

Natural Killer Cell Therapy May Augment Treatment of Hematological Cancers

By Sarah Bronson

Tough cancer treatments can severely weaken the body's natural ability to attack cancer cells. To improve immune recovery and function in patients who have un-

dergone these treatments, especially those who may later receive a stem cell transplant, researchers are turning to natural killer cells that have been expanded in the laboratory.

In an ex vivo natural killer cell expansion technique developed at MD Anderson, mononuclear cells from peripheral blood are stimulated with irradiated mononuclear cells to induce the expansion of natural killer cells. Then, T cells are removed, and the purified natural killer cells are co-cultured with artificial antigen-presenting cells derived from K562 human chronic myelogenous leukemia cells. Abbreviations: aAPC, artificial antigen-presenting cell; NK, natural killer. Used with permission from Denman CJ, et al. PLoS One. 2012;7:e30264. © 2012 Denman et al.

Treating HIV in Cancer Patients

Concurrent HIV and cancer treatment extends survival

4

House Call

Facts about radiation exposure



7

In Brief

Gene therapy shows promise against B cell cancers

8

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Natural Killer Cell Therapy

[Continued from page 1]

Rationale and development

Treatment of high-risk hematological cancers such as acute myelogenous leukemia and chronic lymphocytic leukemia typically requires myeloablative chemotherapy and/or radiation therapy usually followed by hematopoietic stem cell transplantation. Unfortunately, the myeloablative regimens typically cause patients to become immunocompromised at a time when they would most benefit from a robust immune response to their disease.

“The very cells we have in our body that are able to kill our cancer, we wipe out every time we give cytotoxic therapy,” said Dean Lee, M.D., Ph.D., an associate professor in the Division of Pediatrics at The University of Texas MD Anderson Cancer Center. And the allogeneic stem cell transplants often used to restore the immune system after myeloablative treatment can take a long time to regenerate immune cells and can lead to graft-versus-host disease, which itself can threaten survival.

A promising approach for boosting patients’ immune function is the use of natural killer cells, which have an innate, selective cytotoxicity against all cancerous and precancerous cells. Thus, Dr. Lee and others reason that treatment with natural killer cells—alone or as a bridge to autologous or allogeneic stem cell transplantation—following chemotherapy could improve the immunologic response against cancer and protect against some of the adverse effects of stem cell transplantation.

“We’ve been interested in how immunotherapy with natural killer cells after chemotherapy can be a possible middle ground between chemotherapy alone and chemotherapy followed by an allogeneic transplant in terms of adverse effects,” said Nina Shah, M.D., an assistant professor in the Department of Stem Cell Transplantation and Cellular Therapy.

The great majority of clinical trials that have tested natural killer cell therapy so far have derived the natural killer cells from apheresis, in which white blood cells are removed from a donor’s



“[B]lood banks discard the white blood cells from the typical pint of blood that is donated ... What we routinely throw away may actually be an important clinical product.”

– Dr. Dean Lee

blood, the T cells are removed from the pool of white blood cells, and the remaining white blood cells are given as treatment. For some patients, including some with acute myelogenous leukemia, the results of this treatment have been promising. However, the number of cells that can be obtained by this approach is limited, and such infusions are relatively impure, containing only 20%–30% natural killer cells.

A recent breakthrough has enabled researchers to achieve higher concentrations of natural killer cells for patient infusions. Dr. Lee said, “Our laboratory genetically engineered a feeder cell with all the right signals that a natural killer cell needs to proliferate. Now we can grow billions of natural killer cells from a vial of blood in a couple weeks.”

The method for expanding natural killer cells *ex vivo* developed by Dr. Lee’s laboratory uses artificial antigen-presenting cells expressing membrane-bound interleukin-21. This method has yielded greater expansions of natural killer cells after 3 weeks of culture than any other method so far, with a final concentration of natural killer cells greater than 99%. Using this expansion technique, MD Anderson researchers have launched a series of phase I clinical trials testing natural killer cells for patients with hematological cancers, brain cancers, and other solid tumors.

Ready availability

In addition to its potential selective effects against cancer, natural killer cell therapy would likely be easier to obtain than other immune cell therapies. In

contrast to T cell therapy, for which T cells that recognize the specific tumor must be selected or engineered, natural killer cells already have the receptors for recognizing cancerous cells. “We don’t have to individually select just the right natural killer cell for every single patient,” Dr. Lee said. Furthermore, the evidence so far suggests that natural killer cells can treat all kinds of cancer. Thus, natural killer cells may not need to be produced in different ways for different types of cancer and would likely be less costly than custom-made cell therapies.

