LifeTrac News Links

- LifeTrac Press Release – June 2018
- Trends in Transplantation - Volume 3
- Trends in Transplantation - Volume 2
- BiologicTx – the latest addition to LifeTrac
- Trends in Transplantation - Volume 1

Industry Articles

Cancer Immunotherapy: The Year in Review and a Look at the Year Ahead (February 2019) ................................................................. 2

Engineered immune cells target broad range of pediatric solid tumors in mice (February 2019) .............................................................. 3

Frailty tied to liver transplant wait-list mortality in cirrhosis (February 2019) ........... 4

My Husband’s Kidney: Doing Well After 26 Years (January 2019) ......................... 5

UChicago Medicine performs historic back-to-back triple-organ transplants (January 2019) ........................................................................................................ 6

Novoeight Safe, Effective in Hemophilia A Patients Over Long Term, Phase 3b Trial Shows (January 2019) ......................................................... 7

Risk adjustment ‘negates benefit’ of stem cell transplant for acute myeloid leukemia (December 2018) ................................................................. 8

Liver transplant from HIV+ living donor to negative recipient: the unanswered questions (December 2018) ............................................................... 9

‘Exciting’ but early results in trial of immunotherapy for myeloma (December 2018) 10
Cancer Immunotherapy: The Year in Review and a Look at the Year Ahead (February 2019)

January 16, 2019
Arthur N. Brodsky, Ph.D.

2018 was a big year for cancer immunotherapy, with several approvals in new cancer types as well as a number of promising breakthroughs with the potential to dramatically improve how patients are treated in the future.

To recap the highlights of the past year and discuss what’s next in cancer immunotherapy, the Cancer Research Institute (CRI) hosted a webinar for patients and caregivers with Elizabeth M. Jaffee, M.D., who currently serves as a member of the CRI Scientific Advisory Council, president of the American Association for Cancer Research (AACR), and deputy director of the Sidney Kimmel Comprehensive Cancer Center as well as the associate director of the Bloomberg~Kimmel Institute for Cancer Immunotherapy at Johns Hopkins University in Baltimore, MD, among other positions.

In this webinar, which you can watch in full, Dr. Jaffee primarily highlighted the following areas:

**New Immunotherapy Approvals**

In 2018, the U.S. Food and Drug Administration (FDA) approved checkpoint immunotherapies targeting the PD-1/PD-L1 pathway for several new populations of cancer patients. Starting in February, durvalumab was approved for patients with stage III non-small cell lung cancer (NSCLC), the most common type of lung cancer. Previously, checkpoint immunotherapies were only approved for patients with more advanced, metastatic NSCLC. In June, pembrolizumab was approved to treat advanced cervical cancer; in August, nivolumab was approved to treat metastatic small cell lung cancer (SCLC); and in September, cemiplimab was approved for patients with cutaneous squamous cell carcinoma (CSCC), the second most common skin cancer and the deadliest non-melanoma skin cancer. Each of these immunotherapies became the first to be approved by the FDA for these respective patient populations.

Additionally, several combination treatments involving checkpoint immunotherapy were approved in 2018 as first-line options, meaning that patients can now receive them following their initial diagnosis. In April, the combination of nivolumab and ipilimumab—checkpoint immunotherapies that target the PD-1 and CTLA-4 pathways, respectively—was approved for first-line treatment of renal cell carcinoma (RCC), the most common form of kidney cancer, whereas there were two different combinations—pembrolizumab (anti-PD-1) plus chemotherapy as well as atezolizumab (anti-PD-L1) plus bevacizumab, a VEGF-targeting antibody—approved for first-line treatment of patients with metastatic NSCLC.

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

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return to Table of Contents
Engineered immune cells target broad range of pediatric solid tumors in mice (February 2019)

Jan 17, 2019 by Erin Digitale

In mouse studies, a Stanford-led team has developed an engineered immune cell that eliminates several types of childhood tumors. The innovation may help patients with relapsed or metastatic disease.

Immune cells engineered to attack childhood cancers were able to eradicate different types of pediatric tumors in mice, according to a new study from the Stanford University School of Medicine.

