

WITH AN INTERVIEW Expert



ABOUT ALLYSON J. OCEAN, M.D.

Dr. Allyson J. Ocean is Associate Professor of Clinical Medicine at Weill Cornell Medical College of Cornell University, medical oncologist and attending physician in gastrointestinal oncology, Solid Tumor Division, at New York-Presbyterian Hospital/Weill Cornell Medical Center, and practices medical oncology at The Jay Monahan Center for Gastrointestinal Health. Board certified in internal medicine, hematology, and medical oncology, Dr. Ocean's primary interest is in the biology and treatment of gastrointestinal malignancies. She has published numerous peer-reviewed manuscripts, book chapters, and abstracts and is an active member of several professional societies, including the American Society of Clinical Oncology, American Association for Cancer Research, and the Pancreatic Cancer Research Team. Dr. Ocean is currently leading numerous clinical trials investigating radiolabeled antibodies, antibody-drug conjugates, oncolytic viruses, and targeted therapies in pancreatic cancer. Dr. Ocean is Chair, Scientific Advisory Board and Co-Founder of Let's Win! Pancreatic Cancer. She is also an expert cohost of the PancChat, a monthly Twitter chat focusing on various aspects of pancreatic cancer.

Clinical Trials Update

Q&A with Allyson J. Ocean, M.D.

What is a clinical trial?

Clinical trials are scientific experiments that move medicine forward to help people live longer and live well. Clinical trials are the backbone of advancing medicine, and in some instances, a clinical trial can lead to a cure for a disease. They involve rigorous study and are designed to answer many questions including if a potential treatment is safe, if it works, how it works, if it is more effective than other treatments currently available, if there are any side effects and which patients will benefit most from a particular treatment. Before any new cancer treatment is tested in people, it is studied extensively in the laboratory.

A trial can examine drugs not yet approved or investigate approved drugs to determine how they might be used in new or different ways. For example, we can study different methods to administer treatments, such as in pill form if the treatments are usually given intravenously, or study new ways to track the disease and detect it earlier. Funding for trials often comes from private foundations, governmental agencies and pharmaceutical companies developing new treatments—it's not unusual for drug companies to partner with universities and cancer centers to carry out clinical trials.

Are there different types of clinical research?

You may be familiar with clinical trials looking for better ways to treat pancreatic cancer with medications, surgery, radiation, immunotherapy and other modalities. However, we might also look at prevention and better methods to diagnose the disease or conduct research examining screening and quality of life. Genetic studies are another area of intense research, especially with the focus on precision medicine, or tailor-made treatment based on an individual's genetic makeup or the molecular makeup of his or her individual tumor. There also are epidemiological, or data-driven studies focused on patterns and causes of disease in groups of people.

Who is eligible to participate in clinical trials?

Every study has its own rules, and participation is guided by a trial's eligibility requirements to ensure certain variables are controlled. Eligibility can include factors like age, gender, the patient's health prior to diagnosis and any other conditions the patient may have. In cancer studies, research may be geared to those with early-stage disease or metastatic disease. Treat-

ment history is often factored into eligibility, as some potential participants may be excluded based on prior treatment.

What are the different clinical trial phases?

Generally speaking there are five phases that are meant to answer specific questions and build on information from the previous phase. Sometimes researchers begin with a Phase 0 trial, which is the first trial among humans after pre-clinical research is completed. Here, scientists want to learn how a drug is metabolically processed and how it might affect the body. Researchers use very small doses of a drug and the trial itself involves only 10 to 15 people.

