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Is Clinical Research an Aid to Society?

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Abstract

Clinical trials, also known as "Clinical Studies" are research studies in which the scientists and doctors test new drugs, devices and treatments to see if they will improve health and whether they are beneficial to human without causing any adverse effects or side effects. Many of the treatments which are available now a day's for cancer are based on the work and results of past clinical trials. Many people treated for cancer are now living longer because of progress made through clinical trials. Clinical trials are divided into various phases, the preclinical trials using laboratory animals and clinical trials phases involving humans. Responsible persons like Sponsors, Investigators, Doctors, Monitors, Coordinators and their staff involved in trials takes care of all the necessary documents like Informed Consent Forms, Case Report Forms, Visitor forms, Site Feasibility Forms which are necessary for trials. The main aim of conducting clinical trials is to provide improvement in human lives for betterment of the society. Ethical issues rose during trials or study were managed by Independent Ethical Committees (IEC), Institutional Review Boards (IRB's) and the regulatory bodies in trials. Healthy Volunteers and also the patients were considered during various phases of trials and types of trials. This review article aims to explain the current status of clinical trials for the benefits and harms of participants and the patients to improve the human life for further implementation of clinical trials in present scenario.

Keywords: Clinical research; Drug; medical device; Phases; Types of phases; Ethical issues; Benefits; Harms

Introduction

Clinical Research is a systematic study for chemical molecules or new drugs in human subjects to generate a data for discovering or verifying the Clinical, Pharmacological (including pharmacodynamic and pharmacokinetic) or adverse effects with the objective of determining safety and efficacy of the new drug [1]. Clinical research is a branch of medical science that determines the safety and efficacy of medications, and effectiveness of devices, diagnostic products and treatment regimens intended for human use [2]. These may be used for prevention, diagnosis and treatment, or for relieving symptoms of a disease [3]. The term clinical research refers to the entire bibliography of a drug from its discovery in the lab to its introduction to the consumer market and beyond. Once the promising candidate or the molecule is identified in the lab, it is subjected to pre-clinical trials (using animals) [4] and Clinical trials (using Humans) where different aspects of the drug including its efficacy and toxicity are studied [5]. Clinical trials include different phases like Pre-clinical phase to the post marketing phase. Healthy Humans or volunteers are considered in phase-1 trials whereas patients are considered in remaining phase trials. Humans or Subjects participating in clinical trials were informed regarding the type of clinical trial and the phase in which they are participating before starting the trials [6]. The subject or patient's safety is safeguarded by certain rules and regulations given by U.S. Food and Drug Administration [7]. Ethical concerns and ethical issues were resolved by Independent Ethical Committees, Institutional Review Boards, and the governing bodies which work for safeguarding the subjects or patients rights [8]. Benefits and harms of the various clinical trials and the phases were explained to the participants before allotting them with the Informed Consent forms [9]. All the respective members like Sponsors, Investigators, Doctors, Coordinators etc who are responsible during clinical trials takes care of all the necessary information like Authorized Protocol, important documents, data records, site, lab instruments, availability of drugs etc which are required for conducting good clinical trials.

Clinical trials

Clinical research is a branch of medical science that determines the safety and effectiveness of medications, devices, diagnostic products and treatment regimens which are intended for human use [10]. These may be used for prevention, diagnosis and treatment of a disease or for relieving symptoms of a disease [11]. It's a study of testing of a chemical molecule for its safety and efficacy or a medical device for its effectiveness causing without any side effects to humans [12]. It is the entire bibliography of a drug/device/biologic, in fact any test article from its inception in the lab to its introduction to the consumer market [13]. Once the promising candidate or the molecule is identified in the lab, it is subjected to pre-clinical studies or animal studies where different aspects of the test article (including its safety toxicity if applicable and efficacy, if possible at this early stage) are studied [14]. Clinical trials are conducted to collect the important and necessary data related to the safety and efficacy of new drug or medical device development [15]. Before a drug or device can be sold in the consumer market, there are several steps and stages of approval in the clinical trials process [16]. Extensive laboratory research with years of experiments using animals and human cells is involved for testing a new drug or a medical device [17]. The researches send the related data to the Food and Drug Administration (FDA) for approval to continue the research and testing in humans, if the initial laboratory research using animals is successful. Where devices are concerned the submission to the FDA would be for an Investigational Device Exemption (IDE) application if the device is a significant risk device or is not in some

