News

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FDA approves CAR-T cell therapy to treat adults with certain types of large B-cell lymphoma (October 2017)

Yescarta is the second gene therapy product approved in the U.S.

October 18, 2017

The U.S. Food and Drug Administration today approved Yescarta (axicabtagene ciloleucel), a cell-based gene therapy, to treat adult patients with certain types of large B-cell lymphoma who have not responded to or who have relapsed after at least two other kinds of treatment. Yescarta, a chimeric antigen receptor (CAR) T cell therapy, is the second gene therapy approved by the FDA and the first for certain types of non-Hodgkin lymphoma (NHL).

"Today marks another milestone in the development of a whole new scientific paradigm for the treatment of serious diseases. In just several decades, gene therapy has gone from being a promising concept to a practical solution to deadly and largely untreatable forms of cancer," said FDA Commissioner Scott Gottlieb, M.D. "This approval demonstrates the continued momentum of this promising new area of medicine and we're committed to supporting and helping expedite the development of these products. We will soon release a comprehensive policy to address how we plan to support the development of cell-based regenerative medicine. That policy will also clarify how we will apply our expedited programs to breakthrough products that use CAR-T cells and other gene therapies. We remain committed to supporting the efficient development of safe and effective treatments that leverage these new scientific platforms."

Diffuse large B-cell lymphoma (DLBCL) is the most common type of NHL in adults. NHLs are cancers that begin in certain cells of the immune system and can be either fast-growing (aggressive) or slow-growing. Approximately 72,000 new cases of NHL are diagnosed in the U.S. each year, and DLBCL represents approximately one in three newly diagnosed cases. Yescarta is approved for use in adult patients with large B-cell lymphoma after at least two other kinds of treatment failed, including DLBCL, primary mediastinal large B-cell lymphoma, high grade B-cell lymphoma and DLBCL arising from follicular lymphoma. Yescarta is not indicated for the treatment of patients with primary central nervous system lymphoma.

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

https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm581216.htm

Credit to the U.S. Food and Drug Administration

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Popular Hybrid Congenital Heart Procedure without Cardiopulmonary Bypass (October 2017)

Front. Surg., 06 March 2017
Aamisha Gupta and Zahid Amin

Division of Pediatric Cardiology, Children's Hospital of Georgia, Augusta University, Augusta, GA, USA

As surgical and catheter interventions advance, patients with congenital heart disease are now offered alternative treatment options that cater to their individual needs. Furthermore, collaboration between interventional cardiologists and cardiac surgeons have led to the development of hybrid procedures, using the best techniques of each respective field to treat these complex cardiac entities from initial treatment in the pediatric patient to repeat intervention in the adult. We present a review of the increased popularity and trend in hybrid procedures in congenital heart disease without the use of cardiopulmonary bypass.

Common and Popular Hybrid Procedures

- 1. Hybrid Stage I palliation for hypoplastic left heart syndrome (HLHS).
- 2. Perventricular ventricular septal defect (VSD) closure; muscular and perimembranous.
- 3. Perventricular pulmonary valve implantation.
- 4. Hybrid pulmonary valvuloplasty for pulmonary atresia.
- 5. Hybrid aortic valvuloplasty.
- 6. Hybrid stent placement in the branch pulmonary arteries.
- 7. Per-atrial atrial septal defect closure.

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

https://www.frontiersin.org/articles/10.3389/fsurg.2017.00009/full

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F.D.A Approves Second Gene-Altering Treatment for Cancer (October 2017)

By DENISE GRADY Oct. 18, 2017

The Food and Drug Administration on Wednesday approved the second in a radically new class of treatments that genetically reboot a patient's own immune cells to kill cancer.

The new therapy, Yescarta, made by Kite Pharma, was approved for adults with aggressive forms of a blood cancer, non-Hodgkin's lymphoma, who have undergone two regimens of chemotherapy that failed.

