# Clinical Trials 101: Common Myths and Facts

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# Clinical Trials 101

## What is a clinical trial?

- A clinical trial or study is a research study involving humans to explore whether a medical strategy, treatment, or device is safe and effective.
- **Participation in any clinical trial is voluntary. You have the right to refuse treatment or stop participation at any time.**

## Clinical trials are conducted to:

- assist doctors and researchers in learning more about a disease
- improve health care and outcomes for people in the future
- advance medicine & science
- find better treatment strategies (i.e. new treatments, different ways to use currently approved treatments, study treatments in a new population)
- provide access to new, experimental therapies when no other options are available

# Types of Clinical Trials

**Prevention***
- Prevent a disease in people who never had the disease or prevent from returning or worsening
- Example: HIV vaccine

**Treatment**
- Test new therapeutic approaches: drugs, surgical, or radiation techniques
- Example: targeted therapies for NSCLC patients with biomarker positive tumors

**Screening**
- Test new ways to detect disease
- Example: prostate specific antigen (PSA) levels

**Behavioral**
- Evaluate behavioral changes to improve health
- Example: smoking cessation to prevent cancer

**Diagnostic**
- Study tests or procedures to diagnose disease
- Example: HER2 positive breast cancer

**Quality of Life***
- Examine ways to improve comfort & quality of life for those with illnesses
- Example: tracking negative side effects of a therapy

Interventional studies: tests a drug, medical device, or procedure
*Observational studies: do not include therapies or interventions

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National Institutes of Health, “NIH Clinical Research Trials and You: the Basics”,. https://www.nih.gov/health-information/nih-clinical-research-trials-you/basics, Accessed 7/10/2024

# Phases of Clinical Trials


- Learn about safety/side effects of therapy & determine safest dose
- 20 – 100 participants
- Trial time frame: < 1 year

- Examine effectiveness & continue to study safety of therapy
- 100 – 300 participants
- Trial time frame: few months – 2 years

- Therapy is examined in larger population & compared with similar or standard treatments to confirm effectiveness, monitor side effects,& continue to study safety
- 300-3000 participants
- Trial time frame: 1-4 years

- Continued monitoring of safety & benefits of a treatment after FDA approval
- Several thousand participants
- Trial time frame: many years



National Institutes of Health, “NIH Clinical Research Trials and You: the Basics”,. https://www.nih.gov/health-information/nih-clinical-research-trials-you/basics, Accessed 7/10/2024

# Key Terms Used in Clinical Trials

## Placebo

A product that looks like the new treatment being tested, but does not have any therapeutic value

- Placebos are given with standard of care treatments to compare to the experimental or new therapy. They are not used if it puts patients at risk of not receiving effective therapy.
- You will be informed if a trial uses a placebo before entering the trial
- Some trials allow patients in the placebo group to receive the new therapy later if it works best

## Randomization

Participants enrolled in a clinical trial have treatments randomly assigned to them by chance rather than assigned by choice

- Randomization is necessary in some trials to prevent bias in assigning patients to one treatment or another
- The trial will be stopped if one treatment is found to be highly effective compared to the other, to allow all participants to receive that treatment

## Blinded

Patients and/or the researchers do not know what therapy is being given to each participant to avoid influencing results & ensure accuracy of the data

- Single-blinded: participants do not know the therapy they are receiving but researchers do
- Double-blinded: both participants and researchers are not told which therapy is being given



National Institutes of Health, “NIH Clinical Research Trials and You: the Basics”,. https://www.nih.gov/health-information/nih-clinical-research-trials-you/basics, Accessed 7/10/2024

# What to Expect When Participating in a Clinical Trial

## Prior to Enrollment

### Pre-Screening

Process of identifying individuals who may be eligible for a clinical trial (i.e. patient demographics, cancer type & stage)

### Informed Consent

Explains the purpose & type of clinical trial & how it will be conducted (i.e. length of trial, description of procedures, potential & benefits), what is paid for by the study & costs to the patient, how the data will be used including patient confidentiality, patient rights, contact information when questions arise. A signed form is required prior to participation, acknowledging your understanding of the information.