A Phase 0 trial is often combined with a Phase I trial, which is designed to find the best dose of a new drug with the fewest side effects. It's focused on safety and involves only 10 to 20 participants who may receive higher doses until side effects become too pronounced or until researchers see the desired effect. If a new drug is found to be safe and tolerable, it moves to a Phase II trial. In this phase, the goal is looking at safety and efficacy—does it work? Phase II trials typically have

CLINICAL TRIALS: TESTING PROMISING NEW PANCREATIC CANCER TREATMENTS

Research is changing the way patients are being treated, and a clinical trial may be the best option for some patients. Below are some resources to identify a clinical trial:

Lustgarten and Let's Win Clinical Trial Matching Service

<https://app.emergingmed.com/lustgarten/home>

This matching service provides free and unlimited access to current, verified clinical trial information. People who are interested can visit the website above or call 1-800-535-1867 Monday-Friday 8:30am-6pm EST to speak with a Clinical Trial Navigator. Services also are available in Spanish.

Pancreatic Cancer Collective

<https://pancreaticcancercollective.org/clinical-trial-finder/>

The Pancreatic Cancer Collective is an initiative of the Lustgarten Foundation and Stand Up To Cancer to accelerate research for pancreatic cancer patients who desperately need better treatments. The Collective has assembled experienced research teams to develop the most cutting-edge therapies and has conducted nearly 30 clinical trials at approximately 70 participating institutions involving more than 400 research investigators to date.

National Institutes of Health

<https://clinicaltrials.gov>

ClinicalTrials.gov is a database of privately and publicly funded clinical studies being conducted worldwide. Patients and families can search for studies actively recruiting patients and determine if they may be eligible to participate. Patients can also learn about new interventions/treatments under consideration.

about 50 people enrolled and participants are followed and monitored very closely. If everything looks favorable (i.e., the tumor is shrinking or cancer markers in the blood go down) and researchers believe a drug may be working, then the drug progresses to a Phase III trial.

Phase III trials are bigger and compare a new drug to standard-of-care treatment to determine if it is better than, as good as, or not as good as the standard-of-care treatment. A higher number of participants and more data allow researchers to reach statistically significant results. The goal of Phase III trials is to prove efficacy. Generally, these trials enroll at least 100 participants, and these participants are often randomized, which is the gold standard. This means participants are randomly placed by a computer into treatment groups called arms. Randomization ensures the people in the arms are alike and lets us know the results of the trial are because of the treatment, rather than differences in the group.

Sometimes, there are Phase IV trials. These test new drugs that are approved by the FDA but continue to be studied in thousands of patients to examine long-term safety and benefits.

What are the benefits of participating in a clinical trial?

Pancreatic cancer is a tough disease with limited treatment options, and clinical trials aid in identifying new, better treatments. One of the benefits of participating is societal, as patients help advance medicine, potentially enabling future generations of patients to have more treatment options. When patients participate in a clinical trial, they may also be helping themselves, as a clinical trial will provide access to a promising therapy that may be more effective than standard-of-care treatment.

Is there a downside?

Going into a trial can be scary, but so is having pancreatic cancer. There can be risks in early phase trials, as the drugs being tested are new and the side effects are unknown—which is precisely why the trial is being conducted in the first place. I tell my patients I feel the risk of passing away from pancreatic cancer is much greater than the risk of severe adverse events from a clinical trial.

The informed consent form, which is given to every patient prior to enrolling in a clinical trial, usually contains 15-30 pages. I can see the fear in people's eyes when they read it because the document outlines everything that could possibly go wrong. It's important to know the things that may go wrong are usually minor and treatable. People would be nervous if they read everything that could go wrong with taking an aspirin! I really try to counsel patients and spend a lot of time with them.

When in the treatment process should pancreatic cancer patients explore participating in a clinical trial?

Ideally, pancreatic cancer patients could explore clinical trials at the point of diagnosis before treatment (typically with a standard-of-care therapy) even starts. The National Comprehensive Cancer Network, a consortium of 30 leading cancer centers, includes clinical trials as a preferred option at every stage of pancreatic cancer treatment. However, it is important to note that there may not be a trial open at a patient's particular treatment center so they often start with standard-of-care therapy.

I think it is especially important for patients with metastatic disease to explore clinical trial options. Treatments for metastatic pancreatic cancer have improved, but we need more.