The treatment, considered a form of gene therapy, transforms the patient's cells into what researchers call a "living drug" that attacks cancer cells. It is part of the rapidly growing field of immunotherapy, which uses drugs or genetic tinkering to turbocharge the immune system to fight disease. In some cases the treatments have led to long remissions.

"The results are pretty remarkable," said Dr. Frederick L. Locke, a specialist in blood cancers at the Moffitt Cancer Center in Tampa, and a leader of a study of the new treatment. "We're excited. We think there are many patients who may need this therapy."

He added, "These patients don't have other options."

About 3,500 people a year in the United States may be candidates for Yescarta. It is meant to be given once, infused into a vein, and must be manufactured individually for each patient. The cost will be $373,000.

The treatment was originally developed at the National Cancer Institute, by a team Dr. Steven Rosenberg led. The institute entered an agreement with Kite in 2012, in which the company helped pay for research and received rights to commercialize the results.

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

https://www.nytimes.com/2017/10/18/health/immunotherapy-cancer-kite.html

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FDA Approves CAR T-Cell Therapy for Leukemia (September 2017)

'First gene therapy available in the United States,' says agency

by John Gever, Managing Editor, MedPage Today August 30, 2017

WASHINGTON -- The FDA on Wednesday approved a chimeric antigen receptor (CAR) T-cell therapy for treatment of certain pediatric and young adult patients with relapsed or refractory B-cell precursor acute lymphoblastic leukemia.

Calling it a "historic action," the agency said the approval marks the "first gene therapy available in the United States."

The treatment, to be tradenamed Kymriah and carrying the generic name tisagenlecleucel, is sold by Novartis.

In this type of therapy, patients' own immune cells are modified *ex vivo* to include a gene for the CAR protein, which directs them to attack leukemia cells carrying the CD19 antigen.
An FDA advisory committee had unanimously recommended the approval at a meeting last month.

However, tisagenlecleucel (also known as CTL019) can cause severe side effects, particularly a condition called cytokine release syndrome (CRS) that can become life-threatening.

The FDA is including a boxed warning for CRS and, in an unusual move, also approved a new indication for the rheumatologic drug tocilizumab (Actemra) as a treatment for CRS. The agency said that 69% of patients developing the condition during CAR T-cell trials "had complete resolution of CRS within 2 weeks following one or two doses" of tocilizumab, which inhibits interleukin-6.

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

https://www.medpagetoday.com/HematologyOncology/Leukemia/67615?xid=NL_breakingnews_2017-08-30&eun=g999591d0r

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Hearts with improving LVSD can be safely transplanted (September 2017)

Aug 30, 2017 | Daniel Allar

Donor hearts with left ventricular systolic dysfunction (LVSD) can be revived and transplanted as successfully as other hearts, according to a study in the *Journal of the American College of Cardiology*.

After reviewing transthoracic echocardiograms (TTEs) from nearly eight years of transplants in the United Network of Organ Sharing database, researchers identified 472 donor hearts with LVSD that resolved during donor management. These donors demonstrated a left ventricular ejection fraction (LVEF) of 40 percent or less on the initial TTE but later showed LVEF of at least 50 percent.

When compared against "normal" donors with LVEF of at least 55 percent on the initial TTE, no significant differences in mortality were detected at 30 days, one year, three years and five years of follow-up. There were no differences in cardiac allograft vasculopathy or primary graft failure, either.

"These results provide concrete evidence that donor hearts with LVSD on the initial echocardiogram, if appropriately managed, can be successfully resuscitated and have good short- and intermediate-term outcomes," wrote the study's authors, including lead researcher Shivank Madan, MD, of the division of cardiology at Albert Einstein College of Medicine in New York. "Considering that LVSD accounts for 25 percent to 30 percent of nonuse of donor hearts, the findings of this study should be encouraging and help to increase donor utilization rates."

Madan also headed recent research showing hearts from early adolescent donors can be safely transplanted to adults. The combination of these findings could reduce the gap between organ need and availability.

