GLOSSARY: COMMON TERMS IN CLINICAL TRIALS

By Taymeyah Al-Toubah,
Clinical Researcher, Moffitt Cancer Center

NIH Definition	Tay's Definition/Expansion
Adverse Event	
Any unfavorable or unintended disease, sign, or symptom (including an abnormal laboratory finding) that occurs in temporal association with the use of a medical therapy or procedure. This event may or may not be directly related to the medical therapy or procedure and can be related to any aspect of the treatment, such as the therapy itself, the dose, the route of administration, the patient, or an interaction with another drug or procedure. Adverse events can occur before and after a therapy has received marketing approval. The U.S. Food and Drug Administration (FDA) has systems in place to report adverse events that may be associated with a treatment already available in the clinical setting.	Any change in any function, physical, physiological, or psychological, from baseline status, including anything new that occurs. This does not have to be related to the study drug or intervention and includes any changes in cancer symptoms.
Arm	
In the context of clinical trials refers to a group or subgroup of participants who receive a specific intervention, or no intervention, as per the trial's protocol. Types of arms can include experimental, control, placebo comparator, sham comparator, and active comparator arms.	The portion of the study a patient will enroll in will define the patient's schedule. This could be a separate drug, a separate schedule of the same drug, or an arm with additional testing.
Cohort	
A group of people with a particular characteristic, such as age or a medical condition. Clinical trial participants may be recruited from a specific cohort, like pregnant women, children under a certain age, or individuals living with a particular condition like HIV.	The group of patients that qualify for a trial based on a particular characteristic. This term is also used interchangeably with "arm," depending on context.

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Control	
In a clinical trial, it is a standard of comparison for checking or verifying the results of an experiment. New patient treatments are often compared to standard ones to assess their effectiveness. In some cases, placebos are used as a control.	The arm or cohort we are comparing to may not always be a separate arm on a trial. It could be a historical control, meaning data we have on a particular patient population.
Controlled Trial	
This type of clinical trial includes a control arm, which is essential for comparing outcomes with those of the experimental arm to determine any differences, such as safety and effectiveness. This comparison is crucial in establishing the efficacy of a new treatment or intervention against the existing standard or a placebo.	A trial with at least two arms, one of which is a control and either non-active treatment or a currently established standard of care therapy.
Clinical Trial	
A type of clinical research designed to explore new ways to prevent, detect, or treat diseases. They are conducted in phases and rely on healthy volunteers and those with the disease or condition being studied. The goal is to determine the safety and effectiveness of new treatments, diagnostic methods, or other medical interventions. These trials follow a specific research plan or protocol and are subject to strict rules and regulations, monitored by bodies like the NIH and the FDA.	A regulated method for conducting an experiment in which we are testing drugs or interventions on humans that can vary in size and purpose to answer a question, improve upon a current standard, or establish a new therapy/intervention.
Crossover	
A clinical trial where participants receive multiple interventions in a specific sequence. For instance, in a two-by-two crossover, one	The majority of "crossover" studies are in randomized-control trials where a patient who may have been enrolled in the control arm can

group might receive Therapy A, then Therapy B, while the second group starts with Therapy B and then receives Therapy A. This way, all participants "cross over" to the other therapy during the trial, ensuring each one experiences both A and B.	eventually receive the "active" therapy/intervention either on the study itself or by another method (free drug from the company, single-patient IND protocol, etc.)
Double-Blind	
A clinical trial method where neither the medical staff, the patient, nor the individuals analyzing the results know which specific treatment the patient receives until the trial concludes. This design is essential to prevent bias and usually involves at least two groups, or arms, receiving different treatments or a treatment and a placebo.	NIH definition is straightforward; just understand that **no one** involved in the trial in these studies can unblind unless there is a medical, life-threatening emergency that would be resolved if unblinded (not all emergencies qualify).
Eligibility Criteria	
In a clinical study, there are requirements that participants must meet to join the study. These criteria are split into inclusion criteria, which participants must meet to be part of the study, and exclusion criteria, which would disallow someone from participating. This ensures that participants are similar in specific factors, improving the likelihood that the results are due to the treatment being tested rather than other variables.	The checklist that we must have every patient meet to be *safely* enrolled in the trial. These include lab criteria, medical history, current physical status, and prior therapies, among other criteria. This also contains timelines a patient must meet regarding wash-out periods, concomitant medications, etc.
Informed Consent Form (ICF)	
In a clinical study is a critical document that communicates the risks, benefits, and scope of the study to potential participants. It ensures that individuals are fully informed before agreeing to participate. The ICF contains details like the study's purpose, procedures, potential risks and benefits, and alternatives to participation. Signing this form indicates that the	While the informed consent form itself is the legal document that must be signed before any study procedures occur, informed consent itself is an ongoing process that should be part of every patient visit. Ensuring that the patient is aware of and understands every aspect of their care to the extent that the patient can and is involved in the decision-making of their care is part of informed