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way exempt from prior submission to the FDA [18]. Once approved from FDA and also the IDE, human testing of experimental drugs and devices can begin and is typically conducted in four phases [19]. Each phase is considered as a separate trial and, after completion of a phase, investigators are required to submit their relevant data for approval from the FDA before continuing to the next phase [20]. Additionally clinical research requires Institutional Review Board (IRB) or Research Ethics Board (REB) [21] and possibly other institutional Committee reviews, Privacy Board, Conflict of Interest Committee, Radiation Safety Committee, Radioactive Drug Research Committee, approval whether or not the research requires prior submission to the FDA. All these committees resolve the ethical issues related to the trials. There are four phases in trials after the completion of pre-clinical trials including phase-1, phase-2, phase-3 and phase-4 trials [22]. In phase-1 trials only the healthy human volunteers are being considered where as in remaining 3 phases patients are taken into consideration. While conducting the trials all the responsible persons involving in trials like Sponsors, Principle Investigator, Monitors, Coordinators, Doctors, Nurse etc takes care of all the necessary requirements like site selection, site feasibility, enrolling the subjects, subject's protection of rights, drug availability, drug records, various documents including Site approval forms, permission from independent ethical committees, Informed consent forms, Authorized Protocol approvals, Case report forms, data record sheets visitors forms and many other forms related to trials. Also they consider the adverse events and serious adverse events [23] and various tests related to trials [24]. After the approval from authorities, participants are enrolled and Informed consent form is signed [25]. If the subjects suffering with adverse effects or serious adverse effects then within short period of time the subject's condition and the status is informed either to the sponsor or to the investigator and also to the FDA so that further process whether to proceed with the trial or to terminate the subject or patient is decided in order to continue with the trials [26]. Clinical research review criteria will depend on which Federal regulations the research is subject to (e.g., (Department of Health and Human Services (DHHS) if Federally funded, FDA as already discussed) and will depend on which regulations the institutions subscribe to, in addition to any more stringent criteria added by the institution possibly in response to state or local laws/policies or accreditation entity recommendations.

Phases of Clinical Trials

Clinical trials are studies, managed by government agencies, educational institutions, private not-for-profit organizations, or commercial businesses, to develop, produce, and evaluate the effectiveness of new treatments for diseases. Before starting the trials involving human's pre clinical trials [27] using lab animals were conducted *in vivo*, and submitted to the Investigational New Drug Application (IND) [28,29], after getting approval from Investigational New Drug Application (IND) from FDA [30], further proceedings involving humans trials were conducted [31]. The human studies are conducted in four phases in research subjects that give consent to participate in the clinical trials. Clinical research progresses in an orderly series of steps or phases. Clinical trials are done to determine the safety and effectiveness of a new drug or procedure in people [32]. During this process, the treatment goes through "phases," beginning with the first use in people through approval for general use by the Federal Drug Administration (FDA).

Phase 1 clinical trials

These trials were conducted to detect whether the treatment is safe to the participants. After the completion of pre-clinical trials or after an experimental drug or treatment has been tested in the lab and/or on animals, it enters a phase 1 trial [33]. These trials involve a small number of patients to test safety in humans and determine the correct dose of a drug [34]. These trials also help determine the best way to give the drug, or to administer the drug, whether oral or intravenously [35]. These are the first studies to evaluate how a new therapy should be administered, how it should be given, how often, and in what dosage [36]. The focus is to determine safety (drug dose, device safety, or other therapy's safety) for the next phase of testing.

Phase 2 clinical trials

Trials conducted to know how the treatment works. After determining that a treatment is reasonably safe in people, it enters phase 2 trials [37]. These are done to test for effectiveness of the drug or device since a larger number of people are studied, more number of people than the phase-1 trial are involved in phase-2 trial [38]. These are the studies to evaluate the efficacy of the drug and effectiveness of device, further information is gained on safety during phase 2 trials [39]. These studies provide preliminary information about how well the new therapy works, and generates more information about its safety and benefits [40].

