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**Novel program offers new options for adult congenital heart patients (September 2018)**

Reviewed by Alina Shrourou, BSc Aug 29, 2018

Experts at the Vanderbilt Heart and Vascular Institute are forging new ground in the development of a first-of-its-kind program aimed at adults with congenital heart disease (ACHD).

The novel program in Advanced Congenital Cardiac Therapies (ACCT) allows for patients to be evaluated for heart transplantations and ventricular assist devices (VAD) - a foreign concept to Michael Sharpe, 39, who received a new lease on life in May.

Diagnosed at 9 months old with tetralogy of Fallot, Sharpe had resigned himself to the lifelong condition caused by the combination of four heart defects present at birth. He had already undergone the routine surgeries and procedures to improve the oxygen-poor blood flow out of his heart to the rest of his body.

"I did not know that transplant was an option for congenital heart patients," said Sharpe. "My parents were with me when the doctors mentioned it and they were shocked too.

"This has allowed me the incredible option to watch my son grow up. Evan is my motivator. When they told me that I was in heart failure, the thought of not seeing him grow up hit me the most.

"I know people don't live very long in heart failure and I kept thinking, 'I'm getting maybe two to five more years.' But now? I have 20, 30-plus years. That's the absolute best part."

Sharpe is one of three patients with ACHD transplanted at Vanderbilt within the last year. An additional three patients are currently listed for heart transplant and another three have undergone VAD implants.

To view the full article, please click on this link:


Source: [https://ww2.mc.vanderbilt.edu/News-Medical.net - An AZoNetwork Site](https://ww2.mc.vanderbilt.edu/News-Medical.net)

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Spark Reports Progress on Hemophilia A Gene Therapy (September 2018)

AUGUST 8, 2018

Spark Therapeutics recently reported preliminary phase 1/2 data for SPK-8011, the company’s investigational gene therapy candidate for hemophilia A. The therapy is administered via a one-time intravenous infusion, which is designed to elicit the production of therapeutic levels of factor VIII (FVIII), a protein that is normally deficient in individuals with hemophilia A. Spark Therapeutics’ proprietary bioengineered adeno-associated viruses (AAVs) act as delivery vehicles, or vectors, to carry the genetic codes that prompt the FVIII production. The approach being tested in this trial uses a modified novel AAV vector genome (vg) to deliver the corrected FVIII gene into liver cells where the protein is normally generated.

According to a new press release, as of the July 13, 2018 data cutoff, 12 participants in the phase 1/2 trial have received a single administration of investigational SPK-8011. The dose sizes administered to trial participants have varied amongst the study participants with two patients receiving a low dose of 5 x 1011 vg per kilogram (kg) of body weight, three at a mid-range dose of 1x1012 vg per kg of body weight and seven at a high dose 2 x 1012 vg per kg of body weight. Across all participants, there has been a 97% reduction in annualized bleeding rate and a 97% reduction in annualized infusion rate. In addition, the first two trial participants, who have been followed for more than one year, have shown stable FVIII activity levels since reaching “plateau” for up to 66 weeks. Monitoring of trial participants is ongoing.

The company also addressed possible immune responses and incidences of elevated levels of alanine aminotransferase (ALT) enzymes in some of the patients – elevated ALT levels can lead to subsequent adverse effects on liver function if not properly addressed. Oral steroids were subsequently administered to positive effect.

To view the full article, please click on this link:


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Source: Spark press release dated August 7, 2018

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Societies Release Updated Guideline for Treating Adult Congenital Heart Disease Patients (September 2018)

Document offers guidance for treatment in relatively new, growing population

August 16, 2018 Categories: Scientific Statements/Guidelines

Embargoed until 1 p.m. CT / 2 p.m. ET Thursday, August 16, 2018

WASHINGTON, August 16, 2018 — The American College of Cardiology and the American Heart Associated today released an updated guideline for the management of adult congenital heart disease (ACHD) patients.

CHD encompasses a range of structural cardiac abnormalities present before birth and attributable to abnormal fetal cardiac development. Congenital heart defects are the most common type of birth defect. The prevalence of ACHD is growing due to the success of treating these patients during their childhood. Survival to age 18 years is now expected in 90 percent of children diagnosed with severe CHD.

