Development and validation of clinical next generation sequencing assay for sensitive detection of mutations of BTK and PLC gamma genes in chronic lymphocytic leukemia patients treated with BTK inhibitor Ibrutinib

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Chronic lymphocytic leukemia (CLL) is the most common B cell lymphoid malignancy in the western world. Leukemic cells are characterized by autonomous activation of B cell receptor (BCR) pathway and variable genetic and molecular lesions that are reflected by a highly varied clinical course. Some patients may never require therapy while others must be treated with chemo-immunotherapy to survive. Of treated patients, a large subset will relapse with disease that becomes resistant to all available classical therapies. Recently approved BCR pathway inhibition by irreversible inhibitor of Burton Tyrosine Kinase (BTK), Ibrutinib, affords effective treatment of these patients. Continuous therapy with Ibrutinib results in durable remission with marked reduction of tumor burden and improvement of disease symptoms. Unfortunately, a small subset of Ibrutinib treated patients will develop resistance to Ibrutinib that is mediated by mutation in drug binding site of BTK gene and/or activating mutation of PLC-gamma gene. CLL with fully developed acquired resistance to Ibrutinib is characterized by an aggressive clinical course that limits effective intervention in these patients. Sensitive and accurate early detection of these mutations at low allelic burden allows preemptive alteration in therapy in these patients. The ideal test should afford very deep coverage of BTK and PLCg genes with high sensitivity even in samples with low number of leukemic cells. This presentation will describe our experience of development and validation of Ion Torrent based BTK and PLCg mutation detection assay that we currently use in CLIA certified molecular laboratory for CLL patients treated with Ibrutinib.

Biography
Gerard Lozanski completed his graduate medical education at Karol Marcinkowski Medical Academy in Poznan, Poland in 1987. He finished his residency in Pathology at Summa Health System in Akron and fellowship in Hematopathology at Cleveland Clinic in Cleveland OH. Dr. Lozanski joined Ohio State University as faculty in 2002, and is currently Associate Professor of Hematopathology, Director of Hematopathology division, medical director of clinical flow cytometry laboratory and medical director of Hematopathology fellowship program. His research interest focuses on low grade lymphoproliferative disorders with an emphasis on CLL, Follicular Lymphoma and Minimal Residual Disease detection by flow cytometry.

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