Phase 3 clinical trials

Here the comparison of new treatment with the standard treatment [41,42], whether the new treatment works better than the standard treatment can be observed in this phase [43,44]. After determining the efficacy of a new drug, a phase-3 trial includes more number of people [45]. Phase 3 trials test the new drug or treatment on hundreds or thousands of individuals [46]. These studies are often "double-blind" trials [47], which mean that neither the patient nor the investigator knows which treatment is being used [48]. They are designed to answer the question how does the new drug or new treatment work, is new treatment better, or has fewer side effects, than the standard treatment [49]. It compares a promising new therapy, combination of treatments, or procedure with a current standard of treatment [50]. These trials often enroll large numbers of people and may be done at many doctors' offices, clinics, and cancer centers nationwide, or even worldwide.

Phase 4 clinical trials

Confirmation of treatment can be done, whether the treatment is safe over time. These trials are also called as "post marketing trials". Phase 4 trials are less common and serve to answer questions after the FDA has already approved a drug for general use [51]. These can address questions such as long-term safety of a drug, or other circumstances in which the drug may be helpful [52]. The safety and efficacy of the drug or device is confirmed in this phase [53]. It includes the continuing evaluation that takes place after FDA (Food and Drug Administration) approval, when the therapy is already available for general use.

Types of Clinical Trials

People often think of clinical trials as a method of studying new drugs, or medical devices but many different types of trials are in process to evaluate the disease or cancer [54]. Different types of trials include:

Prevention trials

Prevention trials look at substances and lifestyle factors that may raise or lower the risk of developing disease or cancer [55]. These trials are designed to keep disease or cancer from developing in people who

have not previously had them. Prevention trials designed to prevent a new type of disease or cancer from developing or keep cancer or disease from coming back in people who have already had them.

Early detection or Screening trials

Screening trials study methods to diagnose the disease in its early stages when it is often more curable [56]. Screening trials helps to find disease or cancer, especially in its early stages [57].

Diagnostic trials

Diagnostic trials are done to look for the best methods of finding out if a person has any kind of disease or cancer [58]. These trials help to accurately determine the stage of disease or cancer that is present.

Treatment trials

Treatment trials evaluate the ability of drugs, radiation, surgery, or other measures to treat the disease or cancer. These trials help to test new therapies in people who have disease or cancer.

Supportive care trials

Supportive care trials are also called as "quality-of-life trials". These trials were conducted to study the ability of a drug or procedure to lessen the symptoms of disease or cancer or symptoms related to the treatment of disease or cancer [59]. These trials are conducted to improve comfort and quality of life for people who have disease or cancer.

Significance of Clinical Research

People being cared from past research and continue to benefit from research that is currently being carried out. Healthcare professionals know a great deal about health, disease and medicines, but much remains uncertain. Research can find answers to the things that are unknown, filling gaps in knowledge and changing the way that healthcare professionals work [60]. This means treatment, care and patient's quality of life are improved and avoidable early deaths are prevented [61]. Large cancer centers, university hospitals, local medical centers, or physician offices; all may be included in managing clinical trials [62]. Informed consent is a process designed to protect potential participants through detailed description of important facts about a specific clinical trial. There may be only one or two locations involved in a particular study, or hundreds around the country, or even around the world.

Benefits of Participating in Clinical Trials

Clinical trials are done with the sole aim of testing medicines, medical devices and treatments that will ultimately be made available for human health [63]. Although clinical trials offer no guarantees, physicians have a strong belief that the study drug or cancer treatment will provide benefits equal to or better than the current standard therapies [64]. The potential benefits of participating in a clinical trial include the following:

- Access to promising new therapies and approaches often not available outside the clinical trial setting.
- An individual may get treatment that may be more effective than the standard approach [65].
- Close monitoring of an individual or participant for possible adverse events by a research team of doctors and other health professionals [66].
- Participant may get an opportunity to be the first to benefit from the new method under study [67].
- Cancer study, possibly leading to improved options in the future.
- An individual may obtain medical care at free of charge.
- Contribution of an individual to medical research that may result in the advancement of medicine and healthcare in general thereby helping other fellow human beings.
- All sponsors reimburse the persons or individuals who participate in trials for all reasonable expenses related to participating in the trial, including travel expenses, food, medical care and compensation for provable and insured adverse events that are related to the trial.
- If a person is suffering with disease which cannot be treated with an existing drug or regimen, then participation in a clinical trial perhaps provide with a successful treatment before it becomes available to others [68].
- If a person lacks strength in some way, then can have the opportunity to test a regimen that would improve the quality of life.
- If a person gets qualified to participate in a study for a particular disease or condition, and have had trouble finding good care for disease or condition to that point, then may find access to improved care since the investigators involved in the study focus directly on the medical problem being studied.
- Participants are provided with drugs and protocols at no cost during clinical trials. Patients who have trouble in affording the drugs or treatment may need to enroll in a clinical trial in order to access the protocols that may help them.
- Some patients who doesn't have alternatives for treatment and are permanently weakened, in such cases participating in clinical trials may give them a hope or possibilities that do not exist otherwise.
- An individual may have interest in humanitarian and his or her reasons to participate include: For Example, many drugs, devices and therapies have previously been tested on men, and found safe and useful. Fewer trials have been designed and run for women, minorities, or children. Participation in a clinical trial that broadens the use of a good drug for one of these less-tested groups is useful to humanity.
- An individual may be curious about a treatment possibility and fit the profile needed for the trial.