participant understands the study and agrees to partake. An Institutional Review Board (IRB) must review and approve this form before the study commences.	consent. Ensuring the patient understands and agrees to procedures, treatment changes, dose reductions or modifications, scheduling changes, etc., is part of informed consent.
Institutional Review Board (IRB)	
A group composed of medical, scientific, and non-scientific members. Its primary role is to protect the rights, safety, and well-being of humans participating in research studies in compliance with regulatory requirements. The IRB is responsible for reviewing and approving the study protocol, any amendments, and the informed consent process. IRBs can be established by research institutions or operate independently, and they may review studies from affiliated and unaffiliated researchers.	The IRB must approve all documents related to the trial, including any patient handouts, to be sure that the language is written in a way that is easy to understand for patients reading. Depending on the practice field, IRB documents must be no more complicated than a 5th or 8th-grade reading level.
Monitoring	
A clinical trial refers to the continuous oversight of the trial's process to ensure participant safety, the validity and integrity of data, and compliance with the study protocol. This includes regular data collection and analysis, and it is a critical component for protecting participants' rights and maintaining the trial's quality. For detailed guidelines on clinical trial monitoring, one can refer to the resources provided by the National Institute of Neurological Disorders and Stroke (NINDS) and other NIH institutes.	Clinical trials have many tiers, but it is easiest to think of them as 3: pharmaceutical company (sponsor), middleman (clinical research organization – CRO; contracted by the pharmaceutical company), and site/patients/doctors. The pharmaceutical company provides the drug and funding (in most cases), and the site provides the patients and day-to-day operations; the CRO is the hand responsible for making sure that the data we are providing to the pharmaceutical company is, in fact, accurate and without any errors. A third-party system like this ensures that a neutral party is involved in checking work and ensuring that what the pharmaceutical company reports is accurate. For trials where the site is both the sponsor and site, one can contract out to a CRO or utilize internal

	monitoring systems/personnel dedicated to the same task.
Outcomes	
Any observable and measurable change in a patient's health, symptoms, ability to function, quality of life, or survival due to medical care or treatment. In clinical trials, these outcomes can serve as endpoints to assess the effectiveness and safety of a tested therapy.	The schedule of events that the protocol requires patients/sites to adhere to is set up to ensure that all patients have the same schedule and timelines of procedures, evaluation of tumor growth/regression, etc., and veering off course or missing too many of the set procedures can impact outcomes. It is crucial not to deviate from the protocol as best as possible.
Overall Survival (OS)	
Considered the gold standard endpoint in cancer clinical trials. It is defined as the duration from the start of the trial to the death of patients from any cause. OS is clear, unbiased, and of utmost clinical relevance, confirming that treatment can extend a patient's life. It remains the definitive measure of a drug's impact in oncologic trials despite the exploration of surrogate endpoints.	Not all protocols utilize overall survival as an endpoint, nor is it always the "gold standard" in practical terms, because proving a benefit in overall survival, particularly for slow-growing cancers (e.g., neuroendocrine tumors), can be nearly impossible or take well over a decade or more to prove. In addition, designing trials with OS as an endpoint often requires large numbers of patients (>500), which can be unfeasible in many cases. This does NOT mean that a trial has no proven benefit if we cannot clearly state that OS has improved.
PKs/PDs	
Pharmacokinetics refers to how a drug is absorbed, distributed, metabolized, and excreted in the body, while pharmacodynamics involves the study of the biochemical and physiological effects of drugs and their mechanisms of action. These areas are crucial in understanding a drug's effects and behavior in the body, especially during drug development and clinical trials.	Most trials with PKs/PDs are phase I clinical trials (first in human or dose-finding trials), although some phase II and III studies may also have some PKs/PDs. Depending on the trial and the drug's half-life, these tests can involve many additional blood draws or urine collections over a day, week, month, etc. Ask your study coordinator at consent what this will look like for you and whether the additional labs are optional or mandatory. These

