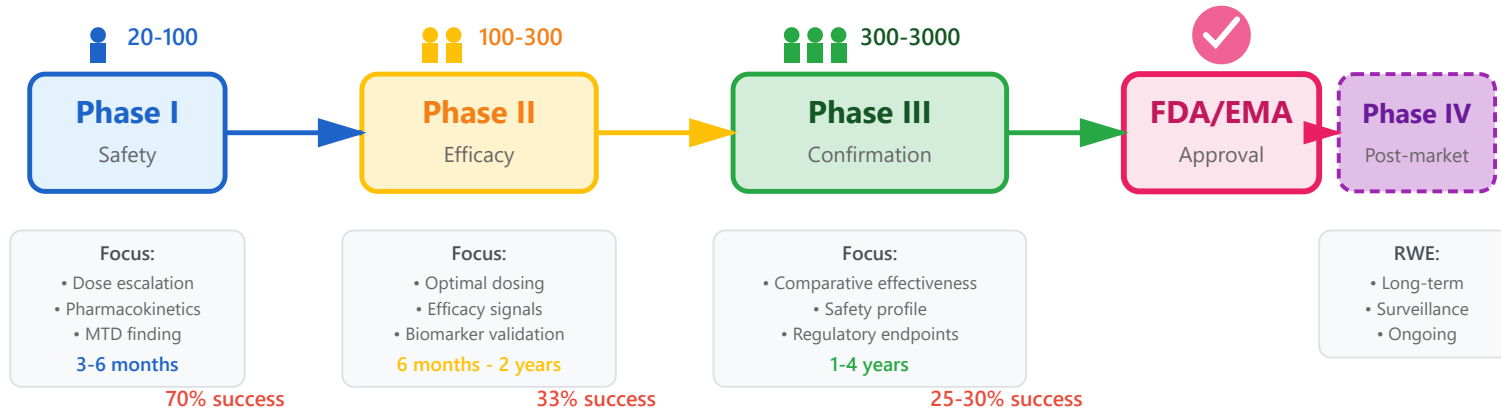


Clinical Trials



Biomarker Strategies

- Patient selection
- Response monitoring
- Surrogate endpoints
- Precision medicine

Adaptive Trials

- Dose finding
- Sample size re-estimation
- Seamless phase transition
- Bayesian approaches

Real-World Evidence

- EHR data mining
- Claims analysis
- Registry studies
- Digital biomarkers

Total: 10-15 years, \$1-3 billion

Biomarker Strategies in Clinical Trials

Overview

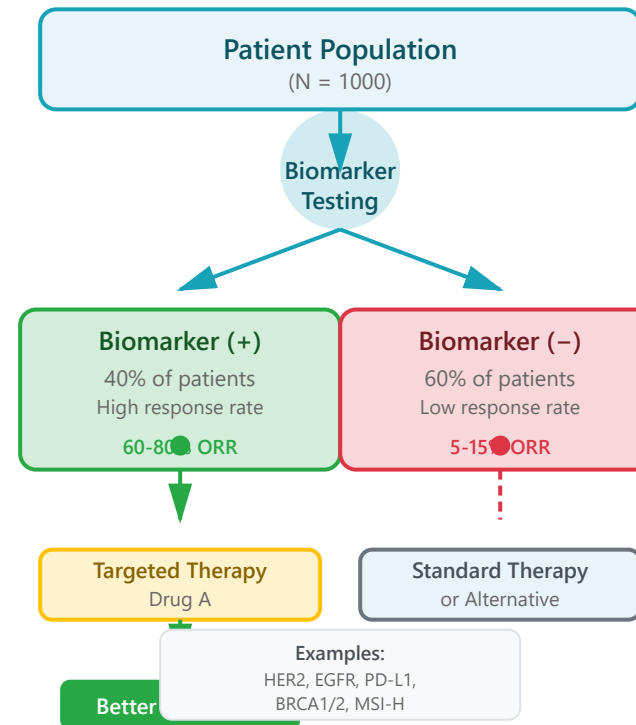
Biomarkers are measurable indicators of biological states or conditions that guide clinical decision-making throughout drug development. They enable precision medicine by identifying which patients will benefit most from specific treatments.

Key Applications

- **Patient Selection:** Identify patients likely to respond based on molecular profiles (e.g., HER2+ breast cancer, EGFR+ lung cancer)
- **Response Monitoring:** Track treatment efficacy through circulating tumor DNA, protein markers, or imaging biomarkers
- **Surrogate Endpoints:** Use validated biomarkers as early indicators of clinical benefit to accelerate approvals
- **Dose Optimization:** Achieve target drug exposure or pharmacodynamic effects

Clinical Impact: Biomarker-driven trials reduce failure rates by 30-40% and decrease development timelines by 1-3 years through better patient stratification.