### Determining Eligibility

Process of confirming whether a patient is eligible to participate in a clinical trial including review of medical history, physical exam, additional tests & procedures.

# What to Expect When Participating in a Clinical Trial

## After Enrollment (example)

| | Screening | Cycle 1 | | | | | Cycle 2 & Beyond | | | | | Off study assessment |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Day | -14 to -1 | 1 | 4 | 8 | 13-27 | 28 | 1 | 4 | 8 | 13-27 | 28 | |
| Experimental medication[a] | | → | | | | | | | | | | |
| Written informed consent | X | | | | | | | | | | | |
| Tumor paraffin block from primary tumor | X | | | | | | | | | | | |
| Medical history | X | | | | | | | | | | | |
| Physical Exam | X | X | | | | | X | | | | | X |
| Vital signs | X | X | X | X | | | X | | | | | X |
| Adverse events | X | X | X | X | X | X | X | X | X | X | X | X |
| CBC w/diff & platelets | X | X | X | X | | | X | | | | | X |
| Liver function tests | X | X | X | X | | | X | | | | | X |
| MUGA scan[a] | X | | | | | X | | | | | | |
| CT scan[b] | X | | | | | | | | | | X | X |

[a]Experimental medication is self-administered at home daily

[b]MUGA scan to be performed within 14 days of enrollment, at end of cycle 1, and then after every 2 cycles while on therapy. A final scan is required as part of the off study assessment, unless the last scan was performed within 28 days of the off study assessment.

[c]CT scan to to be performed within 14 days of enrollment, at end of cycle 2, and then after every 2 cycles while on therapy. A final scan is required as part of the off study assessment, unless the last scan was performed within 28 days of the off study assessment.

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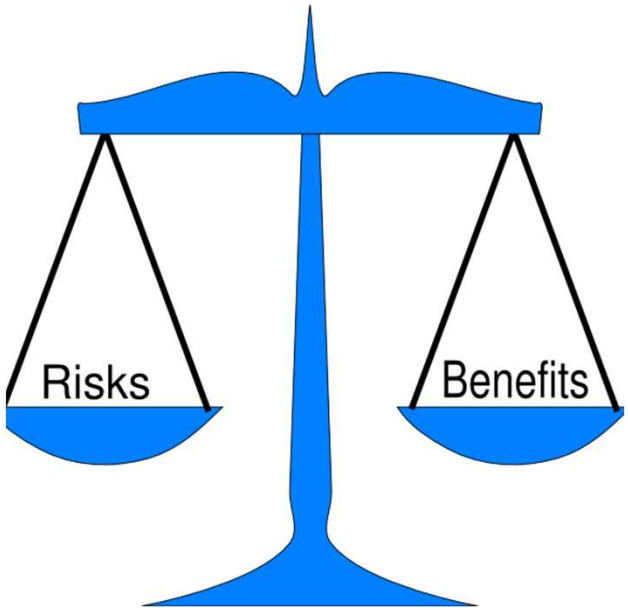
# Potential Risks & Benefits When Participating in a Clinical Trial

## Risks

- The experimental treatment may not be effective for you or other participants
- You may experience unwanted side effects
- Additional testing, appointments, etc. may be required as part of the study
- You may be randomly assigned to receive standard of care therapy and/or placebo

## Benefits

- Access to new, experimental treatments that are not available anywhere else that may be effective
- Your healthcare is managed by a specialized team to provide additional support and help you to keep track of all appointments, tests, and monitor/manage side effects
- Opportunity to learn more about your disease, advance science/medicine, and help others by identifying new treatment strategies



# Examples of Pivotal Clinical Trials That Have Changed How We Treat Cancer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# LANDMARK TRIALS IN LOCOREGIONAL TREATMENT

