Patient Handbook on Stem Cell Therapies

Appendix I of the Guidelines for the Clinical Translation of Stem Cells

December 3, 2008
INTRODUCTION

We have all heard about the extraordinary promise that stem cell research holds for the treatment of a wide range of diseases and conditions. However, there is a lot of work still needed to take this research and turn it into safe and effective treatments.

The International Society for Stem Cell Research (ISSCR) is very concerned that stem cell therapies are being sold around the world before they have been proven safe and effective.

Stem cell therapies are nearly all new and experimental. In these early stages, they may not work, and there may be downsides. Make sure you understand what to look out for before considering a stem cell therapy.

Remember, most medical discoveries are based on years of research performed at universities and companies. There is a long process that shows first in laboratory studies and then in clinical research that something is safe and will work. Like a new drug, stem cell therapies must be assessed and meet certain standards before receiving approval from national regulatory bodies to be used to treat people.

What does this really mean for you as a patient, doctor, friend or family member? Below we hope to answer some of your questions on stem cells and stem cell therapies and give you the resources you and your doctor need to make the best decisions possible for treatment.

The ISSCR is a non-profit professional stem cell research organization with a commitment to ensure the promise of stem cell research is delivered to patients in a safe, effective and fair manner.

FREQUENTLY ASKED QUESTIONS

The ISSCR receives many questions regarding clinical therapies using stem cells and the availability of stem cell clinical trials. Below, we seek to address some of the important elements that underlie these questions.

1. What are stem cells?
2. What is a stem cell therapy?
3. For what diseases or conditions are stem cell treatments well established?
4. What are some of the special considerations for stem cell therapies?
5. What is the usual process for developing a new medical treatment?
6. What are the differences between an approved clinical treatment and an experimental intervention?
7. What is a clinical trial?
8. What is an informed consent form or treatment consent form?
9. How do I know if an approved stem cell therapy is safe?
10. What should I look for if I am considering a stem cell therapy?
11. What should I be cautious about if I am considering a stem cell therapy?
12. What else should I ask?
13. Should I get a second opinion?
14. How can I find out about clinical trials that use stem cells?
1. WHAT ARE STEM CELLS?

Stem cells are defined by two properties. First, they can ‘self-renew,’ that is they can divide and give rise to more stem cells of the same kind. Second, they can mature or ‘differentiate’ into specialized cells that carry out a specific function, such as in the skin, muscle, or blood.

There are many different types of stem cells. These include embryonic stem cells that exist only at the earliest stages of development; and various types of ‘tissue-specific’ stem cells (sometimes referred to as ‘adult’ or ‘somatic’ stem cells) that are found in various tissues in our bodies. Recently, cells with properties similar to embryonic stem cells, referred to as induced pluripotent stem cells (iPS cells), have been engineered from specialized cells such as skin cells.

Visit the ISSCR Web site to read Stem Cell Facts: The Next Frontier, for more information on stem cells, stem cell research, a stem cell glossary and some of the challenges that need to be addressed in order to use stem cells in treating a wider range of diseases: http://www.closerlookatstemcells.org/docs/default-source/patient-resources/stem-cell-facts.pdf

2. WHAT IS A STEM CELL THERAPY?

A stem cell therapy is a treatment that uses stem cells, or cells that come from stem cells, to replace or to repair a patient’s cells or tissues that are damaged. The stem cells might be put into the blood, or transplanted into the damaged tissue directly, or even recruited from the patient’s own tissues for self-repair.

3. FOR WHAT DISEASES OR CONDITIONS ARE STEM CELL TREATMENTS WELL ESTABLISHED?

The range of diseases for which there are proven treatments based on stem cells is still extremely small. Disorders of the blood and immune system and acquired loss of bone marrow function can, in some cases, be treated effectively with blood stem cell transplantation.

Doctors have been transferring blood stem cells by bone marrow transplant for more than 50 years, and advanced techniques for collecting blood stem cells are now used clinically. Umbilical cord blood, like bone marrow, is often collected as a source of blood stem cells and is being used experimentally as an alternative to bone marrow in transplantation.