Most of the time treatment doesn't need to start immediately upon diagnosis. What needs to begin right away is dealing with any issues of pain or problems like biliary blockage. Knowing what clinical trial options are available and where they are available is also part of that immediacy.



**CLINICAL TRIALS ARE THE BACKBONE OF
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What resources would you recommend to help patients find out about which clinical trials are available and which ones they would qualify for?

The first step will be the treatment team, especially if the patient is receiving care at an academic center. Many times there are trials right at that institution. Other resources include disease-specific groups like the Lustgarten Foundation and Let's Win! Pancreatic Cancer, which are focused on pancreatic cancer. Another excellent resource is clinicaltrials.gov, which is a service offered by the National Institutes of Health. The National Cancer Institute and the Center for Information and Study on Clinical Research Participation also provide online search options. The hard part is weeding through the information. Again, the care team should be able to help patients navigate the information, and patient advocacy groups often have trained staff dedicated to assisting patients with finding trials.

What are some key questions patients should ask prior to enrolling in a clinical trial?

Aside from obvious questions such as what the purpose of the trial is, patients should really understand the protocol. A protocol is a carefully designed plan to safeguard the health of the participants and answer specific research questions including eligibility, procedures, dosages and trial length.

Another important question is to determine who is in charge of the patient's care. Clinical trial participants are very closely followed, often more than patients treated outside clinical trials, because the protocol requires frequent check-ups and thorough monitoring. In general, a clinical trial research team will work with the patient's doctor, if he or she is not part of the study team.

Ask about time commitments. That's part of the protocol, but I think it should be emphasized that sometimes patients have to come in once a week, maybe twice a week, maybe five days in a row. In other words, patients need to really understand the time commitment, which may involve some significant travel as well as the treatment time itself.

What safeguards are in place to protect clinical trial participants?

Clinical trials have multiple safeguards in place. Even in early-stage trials, there are evaluation points where doctors examine factors like toxicity. To be clear, treatments have been thoroughly tested in laboratory trials before they are ever tested with groups of patients. The trial protocol is reviewed and approved by an Institutional Review Board before it is even implemented. Participants' privacy is protected by HIPAA (Health Insurance Portability and Accountability Act of 1996) so participants' names remain secret and are not mentioned in any reports. And, as I mentioned before, there is a very robust informed consent procedure detailing every aspect of the trial.

Can participants choose to withdraw from a trial once it has begun?

Yes, absolutely, early withdrawal can happen at any point in the trial. Patients may choose to discontinue their participation for many reasons, and every researcher will respect those reasons.

What costs are associated with joining a clinical trial? Does the patient pay for the trial?

In the majority of trials the drug being investigated is paid for by the drug company or sponsor of the trial. If the trial includes other drugs that are standard of care, those are paid for by the patient's insurance. Other expenses, including travel or transportation, are frequently figured into the study and are often

reimbursed. During a trial, a patient's insurance generally covers doctor visits, hospital stays, standard treatments, lab tests and imaging. Research costs related to the trial, including the study drug, lab work, x-rays or other imaging solely used for the trial, are covered by the trial's sponsor. I advise patients to check with their insurance provider to determine coverage.

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What about travel and transportation if the study site is far from home?

As I mentioned, there is often reimbursement built into a study to cover costs of more frequent travel or transportation when taking part in a study. That can become harder if a patient is traveling a good distance, say to another part of the state or another state altogether. However, nothing is impossible. I recommend speaking to the research coordinator of the trial to see what arrangements can be made.

So trials can be conducted at numerous sites, and sometimes one of those sites may not be near a patient?

Yes, and it can be tough for patients in rural areas or those with transportation difficulties. A trial may be open at only one or a handful of institutions, or a trial can be multi-site, with numerous locations across the U.S. or around the world. Patients must consider travel to the trial site, since travel and, in some cases, even living accommodations will be necessary for the trial duration.

What happens if a patient's medical status changes during the course of a trial?