The study, which was published online Jan. 17 in Clinical Cancer Research, provides evidence that these engineered cells can target many types of pediatric solid tumors, including brain tumors. Better treatments are badly needed for children with these tumors, particularly when traditional therapies fail.

“The prognosis for children with relapsed brain tumors or solid tumors or metastatic disease generally is dismal,” said Robbie Majzner, MD, the lead author of the new study and an instructor in pediatrics at Stanford. “We’re excited that we have a potential therapeutic representing a completely new modality to treat these children.” The study’s senior author is Crystal Mackall, MD, the Ernest and Amelia Gallo Family Professor and a professor of pediatrics and of medicine.

Immunotherapies that work well for adult cancers do not always succeed against childhood cancers, Majzner noted. One approach, called checkpoint inhibition, targets gene mutations that are limited in most pediatric cancers.

Another immunotherapy method, using chimeric antigen receptor T cells, or CAR-T cells, is the basis of a treatment for one form of relapsed childhood leukemia. Leukemia is a type of blood cancer. That therapy, tisagenlecleucel (brand name Kymriah), employs synthetic biology to make immune cells that react to a surface marker found on the leukemia cells.

**CAR-T for pediatric solid tumors**

Majzner and his colleagues decided to try to make CAR-T cells for pediatric brain tumors and solid tumors, including tumors found in bone and muscle. These cancers do not carry the same surface markers as leukemia, so the scientists’ first step was to look for another marker that engineered immune cells could target.

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


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[return to Table of Contents]
Frailty tied to liver transplant wait-list mortality in cirrhosis (February 2019)

February 4, 2019

(HealthDay)—In patients with cirrhosis, frailty is more frequently observed in those with ascites or hepatic encephalopathy (HE) and is independently associated with liver transplant wait-list mortality, according to a study published online Jan. 19 in Gastroenterology.

Jennifer C. Lai, M.D., from the University of California-San Francisco, and colleagues evaluated 1,044 adults without hepatocellular carcinoma who were on the liver transplant wait list at nine U.S. centers. For the evaluation, the researchers used the Liver Frailty Index (LFI), which uses data from grip strength tests, timed chair stands, and balance tests.

The researchers found that 36 percent of patients had ascites, 41 percent had HE, and 25 percent were frail. The odds of frailty were higher for patients with ascites (adjusted odds ratio, 1.56) or HE (adjusted odds ratio, 2.45) versus patients without these features. Compared with nonfrail patients, higher proportions of frail patients with ascites or HE died while on the wait list. Ascites (subhazard ratio [sHR], 1.52), HE (sHR, 1.84), and frailty (sHR, 2.38) were all associated with wait-list mortality. However, in adjusted models, only frailty remained significantly associated with wait-list mortality (sHR, 1.82).

"LFI scores can be used to objectively quantify risk of death related to frailty—in excess of liver disease severity—in patients with cirrhosis," the authors write.

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


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return to Table of Contents
My Husband’s Kidney: Doing Well After 26 Years (January 2019)

By Amy Schwab

January 4th 1983 is a special day in my husband, Rick's, life. It is the day he received a kidney from his younger sister, Beth. Now, 26 years later, Rick is living a healthy, happy life.

Rick was diagnosed in high school as having "kidney problems". Over the next few years, doctors kept an eye on things with his kidney problems, but nothing really changed. After we were engaged, things began to change. Seeking answers, we went to another facility for a second opinion and were told it could be 5-10 years before he was in end-stage renal disease. But in a mere 18 months, he would be starting dialysis 3 days a week for 5 hours each time. Rick was only 24. We had been married less than a year. For the next 6 months he went to dialysis while he continued to work.

During that time family members were tested as a possible match. Rick is one of nine children, so fortunately there were lots of possible matches. His younger sister Beth was a prefect match! She was in college at the time, but that didn't matter to Beth. She never complained about the testing, the scar, the recovery discomfort, or anything except having to remove her nail polish for surgery!

The surgeries began early in the morning on January 4th. Rick remembers them saying they were ready for the kidney and then hearing the basin "clink" on the table. The next thing he remembers was the nurse telling him the kidney was working! He and Beth both had a long day that day, but once Rick was settled into ICU, they served him a spaghetti dinner!