Risks of Participating in Clinical Trials

Patients participating in clinical trials do not know about the drug and the treatment, whether they are receiving the experimental drug or treatment, or a previously approved drug or treatment, or even a placebo (a false or dummy treatment.) Therefore, if the reason if an individual decides to participate in a trial is because he / she hopes to try a treatment which would not be available publicly, but which can be have usually, at best, a 50% chance of receiving that treatment. The clinical trial process is not risk-free [69]. Study investigators anticipate many of the side effects, but not all can be known ahead of time.

Remember, most standard cancer treatments also have side effects, which can include nausea, hair loss and lowering of the blood counts. Many side effects can be managed with medication.

- There may be unpleasant outcomes and side effects which may last only for a short period of time, or they may affect for the rest of life [70].
- The treatment being studied may have no positive effects at times; this is because an individual may not really receive the treatment being studied or because the treatment isn't appropriate to help an individual.
- The participant's time and attention required may be long and involved. It may require hours of testing, miles of travel, hospital stays or even complicated dosing [71].
- New therapies, medications or devices doesn't always mean better.
- Not all clinical trials are as objective as they need to be. Ideally they are set up to be totally objective, but patients are wise to look at who/what organization is doing the investigation to be sure that the study is not biased by financial gains that can be made from any specific outcome.
- An individual may not use certain medications including the traditional medications without the approval of a trial doctor.
- An individual may need to set aside time for trial related activities like visiting the trial site.
- An individual's personal or social life may get affected, e.g. reproductive functioning, consumption of alcohol, tobacco or other drugs of abuse, etc.
- A patient or an individual may need to consult usual healthcare provider for all other illnesses that are not related to the trial, but still a person or patient need to inform this to the provider that he / she is a part of trial and that certain medications or treatment options may not be compatible with trial protocol.
- Health insurance and managed care providers may not cover all patient care costs in a study. It is extremely important that a patient should verify that the sponsor of the trial has an appropriate comprehensive insurance cover for him / her.
- There may be serious adverse events (SAEs) that are related to the medications used or procedures that are done in the trial.
- Participants may be required to make more visits to the doctor than they would if they were not in the clinical trial.
- Even if a new treatment has benefits, it may not work for patients at times.
- New treatments and therapies may have side effects or risks that doctors do not expect or that are worse than standard care [72].