“Patients with ACHD are a heterogeneous population,” said Karen K. Stout, MD, professor of medicine and pediatrics in cardiology at the University of Washington and chair of the writing committee for the guideline. “Although the prevalence of ACHD is increasing, the population of patients with a given congenital abnormality or specific repair may be relatively small, which can make accruing evidence to guide treatment challenging.”

This full revision of the original guideline, published in 2008, incorporates new data and growing ACHD expertise. Despite the difficulty in studying ACHD populations, there is a growing body of high-quality data in these patients to guide the care of this relatively new population. These data were used to develop the recommendations.

To view the full article, please click on this link:


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FDA Accepts First Allogeneic CAR T-Cell Therapy Trial (September 2018)

Samantha DiGrande

Newsroom – Published on: August 04, 2018

Celyad, a biopharmaceutical company that focuses on the development of chimeric antigen receptor (CAR) T-cell therapies, recently announced that the FDA accepted its Investigational New Drug (IND) application for CYAD-101, the first non-gene-edited allogeneic clinical program.

Traditionally, CAR T-cell therapies are created by genetically modifying a patient’s own immune cells to target specific cancer cells before injecting them back into the patient. However, this can be difficult because researchers aren’t always able to collect enough cells from a patient to create the treatment. Conversely, in an allogeneic CAR T-cell therapy, immune cells are instead collected from healthy donors, rather than the patient.

The trial, titled Allo-SHRINK, looks to evaluate the safety and clinical activity of CYAD-101 in patients with unresectable colorectal cancer in combination with standard chemotherapy.

“We are pleased to have achieved this important milestone. Celyad is the first company clinically evaluating a non-gene edited CAR T candidate, which, we believe, offers significant advantages over gene-edited approaches,” Christian Homsy, MD, CEO of Celyad, said in a statement.

CYAD-101 is based on features of the company’s investigational autologous CYAD-01 CAR T with a novel peptide, TCR Inhibiting Molecule (TIM). This prevents the patients’ immune system from recognizing the cells as foreign. The cells in CYAD-01 produce a chimeric receptor called natural killer group 2D (NKG2D) that recognizes multiple tumor proteins.

To view the full article, please click on this link:

https://www.ajmc.com/newsroom/fda-accepts-first-allogeneic-car-tcell-therapy-trial

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Road to Recovery: Woman is Youngest Patient in United States to Receive Face Transplant (August 2018)

AUGUST 14, 2018 / FEATURES & UPDATES

Katie Stubblefield’s wit shows through when she describes her face transplant surgery. “Longest nap of my entire life,” she says.

Those unfamiliar with Katie’s still-developing speech pattern may not easily make out those words, but her parents are usually there to interpret. Robb and Alesia Stubblefield have been by her side – helping her “take four steps forward, two steps back,” as Robb describes it – since Katie, then 18, endured severe facial trauma and significant complications from a self-inflicted gunshot wound on March 25, 2014.

It would take a team of 11 Cleveland Clinic surgeons and multiple specialists to perform the hospital’s third face transplant – and its first total face transplant – on Katie. At 21, Katie was the youngest person in the United States to receive a face transplant.

And, indeed, it was extensive: The surgery included transplantation of the scalp, the forehead, upper and lower eyelids, eye sockets, nose, upper cheeks, upper jaw and half of lower jaw, upper teeth, lower teeth, partial facial nerves, facial muscles, and skin – with 100 percent of her facial tissue effectively replaced.

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Face Transplants: The Changing Face of Medicine (August 2018)

AUGUST 14, 2018 / FEATURES AND UPDATES

To many, the human face defines personhood. When it is devastated beyond the reach of conventional plastic or restorative surgery, a patient may lament both the loss of their appearance and simple functional abilities such as smiling, talking, eating, or breathing on their own.

In these rare instances, a face transplant may be the only solution that can sufficiently restore the patient’s quality of life and function.

Cleveland Clinic face transplant evolution

A face transplant is an intricately complicated, personalized medical procedure that replaces as much as 100 percent of the recipient’s facial tissue with that of a deceased donor. The surgery can integrate many different functional components, such as nose and lower eyelids as well as different tissue types including, skin, muscles, bony structures, arteries veins and nerves.

As of August 2018, around 40 face transplants have been performed worldwide. In 2008, Cleveland Clinic became the first hospital in the United States to perform a near-total face transplant, and remains one of just six U.S. institutions to have conducted the surgical procedure.

