

VIDEO TRANSCRIPT

Scleroderma: Cyclophosphamide Or Transplantation

STUDY-PROCEDURE PHASE

Length 15:15 minutes

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| SCOT logo Study-Procedure Phase Length: 15:15 | Music |
| SCOT logo Text on screen: Study-Procedure Phase | Music |
| Dr. Leslie Crofford, University of Kentucky, sitting in a chair. | Dr. Leslie Crofford: Hello. I am Dr. Crofford, a rheumatologist at the University of Kentucky and an investigator in the SCOT study. SCOT stands for Scleroderma Cyclophosphamide Or Transplantation. |
| Image of physicians looking at x-rays. | Dr. Leslie Crofford: The SCOT study is being done because more information is needed about treating patients with severe scleroderma. Approximately 226 participants across the U.S. and Canada will take part in SCOT. |
| Text on screen: High-dose immunosuppressive therapy followed by stem cell transplantation vs. High-dose monthly Cytosan (cyclophosphamide) Image of laboratory pipettes. | Dr. Leslie Crofford: Half will receive a stem cell transplant and half will receive a high-dose monthly chemotherapy medication called Cytosan, also known as cyclophosphamide. Through this clinical research study, we hope to determine if these 2 interventions can slow down or stop scleroderma from becoming more severe or possibly reverse the effects of the disease. |
| Image of patient having blood pressure taken. Rotating image of a coin. Profile image of a female. | Dr. Leslie Crofford: As we discussed in the other SCOT video, eligible participants who decide to take part will be randomly assigned to 1 of 2 study groups. "Randomly assigned" means you or your doctor will not be able to choose which intervention you will receive. Assignment to a study group will be done by chance—sort of like a flip of a coin. In this video, I'd like to tell you more about the 2 procedures being studied and describe what will be required of you should you choose to participate. Let's begin by discussing the stem cell transplant group. |
| Text on screen: Stem Cell Transplant Group | Dr. Leslie Crofford: The goal of stem cell transplantation is to destroy immune cells that are thought to be activating your scleroderma and then to |

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| <p>Illustration of blood cells in the human body.</p> <p>Human figure with a central venous catheter on chest, blood bag, blood processing machine, frozen lab specimen, receiving an injection and radiation</p> | <p>give your body new cells that will function normally.</p> <p>As you may already know, this will be an “autologous” transplant of your own blood stem cells. “Autologous” means that the stem cells will come from your own body. The SCOT study does not involve the use of any stem cells from embryos or stem cells from another person.</p> <p>Now, let’s go over how the transplant will be done.</p> |
| <p>Illustration of human figure with central venous catheter on chest.</p> | <p>Dr. Leslie Crofford:</p> <p>First, before the stem cell transplant process begins, a central venous catheter will be inserted under the skin on your chest and threaded inside a vein until the end of the catheter is close to your heart. This will be done to help you avoid experiencing numerous needle and IV sticks. This catheter will remain in place throughout your transplant. It’s small and not typically noticeable underneath clothing. You’ll be taught how to care for it.</p> |
| <p>Illustration of different types of blood cells.</p> | <p>Dr. Leslie Crofford:</p> <p>Next, your doctors will give you injections of blood stimulants called growth colony stimulating factor or G-CSF. This medication stimulates your bone marrow to make new stem cells and then release them into your bloodstream. This step is called stem cell mobilization.</p> |
| <p>Human figure with catheter connected to a blood bag.</p> <p>Pheresis machine.</p> | <p>Dr. Leslie Crofford:</p> <p>Then, through a process called leukapheresis, the study doctors will collect the stem cells from your blood. This is done by connecting your central venous catheter to a pheresis machine. As your blood circulates through it, the machine will pull out the stem cells. The cells will be stored for future use. The remainder of your blood will be returned to your body through the catheter. In total, about 20 to 40 pints of blood will be removed and returned to you. Approximately 1 to 5 leukapheresis collections will be needed, and each collection will take about 4 hours.</p> |
| <p>Blood processing machine.</p> <p>Tube of frozen blood sample.</p> <p>Image of hospital admission area.</p> | <p>Dr. Leslie Crofford:</p> <p>Next, your blood cell samples will undergo a process called CD34 selection where specific types of stem cells with a protein called CD34 are chosen. These CD34 cells will be frozen and stored until the time of your transplant. This is called cryopreservation. Cells thought to be associated with activating scleroderma will be removed during the selection process.</p> <p>You will then be admitted to the hospital for the conditioning</p> |

