The new FDA-regulated Gene Therapy Clinical Trial for Patients with Fanconi Anemia is now open and recruiting patients.

Who is eligible?
The trial is for adults with Fanconi anemia, ages 18 and older in the complementation group A (FANCA). Adult patients from the United States and around the world may enroll in the study. The expected enrollment is three to five patients, with a maximum of 10. Patients need to meet specific inclusion criteria, but they need not be in severe bone marrow failure in order to participate. (Specific criteria can be found at www.clinicaltrials.gov . The registry number for the trial is #01331018.)

What is the time commitment?
Patients who successfully enroll in the trial are expected to be in Seattle for 6-8 weeks.

Where does the trial take place?
All procedures will be done on an outpatient basis at the Seattle Cancer Care Alliance.

What is the gene therapy process?
The first 2-3 weeks of the trial include pre-treatment evaluations and the placement of a central line for intravenous injections. Patients will then receive growth factor injections, twice daily for 4-6 days to mobilize the stem cells from the bone marrow to the blood. Peripheral blood will then be collected through a special process that should take about 4-5 hours. Researchers will examine the number of stem cells in the collection. If there are enough stem cells, the cells will incubate overnight in the presence of a reducing agent to correct the defective FANCA gene. The next day, the researchers will infuse the gene-corrected cells back into the patient via the central line. If there are not enough stem cells collected, growth factor injections may be repeated for a second round followed by another collection of peripheral blood. If there still aren't enough stem cells, a bone marrow aspiration will be offered. Once there are enough stem cells collected, the cells will be treated overnight and then infused into the patient the next day. After patients receive the gene-corrected cells, they will be monitored in Seattle for engraftment through peripheral blood samples taken once a week for four weeks. If successful, researchers will notice a *sustained* increase in patient blood counts, essentially curing the bone marrow failure aspects of FA.

What happens next?
Once the patient returns home, i.e., in month 2 after the infusion, peripheral blood collection and testing is done every two weeks. In months 3 through 12, the collection and testing drops to once per month. These samples can be taken in a patient's local community and shipped overnight to Seattle for testing. Patient follow-up continues for 15 years after the infusion.

What if the gene therapy doesn't work?
Unsuccessful gene therapy does not preclude a stem cell transplant in the future if needed. There is no impact, one way or the other, on the future success (or failure) of a more traditional stem cell transplant.

What are the risks?
According to Dr. Kiem, the infusion procedures involved in this trial are considered "standard" and there are no expected side effects of infusing a patient's own cells. The lentivirus vector that is used to transport the corrected cells into the body "has now been used for many years—more than a decade," said Dr. Kiem. In France, researchers have used this same type of vector in gene

therapy to treat adrenoleukodystrophy or “Lorenzo’s Oil” disease, beginning about 3-4 years ago. These patients are doing well, with no side effects from the gene therapy. In addition, ongoing studies in Europe use similar vectors to treat patients with storage diseases, such as metachromatic leukodystrophy disease.

What about the costs?
The treatment-related medical expenses of this trial are covered by the institutions participating in the trial. Patients will be responsible for travel and living expenses while in Seattle, such as airfare, lodging and food. As a reminder, the Fanconi Anemia Research Fund can assist with making referrals to potential resources that patients may qualify for. In addition, the Fund has limited resources for which patients may apply for help with travel and living expenses while participating in certain clinical trials, including this one.

Not FANCA?
While this trial is specifically for FANCA patients, the researchers are hopeful that with success, future gene therapy trials will open for patients in all complementation groups.

Additional questions?
For questions about the clinical trial, please contact Jennifer Adair, PhD at (email: jadair@fhcrc.org or telephone: 206-667-7110). For questions about the Fund’s clinical trials scholarship fund, please contact Teresa Kennedy (email: teresa@fanconi.org or telephone: 1-888-326-2664).