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Potential breakthrough for T-Cell lymphoma patients with drug that mimics folic acid

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Preliminary results of a pivotal Phase 2 clinical trial of pralatrexate (PDX), a drug that partially works by mimicking folic acid, showed a complete or partial response in 27 percent of patients with recurrent or resistant peripheral T-cell lymphoma (PTCL).

PROPEL (Pralatrexate in patients with Relapsed Or refractory PEripheral T-cell Lymphoma) findings were presented by the study's principal investigator, Dr. Owen A. O'Connor of the Herbert Irving Comprehensive Cancer Center at Columbia University Medical Center and NewYork-Presbyterian Hospital, at the 50th Annual Meeting of the American Society of Hematology (ASH) in San Francisco.

The international, multicenter PROPEL trial is the largest ever conducted in patients with peripheral T-cell lymphoma -- a biologically diverse group of blood cancers that account for as many as 15 percent of non-Hodgkin's lymphoma (NHL) cases in the United States. There are currently no pharmaceutical agents approved for use in the treatment of either first-line or relapsed or refractory PTCL, and average five-year survival is approximately 25 percent.

"These results indicate that pralatrexate produces a major durable response in patients for whom numerous prior treatments have been unsuccessful," says Dr. Owen A. O'Connor, director of the Lymphoid Development and Malignancy Program and chief of the Lymphoma Service at the Herbert Irving Comprehensive Cancer Center at NewYork-Presbyterian Hospital and Columbia University Medical Center, and

associate professor of medicine at Columbia University College of Physicians and Surgeons.

Prior to enrolling in the trial, eligible patients had received a median of three (range of 1 to 12) prior systemic treatment regimens, including 16 percent of patients who had previously undergone an autologous stem cell transplant.

"Presently, there are no FDA-approved drugs for patients with PTCL, whether it is in the front-line or for patients with relapsed or refractory disease. This underscores the need for new therapies to treat this challenging disease. Pralatrexate has the potential to play a clinically meaningful role in the treatment of these patients," adds Dr. O'Connor. Pralatrexate, designed to look like the natural vitamin folic acid, disrupts DNA synthesis in tumor cells. The drug is designed to selectively accumulate in tumor cells, after which it then induces programmed cell death, or apoptosis, in the cancer cell.

A total of 109 evaluable patients received 30 mg/m2 of pralatrexate intravenously once every week for six weeks followed by one week of rest per cycle of treatment. Patients also received vitamin B12 and folic acid supplementation. Response was assessed using standard International Workshop Criteria (IWC).

In the trial, 69 percent of patients who responded did so after cycle one of therapy. The median duration of treatment in responding patients was 179 days at the time of this analysis. The duration of response exceeded three months in 17 of 29 responders (59 percent), including 6 of the 17 patients who continued on treatment. An accurate estimate of the median duration of response cannot be reported at this time due to the current length of follow up. Patients will continue to be followed until the median duration of response can be accurately estimated.

The PROPEL trial is organized by Allos Therapeutics Inc., the maker of the drug. Since PROPEL has been given fast-track status, the company will submit pralatrexate for FDA approval once the Phase 2 data has been finalized -- sometime in the first half of 2009.

Pralatrexate was developed by a team of researchers at Memorial Sloan-Kettering Cancer Center (MSKCC) and the Southern Research Institute, including Dr. O'Connor, while at MSKCC. Dr. O'Connor and his colleagues identified the unique activity of pralatrexate in patients with lymphoma. Dr. O'Connor has continued to study pralatrexate at NewYork-Presbyterian/Columbia, now focusing on determining how the drug works in T-cell lymphoma, and on how best to combine it with other drugs to improve the treatment of patient with hematologic cancers.

Peripheral T-Cell Lymphoma

According to the American Cancer Society, approximately 66,000 patients are expected to be diagnosed with non-Hodgkin's lymphoma in the United States in 2008. Annual prevalence is estimated to be approximately 9,500 patients. In addition to the 30 to 50 percent of PTCL patients that do not respond to first-line treatment, a significant number of first-line multi-agent chemotherapy responders relapse or become refractory after treatment.

Source: New York- Presbyterian Hospital