BREAST SURGERY

NSABP B04

NSABP B06

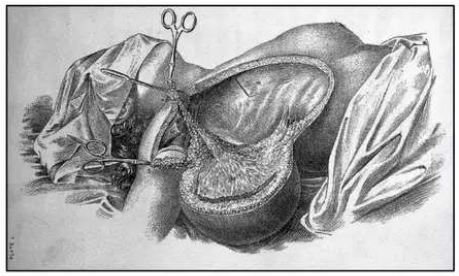
MILAN TRIAL

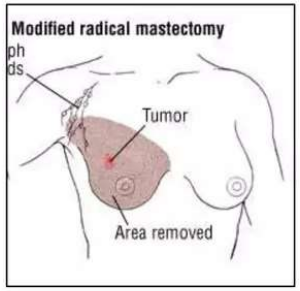
Halsted/ Radical Mastectomy

Total mastectomy + Radiation

Early Breast Cancer patients suitable for BCS

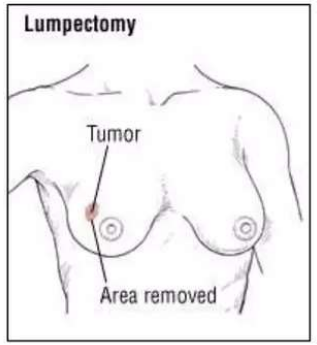
Breast Conservation Surgery + Radiation






Other Mastectomy versus BCS Trials:

- Institut Gustave Roussy (1972-84)
- NCI (1979-87)
- EORTC (1980-86)
- Danish (1983-89)




NSABP B04 and B06 were Phase III randomized trials

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Das, N. (2023) *Landmark trials in treatment of carcinoma breast* [PowerPoint slide]. SliderShare. https://www.slideshare.net/slideshow/landmark-trials-in-breast-cancerpptx-256219071/256219071

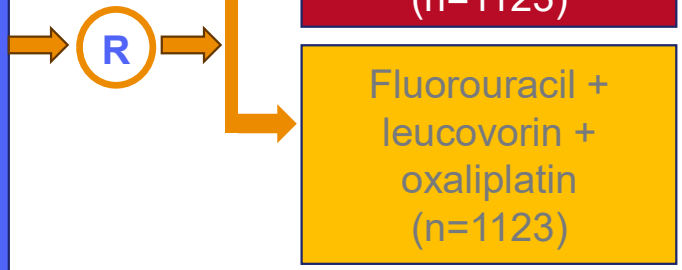
# Phase 3 Trial: Oxaliplatin, Fluorouracil, & Leucovorin as Adjuvant Treatment for Colon Cancer

## Study objective

- Evaluate effectiveness of treatment with fluorouracil, leucovorin plus oxaliplatin in patients with Stage II or III colon cancer in the postoperative setting

Key patient inclusion criteria
- Complete resection of histologically proven Stage II or III colon cancer
- No prior chemo, immunotherapy, or radiation
- Age 18-75

N=2246




**Practice Implications:**

- Adding oxaliplatin to fluorouracil & leucovorin improves the treatment of colon cancer after surgery



