Helping patients’ own immune systems to kill cancer cells is a story that appears with increasing frequency across print, digital and broadcast media. Last December, Science magazine declared forms of cancer immunotherapy as the 2013 Breakthrough of the Year.

It highlighted immune T cells genetically engineered to target a protein found on many B-cell cancers, called CD19. LLS-funded researchers at University of Pennsylvania and Memorial Sloan Kettering are getting astonishing results, including stable remissions in adults and children for whom standard leukemia therapies had not worked. But the T-cell therapies also kill normal cells with CD19 and can compromise immune responses. Therefore, investigators are now also developing T cells that selectively attack cancer-specific abnormalities.

Recently, researchers at the National Cancer Institute sequenced the genome of a bile duct cancer and carefully selected T cells from the patient’s blood that attacked a specific mutation. The cells were expanded in the lab and returned to the patient where they rapidly began attacking the cancer. This is the first report of what could be many more successes with this high-tech approach.

A different immunotherapy that uses natural (not engineered) T cells is being tested at Johns Hopkins University where the LLS Therapy Acceleration Program is investing in a Phase II clinical trial for myeloma patients. Tumor-specific T cells known as marrow infiltrating lymphocytes (MILs) can be easily obtained from patients and inexpensively activated and expanded in number. When returned to the patient, the MILs migrate and safely kill myeloma cells. In the trial, toxicities have been short term and patient responses have been longer lasting than with other therapies. Another LLS-funded study at the university is testing MILs to prevent relapse after stem cell transplantation.

And there are other immunotherapy approaches such as a new class of antibody drugs that target molecular brakes in the immune system. These proteins, known as immune checkpoints, normally keep our immune system from over-reacting and damaging healthy organs, but cancers can use them to escape immune surveillance.

One immune checkpoint involves a protein called PD-1. This biomarker indicates that a T cell is exhausted and ready for the programmed death process known as apoptosis. PD-1 lowers the threshold for apoptosis and prematurely puts the brakes on the immune system’s ability to fight cancer. The antibodies essentially remove the brakes and allow immune cells to get back to work.

All these approaches are likely to have broad utility across blood cancer and solid tumor therapies.
**Immunotherapy as Good Business**

By bolstering patients’ own immune systems, it is possible to save lives without aggressive chemo- and radiotherapies that can produce secondary tumors and other long-term side effects. Some immunotherapies use antibodies, natural immune cell products that can now be produced commercially. The first anti-cancer antibody drug approved in the U.S. was Rituxan® in 1997. Used to treat patients with non-Hodgkin lymphoma, it was later approved as therapy for chronic lymphocytic leukemia. Rituxan binds a specific molecule on these cancers, activating anti-cancer immune responses and also having direct killing effects.

Today, LLS is testing a new antibody drug for Hodgkin lymphoma (HL) patients in a partnership with Affimed Therapeutics, AG of Heidelberg, Germany. The unique element of Affimed’s drug, AFM13, is its two binding sites. One binds the CD30 target on malignant cells; the other recruits the immune system by binding a protein (CD16A) found on natural killer cells that are vital warriors in the immune cell army.

CD30 is a good target that is universally found at much higher levels on HL cells than on normal ones. Phase I data showed Affimed’s new therapy was well tolerated and active even in patients who did not achieve remissions with Adcetris®, a recently approved drug that also targets CD30. LLS and Affimed are now co-funding a phase II trial with HL patients for whom current treatments have failed.

**LLS plays a crucial role, funding research based on patient needs rather than financial return.**

As a privately held company, Affimed’s unique antibody technology and promising early data didn’t necessarily align with investors’ interests in larger markets and proven clinical value. This is where LLS plays a crucial role, funding research based on patient needs rather than financial return. After evaluating the potential for patients, LLS committed $4.4 million that was matched by Affimed and the trial is ready to begin. AFM13 received orphan drug designation by both the U.S. F.D.A. and the European Medicines Agency that will facilitate its development.

Over the past two years, half a dozen projects in the LLS Therapy Acceleration pipeline have led to large investments by pharmaceutical and biotechnology firms with the resources for late-stage clinical trials and product development. LLS believes that Affimed is another good pick.

For more about immunotherapy as good business, read an article in the May 26th issue of *Forbes* titled “Is This How We’ll Cure Cancer?”

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**LLS Convenes CML Expert Expert Summit**

Gleevec® and newer, more potent Bcr-Abl inhibitors are saving lives of people with chronic myeloid leukemia (CML). Whether they are truly curative remains to be proven; for now patients must continue treatment to control their disease. Further, available treatments offer more limited benefit in accelerated and blast phases of CML. Recently, with financial support from Pfizer and Ariad Pharmaceuticals, LLS gathered experts to identify strategies to make CML a more completely treatable disease.

Participants at the summit shared their direct experiences as patients, clinicians, or health advocates. The discussion was a critical step toward identifying what remains to be done to improve CML patients’ quality of life and to continue research towards a cure. The exchange of information provided compelling direction for implementing strategies that focus on healthcare practices and policy.