Ethical Concerns in Clinical Trials

As clinical research involves human participants, researchers and their teams are legally and ethically need to protect them and safeguard the patient's rights [73]. In clinical practice interventions may be used that have a reasonable expectation of success and are designed solely to enhance the wellbeing of an individual patient. Clinical research is designed to test a hypothesis; here the participant or the patient may not get the best known treatment and therefore the obligations on the researcher are more. The Declaration of Helsinki (available at http://www.wma.net/e/policy/b3.htm) which forms the basis of clinical research today, was first accepted by the 18th World Medical Assembly in 1964 and has been revised five times since and the latest version was published in 2000 at the 52nd World Medical Association, Edinburgh, Scotland. It contains 32 principles and has made informed consent a central requirement for ethical research and clearly mandates that "all protocols must be submitted to an ethics committee for review, which must be independent of the investigator, the sponsor or any other kind of undue influence" [74]. It is expected that all institutions in various countries which carry out any form of biomedical research involving human beings should follow guidelines [75] to protect the safety and wellbeing of all research participants. The two important principle protections offered to an individual taking part in any clinical research are written informed consent and ethics committee review. All and any kind of research in humans must be preceded by permission from an ethics committee [76]. The type of research could be an invasive, experimental study involving a new drug or new device (or even an old drug or device) or a "simple" questionnaire-based study, in normal subjects or in patients, a study looking at histopathology specimen or serum samples, a company-sponsored project or a Government-sponsored one, an academic project or a student's thesis. As long as it involves research on human beings, the investigator must obtain ethics committee permission [77]. Ethics is the application of values and moral rules to human activities and bioethics is a part of applied ethics that uses ethical principles and decision-making to solve actual or anticipated dilemmas in medicine and biology [78]. There can very few arguments against the need for ethical review of protocols for human research before starting the research [79]. The ethical conduct of a clinical trial does not end with the clinical study design and a signature on the informed consent form [80]. Protecting the rights, interests, and safety of research subjects involved in clinical trials must continue throughout the study duration [81]. Subject safety monitoring is the first and foremost responsibility of several groups, including research ethics committees (RECs) [82] or institutional review boards (IRBs), investigators and their research staffs, sponsors, and data monitoring committees (DMCs), also called data and safety monitoring boards (DSMBs), especially in the United States. Lack of maintenance and deficiencies in the monitoring of clinical trials and reports related to deaths of research subjects during the last few years have raised serious concerns regarding the systems and processes by which subject safety is currently monitored [83]. The unexpected and fatal adverse events occurred in "first-in-human trial" involving a drug called "TGN1412" highlighted ethical issues in clinical study design and safety monitoring. Despite the findings and investigations from the Medicines and Healthcare products Regulatory Agency (MHRA), found no association between the drug administration and the adverse incidents, concerns remain regarding whether the drug was administered to the participants within a shorter time than what was approved and whether the drug company should have known the drug would provoke the catastrophic reactions seen in humans. Monitoring ongoing research ensures that the research or study is conducted as planned. Such monitoring entails several activities:

- An adequate process of informed consent.
- Sticking or Adherence to approved protocols.
- The proper collection of adverse events and the side effects, ensuring the integrity of the collected research data.

- The annual review of continuing research and studies to assess the appropriateness of fair subject selection and the continued adequacy of a reasonable risk/benefit profile.

Essentially, one need to ensure that the integrity and safety of the research or study remains intact and that both anticipated and unanticipated harms can be rapidly detected and contained (i.e., being able to revise the protocol or stop the study if necessary). The groups responsible for safety monitoring, who have major monitoring responsibilities in a clinical trial includes: IRBs, the DSMBs, the study sponsors, and investigators and their research staffs.

Institutional Review Boards (IRBs)

The IRB has numerous protection responsibilities that include initial and continuing review of the trial or study protocol and related documents, review of the informed consent documentation and review reports of unanticipated problems (UAPs) and adverse events (AEs) [84]. An important mechanism of ensuring subject safety is reporting of UAPs and AEs. The Adverse Event report needs to present an accurate and expanding picture of harms occurring during the study [85]. When first formed, IRBs were expected to be able to monitor the progress of a clinical trial at their site, but such expectations have become unreasonable for multicenter studies and complex single center studies. IRBs are often flooded with all individual AE reports from their site and the other study sites in a multicenter trial, yet such reports are largely un interpretable, because the IRB does not know enough about their context. IRBs receive little guidance on how to handle reports. IRBs should collect relevant information and be responsible for considering the continued acceptability of trials at the study site(s) they oversee. IRBs are also calling for more restricted definitions of AE (i.e., "probably" or "definitely related" to the study intervention), which would be determined by the investigator and/or sponsor. They also are asking for clearer Federal guidance on how to handle AE reports. In addition to the review of the research protocol and informed consent form IRBs should have three major roles in a multicenter trial:

- IRBs should ensure that a monitoring plan exists for each individual study site, and also there is a data monitoring program for multi-site studies.
- IRB should certify investigators' understanding of compliance with regulations governing the subjects' safety during the trial, including AE reporting and the collection of relevant study documents.
- IRB should review the query investigators and the DSMB reports as needed to determine whether additional safeguards are necessary.

These recommendations seem reasonable, because the structure and function of IRBs would enable them to perform these roles better than the other entities involved in the monitoring of clinical trials. In addition, the suggested roles would add an efficient framework to the role that IRBs can play in the safety monitoring of human subjects during the course of a clinical trial.