Andre T et al. N Engl J Med 2004; 350:2343-2351

# Clinical Trials Focused on Precision Medicine

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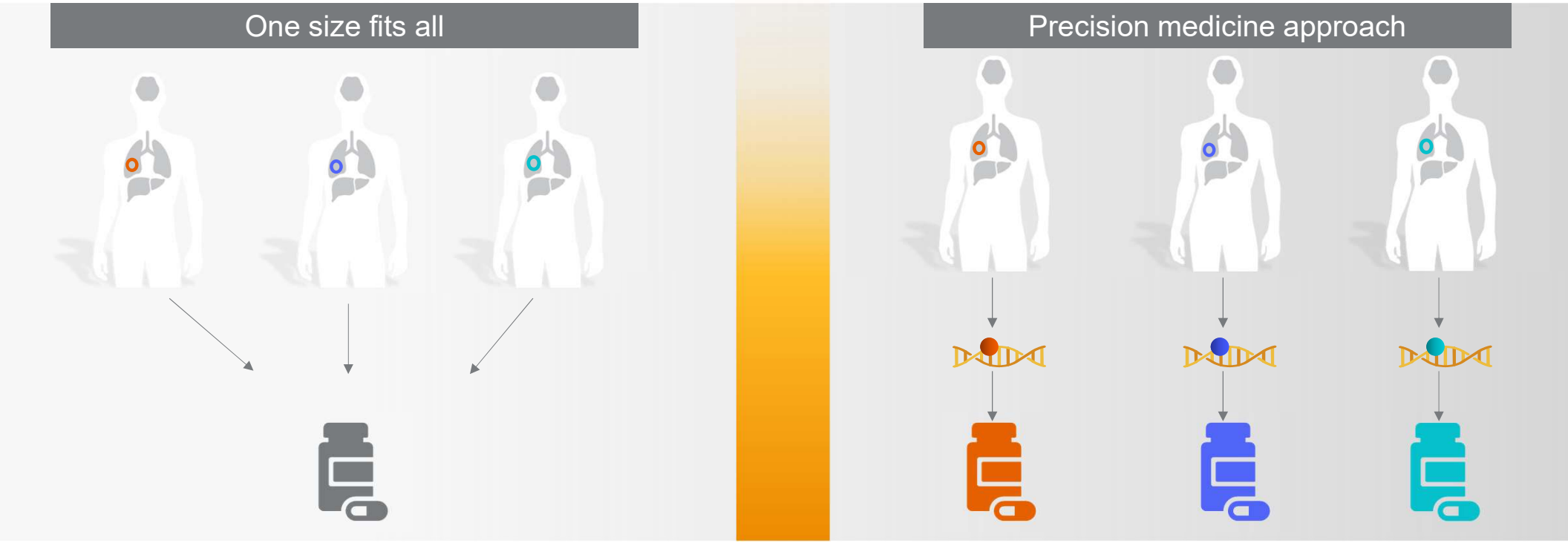
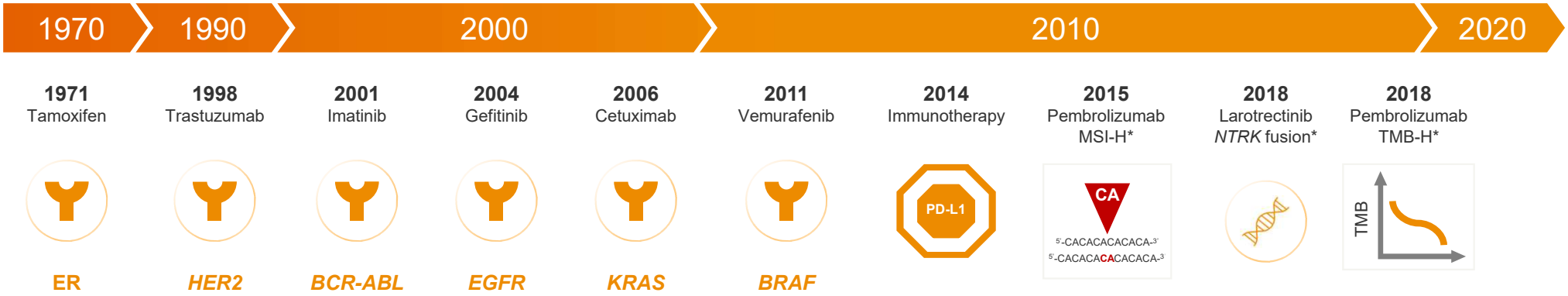
# Understanding Precision Medicine

Precision medicine is matching the ***right treatments*** to the ***right patients***, based on a genetic or molecular understanding of their disease.



# Precision Medicine: 20 Years of Advances




**Therapeutic Landmarks and Molecular Targets**

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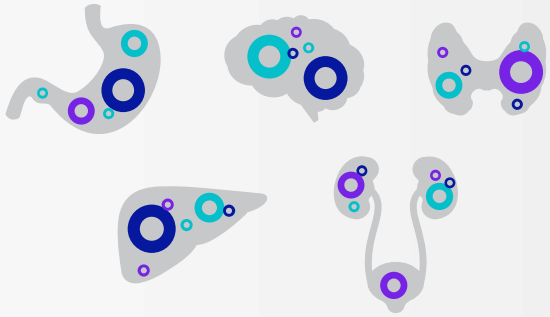
*Tumor agnostic approvals
ER=estrogen receptor; MSI-H=microsatellite instability-high; TMB=tumor mutational burden; TMB-H=tumor mutational burden-high
Adapted from: Colomer R, Mondejar R, Romero-Laorden N, et al. EClinicalMedicine. 2020;25:100487

