

Clinical Trials: A Start



Clinical trials can often be a complex and scary treatment option to consider. This is precisely why a small group of ovarian cancer patients, survivors and caregivers came together to develop this educational brochure for newly diagnosed and recurrent ovarian cancer patients and their caregivers in the U.S. We hope that it provides you with a helpful introduction to cancer clinical trials and makes it easier for you to discuss this potential treatment option with your healthcare provider.

We realize that this brochure cannot provide answers to all of your questions or describe every possible type of clinical trial, but we hope it is a meaningful start. We encourage you to speak to your Gynecologic Oncologist, and to use this clinical trial brochure as a guide throughout your treatment process.

We send you our warmest and best wishes on this road towards better health!



SANDY ROLLMAN
ovarian cancer
foundation



Disclaimer: All photos are stock photos posed by models.

The Basics

Clinical trials (trials) are research studies to test the dosing, safety and effectiveness (efficacy) of an investigational drug (test article) to support government approval for a pharmaceutical company to market and sell the drug for a specific type of cancer (indication).

Typically, a drug will progress through at least 3 clinical trial phases over a multi-year period.

Phase 1

Key Goal: Determine Initial Safety and the Dose

A test of the drug's safety, tolerability, dosage and administration schedule in a small number of patients (e.g., <50). This is the first time the drug is used in humans.



Phase 2

Key Goal: Assess Initial Efficacy and Continue Safety Study

Using the dosing schedule determined in Phase 1, the drug's safety, tolerability, and preliminary effectiveness are tested in a larger number of patients (e.g., <200).

Phase 2 clinical trials can be:

- single-arm clinical trials to test the investigational drug in combination with the standard of care (SoC); or
- placebo-controlled clinical trials to compare the SoC plus the investigational drug to the SoC plus a placebo.



Phase 3

Key Goal: Confirm Safety and Efficacy

- The main purpose is to statistically confirm the efficacy of the drug seen in Phase 2, and further assess safety. A large number of patients (e.g., 500+) are electronically assigned (randomized) to receive the investigational drug with the SoC (experimental arm) or a placebo with the SoC (control arm).
- The gold standard is a “blinded” study, i.e., the pharmaceutical company, physician and patient are not informed of the assigned treatment, nor do they get to choose the assigned treatment. Blinding ensures the study results are not biased by those with a vested interest in the study results. The treatment can be “unblinded” to assist healthcare providers caring for a patient in an emergency situation.

The Treatments

Standard of Care (SoC)

A SoC is a single drug or drug combination with a proven clinical benefit. Since the clinical benefit is recognized by leading physicians in national treatment guidelines, it would be unethical to not offer cancer patients the SoC. This is why an investigational drug is typically added and compared to the SoC. When a SoC does not exist, the healthcare provider chooses an appropriate treatment.

Investigational Drug

An investigational drug is one that is not approved by the FDA for the disease being studied. It is a drug that showed a potential efficacy or safety benefit in the laboratory that now needs to be proven in clinical research with patients. Access to an investigational drug and its potential benefit is limited to patients in a clinical trial.



As the drug moves through each clinical trial phase, safety and efficacy data are collected so that physicians and patients have current information when deciding whether or not to voluntarily participate in a clinical trial. However, not all safety and efficacy information will be known at clinical trial time. Therefore, there is a risk that new safety or efficacy concerns may be discovered as the drug progresses from laboratory research through the clinical research process.

Placebo (PBO)

A placebo is an inactive agent (e.g., sugar pill or saline solution) that looks just like the investigational drug. It is used as a control for comparison to the investigational drug. Typically, patients in the “control arm” of a clinical trial receive the placebo plus the SoC.

The Clinical Trial Design

Study Protocol

The clinical trial design is detailed in a *Study Protocol* for healthcare providers and described in the *Informed Consent* for patients. It typically includes the:

- Clinical trial phase (e.g., Phase 1, 2 or 3)
- Study objectives, e.g., to evaluate the:

Phase 1 First-in-Human Studies	<ul style="list-style-type: none">• Recommended dose• Safety, side effects and tolerability
Phase 2 and Phase 3 Efficacy and Safety Studies	<ul style="list-style-type: none">• Objective Response Rate (ORR) <i>the % of patients responding to treatment</i>• Progression-free Survival (PFS) <i>the time between treatment start and disease progression</i>• Overall Survival (OS) <i>the survival time after start of treatment</i>

- Study design (e.g., global, blinded, randomized, placebo-controlled study)
- Number of patients (human “subjects”)
- Inclusion criteria—the types of patients eligible to enroll in the trial
- Exclusion criteria—the types of patients not eligible to enroll in the trial
- Treatments and dosing schedules
- Planned analyses—e.g., primary, interim safety and/or futility analyses
 - A primary analysis is a statistical test to determine if the trial met its study objective (e.g., improving PFS).
 - A futility analysis measures the likelihood of a clinical trial achieving its objectives.
 - A trial can be stopped early if it is ineffective (meets futility) or poses a serious safety issue. Patients are then switched to a treatment recommended by the healthcare provider.
 - A trial can be stopped early if it offers a significant clinical benefit. Patients may be allowed to “crossover” from the control to the experimental arm to try to achieve the clinical benefit.