In fact, Dr. Lee said that natural killer cells probably could be obtained from ordinary blood donations. “Right now, blood banks discard the white blood cells from the typical pint of blood that is donated,” he said. “But we’ve figured out that you can take those white blood cells and use them to grow large numbers of natural killer cells. What we routinely throw away may actually be an important clinical product; we just have to rescue and process it.”

If natural killer cells can be obtained and prepared efficiently, then natural killer cell therapy could become readily available to cancer patients. One of the upcoming solid tumor studies will test whether natural killer cells can feasibly be generated from blood bank products as an off-the-shelf product to be stored frozen and ready to thaw and infuse into patients.

Although most of the natural killer cell trials that are starting up at MD Anderson derive those cells from peripheral blood, Dr. Shah has adapted

the approach to grow natural killer cells obtained from umbilical cord blood. In her research, Dr. Shah made use of the large cord blood bank at MD Anderson headed by Elizabeth Shpall, M.D. “An advantage of using banked cord blood is that it’s an already collected unit sitting in a freezer, so nobody has to go through the procedure of drawing blood,” Dr. Shah said.

Furthermore, with the help of the new artificial antigen-presenting cells to expand the cord blood’s natural killer cells, it can take as few as 2 weeks to grow enough cells for use in natural killer cell therapy. “People have expanded natural killer cells from cord blood before,” Dr. Shah said, “but not this quickly or reliably and not in a way that translates to the clinic like we’re able to do.”

Dr. Shah has been leading a phase I trial in which these cord blood–derived natural killer cells are given in combination with high-dose chemotherapy followed by autologous stem cell transplantation to patients with multiple myeloma. The patients thus receive an allogeneic immunotherapy without undergoing an allogeneic stem cell transplant.

Variations

Natural killer cells do not need to be matched to the recipient to achieve a therapeutic effect. In fact, certain major histocompatibility complex (MHC) mismatches between donor and recipient result in more effective natural killer cell therapy than do MHC matches. In studies of patients with hematological cancers who received MHC-mis-

matched bone marrow transplants, certain mismatches predicted better natural killer cell responses and longer survival times. Furthermore, the inheritance of certain genes that affect natural killer cell function varies widely, so it is possible that donors with favorable immunogenetic traits could be tapped as sources of particularly effective natural killer cells.

In addition, natural killer cell therapy could be delivered directly to the tumor site rather than intravenously. In a recently approved trial at MD Anderson, patients with brain cancer will receive infusions of their own expanded natural killer cells into the locations from which their brain tumors have been resected. This trial will test the hypothesis that natural killer cells are able to recognize brain tumors but

CLINICAL TRIALS: Natural Killer Cells

A phase I/II clinical trial testing the safety and feasibility of interleukin-21–expanded natural killer cells for induction in relapsed/refractory acute myeloid leukemia (2012-0079).

Principal investigator (PI): Dr. Dean Lee. The goal of this study is to find the highest tolerable dose of natural killer cells that can be given with cytarabine and fludarabine to patients with acute myeloid leukemia. The safety and effectiveness of this treatment will also be studied.

Natural killer cells with human leukocyte antigen–compatible hematopoietic transplantation for high-risk myeloid malignancies (2012-0819). PI: Dr. Richard Champlin.

The goal of this phase I/II study is to find the highest tolerable dose of alloreactive natural killer cells that can be given with busulfan, fludarabine, and interleukin-2 followed by stem cell transplantation to patients with acute myeloid leukemia or myelodysplastic

syndromes. The safety and effectiveness of this treatment will also be studied.

Phase I/II study of umbilical cord blood–derived natural killer cells in conjunction with high-dose chemotherapy and autologous stem cell transplant for patients with multiple myeloma (2011-0379). PI:

Dr. Nina Shah. The goal of this study is to find the highest tolerable dose of cord blood–derived natural killer cells that can be given with lenalidomide, melphalan, and interleukin-2 followed by autologous stem cell transplantation to patients with multiple myeloma. The safety and effectiveness of this treatment will also be studied.

Natural killer cells in allogeneic cord blood transplantation (2011-0493).

PI: Dr. Chitra Hosing. The goal of this phase I study is to find the highest tolerable dose of cord blood–derived natural killer cells that can be given in

combination with fludarabine, melphalan, lenalidomide, and a cord blood transplant to patients with lymphoid malignancies. The safety and effectiveness of this treatment will also be studied.