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

https://www.kidney.org/transplantation/transaction/TC/summer09/TCsm09_HusbandDoingWell

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return to Table of Contents
**UChicago Medicine performs historic back-to-back triple-organ transplants (January 2019)**

January 4, 2019

Written By Ashley Heher

Two 29-year-old patients from Michigan and Illinois are recovering following back-to-back triple-organ transplants to replace their failing hearts, livers and kidneys, marking a first in U.S. health care history.

The two surgeries, which lasted more than 17 and 20 hours each from Dec. 19 to 21, were performed by a team at the University of Chicago Medicine. According to federal statistics, this marked the first time a U.S. hospital has ever performed more than one of these complex procedures within one year, much less within 27 hours. These cases are the 16th and 17th time this type of triple-organ transplant has been performed in this country.

With the addition of these two cases, no other institution in the world has performed more of these procedures. UChicago Medicine also performed heart-liver-kidney transplants in 1999, 2001, 2003 and 2011.

“Rare transplant cases like these provide a unique and memorable legacy for that donor and the donor’s family,” said Kevin Cmunt, president/CEO at Gift of Hope Organ & Tissue Donor Network, a not-for-profit organ procurement organization that coordinates organ and tissue donations and provides donor family services and education in Illinois and Northwest Indiana. “We at Gift of Hope take pride in collaborating with our esteemed transplant centers, like the UChicago Medicine, that helps bring the gift of donation to even more families”

While the UChicago Medicine teams had spent nearly two months preparing for these cases, they hadn’t planned for the near-simultaneous occurrence of two triple-organ transplants.

“We never in our wildest dreams imagined both would take place at virtually the same time,” said John Fung, MD, a transplant surgeon and co-director of the UChicago Medicine Transplantation Institute. “Pulling this off can feel like trying to perform a high-wire ballet in the middle of running a marathon. But we were always confident in our patients as well as our team’s abilities.”

To view the full article, please click on this link: https://www.uchicagomedicine.org/forefront/transplant-articles/2019/january/uchicago-medicine-performs-historic-back-to-back-triple-organ-transplants

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return to Table of Contents
Novoeight Safe, Effective in Hemophilia A Patients Over Long Term, Phase 3b Trial Shows (January 2019)

January 7, 2019

by Joana Carvalho

Long-term treatment with Novoeight (turoctocog alfa) is safe and effective at preventing bleeding episodes in patients with hemophilia A of all ages who had already received prior treatment, a Phase 3b extension trial shows.

The study, "Long-term safety and efficacy of turoctocog alfa in prophylaxis and treatment of bleeding episodes in severe haemophilia A: Final results from the guardian 2 extension trial," was published in Haemophilia.

Hemophilia is a genetic blood disorder that affects the body’s ability to make blood clots to prevent excessive bleeding. In hemophilia A, this inability of the blood to clot is caused by the lack of a specific clotting protein, called factor VIII (FVIII).

Current treatments for hemophilia A are based on providing the missing FVIII to patients as a prophylaxis, or preventive measure, to avoid spontaneous bleeding episodes.

Novoeight, a third-generation recombinant (lab-made) FVIII developed by Novo Nordisk, is approved by the U.S. Food and Drug Administration for the treatment and prevention of spontaneous bleeding in patients with hemophilia A.

In two previous Phase 3 trials — guardian 1 (NCT00840086) and guardian 3 (NCT01138501) — Novoeight achieved positive results in both adults/adolescents and children with severe hemophilia A who had already received prior treatment, respectively.

The non-randomized, open-label, multicenter Phase 3b extension study (NCT00984126), called guardian 2, focused on assessing the long-term safety and efficacy of Novoeight in pretreated patients with severe hemophilia A.

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

https://hemophilianewstoday.com/2019/01/07/novoeight-safe-effective-phase-3b-trial/

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Risk adjustment ‘negates benefit’ of stem cell transplant for acute myeloid leukemia (December 2018)

December 10, 2018

SAN DIEGO — The addition of a transplant-specific comorbidity score to risk stratification appeared to negate the survival benefit of hematopoietic stem cell transplantation among older patients with acute myeloid leukemia, according to results of a prospective, multicenter, longitudinal study presented at ASH Annual Meeting and Exposition.

