Evaluating the risks of additional B-cell lymphoid malignancies

Charles Springer; Private Investigator Dr. Clive Zent

Background: Lymphoid malignancies are the fourth most prevalent cancer and rank as the sixth leading cause of cancer-related fatalities in the United State. B cell malignancies are classified according to the presumed stage of cellular maturation by analysis of morphology, histology, immunophenotype, and molecular characteristics. Survivors of lymphoid malignancies have been reported to have higher risks of developing second malignancies when compared to the general population. The cause of this increased propensity currently is unknown, but could be associated with inherited genetic risk, immunodeficiency, lifestyle, and various environmental factors. There are limited investigations that quantify differences in risk of subsequent lymphoid malignancies in patients with an established diagnosis of one B cell malignancy. This study will expand the current literature by examining the clonality of B cell malignancies in a cohort with multiple B cell malignancies using clinically available data.

Methods: This study utilizes an existing cohort at the University of Rochester James P. Wilmot Cancer Institute (WCI), including all patients with a confirmed diagnosis of primary lymphoid malignancies with a first visit to the WCI lymphoma/CLL clinic from April 1, 2014 to April 1, 2024. Surveillance, Epidemiology, and End Results (SEER) is a national cancer surveillance database containing data from the years 1975 to 2021 from up to 48% of the total population of the United States. This database serves as a representative sample of the United States population.

Outcomes: We hypothesize that patients with a lymphoid malignancy have a higher risk of developing an additional lymphoid malignancy compared to the rate of first diagnosis of lymphoid malignancy in the general population. To test this hypothesis when compared to an age-, sex-, and race-matched general population, standardized incidence ratios and 95% confidence interval of incidence of additional lymphoid malignancies will be calculated, using the SEER data as the reference population. Data is currently undergoing analysis. Determination of clonality is based upon pathology data from immunophenotyping, flow cytometry of B cells to evaluate light chain expression, and genetic analysis of VDJ rearrangements and IGHV family use and somatic hypermutations. If there is insufficient data on an individual's additional lymphoid malignancy to determine clonality, then we will exclude them from our clonality analysis. Cumulative incidence functions will be used to estimate the overall risk of second malignancy from the time of initial diagnosis, treating death as a competing risk. A Pearson's Chi-Squared Test then will be used to compare prevalence of two lymphoid malignancies among those in the WCI database with prevalence among those in the SEER database. Within the WCI cohort, we will compare demographic and clinical characteristics between patients with only one diagnosis of mature B cell malignancy versus those developing a subsequent diagnosis, to look for any associations in subgroup analysis between any host factors and the presence of a subsequent lymphoma diagnosis.