TIP: You may want to initially focus on the clinical trial phase. As the phase increases from 1 to 3, knowledge builds about the safety and potential efficacy of the investigational drug. If the trial is blinded, you will not know the treatment you receive. If there is a placebo control, you may or may not receive the investigational drug. The randomization (e.g., 1:1 or 2:1) tells you the chance of receiving the investigational drug vs. placebo.

The Oversight

Patient Safety

Multiple individuals and institutions are involved in the conduct of a clinical trial. Below are just a few of those who play a key role in ensuring the safety and well-being of clinical trial patients.

Key Study Personnel

- **Clinical Investigators** — The physicians recruited and paid by the trial's Sponsor to care for patients and collect data according to the *Study Protocol*. The Clinical Investigator and his/her Clinical Trial Nurse are the main points of contact for patients.
 - An important potential benefit of clinical research is the increased oversight of the patient's care through more frequent visits with healthcare providers.
- **Institutional Review Board (IRB)** — A team from the Clinical Investigator's hospital (site) that reviews the *Study Protocol* and *Investigator's Brochure* to ensure the clinical trial meets guidelines and is appropriate for patients. The IRB monitors the ethical conduct of the clinical trial to ensure patient safety.
- **Data Safety Monitoring Board (DSMB)** — An independent team that is unblinded, meaning they know which patients are on which treatment arm. The DSMB is responsible for verifying at certain points in time that there are no safety or efficacy concerns to indicate the trial should be stopped early and patients taken off the investigational drug.
- **Medical Monitor** — A physician who is employed or contracted by the Sponsor to help design the *Study Protocol*, monitor adverse events (side effects), and consult with Clinical Investigators on how best to manage adverse events.
- **Sponsor** — Most commonly, the pharmaceutical company that designs the *Study Protocol* with input from leading physicians, seeks FDA approval to proceed with the trial, and covers certain trial costs.

The Informed Consent

Patient's Role and Expectations

The *Informed Consent* is a lengthy document detailing critical clinical trial information for patients considering participation. A member of the Clinical Investigator's staff is required to sit down with the patient to review the *Informed Consent* in detail and answer any questions.



TIP: Bring someone with you to this appointment, as the information can be overwhelming during an already difficult time. An extra set of eyes and ears will help you to carefully consider whether the trial is right for you.

After careful consideration, if the patient wants to voluntarily enroll in the trial, she and the staff member are required to sign the *Informed Consent* to confirm that the discussion took place and that the information is understood. The patient does not have to enroll in the trial. Additionally, the patient has the right to withdraw from the trial at any time and for any reason.



Examples of Information Provided

- Purpose of the clinical trial
 - Investigational drug and SoC along with their common side effects
 - Treatment schedule (e.g., i.v. every 3 weeks until disease progression)
 - Process used to assign patients to the experimental and control arms
 - Schedule of required visits to the Clinical Investigator's office
 - Required blood tests and procedures (e.g., tumor biopsies)
 - Required biomarker testing of the patient's blood, urine and/or tumor
 - Expectations of the patient (e.g., providing complete medical records, keeping scheduled appointments, reporting all side effects)
 - Reimbursement provided for reasonable travel expenses
- [Note: Patients are not paid to participate in clinical trials.]
- Costs covered by the Sponsor, patient's insurance provider or patient
 - Required testing and visits after treatment stops (regardless of reason)

Unrelated to an *Informed Consent* for a clinical trial, a healthcare provider may ask a patient to sign a consent form related to research that does not directly benefit the patient (e.g., tumor tissue collection), but may benefit future patients.

The Importance of Privacy

Study Anonymity

In adherence with the Health Insurance Portability and Accountability Act (HIPAA), the identity of the patients enrolled in a clinical trial and their medical records are kept confidential. Only the Clinical Investigator (the patient's healthcare provider) and certain members of the clinical trial team know the identity of the patient. Each patient is assigned a unique "subject" number under which all of the medical records and tests identified in the *Informed Consent* are collected for the purpose of conducting the clinical trial.