A phase I/II clinical trial of natural killer cell administration to prevent disease relapse for patients with high-risk myeloid malignancies undergoing haploidentical stem-cell transplantation (2012-0708). PI: Dr.

Stefan Ciurea. The goal of this study is to find the highest tolerable dose of natural killer cells from an MHC-mismatched family member that can be given with standard chemotherapy and a stem cell transplant from that same family member. The safety and effectiveness of this treatment will also be studied. ■

FOR MORE INFORMATION

Visit www.clinicaltrials.org.



Natural Killer Cell Therapy

[Continued from page 3]



“People have expanded natural killer cells from cord blood before, but not this quickly or reliably.”

– Dr. Nina Shah

unable to reach them because of the blood-brain barrier.

Unanswered questions

Allogeneic natural killer cells, even those expanded using the new artificial antigen-presenting cells, may have limited lifespans after infusion. “We don’t know whether natural killer cells proliferate in the body in response to the tumor the way T cells do,” Dr. Lee said. In leukemia patients who undergo T cell therapy, under the right circumstances the T cells will grow to outnumber the tumor cells, but patients who undergo natural killer cell therapy will likely require multiple infusions or some other means of sustaining the number of cells.

It also is not known how well natural killer cell therapy will be tolerated by recipients, and any patient characteristics that may be contraindications to this treatment have yet to be determined. Although infusions of natural killer cells are unlikely to cause graft-versus-host disease, the allogeneic natural killer cell infusions still could have adverse effects related to their stimulation of the immune system. Such effects might include allergic responses, fever, leaky blood vessels, or low blood pressure; however, these adverse effects have not been seen in any of the natural killer cell therapy trials ongoing at MD Anderson. The upcoming phase I trials at MD Anderson will continue to test patients’ tolerance of this treatment.

Future directions

Although natural killer cells are associated with fewer adverse effects

than allogeneic stem cell transplantation, they also are less specific than T cells, which target particular tumor markers. Engineering natural killer cells to recognize certain tumors may increase the effectiveness of natural killer cell therapy. Dr. Shah’s group is currently studying ways to engineer natural killer cells to target an antigen on myeloma cells.

Another possibility is banking a patient’s own natural killer cells and then re-infusing those cells after chemotherapy. Dr. Lee said, “For a long time we thought that if a patient develops cancer, then the patient’s own natural killer cells must not be very effective, suggesting that natural killer cells from a donor would be better. But now we have reason to believe that the patient’s cells can still be beneficial if given in high enough numbers or delivered to the right location.”

Yet another possibility for natural killer cell therapy is the creation of a product that clinicians can store and use when needed rather than searching for a specific donor or generating an individualized treatment. Because natural killer cells can be derived from existing peripheral blood banks and cord blood banks, expanded to very large numbers relatively quickly, frozen until needed, and then used to treat all kinds of cancer cells, this scenario seems within reach. ■

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Concurrent Treatment Improves Survival

By Bryan Tutt

Concurrent HIV and cancer patients in the clinic, regardless of who is first. The simultaneous treatment is complicated by patients’ weakened immune systems and the lack of routine HIV screening between drugs. Infectious diseases experts at the University of Texas MD Anderson Cancer Center are studying ways to timely treat HIV in cancer patients and ways to overcome these challenges.

HIV and cancer

The relationship between HIV and cancer is not fully understood, but the virus is known to confer a high risk for various cancers.

“For many years, we had a group of cancers that were associated with HIV, the so-called AIDS-defining cancers: cervical cancer, Kaposi sarcoma, and non-Hodgkin lymphoma,” said Harrys Torres, M.D., an assistant professor in the Department of Infectious Diseases. “Now, with advances in HIV treatment, patients are living longer and developing non-AIDS-defining cancers.”

Compared with the general population, people with HIV have higher rates of lung cancer, melanoma, head and neck cancer, and anal cancer. “The immunocompromised state predisposes patients to the development of cancer, similar to what is seen in solid-organ-transplant patients,” said Bruno Granwehr, M.D., an associate professor in the Department of Infectious Diseases.

The high rates of cancer among HIV patients have a devastating consequence. “One-third of deaths among people with HIV in the United States are cancer-related,” Dr. Torres said. “That may have to do with the late diagnosis of HIV in patients whose cancer is diagnosed first and the limited

Treatment of HIV and Cancer Survival Outcomes

Patients present special challenges when disease is diagnosed. Treatment of HIV and cancer in weakened immune systems, screening, and interactions with disease specialists at The Anderson Cancer Center routinely treat patients and are discovering new challenges.

approach to HIV screening at U.S. cancer centers.”