In both studies, Madan and colleagues noted more than 20,000 patients in the United States may benefit from heart transplantation, yet only 2,000 to 2,400 receive one each year.

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

http://www.cardiovascularbusiness.com/topics/heart-failure/hearts-improving-lvsd-can-be-safely-transplanted?utm_source=CVNW&utm_medium=adcee3b66e&utm_content=article&utm_campaign=newsletter_referral

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Hearts from adolescent donors are underutilized, could reduce CAV risk (September 2017)

Aug 16, 2017 | Daniel Allar

New research suggests greater use of early adolescent (EA) heart donors could save lives and reduce the gap between organ need and availability.

According to a new study, hearts from donors age 10-14 can be safely transplanted to adults and are also associated with a reduced risk of cardiac allograft vasculopathy (CAV).

Using the United Network for Organ Sharing (UNOS) database, the study identified 1,123 adults who received hearts from EA donors over a 21-year span. With propensity scoring, 944 recipients of EA donor hearts were matched to 944 recipients of transplants from donors in the "usual age group"—18 to 55.

Lead researcher Shivank Madan, MD, of the division of cardiology at Albert Einstein College of Medicine in New York, and colleagues published their results in *JACC: Heart Failure*.

They found no difference in recipient survival or primary graft failure (PGF) rates between the two groups at 30 days, one year, three years or five years post-transplant. Further, adult patients who received a heart from a young donor showed a 20 percent decreased risk of CAV.

The authors pointed out more than 20,000 patients in the United States may benefit from heart transplantation, but only about 2,000 to 2,400 transplants are performed in the country each year.

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

http://www.cardiovascularbusiness.com/topics/heart-failure/hearts-young-donors-are-underutilized-study-says?utm_source=CVHF&utm_medium=5df0fdcdb2&utm_content=article&utm_campaign=newsletter_referral

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For women with congenital heart defects, having a baby can be risky (August 2017)

By Tara Haelle
Health & Science
June 4

For years, the one thing standing between Candace Martinez and motherhood was her heart. She was born with a defect that a generation earlier would have led to death as an infant, but modern medicine — open-heart surgery at 5 weeks old to switch two misconnected arteries — had saved her. At age 18 she experienced heart failure: Her heart muscle couldn't pump enough blood to oxygenate her body. At 19, she got a pacemaker.

Martinez survived, but she always assumed that the life modern medicine had given her would not include having children. Pregnancy and childbirth long were thought to be too tough on women with congenital heart defects like hers.

Not anymore. Recommendations adopted in January by the American Heart Association suggest that, with careful supervision and management, many complex congenital heart defects should not be a deterrent to pregnancy.

For Martinez, 33, of Bakersfield, Calif., the recommendations couldn't have come soon enough. After spending the early part of her pregnancy in the Ronald Reagan UCLA Medical Center and the rest of it near the hospital, she gave birth to a baby girl on Valentine's Day. The pregnancy wasn't exactly easy: Martinez's heart at one point started beating abnormally and doctors administered electric shock to get it back to a normal rhythm. But her daughter is healthy and she is, too.

"Where we used to think pregnancy was not feasible or a prohibitively high risk" for women with complex heart defects, said her UCLA cardiologist Jamil Aboulhosn, one of the authors of the new AHA guidelines, "many of these women can actually tolerate pregnancy, but they're still high-risk pregnancies" that should occur in places with appropriate infrastructure and practitioners who know how to care for such patients.

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

https://www.washingtonpost.com/national/health-science/for-women-with-congenital-heart-defects-having-a-baby-can-be-risky/2017/06/02/c7d3cbac-1fb6-11e7-a0a7-8b2a45e3dc84_story.html?utm_term=.118df94207e8

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Congenital heart defects (CHDs) – Data & Statistics (August 2017)

August 1, 2016

Congenital heart defects (CHDs) are the most common types of birth defects, and babies born with these conditions are living longer and healthier lives. Find more statistics about CHDs below.