Michael Mauro, MD, from Memorial Sloan Kettering Cancer Center recently spoke about unmet needs for CML patients. “With higher fractions of patients ultimately achieving deep and stable remissions, we are at the point where CML is truly a chronic disease. Now, a key next area of active research is the investigation of treatment-free remission, which might herald an era where CML therapy is no longer life-long.”

Citing additional unmet needs for CML patients in blast crisis phase of the disease, Dr. Mauro remarked, “We need additional treatment options for patients with sequential resistance to multiple therapies, or early resistance to initial therapies. Additional novel small molecule kinase inhibitors, therapies targeting immune checkpoints, and inhibitors of alternate pathways activated in CML cells, are all being pursued to fill all the ‘chinks in the armor’ of current therapy, to render CML a more completely treatable leukemia.”

A white paper about the summit will be available in coming weeks on www.lls.org.
What is a cure?

This was the question that LLS Interim President/CEO and Chief Mission Officer, Louis J. DeGennaro, PhD, posed to the distinguished panelists at our three-day conference of researchers, volunteers and advocates in Washington, D.C. The panel featured James Bradner, MD, Catherine Wu, MD, and Jennifer Brown, MD, PhD, all from Dana-Farber Cancer Institute, David Porter, MD, from University of Pennsylvania and Gregory Reaman, MD, from the FDA. It also included Sumi Thavarajah and Lokesh Duraiappah whose son Kethan died last summer from ALL, and Tom and Kari Whitehead, whose daughter Emily survived the disease with immunotherapy treatment.

The group collectively defined cure as the durable absence of the disease with no impact on the future, without the threat of death and with the freedom from ongoing treatment. Dr. Reaman added that for patients diagnosed at age five or younger, this was a particularly tall order and emphasized the importance of quality of life. Another panelist rejected remission as an acceptable outcome, calling it a “wishy-washy doctor term” that says we can’t find your disease.

Is disease control with tolerable side effects a good intermediate goal?

There was debate about whether turning diseases into chronic conditions through ongoing therapy was an appropriate end point. Dr. Porter said it was laudable but remaining cells have the potential to mutate. Dr. Bradner stated that cancer as a chronic condition is not good enough. “Our goal is a cure – full stop.” As moderator, Dr. DeGennaro echoed that sentiment saying the LLS won’t settle for disease control.

… cancer as a chronic condition is not good enough. “Our goal is a cure – full stop.”

How should LLS deploy resources? What do we do now?

Kethan’s and Emily’s parents offered advice in this segment requesting a Patient Registry to help access information and care. They felt patients and caregivers in crisis are overwhelmed and can be discouraged from looking elsewhere. Although trials were found with existing LLS resources, it required their personal persistence to speak with the principal investigator to determine if they qualified. They felt a patient registry would be a step toward a team approach for better care.

Of note, LLS is currently developing the Michael Garil Patient Registry under the direction of Larry Saltzman, MD. With a patient’s consent, the registry will store and incorporate patient survey information along with medical records and be available for research purposes as well as specific feedback to patients, families and providers.

You can find the panel discussion in its entirety on YouTube at http://youtu.be/zphIPGmkAO4
I had never been to Capitol Hill but couldn’t resist the LLS invitation this spring to join 400 patients, survivors, families and volunteers and meet with lawmakers on the importance of access to life-saving therapies. As a physician and a researcher focused on hematological malignances, I am devoted to developing new therapies to save lives. Our objective in Washington was to urge lawmakers to support two critical pieces of legislation that would improve access to therapies for blood cancer patients.

“Our objective was to urge lawmakers to support critical legislation improving access to therapies for blood cancer patients.”

One bill, HR460, would limit cost-sharing for patients who require specialty tier drugs in commercial plans. The other, S1365/HR 2827, would allow a patient on Medicare to appeal if a needed prescription drug is placed on a non-preferred tier with high out-of-pocket costs. The bill would allow patients to appeal to have the drug placed on a preferred drug list with lower coinsurance, if the prescribing physician deems it the patient’s only option.

I began my day in Senator Stabenow’s (D-MI) office with Michigan advocates, patients and LLS staff. We focused on the importance of access, shared patient stories and highlighted the need to fund cancer research. As a member of the Senate Finance committee with jurisdiction of the Medicare program, it was important for the senator to hear from Medicare patients who find it difficult to access therapies due to policies that shift the cost burden to patients.

I also met with Senator Carl Levin (D-MI) and his team with the same asks – prioritize cures and access. Afterward, we met with Congressman Dave Camp (R-MI), a recent non-Hodgkin lymphoma survivor and chair of the House Ways & Means Committee, which has jurisdiction over Medicare.

With 329 meetings, 16,000 signatures demanding expanded access to care, and another 175 telephone calls while we were there, LLS obtained 11 new co-sponsors, and counting, to the bills. After years of knowing the importance of LLS in blood cancer research, I appreciated the opportunity to participate in this valuable event and cannot wait to return.

Your support writes these stories. Thank you.

The collective authors of these accounts of progress are the forward-thinking people who sustain LLS with lifetime donations and gifts through their wills. If you’d like to help write the next story by supporting research in a specific type of blood cancer, contact Richard Schneyer, vice president of development, at 1-888-773-9958 or richard.schneyer@lls.org.

My time on Capitol Hill
By Sami Malek, MD