Data Safety Monitoring Boards (DSMBs)

The establishment of DSMBs was based on the recognition in the 1960s. To provide the necessary monitoring, DSMBs usually consist of individuals with pertinent expertise in the disease under study, as well as statisticians, ethicists, and sometimes community representatives [86]. The increasing use of DSMBs has occurred due to:

- The increasing number of industry-sponsored trials with mortality or major morbidity endpoints [87].
- Lack of awareness in the scientific community of problems in analysis that might lead to bias or inaccurate results [88].
- The previously mentioned concerns that IRBs are unable to properly monitor subject safety in multicenter trials.

The focus of DSMBs is on the total safety experience in a trial. The members of the DSMB review data consider differences in the rates of clinical endpoints to determine whether clear benefits or harm might be occurring. They also review individual reports of AEs, Serious Adverse Events (SAEs) and consider the frequency, severity, and types of AEs [89]. A decision to stop a trial is made either when, using preplanned statistical analyses, significant differences in either harms or benefits are observed among the study arms or when there have been an excessive number of AEs in one of the study groups [90]. The US Food and Drug Administration (FDA) issued in March 2006 guidance for clinical trial sponsors for the establishment and operation of clinical trial data monitoring committees (FDA Guidance at http://www.fda.gov/cber/gdlns/clindatmon.pdf).

Sponsors

Sponsors have numerous responsibilities which extend far beyond financing.

- Sponsors must demonstrate in pre-clinical studies that an intervention will be safe enough to justify clinical research.
- Provide medical expertise.
- Ensure that the study or trial design minimizes harms [91].
- Participate in investigator selection, review and initially interpret AEs.
- Protect subjects against injury claims arising from the trial.
- Provide applications, notifications, and submissions of necessary documents to regulatory authorities.
- Confirm IRB review; monitor to ensure Good Clinical Practice (GCP) during the trial.
- Supply and handle the investigational agent maintain records and keep them available for inspection.
- Perform safety evaluation and reporting, monitor and audit the data that have been collected during study or trial [92].
- Secure compliance and report noncompliance, prepare trial reports, and monitor study sites.
- The major role for sponsors in ensuring subject safety serves two purposes:
- Sponsor has the greatest access to information about the study agent, they are in the best position to protect study subjects by making information about risks readily available to investigators and IRBs both before the trial (in the form of the investigator brochure) and during the trial, and then to the FDA after the trial.
- Sponsors are able to report serious and unexpected AEs to IRBs with detailed interpretation of the likeliness of association with the intervention. Sponsors cite an excessive focus on data collection and data auditing and over-reliance on auditing

completeness of case report forms to ensure GCP, such that these processes slow the dissemination of data to the investigator brochure [93]. To be sure, the true purpose of data audits is to ensure the integrity of the safety and efficacy data and completeness of data submitted to the FDA, rather than to identify AEs.

Investigators

Like study sponsors, investigators and their research staffs have a wide range of responsibilities that include sticking or adhering to the protocol and study design, conducting an ethically appropriate informed consent process, ensuring quality data maintenance, quality data collecting, and finally data integrity, maintaining the essential document files, and supplying interpretation of AEs within the data about the intervention [94]. As individuals on the "front line" of the research endeavor, investigators and their research staffs are entrusted with assuring the proper application of the inclusion and exclusion criteria, the proper administration of study treatments, and the accurate monitoring and reporting of Adverse Events. All of these tasks have important implications for subject safety [95].

Conclusion

While experimental study or research is the strongest method for establishing causality, it can be difficult to manage under many scenarios. Clinical research offers many study design alternatives that may be appropriate if planned and executed carefully. Thousands of patients, who have volunteered to participate in clinical trials, have led to many breakthroughs in disease prevention and treatment in the last half-century. Without the willingness of these individuals, many would have suffered a lot with various diseases. It is also important to recognize that "clinical research is not always dedicated to finding the next drug or medical device. Clinical trials also can contribute invaluable information about the benefits and safety of existing therapies, providing doctors and patients with reliable information for choosing between alternative treatments. Ultimately, because "every medicine or medical device must be fully evaluated or examined through closely monitored and highly regulated clinical trials to insure their safety and effectiveness," patients receiving medical care should be encouraged to participate in clinical trials. Participants in clinical trials, are helping to develop new drugs, devices, biologics, and treatments for the future, and improving the care of all people.

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