If a patient's health declines during a trial, perhaps because the cancer has progressed, and it is no longer possible to stay in the trial, then the patient will be taken off the trial.

Can a trial be discontinued while the participant is enrolled?

That's actually very rare but can happen if a drug company can no longer afford to continue funding the trial, or if the drug was deemed too toxic and is found to cause other adverse events.

Would a study participant eventually "complete" a clinical trial?

Yes. If a protocol calls for eight cycles of treatment over eight weeks and the patient completed that regimen, the patient has completed that trial. However, that participant may need to return for follow-up imaging at certain intervals, depending on what the clinical trial protocol states.

Will pancreatic cancer patients ever receive a placebo (a substance which has no active ingredient) while enrolled in a clinical trial?

Yes and no. Some patients may receive the current standard of care plus a placebo, but not the new drug being tested. The only way a patient would receive a true placebo providing no benefit is if no standard treatment option is available. Let's say there is a Phase III randomized trial in which an experimental drug is going to be given. Each participant has a 50-50 chance of getting a placebo in addition to the standard of care, but each participant also will always receive at least the standard of care. Think of it this way: one arm of the study receives FOLFIRINOX plus a new agent and one arm of the study receives FOLFIRINOX plus a placebo. Everyone is getting at least the standard of care.

Currently, less than 5% of pancreatic cancer patients are enrolled in clinical trials. How do you explain the low enrollment rate?

There are so many reasons, but a big one is the false belief that participants are little more than human guinea pigs. That's simply not true. The honest answer is no medical intervention—trial or not—is 100% risk-free. It's important for patients to know all clinical research studies must go through very thorough pre-clinical studies and strict ethical and regulatory checks before they get anywhere near a patient. The U.S. has one of the best records worldwide for patient safety.

As you know, clinical trials also require a time commitment, and patients may be overwhelmed already with a cancer diagnosis. The last thing they want to do is spend more time with doctors and clinics. They may also be worried about potential side effects and concerned about the loss of control over the treatment program.

Unfortunately, sometimes oncologists can be so over-worked and so busy treating patients during the day they just don't have the time to identify clinical trials for individual patients, especially if they aren't involved in research. When that happens, patients may depend on a family member or friend to identify potential clinical trials, or they may try to do it themselves and it just doesn't happen very often.

Sometimes, patients don't participate in clinical trials because previous treatment has disqualified them from trials, or they may have poor performance status. That's why it's so critical to talk about trials upfront.

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PANCREATIC CANCER IS CHALLENGING, BUT WE ARE GETTING CLOSER TO ANSWERS THAT WILL ULTIMATELY HELP PATIENTS. THAT'S THE GOAL AND WE WILL MEET IT.

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Are pancreatic cancer clinical trials increasing now that more researchers are studying this disease?

Yes, and I think that will also help enrollment in trials. There was a time when there were just a handful of trials and now there are hundreds. Pancreatic cancer is still considered a rare disease, though I know it doesn't seem that way. These rare diseases have poor outcomes because historically there hasn't been enough research examining new drugs in the space and there hasn't been enough research funding going to this disease. Thankfully, because of organizations like the Lustgarten Foundation, that has changed and research is exploding both in discovery science and in subsequent clinical trials stemming from those discoveries.

I've been working with pancreatic cancer patients and studying this disease for 20 years, and it is so clear to me we need to spread the message that progress is being made and the survival rate is improving. Doctors who aren't involved in pancreatic cancer research need to know that and so do patients and their families.

What about the patient who simply doesn't want to participate in a clinical trial?

That decision needs to be respected. As a medical oncologist, my primary goal is to help patients live longer and to live well. I want to see a cure for this disease, and that's only going to happen through rigorous clinical trials.

Patients and doctors have to consider quality-of-life issues that often go hand-in-hand with a patient's treatment goals. That's a conversation every doctor really needs to have with his or her patients. Standard-of-care treatment can be time-consuming and difficult, of course, but clinical trials can add another layer of time, and not everyone wants to spend time away from their homes and their loved ones.