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| | phase. |
| <p>Illustration of human figure receiving an injection and radiation.</p> <p>CT image of the lungs.</p> <p>IV bag.</p> <p>IV bottle, vial, syringe.</p> <p>Dr. Crofford.</p> <p>Image of various pills.</p> | <p>Dr. Leslie Crofford:</p> <p>In order to prepare your body for the stem cell transplant, you will be given total body irradiation, a chemotherapy drug called Cytoxan, and a medication called ATGAM. Irradiation will be given twice daily for 2 days in a row. It will be directed at all of your bone marrow sites to eliminate abnormal immune cells. Both your lungs and kidneys will be shielded from the radiation to reduce the risk of damage.</p> <p>In addition to the irradiation, Cytoxan will be given through your central venous catheter for 2 consecutive days. You'll also be given ATGAM if you are not allergic to it. ATGAM is a protein that kills certain kinds of white blood cells that are particularly active in scleroderma. You'll be given a total of 3 doses of ATGAM through your catheter. The goal of this "conditioning" phase is to destroy autoimmune cells and to prepare your body for the transplant.</p> <p>In addition to medications given to you as part of your standard medical care, you'll be given corticosteroids and an ACE inhibitor, which helps to control scleroderma-related high blood pressure.</p> |
| <p>Illustration of blood cells a catheter and arrow pointing toward human figure.</p> <p>Female patient in hospital bed.</p> <p>Laboratory worker handling blood bag.</p> | <p>Dr. Leslie Crofford:</p> <p>On the day of your transplant, your blood stem cells will be removed from the freezer and thawed. These stem cells will be given through your central venous catheter. This will take about 30 minutes.</p> <p>You probably will be hospitalized until your white blood cell levels recover. This may take approximately 14–21 days after transplantation. White blood cells play an important role in fighting bacteria and viruses that may cause infection. During this time, you'll be given antibiotics to protect against infection, and you'll continue to receive ATGAM and corticosteroids. Since your red blood cell counts and platelets will become low, you can expect to receive at least 1 blood product transfusion. Your central venous catheter will be removed when your transplant is complete.</p> |
| <p>Illustration of overall stem cell process—human figure with a central venous catheter on chest, blood bag, blood</p> | <p>Dr. Leslie Crofford:</p> <p>Overall, the stem cell transplant process will take approximately 3 months. The time between your first G-CSF injection and hospital discharge will be about 25–35 days. After hospital discharge you'll need to stay close to the transplant center for another 1–2 months for daily follow-up visits.</p> |