	are critical tests, especially in phase I trials, and if you can participate in even optional draws, the science and future patients will be incredibly grateful.
Placebo	
An inactive substance or treatment that appears identical to the active therapy being tested. It is administered the same way as the active treatment to ensure a controlled comparison of effects. Using a placebo allows researchers to effectively measure the impact of the active therapy by comparing it against the placebo's effects. This is crucial for determining the true effectiveness of the therapy under investigation.	Most trials do **not** have a placebo control, and just because something is randomized does not mean it is randomized to a placebo. Placebos should not affect a patient negatively, and they are not "sugar" pills (diabetic patients often ask if it will affect their glucose levels). They are inactive substances, whether a fluid via IV or a pill. Trials with radiation, surgery, more invasive interventions, etc., usually cannot have placebo controls as it would be nearly impossible (radiation) and possibly dangerous/unnecessary (surgery).
Primary and Secondary Endpoints	
Endpoints are specific outcomes that are statistically analyzed to determine the efficacy and safety of the therapy being tested. They must be validated before use in a clinical trial and are chosen based on the trial's design, the condition being treated, and the expected effect of the therapy. - Primary endpoint: main outcomes used to determine the study's success or, in interventional trials, for regulatory approval. - Secondary endpoints: provide additional information about the therapy's effect on the primary endpoint or other effects on the disease or condition. - Exploratory endpoints are included to explore new hypotheses or capture events less likely to show an effect.	*No addition*
Principal Investigator	

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The individual responsible for overseeing the trial or research. This includes preparing and implementing the study protocol, analyzing data, and reporting the results. The PI is pivotal in ensuring the trial's integrity and compliance with regulatory standards. They are typically a doctor or medical professional leading the research team, focusing on the safety and effectiveness of the study.	Depending on where you enroll on a trial and the system of practice, you may never actually meet the PI, or the PI may already have been your doctor. All doctors who enroll patients in a clinical trial and see patients/treatment must be trained on the trial prior. They are called co- or sub-investigators and discuss your case throughout the trial with the PI. Think of the PI (if not your doctor already) as a second set of eyes.
Progression-Free Survival (PFS)	
Particularly for solid tumors, it is used as an important endpoint. It is the time from randomization in the trial to disease progression or death from any cause. PFS is valuable for evaluating the effectiveness of treatments in preventing disease progression or death. However, various factors can influence the exact moment when disease progression is recorded, affecting its reliability as a primary endpoint.	Most phase III studies consider this an endpoint. Phase I studies usually look at safety, while phase II looks at efficacy (response rate typically). All studies with the power to do so will likely report PFS anyway but understand that it is not always the primary goal of a study.
Protocol	
A document that outlines the objectives, methodology, design, statistical considerations, and organization of a clinical trial. It details the rationale for conducting the study, its objectives, the trial design, the participants' demographics, the treatments and dosages, the data collection and analysis methods, and the procedures for ensuring participant safety. The protocol serves as a guide for conducting the study and is essential for standardizing procedures, ensuring participant safety, and answering specific research questions.	The "bible" of the trial by which the site must adhere (schedule, procedures, eligibility, dose modification/reduction guidelines, etc.). Patients are not given access to the protocols, and these are confidential documents due to the proprietary information they contain. All relevant information is released on CT.gov for any interventional clinical trial regulated by the FDA and/or EMA.
Randomization vs. Registration	