Given the importance of patient privacy, it is not possible for the Sponsor to directly contact clinical trial patients to thank them for their time and contribution to the research process. The Sponsor does not know who the patients are, and "study anonymity" must be preserved to protect the identity of the enrolled patients. This is the reason why a patient who directly contacts the Sponsor is referred back to the Clinical Investigator. Only the Clinical Investigator knows whether a particular clinical trial is an appropriate treatment option for the patient.

Patient privacy is also the reason why the Sponsor cannot connect the patients participating in a clinical trial to form a support group or for any other reason.

The Results

Publication of Results

At the end of the clinical trial, the results may be published in a medical journal and/or presented at a medical conference. Clinical trial results are reported at a summary level. The identities of the patients who participated in the clinical trial are not disclosed in publications or presentations.

The Sponsor does not communicate the results directly to clinical trial patients for the patient privacy reasons mentioned earlier. Consequently, obtaining the study results can be challenging for two main reasons. First, several years can pass between a patient's study participation and the end of a clinical trial. Second, the patient would need to proactively contact the Clinical Investigator or search the Internet for the study results once the clinical trial is completed.



Depending on the clinical trial phase and research objectives, published results may include the:

- Percentage of patients who experienced each side effect and the severity of each side effect
- Percentage of patients who responded to treatment (i.e., ORR)
- Median time from start of treatment until disease progression (i.e., PFS)
- Median survival time from start of treatment (i.e., OS)
- Statistical metrics to indicate the strength or accuracy of the results (e.g., p-values, hazard ratios, confidence intervals)

The Search

Finding a Clinical Trial

The first step is to speak with your healthcare provider about clinical trials that might be appropriate for you. Since not all healthcare providers participate in clinical trials, you may be referred to another clinic or hospital, which may result in additional travel time and expense.

Additional ways to find clinical trials include:

- Searching the Internet for clinical trials being conducted at a cancer research hospital that is nearby or of interest to you.
 - If you know of a cancer research hospital, type its name and the words “clinical trials” in the search bar to quickly get to the right website to begin looking for a relevant clinical trial and contact information.
 - If you do not know of a research hospital, you can search <https://www.cancer.gov/research/nci-role/cancer-centers/find> to locate the closest one to you.
- Contacting a patient advocacy organization that has a relationship with a clinical trial matching service, such as the **Sandy Rollman Ovarian Cancer Foundation**.
- Searching active (open) clinical trials at <https://clinicaltrials.gov>, a service of the U.S. National Institutes of Health. Please be aware that this is a complex resource to search, and the search results will need to be discussed with your healthcare provider.



TIP: Select the ‘Advanced Search’ option to choose the clinical trial criteria of interest to you. For example, you may want to start by:

- Selecting “Open Studies” next to “Recruitment” to focus on active trials;
- Typing “ovarian cancer” in the “Conditions” box; and
- Selecting the clinical trial phase(s) you are willing to consider next to “Phase”.

Clicking on the “Search” button will produce a list of trials matching the criteria you selected. You can then click on any of the trial titles to learn more about the trial and get contact information.

The Match

Qualifying for a Clinical Trial

- Once a potential clinical trial is identified by a healthcare provider or through a personal search, the patient must meet certain criteria to enroll in the trial.
- Each trial has inclusion and exclusion criteria. The Clinical Investigator will review the patient's medical records to preliminarily determine if a patient meets the study criteria.
 - Inclusion criteria ensure the patient population is similar in terms of the cancer type and stage, previous treatments, general health status, etc.
 - Exclusion criteria also ensure the similarity of patients, but mainly prevent patients who may potentially be harmed by the investigational drug from enrolling in the trial.



TIP: It is important to consider with your healthcare provider the inclusion and exclusion criteria of trials to avoid ineligibility for current and potentially future clinical trials.

- Patients who appear to meet all of the inclusion criteria and none of the exclusion criteria are then walked through the *Informed Consent* to decide whether or not to voluntarily enroll in the clinical trial and complete any study-specific tests to confirm eligibility.

Study-specific tests can take some time to complete; therefore, participation in a clinical trial does not start immediately.



- It is possible to complete the *Informed Consent* and then be ineligible for the study based on the study-specific test results.

The Unanswered Questions

What would you like to ask your healthcare provider?



You could start with:

1. What, if any, clinical trial should I consider here at your office or at another hospital?
2. What do you know about the investigational drug and study design?
3. What information is there so far to suggest that the investigational drug might work?
4. What information is there so far on the side effects of the investigational drug?
5. What does the trial require of me?