Cleveland Clinic doctors performed the initial 22-hour procedure on a 40-year-old woman who suffered severe facial injuries from a gunshot to the face. A Cleveland Clinic surgical team integrated functional facial components and numerous tissue types, including skin, muscles, bony structures, arteries, veins and nerves – encompassing about 77 square inches of transplanted tissue.

To view the full article, please click on this link:
https://newsroom.clevelandclinic.org/2018/08/14/face-transplants-the-changing-face-of-medicine/

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**T cell engineering breakthrough sidesteps need for viruses in gene-editing (July 2018)**

*July 11, 2018, University of California, San Francisco*

In an achievement that has significant implications for research, medicine, and industry, UC San Francisco scientists have genetically reprogrammed the human immune cells known as T cells without using viruses to insert DNA. The researchers said they expect their technique—a rapid, versatile, and economical approach employing CRISPR gene-editing technology—to be widely adopted in the burgeoning field of cell therapy, accelerating the development of new and safer treatments for cancer, autoimmunity, and other diseases, including rare inherited disorders.

The new method, described in the July 11, 2018 issue of *Nature*, offers a robust molecular "cut and paste" system to rewrite genome sequences in human T cells. It relies on electroporation, a process in which an electrical field is applied to cells to make their membranes temporarily more permeable. After experimenting with thousands of variables over the course of a year, the UCSF researchers found that when certain quantities of T cells, DNA, and the CRISPR "scissors" are mixed together and then exposed to an appropriate electrical field, the T cells will take in these elements and integrate specified genetic sequences precisely at the site of a CRISPR-programmed cut in the genome.

"This is a rapid, flexible method that can be used to alter, enhance, and reprogram T cells so we can give them the specificity we want to destroy cancer, recognize infections, or tamp down the excessive immune response seen in autoimmune disease," said UCSF's Alex Marson, MD, Ph.D., associate professor of microbiology and immunology, member of the UCSF Helen Diller Family Comprehensive Cancer Center, and senior author of the new study. "Now we're off to the races on all these fronts."

But just as important as the new technique's speed and ease of use, said Marson, also scientific director of biomedicine at the Innovative Genomics Institute, is that the approach makes it possible to insert substantial stretches of DNA into T cells, which can endow the cells with powerful new properties. Members of Marson's lab have had some success using electroporation and CRISPR to insert bits of genetic material into T cells, but until now, numerous attempts by many researchers to place long sequences of DNA into T cells had caused the cells to die, leading most to believe that large DNA sequences are excessively toxic to T cells.

To view the full article, please click on this link:


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How to make CAR-T cell therapies for cancer safer and more effective (July 2018)

Researchers are installing safety switches and adding other features to the immune therapy

By Laurel Hamers

9:00am, June 27, 2018

This wasn’t 15-year-old Connor McMahon’s first time in the hospital. But the 107° fever he’d been running for three days had his dad frightened. The teen was hallucinating, talking gibberish and spouting curses.

“I thought he was going to die,” says Connor’s father, Don McMahon, who stayed close as his son received and recovered from an experimental treatment for leukemia. “It was really hard to watch.” But the fever finally broke, and Connor returned home. Just a month later, in November 2016, he was cancer-free and back on the ice in his hockey skates and pads.

That episode was Connor’s third bout with acute lymphoblastic leukemia. The experimental treatment was a last hope for the boy, who was first diagnosed at age 3. He has spent a total of six years of his life receiving chemotherapy. When the cancer came back in 2016, the doctors said the prognosis wasn’t good.

At that point, “it was about quality of life, not quantity,” McMahon says. But when he and his wife, Michelle, learned about the experimental treatment, called CAR-T cell therapy, the family decided it wasn’t time to give up yet.

McMahon enrolled Connor in a clinical trial for a CAR-T cell therapy at Duke University Children’s Hospital, five hours from the family’s Atlanta home. Days later, doctors extracted immune cells called T cells from Connor’s blood and shipped them off to a lab in New Jersey. There, the cells were genetically modified to target and kill the cancer cells coursing through Connor’s bloodstream.

A month later, doctors injected those modified T cells into the teen’s body, where they multiplied. Over the next few weeks, that five-minute T cell infusion racked Connor’s body but also knocked the levels of cancer cells in his bloodstream down to zero.