Screening cancer patients for HIV

Because many patients with both HIV and cancer are unaware that they have HIV, Drs. Torres and Granwehr believe that HIV screening should be included in the routine workup for cancer patients. Dr. Torres said, “Of the HIV-positive patients who come to MD Anderson for cancer care, 16%–33% don’t know they have HIV until they get tested here.”

Most large cancer hospitals, including MD Anderson, do not currently screen all patients for HIV, although MD Anderson patients with hematological malignancies typically are screened, as are those with other cancers who have HIV risk factors. Dr. Granwehr said HIV screening in cancer

patients is overlooked at cancer centers for numerous reasons, such as assumptions that patients were tested before referral for cancer treatment and confusion about the consent requirements for testing, which vary by state. In addition, older patients—the population most affected by cancer—often are not screened because of the misconception by some clinicians that HIV is an issue among young people only. However, Dr. Granwehr said, “With an increasingly healthy older population, there are more new cases of HIV in people over 50 years old; it’s one of the fastest growing populations of newly diagnosed HIV patients.”

Dr. Granwehr is leading a group that is working to improve the mechanics of HIV testing at MD Anderson. “We’ve proposed incorporating HIV testing into our ‘front door’ consent form,” he said. This measure would facilitate HIV testing and reduce the number of patients in whom screening is overlooked.

Dr. Granwehr added, “If you’re going to use chemotherapy or other treatments that would further suppress a cancer patient’s immune system, you should know as far in advance as possible if a patient has HIV. This test should be considered as necessary at baseline as assessing liver or kidney function. It’s important to test cancer patients for HIV as part of their workup because patients can be treated for their cancer and their HIV simultaneously with success.”

Treating HIV in cancer patients

Studies of patients who have both HIV and cancer have shown that those who receive concurrent HIV treatment and cancer treatment survive longer than do those who receive cancer treatment only. For this reason, patients at MD Anderson with HIV—whether newly or previously diagnosed—are referred to the Infectious Disease Clinic. The infectious disease specialists work closely with oncologists to tailor each patient’s regimen of antiretroviral drugs for HIV treatment according to the patient’s cancer treatment. Also, Dr. Granwehr said, “If a patient is receiving chemotherapy here and HIV treatment from an outside provider, we can work with that provider to modify the antiretroviral regimen if necessary.”

According to Drs. Granwehr and Torres, the most important challenge of treating HIV in patients who are also undergoing cancer treatment is avoiding unwanted interactions between HIV drugs, chemotherapy drugs, and other agents commonly used in cancer patients (e.g., antifungals, antivirals, and immunosuppressants) and the resulting toxic effects.

Although physicians at MD Anderson have successfully treated hundreds of patients who have HIV and cancer, much remains unknown about the interactions between the antiretroviral drugs used in HIV treatment and the chemotherapy drugs and targeted agents used in cancer treatment.

To address this gap in knowledge, Dr. Torres and his colleagues conducted a retrospective analysis of 154 patients who were treated for HIV and cancer and followed up regularly at MD Anderson. The researchers analyzed rates of adverse events, side effects, clinically relevant drug interactions, and efficacy in patients treated with various antiretroviral drug regimens.

Among the commonly used classes of HIV drugs, integrase strand-transfer inhibitors (INSTIs) were tolerated best by cancer patients in the study and had



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– Dr. Harrys Torres

Concurrent Treatment

[Continued from page 5]

the fewest interactions with cancer drugs, although non-nucleoside reverse transcriptase inhibitors (NNRTIs) also were well tolerated with few drug interactions (see figure). INSTI- and NNRTI-based regimens had similar efficacy rates. HIV protease inhibitors were shown to have clinically significant interactions with several cancer drugs, and regimens based on protease inhibitors were less efficacious than INSTI- and NNRTI-based regimens.

Dr. Torres said that without INSTIs, it would be much more challenging to treat HIV in cancer patients. “INSTIs have virtually zero interactions with immunotherapeutic agents and other anticancer drugs,” agreed Dr. Granwehr, a co-investigator in the retrospective analysis.

If toxic effects due to drug interactions or other causes necessitate treatment changes for a patient with HIV and cancer, the antiretroviral regimen typically is adjusted rather than the anticancer regimen. According to Drs. Torres and Granwehr, the cancer treatment is rarely modified, although in a very few cases, the dose of a chemotherapy agent is adjusted.