Number of U.S. Babies Born with CHDs

- CHDs affect nearly 1% of—or about 40,000—births per year in the United States.[1,2]
- The prevalence (the number of babies born with heart defect compared to the total number of births) of some CHDs, especially mild types, is increasing, while the prevalence of other types has remained stable. The most common type of heart defect is a ventricular septal defect (https://www.cdc.gov/ncbddd/heartdefects/ventricularseptaldefect.html) (VSD).[3,4]
- About 25% of babies with a CHD have a critical CHD. Infants with critical CHDs generally need surgery or other procedures in their first year of life. [Read summary]
- The prevalence of all types of CHDs, including critical CHDs, varies by state and by type of defect.

Number of U.S. Children and Adults Living with CHDs

Currently, there are a number of state-based birth defects programs that track CHDs among newborns and young children, but no tracking system exists to look at the growing population of older children and adults with heart defects.

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

https://www.cdc.gov/ncbddd/heartdefects/data.html

Content source: Division of Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention

U.S. Department of Health & Human Services

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Improving Access to Transplant for Patients with Incompatible Donors (August 2017)

July, 2017

M Health – University of Minnesota

Paired kidney exchange programs are bringing together pairs of patients and living donors, improving the odds of identifying compatible matches and achieving better outcomes. Kidney paired exchange programs are giving patients with renal failure and willing, but incompatible donors improved access to transplantation. First established in the United States in the 2000s, databases of incompatible pairs were created in the effort to find suitable matches for donor-recipient pairs. Before paired exchange programs, most patients with incompatible living donors could only opt to join the nation's waiting list for organs from deceased donors. Each year, however, deceased-donor kidneys become available for less than one-fifth of waiting patients, and increased time spent on dialysis increases the rate of complications from kidney disease.[1] Patients who receive kidneys from living donors experience better overall health outcomes and greater longevity than do those who receive kidneys from deceased donors.[2] The chance that a living-donor kidney will fail 5 years after transplant is half that of deceased-donor kidneys.[1]

Donors undergo tissue typing, and recipients are tested for antibodies against human leukocyte antigens (HLA), and their compatibility is then evaluated. Antibodies may develop to HLA after exposure through blood transfusion, pregnancy, or a prior organ transplant and can make a recipient "sensitized." Sensitized patients face increased difficulty in finding compatible donors. Highly sensitized patients can pursue desensitization therapy prior to transplant, but transplant outcomes are inferior to those achieved with the use of compatible donor organs.[3]

The National Kidney Registry, the largest paired exchange program in the United States, expands the pool of potential donors for transplant patients.

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

http://consult.mhealth.org/7-27-2017/improving-access-to-transplant-for-patients-with-incompatible-donors?utm_source=m_health_consult_newsletter&utm_medium=email&utm_campaign=sot_july_2017&utm_source=M+Health+Consult+Newsletter&utm_campaign=b0c9b4da64-EMAIL_CAMPAIGN_2017_07_31&utm_medium=email&utm_term=0_458d22411d-b0c9b4da64-331578581

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Doctors Treat Rare Case of Bleeding in Newborn with Hemophilia A (July 2017)

March 24, 2017

By Joana Fernandes, PHD In News

An infant was diagnosed with severe hemophilia A after developing splenic injury (injury to the spleen), a rare condition among newborns. For the first time, however, a newborn with these conditions was successfully treated with recombinant factor VIII replacement therapy without the need for surgical intervention, doctors reported.

The report, titled "Successful Medical Management Of A Neonate With Spontaneous Splenic Rupture And Severe Hemophilia A," was published in the journal *Hematology Oncology and Stem Cell Therapy*.

Spontaneous rupture of the spleen during the newborn period is very rare and usually associated with an underlying coagulation disorder or abnormalities of the spleen. In most cases, splenic rupture occurs due to increased intrathoracic pressure during delivery, which puts the newborn's spleen at risk of injury during labor.

