City of Hope Researchers Present Data on more than 30 Studies During American Society of Hematology Meeting Dec. 5 to 8 in New Orleans

Topics presented range from targeting dormant cancer stem cells to assessing neurocognitive side effects after bone marrow transplants

Duarte, Calif. (Vocus) December 8, 2009 -- City of Hope researchers will present data from more than 30 studies during the 2009 American Society of Hematology (ASH) meeting Dec. 5 to 8 in New Orleans, focusing on such topics as a new drug combination to target dormant chronic myelogenous leukemia (CML) stem cells, lymphoma patients’ genetic susceptibility to therapy-related leukemia, and neurocognitive impairments after bone marrow transplants.

Research highlights include:

“Effective targeting of Quiescent CML Stem Cells by Histone Deacetylase Inhibitors in Combination with Imatinib Mesylate”
ASH Abstract #190 (Oral)

Imatinib mesylate (Gleevec) has become known as a wonder drug that has dramatically improved the treatment of CML, yet patients can relapse because the disease often lurks in the “quiescent” or dormant stem cells. To understand how cells resist Gleevec treatment and find ways to better target these residual stem cells, clinical research fellow and lead author Bin Zhang, Ph.D., and her City of Hope colleagues conducted a series of experiments on tumor tissue samples from patients. Research team members believe they are the first to demonstrate that histone deacetylase (HDAC) inhibitors in combination with Gleevec can destroy the hidden reservoir of treatment-resistant CML stem cells.

“We’ve shown that these drugs in combination with Gleevec are very effective in killing CML stem cells – including the dormant ones,” said Ravi Bhatia, M.D., director, Division of Stem Cell and Leukemia Research at City of Hope, and senior author on the study. Their research has led to a clinical trial, now in progress. (See Abstract #2194: “A Phase 1 Study of the HDAC Inhibitor LBH589 in Combination with Imatinib for Patients with CML in Cytogenetic Remission with Residual Disease Detectable by Q-PCR.”)

“The ultimate aim would be to give this combination therapy to patients who would go from having temporary remission with residual cells to being completely cured of leukemia,” said Bhatia. Potentially, this combination of drugs also may be successfully applied to other leukemias and cancers, including myelodysplastic syndrome (MDS), acute myeloid leukemia (AML) and perhaps breast and colon cancers.

“Genetic Susceptibility to Therapy-Related Leukemia (t-MDS/AML) After Hodgkin Lymphoma (HL) or Non-Hodgkin Lymphoma (NHL)”
ASH Abstract #199 (Oral)

Treatments for lymphoma can cure patients of their disease but also can lead some to develop acute myeloid leukemia (AML) or myelodysplastic syndrome (MDS), the leading cause of non-relapse death. Currently there is no reliable method to identify which patients are most at risk of developing this therapy-related disease,
known as t-MDS/AML, so that preventive steps can be taken. In partnership with her City of Hope colleagues, molecular epidemiologist Yan Ding, Ph.D., M.S., Division of Outcomes Research at City of Hope, and lead author of the study, explored why certain patients are more susceptible to t-MDS/AML by looking at key groups of genes involved with DNA repair, drug metabolism and apoptosis. Apoptosis is a sort of programmed death most cells undergo when they are damaged or faulty.

“Cancer treatments often target DNA damage and repair and apoptosis pathways to eradicate malignant cells,” said Ding. “We found that patients’ ability to repair their DNA, metabolize drugs and undergo apoptosis affected their risk of getting t-MDS/AML,” she added. The team also found that patients with a genetic susceptibility to developing AML without therapy had an increased risk of t-MDS/AML.

“The study has helped us understand and predict who might be at risk for developing this complication, so we can gear our interventions toward them accordingly,” said Smita Bhatia, M.D., M.P.H., director, Center for Cancer Survivorship at City of Hope, and senior author on the study.

“Neurocognitive Function and its Impact on Return to Work in Patients Treated with Hematopoietic Cell Transplantation”
ASH Abstract # 521 (Oral)

Patients undergoing hematopoietic stem cell transplants are often at risk for neurocognitive impairments such as memory loss caused by conditioning treatments like total body irradiation and drugs used to prevent graft versus host disease.

“We heard anecdotal stories from patients about their neurocognitive losses following treatment,” said Lennie Wong, Ph.D., associate research professor in the Department of Population Sciences at City of Hope. In this three-year study, one of the longest of its kind, lead author Wong and her City of Hope colleagues sought to verify whether there is an increase in deficit and identify which patients may be susceptible. “We wanted to examine longitudinal trends after patients received their transplants to see whether they were getting worse or better, and also to find risk factors to identify patients who may do worse than others. Few studies have systematically assessed the impact of cognitive changes on the ability to return to work -- a practical indicator that patients are recovering and resuming their lives.

The study followed patients who received either allogeneic transplants (blood stem cells from a healthy donor) or autologous transplants, which use a patient’s own, purified blood stem cells. Before and after transplants, patients underwent extensive tests to measure neurocognitive function. Researchers discovered that overall, hematopoietic cell transplantation does not have a major impact on the neurocognitive functioning of the recipients. Allogeneic transplant patients seem to do worse than autologous patients and are more affected by treatments in terms of neurocognitive function, including memory loss, information processing and “executive functioning” (the ability to multitask). Researchers also found that the ability to return to work is affected by impairment in immediate memory and verbal speed. “Targeted surveillance and early intervention may facilitate patients’ smooth reintegration into society,” Wong added.

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