Stanford Children's Health

Bass Center for Childhood Cancer and Blood Diseases

Our Approach to Treating Fanconi Anemia (FA)

Fanconi anemia is a rare, genetic disease that causes every cell in the body to be vulnerable to DNA damage, leading to the death of vital cells or contributing to their transformation into cancers. Through innovative research, Stanford Children's Health has developed groundbreaking new treatments for FA that help children and adults survive and thrive.

Why Stanford Children's Health for Fanconi anemia

- Our team of care providers are among the top doctors in the nation and world for FA; we have handpicked them for their complementary expertise and innovative approaches to treating FA.
- We are a true center of excellence for Fanconi anemia and the top FA treatment center in the West, offering multidisciplinary care and treating children and adults of all ages from California, the nation, and the world.
- Our FA program is housed in our Bass Center for Childhood Cancer and Blood Diseases, which is nationally known for its innovative research in cancer and cell and gene therapy. We also have a dedicated Center for Definitive and Curative Medicine, aimed at accelerating the research-to-treatment process and bringing life-changing therapies to patients, including new hope of cures for FA.

Unique research-driven treatments

While we provide exceptional standard of care treatments for FA, including comprehensive disease monitoring, growth factor therapies, blood transfusions, and stem cell transplants, we are especially proud to also offer leading-edge and novel investigational treatments for FA. These include:

- **Personalized diagnostics and decision-making.** We are one of the few programs in the nation to conduct thorough diagnostic testing to understand the complete genetic cause of FA in your child, and we

additionally encourage detailed testing to understand the full extent of disease in your child's blood and bone marrow using both cutting-edge clinical and exploratory research tests. This information can then be used to tailor our treatments specific to your child, homing in on exactly what care your child needs at each step throughout his or her medical journey.

- **Gene therapy.** For Fanconi patients with subtype A (FA-A), we offer an investigative treatment that is intended to reverse the root cause of the blood disorder associated with FA by placing an intact normal copy of the FANCA gene (the mutated gene that causes FA in a majority of patients) inside the blood stem cells of patients. The goal of the gene therapy is to enable the corrected blood stem cells to grow normally, thereby avoiding or delaying bone marrow failure in children. We have obtained promising results in both our Phase 1 and Phase 2 trials, showing the safety of this treatment, and we hope to be able to offer this treatment to more patients soon.
- **Cutting-edge oral medicines.** We are studying the investigational use of alternative oral medicines with the hope of improving the performance of the blood cells and preventing cancer. For example, we recently received FDA approval to open a clinical trial to use a new drug called an ALDH activator, specifically FP-045, in FA patients to test if it can restore stem cells to normal function and prevent damage.
- **Novel approaches to stem cell transplants.** Stem cell transplants (sometimes called bone marrow transplants) are the only recognized cure for the blood problems associated with FA. We take a unique approach to transplants, including:

  — **Exceptional planning and monitoring.** Our program has decades of expertise in transplanting patients with FA as well as other patients with complex and extremely challenging diseases. We carefully tailor treatment regimens for each patient, taking into account their disease state and donor options. We pay close attention to all details before, during, and after the transplant to ensure excellent outcomes, and our center has a wide variety of innovative treatments and outstanding subspeciality teams available if issues such as graft-versus-host disease (GvHD) or infections unexpectedly arise.

  — **Alternatives for conditioning.** Conditioning is an essential part of the patient preparation for a stem cell transplant. Because FA patients are particularly sensitive to chemotherapy and radiation, which are traditionally used for conditioning, we tailor our conditioning to reduce the use of these agents and prefer to use a combination of low-dose chemotherapy and low-dose radiation with vital organ shielding given

the exceptional outcomes with this approach. We are also developing methods that are free of radiation and busulfan chemotherapy altogether and recently opened an innovative clinical trial with antibody-based conditioning using JSP191, a unique drug directed against the diseased stem cells. We have used this agent to treat children with other diseases with no toxicity concerns, and we are optimistic about its ability to further improve FA treatment as well.

— **Graft manipulation.** Our center has been manipulating donor blood-forming cells prior to stem cell transplantation for many years to enhance engraftment (the act of transplanted stem cells growing and proliferating) while minimizing toxicity concerns such as GvHD. For patients without matched sibling donors, we have adopted these graft manipulations as our hospital's standard approach to care for patients with certain genetic conditions, including FA. Using these approaches, we adjust the elements of donor cells to make them safer. We have historically conducted T-cell depletion to reduce GvHD using CD34+ cell enrichment. However, we now also perform a new specialized graft manipulation called TCR alpha/beta T-cell/CD19 B-cell depleted stem cell transplant to further increase the chance of transplantation success. This innovative technique uses a partially matched donor (often a parent) to expand the donor pool and bring children to transplant more quickly. In this approach, the immune system's fighter cells (TCR alpha/beta T cells) are removed from the donor stem cells, making it less likely that the graft will attack the child's body and cause GvHD. Simultaneously, the gamma/delta T cells and other immune and progenitor cells are preserved to enable faster engraftment and immune recovery. Because we often use a child's parents or siblings for this approach, we also have full control over the collection process to ensure an optimal stem cell graft and remove the need for graft shipment to further minimize risks.

- **Long-term follow up.** Although our stem cell transplant treatments have exceptional outcomes, they still place patients at risk of short-term and long-term complications. Additionally, even without transplant, FA patients can have various health issues, so we follow all of our patients closely. Initially post-transplant, patients stay in the hospital and then in the local vicinity, and once patients have stable immune recovery, they return home while maintaining close communication with our team. We provide telehealth services to provide care at a distance, work closely with local care providers for laboratory work, exams and treatments, and encourage patients to return annually for further follow up. Our team primarily cares for children; however, we are also set up to care for adults with FA and have close relationships with adult providers.
- **Innovative cancer treatments.** Fanconi anemia puts patients at a higher risk for cancers, especially leukemia, a blood cancer. While our goal is to prevent such cancers in FA patients, we also offer the very latest research-driven cancer treatments, such as immunotherapy, for patients who do unfortunately develop various cancers, and we closely monitor our patients to be able to treat these as early as possible to improve outcomes.

For more information

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