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Randomization refers to a method used to prevent bias in research: a computer-generated schedule of random assignments to a treatment group. Registration is the process of recording a clinical trial with a health authority or certification body.	While the "registration" in this context by the NIH refers to the record of the trial, registration for purposes of a patient's enrollment refers to the process of enrolling a patient on trial in situations where there is no randomization required/part of the trial. This can mean different things depending on the protocol, study sponsor, processes, etc.. However, it usually involves a computer system that generates a deidentified code/ID by which a patient is referred to on documentation for the duration of the trial. Registration procedures can be simple (one click) or convoluted (several weeks of steps, procedures, systems). Drugs usually cannot be assigned or ordered until this occurs.
Recist	
A set of published rules that define when cancer patients improve ("respond"), stay the same ("stable") or worsen ("progress") during treatments. These criteria assess the response to treatment in solid tumors, primarily in clinical trials. RECIST provides a standardized way to measure and evaluate the tumor burden and its changes, enabling a consistent way to assess the efficacy of treatments across different studies and settings.	RECIST reads involve an extra step for radiologists and can take more time to report. This is why it is important to space the time of your scan and treatment out by a few hours to a few days, depending on your site, treatment, etc. It is important to have an accurate read/evaluation before we discuss results with the patient. It is also important to note that certain protocols may modify RECIST depending on the type of therapy. Your doctor and coordinator can discuss what that means in your case.
Response Rate	
The proportion of patients whose cancer shrinks or disappears after treatment. This metric is particularly relevant in trials evaluating the effectiveness of cancer therapies. The response rate helps to determine whether a treatment has a significant impact on reducing the size of	This is often determined by the RECIST responses (other metrics for patients with liquid tumors like leukemia). It is important to note that even if a patient does not have a "response" per RECIST, that does not always mean they are not benefiting

tumors and is often used as an important endpoint in oncology trials.	from the treatment. This would impact overall study results/outcomes, but not necessarily
SAE/AE	
SAEs (Serious Adverse Events) and AEs (Adverse Events) in clinical trials refer to any unwanted medical occurrences in a patient or clinical study participant. An AE does not necessarily have a causal relationship with the treatment. An SAE, however, is any untoward medical occurrence that results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, or causes a congenital anomaly/birth defect. Both SAEs and AEs are crucial for assessing the safety profile of medical interventions in clinical trials.	All patients need to know for this is to report any hospital admissions or issues that occur at any hospital other than your study site to determine whether this qualifies as an event. There is a lot of paperwork and reporting to several agencies that need to be done when something of this sort happens on trial, and it can often impact other patients' ability to enroll on trial, depending on the nature of the event. Communication is key to ensuring the safety of everyone, both you and others on trial.
Sponsor	
The organization or individual that takes responsibility for initiating, managing, and/or financing the clinical trial. This can include pharmaceutical companies, academic institutions, government agencies, or other organizations. The sponsor plays a crucial role in designing, conducting, and overseeing the clinical study, ensuring compliance with regulatory, ethical, and scientific standards.	*None*
Standard of Care	
The best-known treatment based on scientific evidence, expert medical knowledge, and patient care guidelines. It serves as a benchmark for evaluating the effectiveness and safety of a new treatment or intervention in	*None*

clinical studies. The standard of care can vary based on disease, patient population, and geographic location, and it is often used as a control comparison in clinical trials to assess new treatments' benefits and risks.	
Unblinding/Blinding	
Whether the participants, healthcare providers, or researchers know which treatment or intervention the participants are receiving. In a blinded trial, this information is concealed to prevent bias in interpreting results. Unblinding occurs when this concealment is removed, usually after the trial's completion, allowing everyone to know who received which treatment. Blinding is crucial for maintaining objectivity, while unblinding is often used in data analysis or in cases where knowing the treatment is necessary for patient safety or care.	Not all trials will involve blinding or unblinding; some blinded studies will never unblind patients, and this is predetermined with the FDA before study activation.
Wash-Out Period	
This is a break between different treatment phases or before starting a new treatment, during which all medications from previous phases are allowed to leave the body. This period helps ensure that previous treatments do not influence the results of the subsequent phase or new treatment. It is particularly important in crossover trials or studies evaluating multiple therapies to avoid carry-over effects and ensure an accurate assessment of each treatment's efficacy and safety.	This is extremely important to discuss with your study coordinator and provider as soon as you start discussing the possibility of enrolling in a clinical trial. Any delays in wash-out will result in delaying enrollment and possibly even losing a slot on a trial.

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Sources:

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