Other tissue-specific stem cells may also play a role in tissue transplants that have been performed for several years. For tissues and organs such as skin and cornea, stem cells contained in these tissues contribute to long-term regeneration.

Other stem cell treatments are still experimental. This means that it has not yet been shown that this treatment is safe or that it will work.

4. WHAT ARE SOME OF THE SPECIAL CONSIDERATIONS FOR STEM CELL THERAPIES?

Therapies based on stem cells are largely new and there is a lot that we still need to learn.

To start, there are particular challenges in preparing stem cells for use as a medicine. Unlike drugs, stem cells cannot necessarily be produced and tested for quality in large batches, and treatments may even be specific to one patient.

For most diseases, it is still being determined which cells will work best to repair a particular damaged or diseased tissue, and how to get those cells to the right place in the body.

Furthermore, side effects and long-term safety must be determined, since transplanted cells may remain for many years in patients’ bodies. Therefore, careful monitoring and extended follow-up of patients who receive stem cell treatments is extremely important.
5. WHAT IS THE USUAL PROCESS FOR DEVELOPING A NEW MEDICAL TREATMENT?

This process is also known as *clinical translation*.

The process starts with very general research into how a tissue or cell usually works and what goes wrong in a particular disease or injury. This information is used to design and develop ways to diagnose, stop or fix what goes wrong.

To test whether and how a new intervention might work for a particular disease or injury, studies are done first *in vitro* (in a dish), and then wherever possible in animals with a disease or injury like ours. These are referred to as preclinical studies; *preclinical studies* should be reviewed by other experts, published and repeated before moving to research in patients.

After demonstrating a reasonable expectation that the treatment will work and be safe, permission is sought to conduct a clinical trial in humans, starting with a very small number of individuals. In some cases, new experimental treatments might be tried on a very small number of people before a clinical trial is started.

As the safety and side effects are better understood and methods to get the treatment to the correct part of the body are improved, the number of patients is gradually increased and the new intervention is compared against existing treatments.

Once safety and effectiveness is demonstrated through this formal process, a national or regional regulatory agency, for example, the US Food and Drug Administration (FDA) or the European Medicines Agency (EMEA), will approve the use of the treatment for particular diseases or conditions.

6. WHAT ARE THE DIFFERENCES BETWEEN AN APPROVED CLINICAL TREATMENT AND AN EXPERIMENTAL INTERVENTION?

An approved clinical treatment is a medical practice that has been shown through a formal process of clinical trials to be reasonably safe and effective for treating a particular disease or condition. Normally, such treatments will be approved by a national or regional regulatory agency, for example, the US Food and Drug Administration (FDA) or the European Medicines Agency (EMEA).

An experimental intervention is new, untested, or different from the usual medical treatment. It has not yet been proven that it is safe or that it will work in treating the particular disease.

7. WHAT IS A CLINICAL TRIAL?

A clinical trial is a research study designed to answer specific questions about a new treatment or a new way of using current treatments. Clinical trials are used to establish whether new treatments are safe and effective. It is very important to understand that the new treatment being tested is *unproven*. It may not be better than, or even as good as, existing treatments.

Some research studies are not trials. In some cases, new experimental treatments might be tried on a very small number of people before a clinical trial is started. Again, the new treatment being tested is *unproven*.

The fact that a procedure is experimental does not automatically mean that it is part of a research study or clinical trial. Experimental procedures should be made part of a formal research study at an early stage in order to determine whether they are safe and effective.

Further information explaining and describing clinical trials written by the National Institutes of Health (USA) can be found at [www.clinicaltrials.gov/ct/info/resources/](http://www.clinicaltrials.gov/ct/info/resources/).
8. WHAT IS AN INFORMED CONSENT FORM OR TREATMENT CONSENT FORM?

