◦ A research study that tracks the medical history of people with a specific condition over time. The foundation's registry is self-reported by all participants.
	
	Steps to developing new drugs:
	1. Scientist will gather as much information as they can to find a "target" to improve.
	2. They will find a substance that will improve these targets and select a Lead Candidate Compound, or the more promising compounds.
	3. Scientist will work to improve this compound to have fewer side effects and last longer in the body
	4. This compound is experimented on in pre-clinical trials and then will move to animal testing to determine its safety and effectiveness.
	5. Clinical trials will start with a small population and then move to a larger population.
	6. The FDA will monitor and regulate clinical trials even before the approval process.

Drug Repurposing	Many times, scientist will research drugs that already exist to treat a different disease in the hopes that it can help improve the symptoms of another condition. For example, Viagra is used to help pulmonary arterial hypertension. In rare diseases, drug repurposing can also lead to more off-label drugs, meaning a drug is used differently from the disease for which it was FDA approved.

How does basic research get funded and how can we support it?	1. Government Grants 2. Investors and Venture Capitalist 3. Corporate Donations 4. Universities/Academic Centers 5. Patient Advocacy Groups/Foundations Patients can help by 1. Donating or fundraising for patient advocacy groups 2. Joining Patient Registries or Natural History Studies 3. Advocating for elected officials to prioritize rare disease research and support from government agencies like the NIH Much of the advocacy we do at Capitol Hill is to increase the amount of money available for GBS, CIDP, and MMN research.
Who initiate clinical trials and who oversees them?	After scientists find promising research in the Pre-clinical research stage, a team of medical professionals, FDA employees, and researchers work to ensure the drug's safety. Drug Sponsors, or the company that makes the drug, will put together a clinical trial team to enroll patients or healthy volunteers. This team will establish a plan of action that determines how the trial will be conducted, what data the drug sponsor needs, and how to make the process more properly made, fair, and ethically sound. The FDA will monitor clinical trials even before the approval process to ensure that the trial meets their standards through reports and inspections. Then Drug sponsors will also use their regulatory staff to help navigate the drug governing process.
What does the typical FDA employee look like?	• Lawyers • Doctors (MD/PhD) • Statisticians • Research Scientists
Patient's role in the Clincal Process	Patients are partners in the research process and will receive care and oversight from physicians. 1. Patients must give consent by signing an informed consent form that explains the trial's risks, how the trial works, whether it is placebo or randomized, etc.

Patient's role in the clinical process (contin.)	2. The trial will then randomize assigned patients to 3 categories ◦ Standard care of treatment: Patients will stay on their same treatment ◦ Placebo: Patients are given a pill without the active drug like a sugar pill ◦ Experiential: Patients are given the drug being tested Patients do not know what group they are in, but patients always have the right to withdrawal from a trial because participation is always voluntary. If a patient does not react will to the experimental drug, patients will be put on emergency treatment, known as rescue protocol. To participate in a clinical trial, patients must talk to their doctor about getting enrolled.
Patient Diversity	The FDA wants to promote diversity in clinical trials and has framed a plan to reduce discrimination by race, ethics, gender, and financial status in two ways: 1. Decentralization a. Doctors can collect data rather than have patients go to a big institution to be monitored b. In some cases, physicians can monitor and collect data for patients who cannot travel 2. Diversity Action Plan a. Drug Sponsors need a diversity action plan to enroll historically underrepresented populations in clinical trials The goal is to meet patients where they are and mitigate cost
How does AI and Big Data change the clinical process?	AI can: • Help scientists in the discovery phase as a superpowered search engine to find compounds that treat "targets" and ultimately speed up the discovery phase process • Run computer simulations to see how a drug will affect the body before the clinical trial starts • Make the Drug Repurposing process easier • Help pre-screen patients for testing • Help tweak issues in the trial to find the strongest way to gather data and spot failures ◦ Saves time and money that would be used on drugs stats that do not work • Collect and analyze data from wearable devices during the trial • Can look through insurance claims to see how a drug is helping patients in everyday life Examples: Alphafold predicts how proteins can affect the body Exscientia can find chemical compounds and have actually helped drugs get to the trial phase faster than other drugs

Once the clinical trial is completed	Researchers analyze data and determine if the drug is safe, effective, and if the benefits outweigh its risks Then the FDA Approval process starts: 1. Drug Sponsors will put all their data in a New Drug Application (NDA) or Biologics License Application (BLA) with information on the treatment a. These applications will show how the drug is used, manufactured, and its potential risks 2. The FDA examines all the evidence provided and will request more data, if needed, to understand its effectiveness and safety 3. The FDA will either decline or approve the drug Patients can always educate the FDA on the lack of treatments, what success means, and what burdens would be released from new treatments whether physical, social, or familial. Early engagement with drug sponsors and the FDA can result in improved drug designs and increased trust between patients and organizations. We are always looking for volunteers to do patients panels like our Externally Led Patient Focused Drug Development meetings (ELPFDD) and Patient Listening Session (PLS) with the FDA.
Role of the Government	Regulation, Funding, and Policy • Shape drug development process with regulation and funding ◦ FDA regulates Drugs ◦ NIH provides funding for research ◦ US patent and trademark office provides patents that last 20 years to prevent another drug of the same composition to treat the same condition What does Congress do: • Create and pass legislation that encourages drug development, like the Orphan Drug Act which: ◦ Provides a 25% tax credit, waiver for drug application, a 7-year exclusivity market cap (no one can make the same drug and have it approved), and provides a priority review voucher for the next drug that the drug sponsor makes ▪ This priority review voucher reduces approval process from 10 months to 6 months ▪ This voucher can be sold to other companies

Realistic Timeline to Approval	Clinical trials testing treatments for non-rare diseases can take 10-15 Years Through programs like Continuing Research, Fast Track, and Breakthrough Design, rare disease trials can take 5-10 years Drugs approved in times of crisis and have a confirmatory trial after its approval to ensure its safety and effectiveness. HIV treatments are an example of a faster approval timeline.
Advice for the Community	• Learn more at NORD's Free Drug Development Webinar • Join patient registries • Join ELPFDD and PLS meetings • Explore Clinical Trials • **Do not underestimate the power of your story**

Relevant Resources

Learn more about our Patient Registry

The Foundation's Research Portal

Clinicaltrials.gov

NORD's Free Drug Development Webinar