Survival rates following allogeneic HSCT have continued to improve for older patients with AML, according to Mohamed L. Sorror, MD, MSc, associate professor of medicine in the division of oncology at University of Washington School of Medicine, associate member in the clinical research division at Fred Hutchinson Cancer Research Center, and physician at Seattle Cancer Care Alliance.

Patients aged 61 to 70 years seem to have the biggest improvement in survival over the last decade,” he said, stressing that the population of individuals aged older than 60 years who undergo transplantation is small.

The fundamental question clinicians face when they have a patient in remission is whether they should receive a transplant, Elihu Estey, MD, professor in the division of hematology at University of Washington School of Medicine, member of Fred Hutchinson Cancer Research Center and hematologist at Seattle Cancer Care Alliance, told HemOnc Today.

“For many years, transplants were restricted to people who were relatively young,” he said. “It was felt that the procedure was too intense for older individuals, and that they would die from it. In the last 20 or 25 years, the idea of a reduced-intensity transplant has been developed, permitting transplantation in people even in their 70s.

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


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return to Table of Contents
Liver transplant from HIV+ living donor to negative recipient: the unanswered questions (December 2018)

November 28, 2018 7:57 am EST

A lifesaving partial liver transplant from an HIV-infected mother to her uninfected child – the first of its kind – was conducted last year at the University of the Witwatersrand’s Donald Gordon Medical Centre in Johannesburg. More than a year later, both mother and child are doing well.

But the crucial question of the child’s HIV infection status remains unanswered. And we don’t expect to have a definitive answer any time soon.

Despite this uncertainty, the story of the transplant is inspiring. To date there have been no published reports of a living organ donation by a person with HIV, or of an intentional transplant from an HIV-positive to HIV-negative individual. The operation was driven by a number of factors. These included life-threatening liver failure in the child, no available deceased or suitable live HIV-uninfected donors, and an HIV-positive mother’s continued pleas to be allowed to save her child.

We’ve learned a great deal from the operation and during the subsequent year. Most importantly, the success of this transplant provides a new therapeutic option for similar cases in high burden HIV countries where deceased donor organs are limited in number, or where access is limited.

But there are still gaps in our knowledge. The biggest is what the long term effect of the transplant will be on the child, and particularly whether the mother’s virus was transferred with the liver.

The journey

The child was 13 months old when the transplant happened. The liver has a remarkable ability to regenerate and grows back to its normal size in the donor in about six weeks.

Although born to an HIV-positive mother, the child did not have HIV. The mother was on antiretroviral therapy during pregnancy, and the child received standard preventative treatment.

To view the full article, please click on this link: https://theconversation.com/liver-transplant-from-hiv-living-donor-to-negative-recipient-the-unanswered-questions-107388

'Exciting’ but early results in trial of immunotherapy for myeloma (December 2018)

Cancer cells disappeared rapidly in patients with high-risk, treatment-resistant disease

December 3, 2018 by Susan Keown / Fred Hutch News Service

The 11 patients had already received treatment after treatment for their cancers, some as many as 20 different courses of therapy. Yet their myelomas, almost all classified by doctors as “high risk,” kept coming back. Their options faded away.

Then they joined a clinical trial to be the first people ever to receive a new experimental, immune-harnessing therapy, whose design includes features based on pioneering research at Fred Hutchinson Cancer Research Center. For several of them, this was the only trial in the world of this type of therapy for which they were eligible.

The industry-funded study was designed to find a safe dose of the experimental immunotherapy, not test its effectiveness. So these first participants got just a low dose, lower than previous studies had suggested could have much of an effect on this blood cancer.

That’s why the researchers were so encouraged when the cancerous cells vanished from every patient’s bone marrow within a month.

Trial leader Dr. Damian Green of Fred Hutch reported initial results from these first patients today at the annual meeting of the American Society of Hematology, which runs through Tuesday in San Diego. The findings after an average of about five months of follow-up have him feeling “very optimistic” about the potential for this strategy.

“I think it was as good as we could have hoped for and maybe better,” said Green, a myeloma specialist. He cautioned that researchers need to study trial participants for years to draw conclusions about how well the experimental therapy will help patients in the long run.

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


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