CASE STUDY #3 Ethics behind the use and study of stem cells

Clinician Perspective:

You're a famous medical doctor and scientist and have recently been contacted by a desperate family in need of help. The Smith's youngest child Eric has recently endured a relapse of Acute Myeloid Leukemia (a deadly type of blood cancer) and his health is rapidly deteriorating. Eric has already received chemotherapy treatment and blood stem cell transplants but none of these conventional approaches have worked. His family is seeking out high-risk last resort therapies to save his life. Your research has shown two drugs that can specifically target and kill leukemia tumor cells but leave the normal healthy cells alone. One drug was previously used in the 1960’s as an antipsychotic to treat schizophrenia but was very quickly discontinued because it showed it sometimes caused serious side effects such as inducing suicidal thoughts and brain hemorrhaging (uncontrolled bleeding), which often led to death. The second drug you discovered to combat cancer was previously used to treat malaria. This drug was only recently discontinued because newer, more potent anti-malarial drugs have been developed. This drug is relatively safe with minimal side effects, but importantly, only guarantees a 40% chance of eliminating the leukemic cells. This is in stark contrast to the 99% efficiency of the antipsychotic drug in destroying cancer cells. Both drugs are expensive to buy and are not covered by the parent's drug plan.

Alternatively, your research group has shown promise in using induced pluripotent stem cells to make immune system cells that can specifically target and destroy tumor cells. This work involves taking skin from a patient and converting them to immune cells that can be transplanted back in to the person to help fight tumor growth. This work is experimental, but has shown incredible promise; however, it has only been demonstrated to work in mice and pigs. Your success with stem cell immuno-therapy has led to a small clinical trial to test in humans. You're feeling uneasy to recommend this option since you have no proof it works in humans; however, based on your animal models it poses no risk to the patient and if it works will permanently eliminate the cancer. This treatment is completely government funded.

Focus Questions:

1. Evaluate your options and choose a treatment for Eric. Take in to consideration tradeoffs between treatment effectiveness with side-effect risks.
2. Should children be subject to risky drugs or non-proven treatments?
3. Should the cost of the drugs or therapy impact what treatment a clinician gives, especially in cases when people do not have drug plans?
4. Should you be able to sue a doctor if a loved one dies when undergoing a risky or experimental treatment?
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Industry Perspective:

Lead scientist Dr. Hwang works for the Human Stem Cell Inc. biotechnology company and is directing a clinical trial for a new stem cell therapy to treat multiple sclerosis. The method involves taking skin cells from the patient, converting them to induced pluripotent stem cells (iPS), and then making them into cells that insulate neurons, which should cure the disease. Dr. Hwang recently got results back from the first cohort that received the stem cell transplant therapy. He found a general trend in 6 of 10 patients that received the stem cell transplants to have significantly better hand-eye coordination and walking ability than the 10 patients that received a placebo (no stem cells). This effect was found within 12 weeks of transplantation. The news of the successful treatment to this incurable disease was leaked to the press that led to numerous requests for interviews from major news corporations and investigations by the media to find out who participated in the study and got better. Stocks in Human Stem Cell Inc. rose by 200% in the weeks following the success of this clinical trial. One year later, of the 6 patients that got better 3 regressed back to their diseased state prior to the stem cell therapy, 1 developed a tumor from the cells that were injected, and the other two continued to progress and live a healthy life. Dr. Hwang, in consultation with the company CEO, decided that this information could not get out to the public since it could dramatically affect company’s fundraising and profits. They thought that this in turn would reduce Dr. Hwang’s team’s ability to identify what went wrong in these people and slow down progress on new stem cell therapies.

Focus Questions:

1. Define a conflict of interest? In this case, identify what constituted a conflict of interest.
2. Is Human Stem Cell Inc. justified to cover-up the deterioration in patient health to ensure research maintains well funded?
3. Is Dr. Hwang being fair to other scientists who are also studying this disease by not disclosing this information?
4. Under the circumstance described here, should there be more or less transparency in the reporting of correct scientific information? Even if it means disclosing to the public the names of people involved in the cover-up or the patients involved?
5. Is insisting there are 6 instead of actually only 2 long-term healthy people dishonest about the application and usefulness of this new stem cell therapy?
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**Patient Perspective:**