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How is Biotech Innovating to Treat Hemophilia? Let’s Review (July 2018)

Clara Rodriguez Hernandez on 13/02/2018

Experts say hemophilia treatment is at a ‘precipice of a therapeutic revolution.’ From antibodies to gene therapy, here are some of the most innovative technologies in the field that might significantly improve the lives of patients suffering from this bleeding disorder.

Hemophilia is a genetic disorder that impairs blood clotting. When one of the genes that encode for blood clotting factors is absent or deficient, the smallest injury can trigger serious bleeding episodes. Since these genes are located on the X chromosome, the disease is much more common in males than females.

Worldwide, there are over 187,000 people with hemophilia. About 80% of them have hemophilia A, which affects the clotting factor VIII. The second most common form, hemophilia B, is due to a deficiency of the clotting factor IX.

There is currently no cure for hemophilia, once known as the mysterious 'Royal Disease' that monarchs across Europe inherited from Queen Victoria. People living with this disease may require up to 3 infusions per week of clotting factors as a prophylactic therapy, as well as emergency treatment in case of an injury. Still, these patients keep experiencing recurrent bleeding episodes. And 30% of patients with severe hemophilia A develop inhibitory antibodies that leave them unresponsive to the standard treatment — recombinant clotting factors.

But the biotech industry is striving to change this situation, with the incentive of tapping a global market expected to hit €20Bn by 2024. A number of technologies, including therapeutic antibodies, RNAi and cell therapy are fighting to become the go-to treatment; Gene therapy might be the first.

To view the full article, please click on this link:

https://labiotech.eu/biotech-hemophilia-treatment/

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Kymriah Ellicits Prolonged Complete Responses in Advanced DLBCL Patients, Trial Data Show (July 2018)

June 25, 2018
By Joana Carvalho

Kymriah (tisagenlecleucel), a chimeric antigen receptor (CAR) T-cell therapy developed by Novartis, is able to elicit prolonged complete responses with minor side effects in adults with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), according to new data from a Phase 2 trial.

The results from JULIET (NCT02445248) were in an oral presentation, “An updated analysis of JULIET, a global pivotal Phase 2 trial of tisagenlecleucel in adult patients with relapsed or refractory (r/r) diffuse large b-cell lymphoma (DLBCL),” given at the 23rdAnnual Congress of the European Hematology Association (EHA) on June 16 in Stockholm.

Kymriah was the first cell-based gene therapy to be approved by the U.S. Food and Drug Administration (FDA) to treat relapsing or refractory acute lymphoblastic leukemia (ALL) or non-Hodgkin’s lymphoma (NHL) in pediatric and young adult patients up to 25 years old.

ALL is the most frequent type of leukemia in children, and is marked by the bone marrow producing too many white blood cells, or lymphocytes, that fail to develop correctly. This excess of abnormal lymphocytes can cause swelling and damage to internal organs, and prevents the body from producing other blood cells, resulting in anemia and a dampened immune response.

In a similar way, DLBCL — the most common form of NHL — is an aggressive cancer of the lymphatic system caused by accumulation of abnormal B-cells.

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Insurers and Government Are Slow to Cover Expensive CAR-T Cancer Therapy (July 2018)

July 17, 2018 8:02 AM ET

Michelle Andrews

Patients whose blood cancers have failed to respond to repeated rounds of chemotherapy may be candidates for a new type of gene therapy that could send their cancers into remission for years. But the two approved therapies, with price tags of hundreds of thousands of dollars, have roiled the insurance approval process, leading to delays and, in some cases, denials of coverage, clinicians and analysts say.

The therapy involves collecting patients' own T cells, a type of white blood cell, genetically modifying them, and then infusing them back into patients, where they hunt down and kill cancer cells. Known as CAR-T cell therapy, it's been characterized as a "living drug" by some researchers.

Two different CAR-T drugs — Kymriah and Yescarta — were approved by the FDA last year to treat patients whose blood cancers haven't responded to at least two other rounds of treatment.

Kymriah is approved for people up to age 25 with a form of acute lymphoblastic leukemia, the most common cancer in children. Kymriah and Yescarta are both approved for adults with advanced lymphomas.

Researchers report that some critically ill patients who received the therapy have remained cancer-free for as long as five years.

"This is what patients need," says Dr. Yi Lin, a hematologist who oversees the CAR-T cell practice and research for the Mayo Clinic. "With the likelihood of getting patients into durable survival, we don't want to deny them the therapy." She says she receives no personal financial support from the drugs' makers.

To view the full article, please click on this link:


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