# Biomarker-Linked Clinical Trials Will Drive New Indications

Number of ongoing clinical trials linked to a genomic biomarker

| All cancer types | NSCLC Patients |
|---|---|
| 4,736 | 310 |

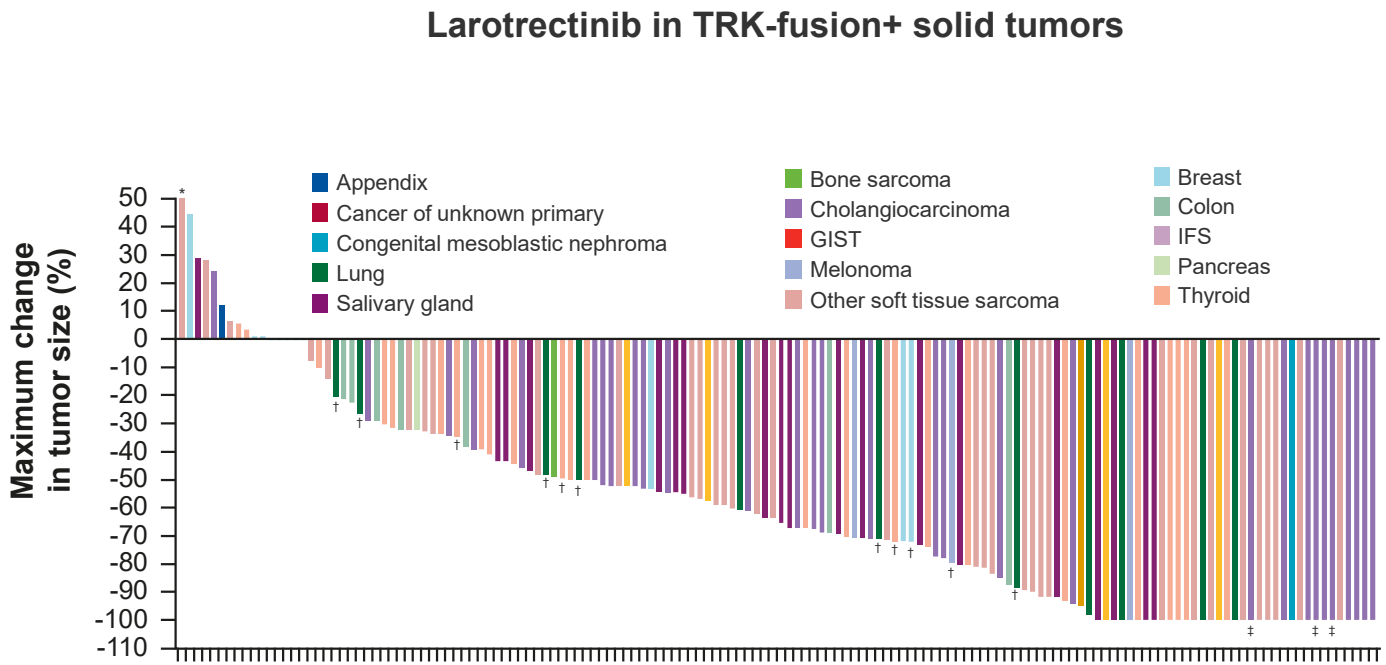


**The robust pipeline of biomarker-linked clinical trials will drive new indications and encourage emerging biomarkers to be added to guidelines over time**



NSCLC=non-small cell lung cancer
www.clinicaltrials.gov (assessed on 03/27/2023; search terms combination: “genetic OR genomic OR DNA OR RNA” with recruitment filters “Not yet recruiting,” “recruiting,” “enrolling by invitation,” and “active, not recruiting.” in “NSCLC” and “cancer”)