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IT'S SO IMPORTANT FOR PATIENTS TO KNOW ALL CLINICAL RESEARCH STUDIES MUST GO THROUGH VERY RIGOROUS PRE-CLINICAL STUDIES AND STRICT ETHICAL AND REGULATORY CHECKS BEFORE THEY GET ANYWHERE NEAR A PATIENT.

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Do you see the role of clinical trials for pancreatic cancer patients changing, and what advice would you give to patients who are considering enrolling in a trial?

People are frightened when they get a diagnosis of pancreatic cancer and they often get paralyzed, not knowing which direction to turn. My advice is for patients to take a deep breath and get their “dream team” aligned. That “dream team” is every doctor who will be involved in a patient's care, as well as the patient's family members, friends and others in their support system. During this process, patients should ask absolutely everything they can think of, get answers from the experts and bring a family member or friend to doctor's appointments to help take notes and remind the patient of questions.

I want to emphasize the importance of pancreatic cancer patients having a gastrointestinal oncologist, someone who focuses on pancreatic cancer. That oncologist will have the breadth of knowledge necessary to guide treatment and will be most aware of new approaches and ongoing clinical trials.

The role of clinical trials has always been, and will always be, patient-centered in the sense that a trial is happening to find ways to better treat those with pancreatic cancer through extensive testing. Now, however, there is also a focus on adaptive trials, enabling researchers to modify a trial after it's started, allowing more flexibility and efficiency. The Lustgarten Foundation has started a new initiative allowing researchers to quickly determine if patients are responding to specific treatments and why. This program, the Robert F. Vizza Clinical Accelerator Initiative, was launched to conduct new clinical studies in a way that shortens the time required to move from concept to study launch and to develop smarter clinical trials generating data to improve patient outcomes.


Additionally, there are now more trials in the first-line setting, or initial treatment, and second-line setting, which is subsequent treatment, than ever before. And, there are more trials in the third-line setting, which is important for patients when prior treatments stop working or aren't effective at all. That's due to research.

There also is a greater emphasis on molecular tumor testing, to determine the specific makeup of the patient's tumor, which can help doctors identify the most effective treatment plan. Recent updates to the National Comprehensive Cancer Network guidelines include the incorporation of germline (genetic) testing for pancreatic cancer, to identify any inherited genetic mutations that could impact a treatment plan. The more we test patients, the more we are uncovering genetic mutations that can impact the therapies a doctor will choose. All of this information is going to lead to the development of new agents targeted to particular mutations.


Are you hopeful about the future of pancreatic cancer research?


I cannot emphasize enough the strides that have been made in just the last few years alone. Pancreatic cancer is challenging, but we are getting closer to answers that will ultimately help patients. That's the goal and we will meet it.

Join the conversation and follow us on social media.

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QUESTIONS TO ASK ABOUT CLINICAL TRIALS*

- Is there a chance I would be given a placebo and not a treatment?
- What is the study goal/purpose of the research?
- What are my other treatment options?
- How much experience do the doctor and the institution have with this treatment?
- Has the treatment been used at other cancer centers? If so, are the results about its safety and efficacy available?
- Is the drug being used to treat other cancers?
- Is the drug already being used in another country?
- What are the known potential risks and potential benefits of the treatment?
- What exactly does the treatment consist of, and how is it carried out?
- If this is a randomized trial, what are the treatment options?
- What are the major side effects seen so far? Minor side effects?
- What phase is this trial?
- Who looks out for me as a study participant?
- What happens if I do not respond to this treatment?
- What happens if I respond to the treatment but then stop responding?
- What are the costs?
- Will I need to come to this institution to receive treatment in this clinical trial? If so, how long can I expect to be here for each treatment?
- What happens when the clinical trial is over?

*Excerpted from *Navigating Pancreatic Cancer: A Guide for Patients & Caregivers*. ©2019 by Lustgarten Foundation National Institutes of Health. NIH clinical research trials and you. <https://www.nih.gov/health-information/nih-clinical-research-trials-you/basics>. Accessed August 23, 2020.