In normal conditions, the body triggers a response to stop spleen bleeding, but in patients with blood coagulation disorders such as hemophilia, the spleen may rupture hours to days later.

The newborn boy was born after an unremarkable delivery. His family had no history of bleeding problems. But four days after his birth, he was admitted to the ER with worsening anemia and was later diagnosed with spontaneous splenic rupture. His symptoms included abdominal distension with a slightly enlarged liver, tachycardia (accelerated heart beat), poor feeding, and worsening yellow skin color.

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

https://hemophilianewstoday.com/2017/03/24/rare-case-bleeding-newborn-hemophilia-spleen-injury-during-birth/

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FDA Advisors Back CAR T-Cell Therapy for B-Cell ALL (July 2017)

Committee unanimously recommends approval of tisagenlecleucel

by Charles Bankhead, Senior Associate Editor, MedPage Today July 12, 2017

WASHINGTON -- An FDA advisory committee today unanimously recommended approval of the CAR T-cell therapy tisagenlecleucel (CTL019) for pediatric and young-adult patients with relapsed/refractory B-cell acute lymphoblastic leukemia (ALL).

The Oncologic Drugs Advisory Committee (ODAC) voted 10-0 in favor of approval after hearing reports from FDA staff and Novartis regarding the development, manufacturing, efficacy, and safety of CTL019, the first-ever CAR T-cell therapy submitted for FDA approval. The therapy consists of genetically modified antigen-specific autologous T cells programmed to target CD19, an antigen expressed by B-cells and tumors of B-cell origin.

As noted in the FDA staff report, the product's efficacy was not in question, but instead its short- and long-term safety. ODAC members expressed satisfaction with Novartis' plan to minimize risk, which includes limiting distribution of the therapy to selected centers experienced with CAR T-cell therapy (at least initially) and plans for extensive, long-term postmarketing surveillance.

"This is a very poor-risk population and represents a very great unmet need in the pediatric population," said Catherine M. Bollard, MD, of George Washington University here. "The clinical responses are remarkable, and I think Novartis has done a great job of putting together a plan for mitigating risk."

Brian Rini, MD, of the Cleveland Clinic, characterized the therapy as "potentially paradigm changing."

Despite unknowns surrounding the therapy, "it is hard to argue with the unprecedented clinical success we have seen in this population of patients who do not have other viable treatment options," added Grzegorz S. Nowakowski, MD, of the Mayo Clinic in Rochester, Minn.

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

https://www.medpagetoday.com/PublicHealthPolicy/FDAGeneral/66592

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What Causes Hemophilia (July 2017)

by Erum Naqvi

Hemophilia is a bleeding disorder usually caused by defects (mutations) in the genes that code for the blood-clotting factors VIII, IX or XI.

What causes hemophilia A and hemophilia B?

Hemophilia A and B are the major forms of hemophilia and affect males more than females. Hemophilia A is the most common type that affects approximately 1 in 4,000 to 5,000 newborn boys, while hemophilia B affects 1 in 20,000 newborn boys.

Mutations in the gene coding for factor VIII cause hemophilia A (also known as classic hemophilia), while mutations in the gene coding for factor IX cause hemophilia B (also called Christmas disease). The genes encoding for factor VIII and factor IX are both situated on the X-chromosome.

Mutations in these genes cause a deficit of blood-clotting factors, which are proteins in the blood that work together with platelets to stop or control bleeding. As a result, blood clotting in hemophilia patients is impaired and results in uncontrolled bleeding.

The genetic material in humans is packaged in 23 chromosome pairs, with the last pair being two X chromosomes in females and one X and one Y chromosome pair in males. If a disease-causing mutation is in a gene located on the X chromosome, a male with this mutation will develop hemophilia.

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

https://hemophilianewstoday.com/what-causes-hemophilia/

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