# Targeted Therapies Have Dramatically Improved Outcomes

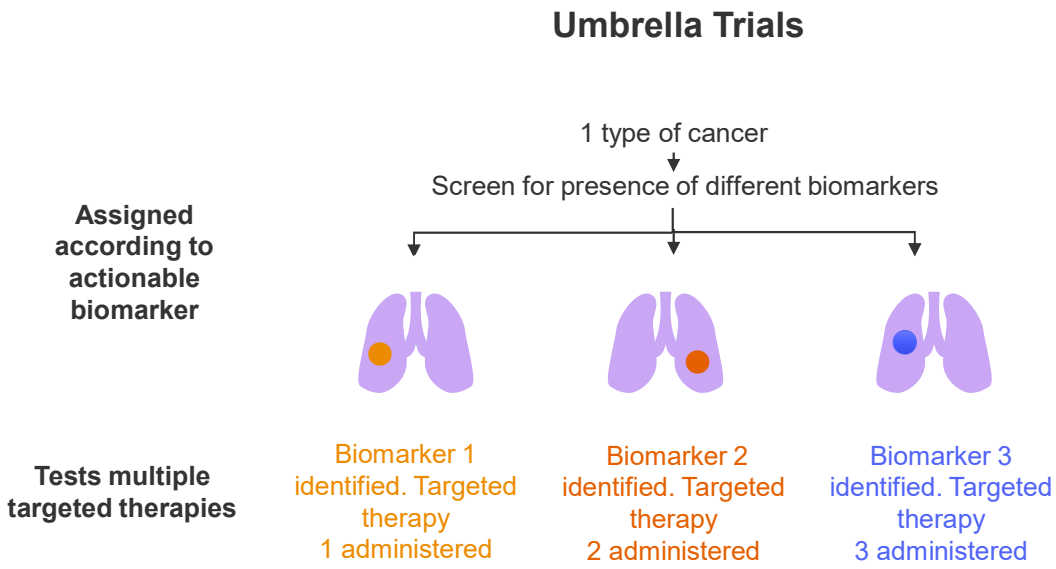


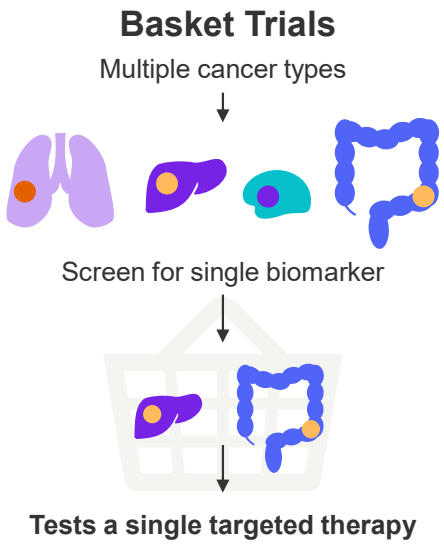

CI=confidence interval; GIST=gastrointestinal stromal tumors; HR=hazard ratio; IFS=infantile fibrosarcoma; NSCLC=non-small cell lung cancer

Hong DS, DuBois SG, Kummar S, et al. Lancet Oncol. 2020;21(4):531-540

# Clinical Trial Design in the Era of Precision Medicine

- Identification of actionable biomarkers in small subgroups of patients
- Trial participants can be from many locations without the need to travel to distant sites
- Rapid testing and approval of new therapies