An Informed Consent Form or Treatment Consent Form outlines your role and what might happen to you. It should clearly provide a detailed description of the treatment or procedure in language you understand. It should explain your options for treatment, the risks, your rights and your responsibilities. A consent form is a good way to get the information you need.

You should receive a consent form for any experimental stem cell treatment, even if the treatment is not part of a clinical trial. It should emphasize the unproven nature of the treatment and outline the specific risks associated with new stem cell therapies.

Once you have read and understood the consent form and have had your questions answered, the form should be signed by you (or your legal representative) and the person providing the information. You should receive a copy of this form.

The informed consent form for a clinical trial should include:

• that the trial involves research and why the research is being done;
• what the study treatment is; if a randomized trial;
• what the chance of you receiving different treatments is (placebo or alternative treatment);
• what other medical options there are;
• what is involved in the research study before, during and after treatment including procedures like blood-draws;
• who will perform the study;
• how long the study will last;
• the risks of the treatment;
• contact details of the point person and contact details of an independent organization that protects patient rights;
• your responsibilities as a subject and information on who may see your research/medical data and your rights to confidentiality;
• your right to be informed of any new information that may effect your decision to continue participating in the research study;
• the circumstances under which you may be withdrawn from the trial;
• your right to withdraw at any time without consequences; and
• how many patients are involved in the study.

The documents should not include language that releases the investigator, the institution, the sponsor or their agents from liability for negligence.

9. HOW DO I KNOW IF AN APPROVED STEM CELL THERAPY IS SAFE?

No medical treatment can ever be described as completely safe. There are risks involved with all medical treatment, some small, some great. These risks, even if they are small, should be explained clearly to you by a medical professional.
10. WHAT SHOULD I LOOK FOR IF I AM CONSIDERING A STEM CELL THERAPY?

You need to be sure that there is good scientific evidence that the treatment is safe and effective, and that your rights as a patient are being respected. To begin, ask for evidence that:

- Preclinical studies (see question 5) have been published, and reviewed and repeated by other experts in the field.
- The providers have approval from an independent committee such as an Institutional Review Board (IRB) or Ethics Review Board (ERB) to make sure the risks are as low as possible and are worth any potential benefits, and that your rights are being protected.
- The providers have approval from a national or regional regulatory agency, such as the Food and Drug Administration (FDA) or the European Medicines Agency (EMEA) for the safe conduct of clinical trials or medical use of a product for this disease.

Some smaller research studies may not need this level of regulatory approval, but must have approval from an independent review committee (see above) and support from the clinical and administrative leadership where the procedure will be done.

11. WHAT SHOULD I BE CAUTIOUS ABOUT IF I AM CONSIDERING A STEM CELL THERAPY?

This is not a comprehensive list but some major warning signs include:

Claims based on patient testimonials. Patients want to believe so much that a treatment is helping them that they can convince themselves that it has. They may even have experienced some recovery unrelated to the treatment. Unless there has been carefully evaluated clinical research it is very difficult to know what is a true effect of the treatment and what you can expect.

Multiple diseases treated with the same cells. Unless the diseases are related, such as all being diseases of the blood, different diseases, such as Parkinson’s disease and heart disease, would be expected to have very different treatments. Also, you want to be treated by a doctor that is a specialist in your disease.

The source of the cells or how the treatment will be done is not clearly documented. This should be clearly explained to you in a treatment consent form (see question 8). In addition, there should be a ‘protocol’ that outlines the treatment in detail to the medical practitioner. The protocol is the ‘operating manual’ for the procedure. While it may not be made available to you automatically, you should be able to request this. For a clinical trial or experimental treatment, protocols should have been reviewed for scientific merit by independent experts and approved by an ethics committee to ensure that the rights and well-being of the participants will be respected. Ask who has approved this protocol and when the approval expires.

Claims there is no risk. There is always risk involved with treatment. Information about the possible risks should be available from preclinical or earlier clinical research.