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| processing machine, frozen lab specimen, receiving an injection and radiation | |
| Text on screen: High-Dose Cytoxan Group Image of healthcare providers talking. Image of a calendar. | Dr. Leslie Crofford: Now, let's discuss what is involved if you are randomized to the high-dose Cytoxan group. The goal of high-dose Cytoxan is to reduce the number of immune cells that are believed to be causing your scleroderma. As you may already know, Cytoxan has been used by doctors to treat autoimmune diseases like scleroderma. However, in the SCOT study, the dose being tested is higher than what is normally given. The length of the intervention is 12 months which is longer than typically prescribed. Here is an overview of what to expect. |
| Image of laboratory worker performing lab test. Female drinking water. Illustration of human figure with IV tubing in the arm, connected to an IV bag. IV bags. | Dr. Leslie Crofford: In order to maximize your safety during the 12 months of high-dose Cytoxan, you'll have a physical exam and several laboratory tests prior to each infusion. A urine specimen will be needed and approximately 1 tablespoon of your blood will be taken each time. To prepare your body for the infusion, you'll be asked to drink 4 to 8 cups of fluid a day for 2 days before your dose. Each Cytoxan infusion will be given through a small intravenous catheter. A new intravenous catheter will be placed each time you come in and then removed at the end of each infusion. Medications will be given to decrease possible side effects, such as nausea and vomiting. |
| Image of female drinking a glass of water. Blood sample tubes and reports. Syringe withdrawing a blood sample from a vial. | Dr. Leslie Crofford: After your infusion, unless you are instructed differently by your doctor, you'll need to drink at least 8 cups of fluid each day for 2 days. You'll also need to urinate often after each infusion, including once during the night following each dose. This will help your body flush out the Cytoxan to avoid prolonged bladder contact with the drug. Ten to 14 days after each infusion, you'll be asked to provide a urine specimen and approximately 1 tablespoon of your blood will be taken. Your doctor will check these samples to be sure your white blood cells, platelets, and kidney function are stable. These tests must also be done to be sure it's safe to administer your next dose of Cytoxan. |
| Text on screen: Follow-up | Dr. Leslie Crofford: Regardless of which intervention you receive, you'll be asked to stay in the study for 5 years for follow-up assessments at the |

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| <p>Image of patient having blood taken.</p> <p>Female patient in exam room.</p> | <p>rheumatology and transplant centers.</p> <p>Frequently over the first year, you'll have physical exams and blood samples taken. After the first year, follow-up visits will occur regularly through year 5. Periodic comprehensive evaluations at the transplant center will be required to evaluate the function of your heart, lungs, and gastrointestinal system.</p> |
| <p>Image of car on the road.</p> <p>Healthcare provider on the telephone.</p> | <p>Dr. Leslie Crofford: Depending on where you live, you may need to travel for annual follow-up visits to evaluate your scleroderma and response to the interventions. SCOT participants will be eligible to receive reimbursement for travel and lodging for these follow-up visits; however, some limits will apply. Please talk with the SCOT study staff to find out more information about your specific travel needs.</p> |
| <p>Images of phones.</p> <p>Female preparing food in the kitchen.</p> <p>Family with 2 children sitting on a couch.</p> | <p>Dr. Leslie Crofford: Every 3 months during the 2nd and 3rd year, a study staff member will contact you to ask questions regarding your health status. Throughout the study you'll be asked to fill out surveys periodically. These will be used to evaluate how you feel and how well you are able to do your usual activities.</p> |
| <p>Text on screen: Risks</p> <p>Female reviewing a form.</p> <p>Dr. Crofford sitting in a chair.</p> | <p>Dr. Leslie Crofford: It is important that you take the time necessary to learn about the risks associated with each intervention. In particular, it is important that you understand the stem cell transplant's intervention may have serious complications including death, particularly in the first year after transplant. Past experience has shown that approximately 10% of patients participating in this study could die as a result of the stem cell transplant. Although taking part is completely voluntary and you may withdraw from the study at any time, if you receive a stem cell transplant and decide to stop in the middle of the procedure, you could die.</p> |