Biomarker-Guided Trial Design



Adaptive Trial Designs

Overview

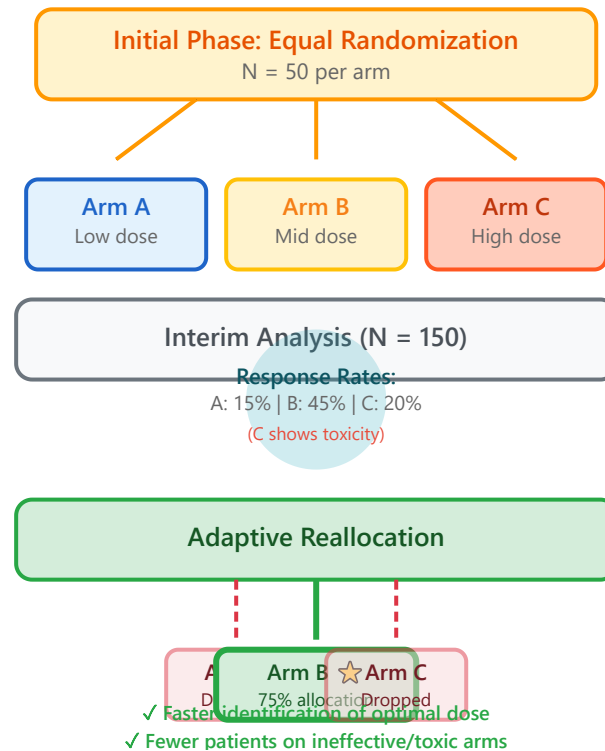
Adaptive trial designs allow modifications to ongoing trials based on accumulating data, making clinical development more efficient and ethical by responding to interim results in real-time.

Key Features

- **Dose Finding:** Identify optimal dose through model-based adaptive randomization (e.g., continual reassessment method)
- **Sample Size Re-estimation:** Adjust enrollment based on observed treatment effects to ensure adequate power
- **Seamless Phase Transition:** Combine Phase II/III into single protocol with interim go/no-go decisions
- **Arm Dropping:** Eliminate poorly performing treatment arms early
- **Bayesian Methods:** Incorporate prior knowledge and update probabilities continuously

Efficiency Gains: Adaptive trials can reduce development time by 20-40% and patient numbers by 15-30% compared to

Adaptive Randomization Design



Real-World Evidence (RWE)

Overview

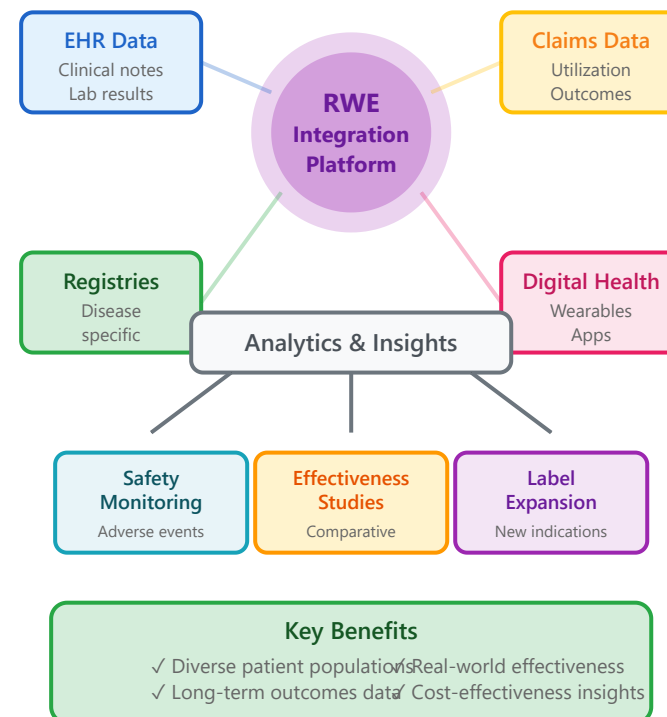
Real-World Evidence leverages data from routine clinical practice to complement traditional clinical trials, providing insights into drug performance in diverse, real-world populations and practice settings.

Data Sources & Applications

- **Electronic Health Records (EHR):** Comprehensive patient histories, treatment patterns, and outcomes from millions of patients
- **Claims/Administrative Data:** Large-scale healthcare utilization, costs, and population-level outcomes
- **Patient Registries:** Disease-specific longitudinal data for rare conditions and long-term safety
- **Digital Health Data:** Wearables, mobile apps, and remote monitoring for continuous patient insights
- **Post-market Surveillance:** Detect rare adverse events, drug interactions, and long-term effects

Regulatory Impact: FDA and EMA increasingly accept RWE for label expansions, safety assessments, and in some cases,

Real-World Evidence Ecosystem



efficacy endpoints—reducing need for additional RCTs.

Comparative Overview: Modern Clinical Trial Approaches

Approach	Primary Goal	Key Advantages	Challenges
Biomarker Strategies	<ul style="list-style-type: none">• Higher success rates• Smaller trial sizes needed• Faster approvals• Better patient outcomes• Enables personalized Rx	<ul style="list-style-type: none">• Biomarker validation• Smaller target population• Testing infrastructure• Regulatory complexity• Companion diagnostic	
Adaptive Trials	<ul style="list-style-type: none">• Reduced development time• Flexible, data-driven trial modifications• Efficient dose finding during conduct• Seamless phase transitions• Resource optimization	<ul style="list-style-type: none">• Complex statistics• Regulatory acceptance• Operational complexity• Type I error control• Pre-planning required	
Real-World Evidence	<ul style="list-style-type: none">• Large, diverse populations• Long-term safety data• Real-world effectiveness• Cost-effective research• Rapid hypothesis testing	<ul style="list-style-type: none">• Data quality/completeness• Confounding factors• Selection bias• Causal inference• Privacy/data access	