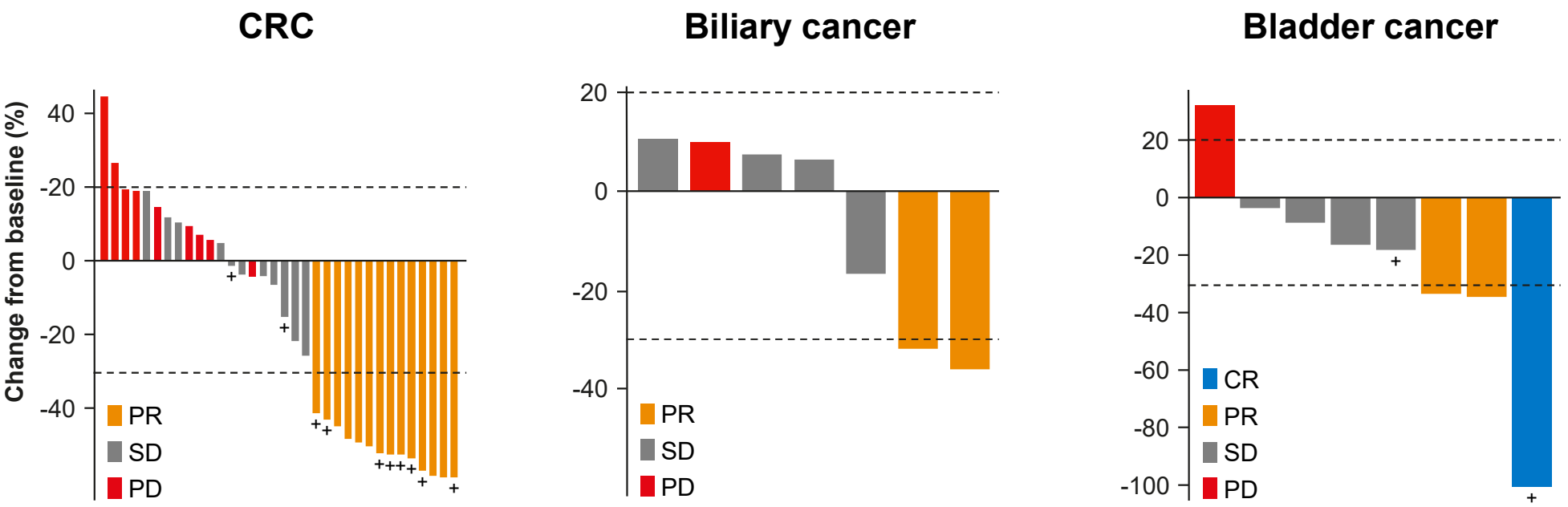






West HJ. JAMA Oncol. 2017;3(3):423

# MyPathway Basket Trial

Objective responses to trastuzumab plus pertuzumab were seen in 9 tumor types with *HER2* amplification/overexpression, including colorectal, bladder, and biliary cancer

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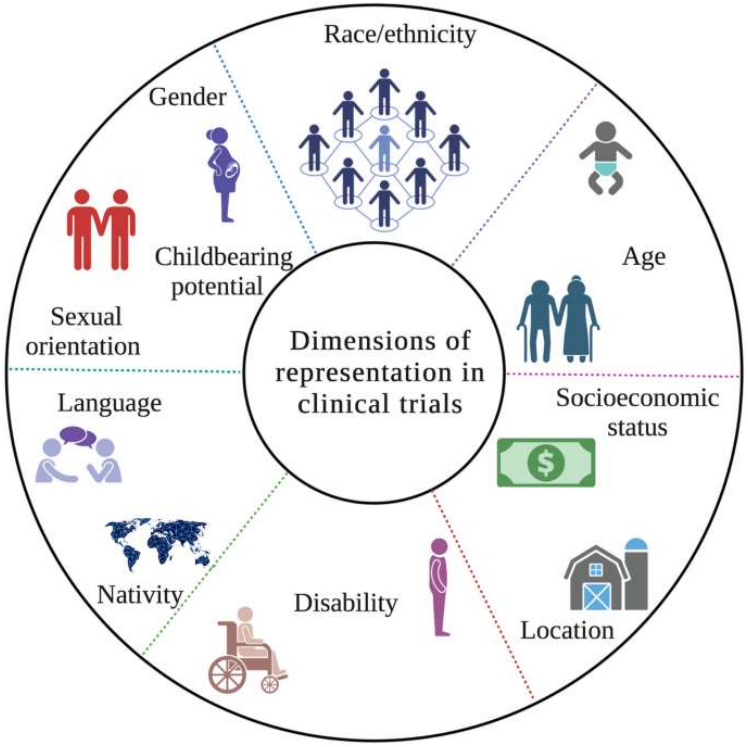
+ indicates treatment was ongoing
CR=complete response; CRC=colorectal cancer; PD=progressive disease; PR=partial response; SD=stable disease
Hainsworth JD, Meric-Bernstam F, Swanton C, et al. J Clin Oncol. 2018;36(6):536-542

# The Need for Diversity in Clinical Trials

Diverse populations may require different approaches to cancer prevention, treatment, and care