Dr. Granwehr added that the timing of cancer treatment is seldom affected by HIV treatment, although if a patient newly diagnosed with HIV has just begun treatment for the virus, surgery for cancer might be postponed to make sure the patient is stable. Otherwise, HIV treatment rarely interferes with surgery or radiation therapy for cancer.

Another challenge of treating HIV in cancer patients is monitoring the patients’ progress. “The two markers typically used to monitor HIV are viral load

The figure describes treatment modifications made to avoid drug interactions in patients who received concurrent cancer and HIV treatment. No clinically significant interactions were seen between INSTIs and anticancer drugs. Abbreviations: ARV, antiretroviral; AVBD, doxorubicin, bleomycin, vinblastine, and dacarbazine; ICE, ifosfamide, carboplatin, and etoposide; INSTI, integrase strand-transfer inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor. Adapted from Torres HA, et al. Clin Microbiol Infect. 2014;20:O672–O679.

and CD4 cell count,” Dr. Torres said. “But the CD4 cell count can be affected by cancer medications, so HIV in cancer patients is best monitored by viral load.”

Improving detection and treatment

Despite the successful treatment of many patients with HIV and cancer, there are no standardized guidelines for HIV treatment in cancer patients. In the report of their retrospective study, Dr. Torres and his co-authors urged a prospective study to further

the development of such guidelines.

In addition, Dr. Granwehr said he hopes more cancer centers will recognize the importance of screening cancer patients for HIV. “Cancer patients who are tested and treated for HIV tolerate their cancer therapy and their HIV therapy very well. Oncologists should not be hesitant to test patients for HIV for fear that their patients might not benefit from cancer treatment.” ■

FOR MORE INFORMATION

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“Cancer patients who are tested and treated for HIV tolerate their cancer therapy and their HIV therapy very well.”

– Dr. Bruno Granwehr

FURTHER READING

Torres HA, Mulanovich V. Management of HIV infection in patients with cancer receiving chemotherapy. *Clin Infect Dis.* 2014;59:106–114.

Torres HA, Rallapalli V, Saxena A, et al. Efficacy and safety of antiretrovirals in HIV-infected patients with cancer. *Clin Microbiol Infect.* 2014;20:O672–O679.



Facts About Radiation

Radiation exposure comes from many sources

We are exposed to radiation every day. This may seem alarming, but much of this radiation occurs naturally and is harmless in small doses.



Knowing how much additional radiation exposure is caused by medical procedures, air travel, and other activities can help us make informed decisions and avoid unnecessary worry.

The average person is exposed to approximately 6.2 millisieverts (mSv, the units used to measure the effective radiation dose) of radiation each year. This level of exposure is well below the international standards for radiation workers, which allow up to 50 mSv per year.

However, we should be aware of the hazards of excessive radiation exposure, especially since the effect of radiation is cumulative over a lifetime. Scientists estimate that for every 1,000 mSv of radiation that we receive, 0.2 mutations occur in our genes. Some of these mutations increase the risk for cancer, but not all mutations are dangerous—the average person already carries 50 gene mutations.

Natural radiation sources

Radiation is classified as ionizing (capable of freeing electrons from atoms or molecules) and non-ionizing. Ionizing radiation (e.g., x-rays) is considered more harmful than non-ionizing radiation (e.g., radio waves).

Most of the natural radiation that we receive is due to radon (a radioactive element) in the air. Airborne radon alone accounts for more than one-third (2.3 mSv) of the average person's annual radiation exposure. Altitude also affects radiation exposure. For every additional foot above sea level, there is a minute increase in radiation per year due to cosmic radiation, or radiation from the sun and outer space.

Terrestrial (ground) radiation accounts for approximately 0.2 mSv (3.2%) of our annual exposure.

What we consume also affects our exposure to radiation: food contains the radioactive isotopes carbon 14 and potassium 40, and some water contains additional radon. This, however, should not be a source of concern: together, food and water typically account for only 0.3 mSv (4.8%) of our annual radiation exposure.

Factors that increase radiation exposure

Although most radiation occurs naturally, environmental and lifestyle factors can increase our levels of exposure. Keep in mind that the amount each factor contributes to a person's level of radiation exposure is usually very small.

Building materials contain varying levels of radon: living in concrete, stone, adobe, or brick buildings increases a person's annual radiation exposure.

Air travel also exposes us to small amounts of radiation. Specifically, for every hour spent traveling by plane, a person is exposed to 0.005 mSv of ionizing radiation. The millimeter wave scanners at security checkpoints use non-ionizing radiation that is not known to be harmful.

