

Vaccine Shows Response in Some Leukemia Patients

A peptide vaccine helped certain patients with leukemia live longer without relapse, M. D. Anderson researchers reported at the annual meeting of the American Society of Hematology in December 2007. The PR1 vaccine, which attempts to elicit an immune response to kill cancer cells in myelodysplastic syndrome, acute myelogenous leukemia, and chronic myelogenous leukemia, was tested in a phase I/II clinical trial from 2000 to 2006.

Patients in whom the vaccine triggered an immune response had an 8.7-month relapse-free survival, compared to 2.4 months for nonresponders. Also, clinical responses—including complete remission—were observed in 36% of the patients with immune responses, compared to 10% of nonresponders. Among the 13 patients who were in remission when they started the trial, four remained in remission for a median of 30.5 months. “We were quite pleased to see the clinical responses and improved relapse-free survival, since we did not expect it in the beginning,” said Muzaffar Qazilbash, M.D., an associate professor in the Department of Stem Cell Transplantation and Cellular Therapy. The vaccine was developed by Jeffrey Molldrem, M.D., a professor in the department.

Disease-specific phase II trials of the vaccine for chronic myelogenous leukemia and myelodysplastic syndrome are planned or under way. To be eligible, patients must be positive for HLA-A2, a histocompatibility molecule.

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Drug’s Redesign Lessens Danger to the Heart

Imatinib (Gleevec)—a drug that has dramatically improved the long-term survival rate for patients with chronic myelogenous leukemia (CML)—has

been redesigned to kill gastric cancer cells with a lower risk of cardiotoxicity. Researchers at M. D. Anderson produced and tested the altered form of imatinib, which was redesigned at Rice University. The development of the new drug, called WBZ-4, is being described as a novel “bottom-up” approach, in which small changes in an agent’s chemical structure are designed to elicit specific, intended effects on biological processes.

Imatinib inhibits proteins including C-Kit kinase, which is involved in the development of gastrointestinal stromal tumor (GIST), and Bcr-Abl kinase, which is involved in CML. The cumulative incidence of complete cytogenetic response in CML with imatinib therapy was 91%, according to a recent M. D. Anderson study led by Hagop Kantarjian, M.D., a professor in and chair of the Department of Leukemia. However, imatinib does carry a low risk of heart failure (one M. D. Anderson study showed that 1.7% of 1,276 patients taking imatinib had symptoms that may have been caused by heart failure). Researchers believe this risk may be related to the inhibition of Bcr-Abl activity.

WBZ-4, unlike imatinib, targets C-Kit but not Bcr-Abl. As a result, the potential for cardiotoxicity is even lower, researchers found in laboratory, animal, and computer testing. WBZ-4 appears to be as effective against GIST as imatinib—but, of course, it has no effect on CML since it does not inhibit the function of the leukemia-associated protein. The new drug was created by adding just four atoms to imatinib at a precise location in its molecular structure, which allowed a reaction with C-kit but not Bcr-Abl.

“This is excellent proof that we can enhance the selectivity of a drug by making a small but significant change in its structure,” said Gabriel Lopez-Berestein, M.D., a professor of experimental therapeutics at M. D. Anderson, who helped oversee testing of WBZ-4 by computer, in cell culture experiments, and in mouse models of GIST and CML. “We know exactly how WBZ-4 works. It’s a completely novel approach

that could be applied to the redesign of other drugs in a way that allows for greater control of their effects.”

Results were published in the *Journal of Clinical Investigation*. Human trials have not been set. ●

Aerosol Therapy May Offer Hope to Infection-Prone Patients

Researchers at M. D. Anderson have developed an aerosol therapy that stimulates an immune system response within the lungs, killing airborne pathogens on contact. Though the therapy has so far been tested only in mice, investigators are hopeful it will lead to new protection for cancer patients and others at risk of infection because of compromised immune systems.

Dubbed the aerosolized lung innate immune stimulant (ALIIS), the therapy is a purified extract of a common bacterium that causes ear and sinus infections in children. When inhaled, ALIIS apparently prompts the innate immune system to flood the thin layer of fluid lining the lungs with polypeptides that destroy invading microbes. What’s more, the ALIIS-stimulated innate immune system appears to wipe out invaders before the adaptive immune system is fully activated and before neutrophils are summoned. That could be important for immunocompromised cancer patients, whose neutrophils are often killed off by chemotherapy, said Burton Dickey, M.D., a professor in and chair of the Department of Pulmonary Medicine at M. D. Anderson and senior author of the ALIIS research.

All mice treated with ALIIS 4 to 24 hours before exposure to the most common pneumonia bacterium survived. When administered 2 hours before exposure, ALIIS was found to prompt an effective response against the bacterium in 83% of exposed mice. Likewise, ALIIS was effective against several other types of bacterial pneumonia, influenza virus, and the mold *Aspergillus*.

The findings were presented at the annual meeting of the American Society for Cell Biology in December 2007. ●