

The drug development process

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OVERVIEW



- **Drug Discovery**
- **Pre-Clinical Testing**
- **Phase I Clinical Trials**
- **Phase II Clinical Trials**
- **Phase III Clinical Trials**
- **Phase IV**

GENERAL PRINCIPLES



THE DECLARATION OF HELSINKI

GOOD CLINICAL PRACTICE GUIDELINES

Drug Discovery



- A hypothesis for a mechanism of treatment/mode of action
- Develop compounds
- 1 of 10,000 reach the market

Pre-Clinical Testing



- Animals
- Toxicity
- Pharmacokinetics: absorption, distribution, metabolism, excretion

Clinical trials on humans



- Phase I-IV (1-4)
- Randomized clinical trials (RCTs)
- Comparator: placebo (usual care) or existing drugs
- Efficacy: selected populations/ideal test situation (phase II-(III))
- Effectiveness: real world populations (phase III- phase IV)
- Efficiency: "cost effectiveness", (phase IV)
- Several years
- Approval: FDA, EMA, countries
- Reimbursement: countries

Phase I



- Healthy subjects (20-100?)
- Determine bioavailability.
- Side effects associated with increasing doses: safety, tolerability, pharmacokinetics, pharmacodynamics
- Early evidence/hint on effectiveness (not powered for that)
- Duration: (weeks) – months
- Costs: 100,000 – 1 mill US\$

Phase II



- Randomized
- Efficacy in treating a particular disease or medical condition
- Safety and side effects are monitored.
- 100-300 patients (or more – phase IIb)
- Duration: months-year(s)
- Cost: 10-100 million US\$

Phase III



- 500-3,000 patients
- Often Multicenter – multi country sites
- Duration: 6 months - 2 years (or more)
- Cost: \$10-500 million
- Confirm efficacy/effectiveness and safety of drug
- Basis for approval process
- Reimbursement (?)

Phase IV



- Post-approval/post marketing studies
- Long term effects
- Observational, non-interventional trials in a naturalistic setting (non-RCT)
- Effectiveness and safety monitoring
- Registry studies (simulated RCTs)
- Cost effectiveness ?

Shorten the process?



- Process takes years.....
- Conditional/stepwise approval/adaptive pathways?
- Disease modifying drugs in AD?



THE END