High cost of treatment or hidden costs. It is not customary for someone to pay to be in a clinical trial (other than perhaps travel and other personal expenses). Consider whether you should pay for a treatment that is unproven. Furthermore, ask about the costs of emergency medical care if something goes wrong, particularly if you are outside your own country. Find out what costs your national health program or health insurance provider will cover, in what circumstances and in what countries.
12. WHAT ELSE SHOULD I ASK?

Ask a lot of questions about the treatment being offered, and seek a second opinion from a doctor you trust. You should not be rushed to make a decision—make sure you understand the entire treatment plan and any risks.

The doctors involved should know a lot about your disease, other treatment options and the evidence that the treatment they are offering will be safe and that it will work. You should be provided with an Informed Consent Form or Treatment Consent Form that should address many of your questions (see question 8). This should be signed by both you and the doctor.

The treatment

- Is the treatment routine for this specific disease or condition?
- Is the treatment part of a formal clinical trial?
- What are the alternative treatment options for my disease or condition?
- If I have this treatment, could it affect whether I get into another clinical trial or am able to have another treatment?
- What are the possible benefits I can expect? How will this be measured and how long will this take?
- What other medications or special care might I need?
- How is this stem cell procedure done:
  - What is the source of the stem cells?
  - How are the stem cells identified, isolated and grown?
  - Are the cells differentiated into specialized cells before therapy?
  - How are the cells delivered to the right part of the body?
  - If the cells are not my own, how will my immune system be prevented from reacting to the transplanted cells?

Scientific evidence and oversight

- What is the scientific evidence that this new procedure could work for my disease or condition? Where is this published?
- Have there been (earlier) clinical trials? What was learned from these trials?
- Is there any independent oversight of the treatment plan, for example, an Institutional Review Board? Can you provide me several names of scientists and clinicians who can give me independent advice?
- Is there any independent oversight or accreditation of the clinic where the treatment will be done and the facility where the cells are processed?
- Is there approval from a national or regional regulatory agency, such as the US Food and Drug Administration (FDA) or the European Medicines Agency (EMEA), for this treatment of this specific disease?

Safety and emergencies

- What are the risks of the procedure itself, and the possible side effects both immediate and long-term?
- Are there any other risks to me in joining in the study?
- What will be done if an adverse reaction (bad side-effect) develops? Who is the person to contact in an emergency or research-related injury? Who will provide emergency medical care?
- Is the clinic adequately prepared to handle emergencies such as a serious allergic reaction?
- What follow-up treatment will be received, and for how long? What will I need to do?
- Who is the doctor in charge of the treatment? What specialized training does this doctor have? How well trained are the other doctors and the technical support staff?
Patient rights

- What are my rights as a participant—for example, confidentiality, my right to be informed of any new information that might come up, my right to withdraw from the treatment process?
- What compensation am I entitled to if I am injured as a result in taking part in this study?

Cost

- What are the costs of the treatment? What does this include? What other costs will I incur?
- What would be the costs of emergency treatment if something goes wrong? Who would provide this and who would pay for this? Before traveling or agreeing to treatment, find out what costs your travel insurance, health insurance provider or national health program will cover, in what circumstances and in what countries.

13. SHOULD I GET A SECOND OPINION?

You are encouraged to ask a lot of questions about the treatment being offered and to seek second opinions from independent qualified doctors. Your doctor should be supportive and help in the process of obtaining a second opinion. Medical records, research protocols, treatment protocols (where not well-established), and informed consent documents should be supplied to the person giving a second opinion.

14. HOW CAN I FIND OUT ABOUT CLINICAL TRIALS THAT USE STEM CELLS?

Ask your medical doctor for advice on what is available in your area for your disease or condition. Different clinical trials are offered at different institutions. Remember that clinical trials have very strict entry criteria to safeguard the safety of participants and to make sure that researchers will be able to answer their research question.

There are some databases that allow you to search for registered clinical trials. For example, the public may search a database of clinical trials sponsored by the National Institutes of Health (USA) at www.clinicaltrials.gov. Note, however, that not all clinical trials are included in these databases.