Drug Discovery and Development [1]

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Doctors and scientists are always looking for better ways to care for people with cancer. To do this, they are constantly creating and studying new drugs. Also, they are looking for new ways to use existing drugs.

A drug goes from being an idea in the lab to something that a doctor prescribes. To do this, it must go through an extensive development and approval process to make sure it effectively treats cancer. Also, it must be safe for people to take. This process often takes many years and significant resources. However, depending on the drug, the actual amount of time and money required varies.

Preclinical research: drug discovery and initial testing

The discovery of new cancer drugs happens in a variety of ways.

- **Accidental discovery.** In the early 1940s, an explosion exposed sailors to poisonous mustard gas. Doctors observed that these sailors developed low white blood cell counts. As a result, they began using nitrogen mustard (mechlorethamine [Mustargen]) to treat Hodgkin lymphoma [3]. This is a cancer of the lymphatic system involving the white blood cells. Nitrogen mustard is still a cancer treatment used today. Accidental discoveries such as this are rare, though.

- **Testing plants, fungi, and animals.** Paclitaxel (Taxol) treats several types of cancer and was first found in the bark of the Pacific Yew tree. More recently, a primitive animal

called a sea sponge was used to create the drug eribulin (Halaven). The National Cancer Institute (NCI) has samples of thousands of plants, marine organisms, bacteria, and fungi. They were collected from around the world in the hopes of finding new cancer treatments.

- **Studying the biology of cancer cells.** Most researchers who are creating cancer drugs start by comparing the genetics found in DNA and cellular processes of cancer cells to healthy cells. This identifies important steps in the cancer growth process that a drug could possibly fix. For example, researchers learned that about 20% of all breast cancers have an abnormal amount of a certain protein. It is called HER2 and controls the growth and spread of cancer cells. Four drugs were created to target HER2: trastuzumab (Herceptin), lapatinib (Tykerb), pertuzumab (Perjeta), and ado-trastuzumab emtansine (Kadcyla). Now, a person with breast cancer has the tumor tested to check for HER2 to find out if these drugs can treat the cancer. Learn more about these targeted treatments [4].

- **Understanding the chemical structure of a drug target.** Scientists may use computers to mimic how a potential drug interacts with its target. This is similar to fitting two puzzle pieces together. Using details from the computer models, researchers can then design chemical compounds that interact with the specific drug target.

Once drugs are created, researchers test them on human tumor cells in the lab to see if they stop the growth of cancer cells. Next, they test the drug in animals to confirm it is still effective at treating cancer. Researchers test the drug in two or more animal species. Testing in animals helps researchers learn how the body uses the new drug. Also, it shows what side effects the drug may cause and what dose of the drug to use in human research trials.

Drug developers and sponsors

The U.S. Food and Drug Administration (FDA) does not develop or test drugs. Instead, drug companies work to discover and test new drugs. Other organizations also do this, such as university medical centers and some government agencies (for example, the NCI). The sponsor is the group that develops a drug. It conducts the research needed for the FDA to approve the drug.

Clinical research: testing in people

Before new drugs are tested in people, the sponsor must submit an Investigational New Drug (IND) application to the FDA. The IND provides important information about the research already done and future research plans, such as:

- Preclinical studies done in the laboratory and in animals

- Plans for clinical trials in people
- How the new drug is made

The FDA approves potential drugs for testing in people if the research shows that the drug is likely to work and be safe. Approval also depends on whether the proposed clinical trials are designed correctly and if the drug can be made the same way every time.

Clinical trials are research studies involving volunteers that assess whether a new drug is safe, effective, and better than the current (standard) treatment. There are usually three phases of a clinical trial [5]. Each following phase involves a larger number of patients and provides more detail about the new drug's safety and effectiveness. Clinical trials frequently take years to complete and may involve hundreds or thousands of patients.

Clinical trials follow a risk-based approach. Earlier phases focus on safety, dosing, and how the body processes the drug. Later phases center on how well the drug works. Later phases include a larger group of clinical trial volunteers. Learn more about clinical trials [6].

Clinical review and FDA approval

If the clinical trials are successful, the drug sponsor submits a New Drug Application (NDA) to the FDA. The NDA requests approval of the drug for physician prescribing. It contains results from the preclinical and clinical studies and details about how the drug will be made and labeled. Also, it includes the drug’s possible side effects and any interactions with food or other drugs.

The FDA may approve the drug if the evidence shows it is effective and safe for use. No drug is completely safe or free from side effects. However a drug is known to be suitable for use if the benefits of taking it outweigh the possible risks.

Post-approval research and post-marketing surveillance

Once a drug receives FDA approval, it is ready for market and can be prescribed by doctors and sold to patients. However, the FDA may require that the sponsor conduct more clinical trials (phase IV trials) to look for other possible side effects or to confirm the benefits of the treatment. Also, the new trials may study the drug in different doses, new combinations, or in different schedules. New trials may also study the treatment in new patient groups, such as older adults or children, or assess its long-term effects. Some drug makers may conduct their own phase IV trials. They may perform new research to gain FDA approval to use the drug in a new way, such as for another type of cancer.

The FDA also monitors the safety of drugs currently on the market and ensures that drug makers report any new or serious side effects to the FDA. The FDA may withdraw a drug from the market if new research suggests it is not safe or effective.

More Information

Drug Approval and Labeling [7]

Video: What are Clinical Trials, with Richard Goldberg, MD [8]

Video: Types of Cancer Clinical Trials, with Louis Weiner, MD [9]

Video: Clinical Trials and Safety with Eric Singer, MD, MA [10]

Patient Safety and Informed Consent [11]

Additional Resource

FDA: Drug Development and Approval Process [12]

Links
[1] http://www.cancer.net/research-and-advocacy/introduction-cancer-research/drug-discovery-and-development
[2] http://www.cancer.net/about-us
[3] http://www.cancer.net/node/31271
[4] http://www.cancer.net/node/24729
[5] http://www.cancer.net/node/24880
[6] http://www.cancer.net/node/24863
[7] http://www.cancer.net/node/24506
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[11] http://www.cancer.net/node/24879
[12] http://www.fda.gov/Drugs/DevelopmentApprovalProcess/default.htm