RIGHTS OF CLINICAL TRIAL PARTICIPANTS*

Patients have the right to be told:

- the purpose of the clinical trial;
- all risks, side effects and discomforts that might reasonably be expected;
- any benefits that can reasonably be expected;
- what will happen during the clinical trial and whether any procedure, drug or device is different from that used in standard medical treatment;
- available options and how they may be better than or worse than being in the clinical trial; and
- medical treatments available if complications occur during clinical trial participation.

Participants may also do the following:

- ask any questions about the clinical trial before giving consent to participate, and at any time during the clinical trial;
- have ample time, without being pressured, to decide whether to agree to participate in the clinical trial; and
- refuse to participate before entering the clinical trial, and leave the clinical trial at any time after it has begun.

*Excerpted from: *Navigating Pancreatic Cancer: A Guide for Patients & Caregivers*. ©2019 by Lustgarten Foundation National Institutes of Health. NIH clinical research trials and you. <https://www.nih.gov/health-information/nih-clinical-research-trials-you/basics>. Accessed August 23, 2020.



Let's Win! Pancreatic Cancer

Let's Win! Pancreatic Cancer (www.letswinpc.org), an affiliate of the Lustgarten Foundation, is an online community that connects doctors, researchers, and patients to the latest science-driven treatment options through a dynamic website and a robust social media program in both English and Spanish. Let's Win also introduces experienced physicians who do not specialize in pancreatic cancer to emerging treatments to combat the disease. The site features an interactive patient and family forum where patients describe their treatment plans; information on promising science; highlights from the latest clinical trials; information about managing care during treatment; current pancreatic cancer news; and inspiring videos from survivors.

ABOUT THE LUSTGARTEN FOUNDATION

The Lustgarten Foundation is the largest private funder of pancreatic cancer research in the world. Based in Woodbury, N.Y., the Foundation's mission is to cure pancreatic cancer by funding scientific and clinical research related to the diagnosis, treatment, and prevention of pancreatic cancer; providing research information and clinical support services to patients, caregivers and individuals at high risk; and increasing public awareness and hope for those dealing with this disease. Thanks to separate funding to support administrative expenses, 100% of your donation goes directly to pancreatic cancer research. For more information, please visit www.lustgarten.org.

GLOSSARY

The following is a list of clinical trial terms you may encounter:

Adverse event: A negative change or medical problem that occurs during a clinical trial or within a certain time period after the trial is completed. The "event" may not be related to the trial, however.

Arms: The assignment of a group or subgroup of clinical trial study participants who receive interventions, or no interventions.

Blinding: A clinical trial design in which one or more parties involved with the trial, such as the research team or participant, do not know which treatments have been assigned to which participants.

Clinical study: A research study conducted in human volunteers to answer specific health questions.

Control: The control or "standard" treatment is compared against the investigational treatment.

Eligibility criteria: The requirements that people who want to participate in a clinical study must meet.

Informed consent: Informed consent protects the participant. The researchers review trial details and answer all participant questions. The same information is also provided in written form.

Institutional Review Board: An IRB (Institutional Review Board) is a group of medical experts, and often members of the community, who have been designated to review and monitor all scientific research that involves humans.

Investigational drug: The drug being evaluated in the trial.

Phase: Categories, defined by the Food and Drug Administration, for describing the clinical trial.

- Phase 0/I trials test an experimental agent in a small group of people to evaluate safety, identify side effects and determine safe dosages.
- Phase II trials involve larger groups of people and are designed to assess whether an experimental treatment is safe and whether it works.
- Phase III trials are large studies comparing the experimental agent to a standard treatment.
- Phase IV trials are performed once a drug has reached the market, to provide additional information about the best use of the drug and its safety.

Protocol: A written document describing eligibility, procedures, medications, dosages, measures that will be evaluated, and study length, among other study requirements.

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