Sandra and John gave birth to baby boy, Eric. At the age of 1 Dylan was excessively fatigued, developing unexplained bruising, and was not eating and as a result lost a significant amount of weight. Upon visiting with Eric’s pediatrician for blood testing and after the recommendation for bone marrow testing, Eric was diagnosed with Acute Myeloid Leukemia (AML), a rare disease but the most common type of leukemia presented in infants. After chemotherapy, Eric’s condition improved and his cancer went into remission. However, within one year Eric relapsed and underwent several rounds of chemotherapy until he was recommended for stem cell transplantation (SCT) therapy, a high-risk treatment option. The parents, upon careful consideration, consented and Eric, now 2 years old, received the transplant. Initially, the transplant appeared to be successful, but again, he relapsed. Now the only avenue to help Eric was in clinical trials.

Sandra and John were recommended by the oncologist for several phase I clinical trials testing new combinations of drug therapy in Canada and the USA, but continued their own desperate search. They discovered a website claiming to have successfully treated children under the age of 10 for AML using hematopoietic stem cells (HSC) derived from patient-specific induced pluripotent stem cells (iPSC) with a 95% success rate, and were currently accepting children for the clinical trial in one month in Thailand. Unknown to Sandra and John, this type of research is only in the basic research phase and is unproven to be successful in generating functional HSC from pluripotent stem cells for potential therapeutic applications. Eric’s parents were immediately hopeful and proceeded to enroll him in the trial. Eligibility for the trial required Sandra and John to pay a sum of money equivalent to the price of their home, in advance.

**Focus Questions:**

1. **Distinguish between basic research and a phase I clinical trial and what is required to move from basic research into the clinical trial phase.**
2. **What is informed consent? What type of information should be provided to Sandra and John prior to providing informed consent for stem cell transplantation therapy?**
3. **Should Sandra and John talk to their doctors about the Thailand trial? What types of questions should they ask?**
4. **What is Stem Cell Tourism and what might be some consequences to basic research studying human pluripotent stem cells?**
5. **How might stem cell tourism impact valid medical services provided by legitimate affiliated medical institutes (in contrast to medical tourism)?**
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Political Perspective:

As the newly appointed Minister of Research and Innovation, you are responsible for governing the Ontario Research Fund (ORF), a fund which provides cutting-edge scientific research developed in Ontario with the funds to advance research into innovative services/products for economic growth. A news story breaks headlining, “Family of child with life-threatening AML duped by discredited Ontario physician practicing in Thailand”. The article describes little boy named Eric who has endured several relapses of Acute Myeloid Leukemia (AML) after receiving various forms of chemotherapy and a stem cell transplant, a high-risk last resort therapy. With his life in serious jeopardy, Eric's desperate parents paid thousands of dollars to Dr. Anthony Shivago, who established a clinical practice in Thailand. Dr. Shivago's treatment claimed the success of using hematopoietic stem cells (HSC) derived from induced pluripotent stem cells (iPSC) taken from the patient to treat various types of leukemia, including AML. Dr. Shivago was once a practicing clinician at Sick Kids Hospital in Toronto and advocate for the clinical use of pluripotent stem cells for the treatment of leukemia. However, he was discredited and his medical license was revoked after publishing a bogus article in Nature claiming the success of patient derived stem cells for treating AML, in which case he misinformed the patients he enrolled in the study.

A few days later, within a pile of grant proposals you are reviewing for the ORF, one is requesting funds to set up a drug screening facility. The proposal claims that: 1) it can generate human iPSCs that can generate normal blood at a high efficiency, 2) has access to primary samples of cord blood and blood from patients with AML, 3) is able to utilize these cell types to screen small molecules to find novel or re-purposed chemicals with the potential to treat patients with leukemia. In addition, this innovative project will likely hold the potential for setting up a phase I clinical trial if successful candidate drugs are discovered.

Focus Questions:

1. When reviewing grant proposals, what will you look for to ensure the authors claims are legitimate?
2. How may bogus claims, such as Dr. Shivago's, influence the future of pluripotent stem cell research regarding governmental policy and scientific funding opportunities?
3. What may be some political/economical reasons for the increase in stem cell tourism havens in foreign countries like Costa Rica, Mexico and China?
4. What could be the public's point of view on the legitimacy of induced pluripotent stem cells and dissemination of government funds for such research?