Targeted Drug Shows Real Potential as a Safe and Effective Treatment for Chronic Lymphocytic Leukemia and Mantle Cell Lymphoma

- Clinical results published online in *NEJM* show ibrutinib significantly prolongs survival in all classes of chronic lymphocytic leukemia (CLL) patients, even those at high-risk of recurrence; Similar results were shown in patients with mantle cell lymphoma (MCL);
- Ibrutinib is the first drug designed to target Bruton's tyrosine kinase, a protein critical in the B-cell receptor pathway for tumor cell survival and growth;
- CLL, the most common form of leukemia, and MCL, a rare, aggressive form of non-Hodgkin lymphoma, are both incurable.
- In CLL, the rate of overall survival at 26 months was an estimated 83 percent.

COLUMBUS, Ohio – Two clinical studies published in the *New England Journal of Medicine* (NEJM) suggest the novel agent ibrutinib shows real potential as a safe, effective, targeted treatment for adults with chronic lymphocytic leukemia (CLL) and patients with mantle cell lymphoma (MCL).

Both studies, co-led by researchers at the Ohio State University Comprehensive Cancer Center – Arthur G. James Cancer Hospital and Richard J. Solove Research Institute (OSUCCC – James) and MD Anderson Cancer Center, were published in the Journal's June 19, 2013 online edition.

Chronic Lymphocytic Leukemia and Ibrutinib

Results from the phase Ib/II trial showed an overall response rate (complete and partial) of 71 percent. At 26 months the estimated progression-free survival rate was 75 percent and overall survival was 83 percent.

"Essentially all CLL patients respond well to ibrutinib, which lacks many of the side effects of chemotherapy and frequently produces long-lasting remissions even in patients with high-risk genetic lesions," says study co-leader John C. Byrd, MD, director of the division of hematology and a CLL specialist at the OSUCCC – James.

CLL is the most common form of leukemia with an estimated 15,000 American diagnosed annually. It is a cancer of B cells, which are a major component of the immune system along with T cells. Ibrutinib (PCI-32765) is the first drug designed to target Bruton's tyrosine kinase, a protein essential for CLL-cell survival and proliferation. Ibrutinib kills malignant B cells but has little effect on healthy T cells – unlike other CLL therapies. This leaves an important arm of the immune system largely intact, enabling patients to remain healthier during treatment.

The trial involved 85 relapsed CLL patients (median age, 66) who took ibrutinib once daily. Fifty-one patients received a 420 mg dose and 34 patients received an 840 mg dose. Long-term therapy was associated with modest side effects such as diarrhea, fatigue, and infection that usually resolved with no treatment delay.

Funding for the study was provided by Pharmacyclics, Inc.; the Leukemia and Lymphoma Society; D. Warren Brown Foundation; Mr. and Mrs. Michael Thomas; the Harry Mangurian Foundation; and the NIH/National Cancer Institute (grant CA140158 and CA095426).

Mantle Cell Lymphoma and Ibrutinib

Results from this phase II trial showed an overall response rate of 68 percent, with 21 percent of patient achieving a complete response and 47 percent achieving a partial response. Estimated overall survival was 58 percent at 18 months.

"This is remarkable because the last agent approved by the Food and Drug Administration for MCL had a 30 percent response rate," says senior author Kristie Blum, MD, associate professor of medicine, and head of the OSUCCC – James lymphoma program. "This

trial suggests that ibrutinib could significantly improve the landscape of therapy options for MCL."

MCL is a type of non-Hodgkin lymphoma, a malignancy that is expected to strike nearly 70,000 Americans in 2013. About 7 percent of those cases will be MCL, a cancer of white blood cells called B lymphocytes, or B cells. Currently, oncologists treat MCL using combination chemotherapy or intensive chemotherapy plus immunotherapy, followed by stem-cell transplantation.

The trial involved 111 patients with relapsed or refractory MCL who took ibrutinib. The trial was conducted at 18 sites. Participants had received one to five prior treatments, which could include the drug bortezomib, an agent sometimes used to treat MCL. The estimated median response duration was 17.5 months and estimated median progression-free survival was 14 months.

Funding for the study was provided by Pharmacyclics, Inc.

About OSUCCC-James

The Ohio State University Comprehensive Cancer Center – Arthur G. James Cancer Hospital and Richard J. Solove Research Institute strives to create a cancer-free world by integrating scientific research with excellence in education and patient-centered care, a strategy that leads to better methods of prevention, detection and treatment. Ohio State is one of only 41 National Cancer Institute (NCI)-designated Comprehensive Cancer Centers and one of only four centers funded by the NCI to conduct both phase I and phase II clinical trials. The NCI recently rated Ohio State's cancer program as "exceptional," the highest rating given by NCI survey teams. As the cancer program's 228-bed adult patient-care component, The James is a "Top

Hospital" as named by the Leapfrog Group and one of the top cancer hospitals in the nation as ranked by U.S. News & World Report.