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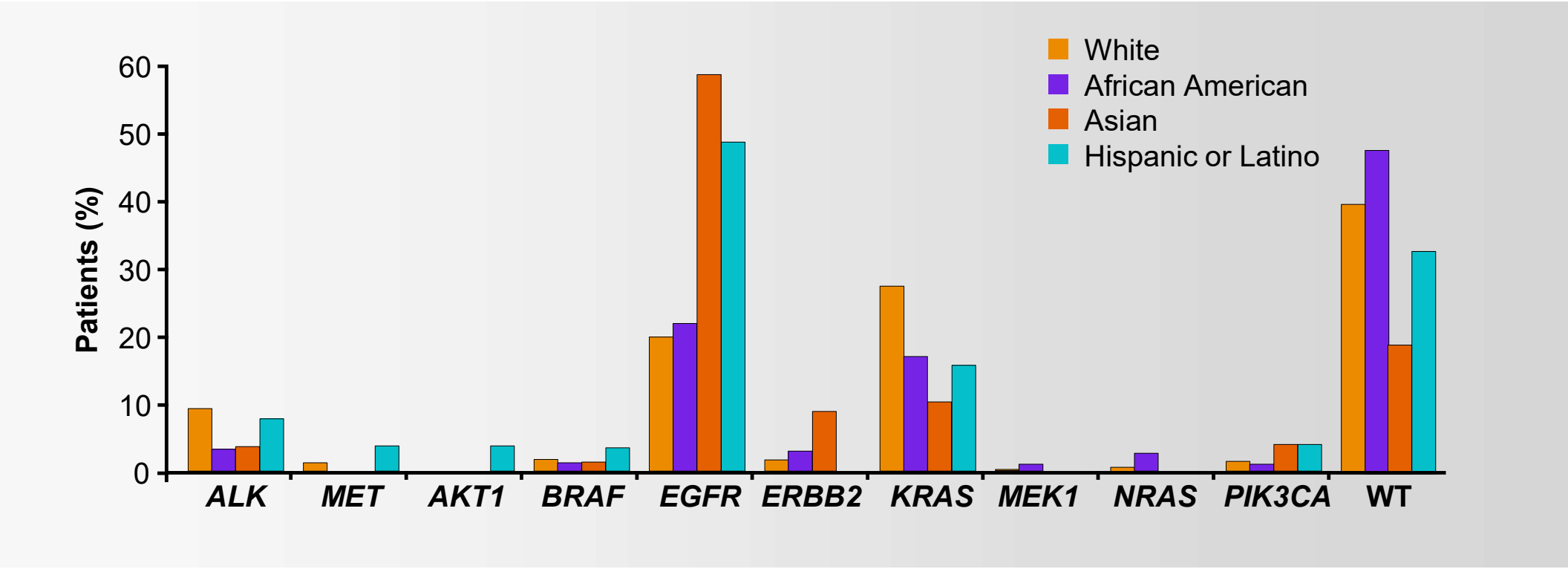
Ogungbe, O et al. Current Cardiology Reports 2023; 25: 1189-1210

# Prevalence of Driver Mutations in NSCLC by Race






NSCLC=non-small cell lung cancer; WT=wild-type

Steuer C, Behera M, Berry L, et al. Cancer. 2016;122(5):766-772

# Common Questions Regarding Clinical Trials

1. Is a clinical trial the right choice for me?
2. How does a clinical trial affect my family?
3. How is my safety and privacy protected?
4. Why would I be removed from participating in a clinical trial?
5. Can I find out what the results are from the trial?
6. How do I find out what clinical trials are available to me?
7. Does the clinical trial pay for my health care?

# Potential Questions to Ask When Considering Participation in a Trial

1. What is the purpose of the study?
2. What are my responsibilities if I participate?
3. What types of therapies, procedures, and/or tests will I receive during the trial?
4. What other options do I have & how do they compare to treatments I would receive in the trial?
5. What are the possible short- & long-term risks and benefits?
6. Who will be part of my care during the trial?
7. Will I have to pay for anything in the trial and if so, what will my health insurance cover?
8. Who do I contact with any questions or concerns I have during the trial?