Welcome to Yale Cancer Center Answers with your hosts doctors Francine Foss, Anees Chagpar and Steven Gore. Dr. Foss is a Professor of Medicine in the Section of Medical Oncology at Yale Cancer Center. Dr. Chagpar is Associate Professor of Surgical Oncology and Director of the Breast Center at Smilow Cancer Hospital and Dr. Gore is Director of Hematological Malignancies at Smilow. Yale Cancer Center Answers features weekly conversations about the research, diagnosis and treatment of cancer and if you would like to join the conversation, you can submit questions and comments to canceranswers@yale.edu or you can leave a voicemail message at 888-234-4YCC. This week you will hear a conversation about pancreatic cancer with Dr. Jill Lacy. Dr. Lacy is Assistant Professor of Medicine at Yale School of Medicine. Here is Dr. Anees Chagpar. MedicalGore Welcome back to Yale Cancer Center Answers. This is Dr. Steven Gore and I am joined tonight by my co-host, Dr. Anees Chagpar and our guest, Dr. Jill Lacy. We are discussing pancreatic cancer clinic trials. Jill, before the break you were telling us that for patients who have had surgery for pancreas cancer, you have been able to prolong their survival with new combinations of chemotherapy is that right? Lacy Actually the advances have been in the treatment of metastatic pancreas cancer. Hopefully, those advances will then apply to patients who have had surgery. Gore Got you. Lacy In 2010, we learned about a large clinical trial for patients with metastatic pancreas cancer. In that trial, half of the patients received what was the standard of care, the drug gemcitabine and the other half received a three drug regimen, traditional chemotherapy drugs. They weren't new drugs but they were combined together. That regimen is referred to as FOLFIRINOX and the results of that study were really quite stunning. The patients who received the three drug regimen FOLFIRINOX lived nearly a year compared to half a year for the patients who received the one drug gemcitabine. In addition, the quality of life was better, because they were having control of the tumor related symptoms, in particular pain. So that was a huge breakthrough and since that time that regimen FOLFIRINOX has worked its way from cancer centers into the community and is being widely used and without a doubt is changing the natural history of this disease. We have actually seen a few patients with metastatic pancreas cancer treated with FOLFIRINOX who are surviving now to three years. So this is something that we never saw before. That was one major advance. The second advance came last year, again in a clinical trial for patients with metastatic pancreas cancer, half of whom again received the single drug gemcitabine, half received gemcitabine plus a newer drug called Abraxane. This is a drug that is used in breast cancer and very effectively and again what we saw was the patients that received the two drug combination lived longer, not quite as long as FOLFIRINOX, about eight and a half months versus six months. So a very effective regimen as well and so now in the metastatic setting we have two standard multidrug chemotherapy regimens that have improved the prognosis for these patients. Obviously, we would not call this a home run. We do not think we are curing folks, but the patients are living longer buying time and in general they are feeling better during that period of time, because it is controlling the tumor related symptoms. Chagpar It seems to

me that the FOLFIRINOX story, as well as the Abraxane story, are both stories of why patients ought to participate in clinical trials. Lacy Absolutely, we really appreciate our patients who are willing to go into clinical trials. It is often not an easy decision and neither of these discoveries would have been made possible if it wasn't for the patients that went into these studies. This is how we make advances in the field. Chagpar Because I can imagine the patients might have looked at you when you were trying to enroll them in clinical trials and saying, why should I take three drugs instead of one drug, even though these are standard chemotherapeutic drugs. Is it really going to make a difference, and yet they had twice the survival. Lacy That is correct and so again we really greatly appreciate our patients. We could not make advances like this without their involvement. Chagpar So what are the next clinical trials on the agenda? Lacy Obviously we have a long race to go. Still only about 5% of patients with this disease are surviving five years. So when you compare this to say breast cancer, which is 90%, prostate cancer is actually 98%, colorectal cancer, about 2/3 of patients survive five years. We have a long ways to go and so progress is going to come through research, understanding the basic biology of this disease, which is very complex, as well as clinical trials. We are actively engaged obviously in that endeavor here at Yale. For example, one of the studies that we have open here at Yale for patients with newly diagnosed metastatic disease is a study where the patients will be receiving FOLFIRINOX and added to that will be a biological agent that is called hyaluronidase. So what is that? It is an enzyme that breaks down the sort of scar like armor that we often see around the pancreas cancer and if you can break that down, the theory is that you will get better penetration of the drugs into the tumor and more effectiveness. So, that is one area of research looking at this sort of scar-like protection around pancreas cancer that has created some challenges in terms of treating it both in terms of drugs penetrating and also creates a hostile environment for the immune system in terms of attacking the tumor. We are also now looking at using these two multidrug chemotherapy regimens in the setting of patients who are able to undergo surgery. The hope is that if we use these more active regimens, either before or after or before and after surgery, that we will be able to increase the cure rate much as we are doing in breast cancer where after mastectomy or lumpectomy most patients or many patients will be getting chemotherapy. So if we can use more effective chemotherapy in pancreas cancer, maybe we can get that cure rate from 20% up to a much higher level. So, we have two studies at Yale looking at that aspect, one is for the patients who already had their surgery and come to us. This is again a randomized trial so sometimes it can be challenging for the patients. Half of them will get gemcitabine after the surgery and half of them will get gemcitabine and abraxane, the two drug regimen and hopefully from that we will learn that maybe two drugs will get that cure rate up higher and then the second study takes a slightly different approach. The patients who present to our surgeons who have localized disease are able to have surgery are offered the option of getting chemotherapy before surgery and there are a lot of reasons why that may be advantageous in terms of increasing the cure rate and the particular chemother-

apy that is a part of this protocol is the FOLFIRINOX regimen so highly active regimen. So they get about three months before surgery, then surgery and then three months after surgery. So those are some clinical trials that we are offering here at Yale.Dr Jill Lacy is Associate Professor of Medicine at Yale School of Medicine. We invite you to share your questions and comments. You can send them to canceranswers@yale.edu or you can leave a voicemail message at 888-234-4YCC and as an additional resource archived programs are available in both audio and written format atyalecancercenter.org. I am Bruce Barber hoping you will join us again next Sunday evening at 6:00 for another addition of Yale Cancer Center Answers here on WNPR Connecticut's Public Media Source for news and ideas.