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| <p>Text on screen: Some of the other side effects which could occur with the SCOT interventions include: * Nausea, vomiting, diarrhea * Hair loss * Decreased appetite and energy</p> | <p>Dr. Leslie Crofford: Some of the other side effects which could occur with the SCOT interventions include: * Nausea, vomiting, diarrhea, * Hair loss, * Decreased appetite and energy, * Decreased white blood cell counts, which increases your risk of infection, * Increased risk for damage to the heart, lungs, brain, kidneys, liver, and/or reproductive organs,</p> |
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| <p>* Decreased white blood cell counts, which increases your risk of infection</p> <p>* Increased risk for damage to the heart, lungs, brain, kidneys, liver, and/or reproductive organs</p> <p>* Increased risk for cancer</p> <p>* Sterility—the inability to conceive children</p> <p>Physician speaking to a patient.</p> | <p>* Increased risk for cancer, and</p> <p>* Sterility—the inability to conceive children</p> <p>Your doctor will discuss all the potential risks with you. These risks are also described in your consent form.</p> |
| <p>Image of healthcare providers, laboratory worker performing lab test.</p> <p>Image of scale.</p> | <p>Dr. Leslie Crofford: Regardless of the group to which you are assigned, it's important to remember that these study procedures are investigational and may not result in your improvement or prevent the progression of your disease. The word "investigational" means that the interventions are still being tested in research studies and are not approved by the U.S. Food and Drug Administration or FDA for the treatment of scleroderma.</p> <p>A benefit of participating in this study is that you will receive one of two investigational interventions not currently offered as standard medical care. In addition, your participation will contribute to our knowledge regarding the safety and effectiveness of these 2 interventions.</p> |
| <p>Text on screen: Important Considerations</p> <p>Image of a man thinking.</p> <p>Man and woman.</p> | <p>Dr. Leslie Crofford: As you consider taking part in SCOT, take all the time you need.</p> <p>Because the interventions used in this research study are investigational and can cause serious side effects, it's important that you fully discuss all of your options with your doctors, family, friends, and supporters.</p> <p>As you consider SCOT, ask yourself the following questions—</p> <p>Will I be satisfied if I am assigned to either one of the study procedures?</p> <p>This is an important question to consider because neither you nor your study doctor will be able to choose which intervention you</p> |

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| <p>Family together.</p> <p>Dr. Crofford sitting in a chair.</p> | <p>receive. If you have a strong preference for a specific study group, you should tell your doctor.</p> <p>Do I have enough support from my family and friends to participate?</p> <p>If you decide to take part in SCOT, you'll need someone to drive you to appointments, help take care of you, and oversee your responsibilities at home.</p> |
| <p>Family talking.</p> <p>Image of cars on the road.</p> <p>Woman thinking.</p> <p>Healthcare provider recording information.</p> <p>Woman thinking.</p> <p>Healthcare provider writing on a form.</p> <p>Reading glasses.</p> | <p>Dr. Leslie Crofford: Will I be able to handle the travel requirements of this study?</p> <p>Depending on where you live, traveling long distances may be necessary. Ask the SCOT study staff to describe when and where you'll need to travel, and write down this information in your SCOT patient brochure. Financial support for travel is available.</p> <p>Am I willing to commit to the length of this study?</p> <p>SCOT participants must agree to return for follow-up visits over the next 5 years. The information collected from these appointments is very important to understanding the safety and effectiveness of these procedures.</p> <p>Do I understand the possible risks and side effects associated with each intervention?</p> <p>Each procedure has associated risks and side effects. Although it's impossible to know how your body will respond, the SCOT study staff will review all the known risks and side effects with you. In particular, they will explain that stem cell transplantation has significant risks and can cause death.</p> <p>Have all of my questions been answered?</p> <p>Before you decide to participate, you should ask all the questions that you can think of.</p> |
| <p>List of SCOT Steering Committee members: Leslie J. Crofford, MD University of Kentucky Daniel E. Furst, MD University of California, Los Angeles Maureen D. Mayes, MD, MPH University of Texas–Houston Health</p> | <p>Dr. Leslie Crofford: For your safety and the safety of each participant, every aspect of this research study has been carefully reviewed by the leaders of the SCOT study, the National Institute of Allergy and Infectious Diseases, and scleroderma specialists nationwide.</p> |

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| <p>Science Center Peter A. McSweeney, MD Rocky Mountain Cancer Centers Richard A. Nash, MD University of Washington School of Medicine Keith M. Sullivan, MD Duke University Medical Center Dennis D. Wallace, PhD Rho Federal Systems Division, Inc.</p> | |
| <p>Dr. Crofford sitting in a chair.</p> | <p>Dr. Leslie Crofford: We need to add to our knowledge about scleroderma. This knowledge can only come from carefully designed clinical research studies such as SCOT. Thank you for your time.</p> |
| <p>Text on screen: Both of the SCOT study procedures are considered investigational and are not available as standard medical treatment.</p> <p>Please carefully review the SCOT study consent forms to decide if this research study is right for you.</p> <p>Text on screen: Produced by Duke Clinical Research Institute, 2005</p> | <p>Music</p> |