Nearly half of the average person's annual radiation exposure is due to medical testing, such as radiography (x-ray) and computed tomography (CT or CAT) scans. An average chest x-ray exposes the patient to around 0.1 mSv of radiation. CT scans, on the other hand, use multiple x-ray beams to form a three-dimensional image of the patient's body. A patient receiving a chest CT scan receives around 7 mSv of radiation. Although radiography and CT scans expose patients to radiation and should not be overused, it is important to keep in mind the life-saving benefits of these imaging studies. Ultrasonography and magnetic resonance imaging do not use ionizing radiation.

An avoidable source of radiation is tobacco smoke. In addition to other carcinogens, tobacco smoke contains

small amounts of the radioactive isotopes lead 210 and polonium 210.

Despite public concerns about cell phones, which use radiofrequency (non-ionizing) radiation, no relationship between cell phone use and cancer has been found. However, because data are not yet available from people who have used cell phones for several decades, the International Agency for Research on Cancer has classified radiofrequency radiation as a possible human carcinogen (cancer-causing agent).

Concerns and misconceptions

There is a common misconception that radiation exposure is one of the leading causes of cancer. This is largely due to well-publicized disasters such as chemical leaks, nuclear reactor meltdowns, and atomic bombings that greatly increased the cancer rates in surrounding areas. However, such disasters involve massive quantities of radiation (around 210 mSv, in the case of the bombing of Hiroshima) that are far above the typical annual exposure. In reality, radiation, when compared with certain chemicals and heavy metals, is one of the weaker cancer-causing sources.

While unnecessary radiation exposure should be avoided, we should keep the small risk of additional exposure in perspective. Medically necessary x-ray or CT scans should not be avoided because of radiation concerns, and patients should discuss any such concerns with their physicians. ■

—N. Danckers

FOR MORE INFORMATION

- Talk to your physician
- Visit www.cdc.gov/nceh/radiation
- To learn about radon, visit www.epa.gov/radon
- To calculate your radiation exposure, visit www.ans.org/pi/resources/dosechart

IN BRIEF

Sleeping Beauty Gene Therapy Shows Promise Against B Cell Malignancies

CD19-directed therapy using T cells genetically modified with chimeric antigen receptors (CARs) shows promise against advanced hematological malignancies, particularly as an adjuvant treatment after stem cell transplantation, according to the preliminary results of four clinical trials.

In the four ongoing clinical trials at The University of Texas MD Anderson Cancer Center, patients with B cell malignancies receive T cells modified by the novel Sleeping Beauty gene transfer system. The Sleeping Beauty system creates a CAR on the T cells that recognizes and binds to CD19, a B cell-specific protein. Thus, the CAR enables the T cells to actively target and kill CD19-expressing cancer cells.

“We are treating patients with advanced CD19-positive hematological malignancies using CAR T cells in combination with conventional blood stem cell transplanta-

In the four ongoing clinical trials at MD Anderson, patients with B cell malignancies receive T cells modified by the novel Sleeping Beauty gene transfer system.

tion,” said Partow Kebriaei, M.D., an associate professor in the Department of Stem Cell Transplantation and Cellular Therapy and the principal investigator of two of the clinical trials of CAR T cells. “We are also treating patients who have active disease but have not received blood stem cell transplantation.”

In the clinical trials, patients with acute lymphocytic leukemia (ALL), chronic lymphocytic leukemia (CLL), or non-Hodgkin lymphoma (NHL) receive patient- or donor-derived CAR T cells after hematopoietic stem cell transplantation or during active treatment.

Dr. Kebriaei and her colleagues reported that, of 5 NHL patients who received patient-derived CAR T cells after autologous stem cell transplantation, 4 remained in complete remission at a median of 12 months after T cell infusion. Of 10 ALL and 3 NHL patients who received donor-derived CAR T cells after allogeneic stem cell transplantation, 6 remained in complete remission at a median of 7.5 months after T cell infusion. And of the 8 ALL, 4 CLL, and 2 NHL patients with active disease who were treated with donor- or patient-derived CAR T cells, 5 showed disease regression at a median of 6 months after T cell infusion. No toxic effects from the CAR T cell treatments were observed.

Dr. Kebriaei and her colleagues presented preliminary results of the studies in December 2014 at the 56th Annual Meeting of the American Society of Hematology in San Francisco. ■

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Made possible in part by a gift from the late Mrs. Harry C. Wiess.

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