The Glossary (A-L)

- **Administration or Dosing Schedule:** the dosing route (e.g., i.v.) and frequency (e.g., weekly) for a drug
- **Agent:** a drug or inactive compound (placebo)
- **Biomarker Testing:** an assessment of the patient's tumor, blood and/or urine to determine if the treatment or clinical trial is appropriate for the patient
- **Blinded Study:** a clinical trial in which the pharmaceutical company, physician and patient are not informed of the assigned treatment, nor do they get to choose the assigned treatment
- **Clinical Research:** the study of a drug in human patients
- **Clinical Trial Matching Service:** a service that provides a nurse or other healthcare provider to help a patient find an appropriate clinical trial
- **Confidence Intervals:** a statistically derived numeric range that most likely contains the clinical result, e.g., median survival time
- **Control Arm:** the treatment (e.g., SoC) that the experimental arm is compared to in a clinical trial
- **Crossover:** the moving of patients from the control arm to the experimental arm when a clear clinical benefit is observed with the experimental arm and the clinical trial design allows for this move
- **Disease Progression:** worsening of the disease
- **Efficacy:** how well the drug works
- **Experimental Arm:** the clinical trial treatment that includes the investigational drug
- **FDA:** U.S. Food and Drug Administration
- **Futility Analyses:** a statistical measurement of the likelihood that a clinical trial will achieve its study objectives; an ineffective trial is one that "meets futility"
- **Hazard Ratio:** measures the relative risk of a particular clinical outcome, such as disease progression; a value under 1.0 is desired
- **Healthcare Provider:** typically, the Gynecologic Oncologist or Medical Oncologist
- **Indication:** the disease for which a drug is approved for use or seeking to be approved for use
- **Informed Consent:** a lengthy document detailing the critical clinical trial information for patients considering participation
- **Interim Analyses:** an early assessment of safety and/or efficacy that takes place at a specified time point before study completion
- **Investigational Drug:** the drug being studied
- **Investigator's Brochure:** a detailed review of the clinical trial design, as well as the clinical and safety data collected for the investigational agent; this document is provided to healthcare providers and institutions

The Glossary (M-Z)

- **Median:** a midpoint wherein 50% of patients fall above and below this value (e.g., number of survival months)
- **Metrics:** measurements
- **Objective Response Rate (ORR):** the percentage of patients who respond either partially or completely to treatment
- **Overall Survival (OS):** the survival time after start of treatment
- **Placebo:** an inactive agent (e.g., sugar pill or saline solution) that looks just like the investigational drug; it is used in the control arm for comparison purposes
- **P-values:** a measurement of the probability of obtaining the desired result; a value of less than 0.05 is typically desired
- **Placebo-controlled clinical trials:** studies that compare the investigational drug plus the SoC to a placebo plus the SoC
- **Progression-free Survival (PFS):** the time between treatment start and worsening of the disease
- **Randomized:** a statistically driven system of assigning patients to either the experimental arm or control arm of a clinical trial
- **Recurrent Ovarian Cancer:** ovarian cancer that has come back after treatment
- **Standard of Care (SoC):** a single drug or drug combination with a proven clinical benefit; the drug(s) routinely used to treat the disease
- **Single-arm clinical trials:** studies without a control arm
- **Subjects:** patients; patients are provided with a “subject” number to protect their identity
- **Study:** another name for a clinical trial
- **Study Anonymity:** the protection of the patient’s identity and medical information during the research process
- **Study-specific tests:** procedures (e.g., biopsies) and/or tests (e.g., blood tests) that are required to determine if the clinical trial is appropriate for the patient, as well as tests done during the course of the study that would not be done if the patient was not being treated on a study
- **Test Article:** the investigational drug being studied
- **Treatment Regimen:** the drug or combination of drugs administered to the patient
- **Tumor Biopsies:** a surgical procedure to obtain a small sample of the cancerous tumor to determine how aggressive the tumor is and if it is likely to respond to certain treatments
- **Unblinded:** the ability to see what treatment has been assigned to a patient in a clinical trial

My Notes

My Notes

The People

Most Importantly, the Patient

Patients are the most important research pioneers in the development of new cancer treatments. It is only through their courage and selflessness that clinical trials are possible. We thank these brave women and their faithful caregivers for their tremendous contribution to making new treatment options available to future women facing an ovarian cancer diagnosis.



We especially thank the women of the **Sandy Rollman Ovarian Cancer Foundation** for their dedication to this project to help educate patients and caregivers on clinical trials. We dedicate this brochure in loving memory of Sarah who was instrumental in identifying some of the challenges patients face when trying to learn about and consider clinical trials.



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