Title: Late health outcomes following contemporary Lymphome Malin de Burkitt therapy for mature B-cell non-Hodgkin lymphoma: a report from the Childhood Cancer Survivor Study

Authors: Matthew J. Ehrhardt1,2, Yan Chen3, John T. Sandlund1, Elizabeth C. Bluhm4, Robert J. Hayashi5, Kerri Beckettle6, Wendy M. Leisenring7, Monika L. Metzger1, Kirsten K. Ness2, Kevin R. Krull2,8, Kevin C. Oeffinger9, Todd M. Gibson2, Mitchell S. Cairo10, Thomas G. Gross11, Leslie L. Robison2, Gregory T. Armstrong2, Yutaka Yasui2, Melissa M. Hudson1,2, and Daniel A. Mulrooney1,2

Affiliations: 1 Department of Oncology, St. Jude Children’s Research Hospital, Memphis TN; 2 Department of Epidemiology and Cancer Control, St. Jude Children’s Research Hospital, Memphis TN; 3 School of Public Health, University of Alberta, Edmonton, Alberta, Canada; 4 Department of Internal Medicine, George Washington University, Washington, DC; 5 Department of Pediatrics, Washington University School of Medicine, St. Louis, MO; 6 Department of Pediatric Hematology/Oncology/Bone Marrow Transplant, Medical College of Wisconsin, Milwaukee, WI; 7 Clinical Statistics and Cancer Prevention Programs, Fred Hutchinson Cancer Research Center, Seattle, WA; 8 Department of Psychology, St. Jude Children’s Research Hospital, Memphis TN; 9 Department of Medicine, Duke University, Durham, NC; 10 Department of Pediatrics, New York Medical College, Valhalla, NY; 11 Center for Global Health, National Cancer Institute, Rockville, MD

PURPOSE: The widely utilized, risk-based Lymphome Malin de Burkitt (LMB) chemotherapy regimen has improved survival rates for children with mature B-cell non-Hodgkin lymphoma (NHL), however associated late effects remain understudied. We assessed late health outcomes after LMB treatment in the Childhood Cancer Survivor Study.

PATIENTS AND METHODS: Multivariable regression models compared chronic health conditions, health status, and socioeconomic and neurocognitive outcomes between NHL survivors treated with the LMB regimen (n=126), non-LMB regimens (n=444), and siblings (n=1,029).

RESULTS: LMB survivors were a median age of 10.2 (range:2.5-20.5) years at diagnosis and 24.0 (10.3-35.3) years at evaluation. Compared to siblings, LMB survivors were at increased risk for adverse health outcomes. However, LMB and non-LMB survivors did not differ with regards to risk of having any chronic health condition, impaired health status, neurocognitive deficits, or poorer socioeconomic outcomes. Increased risk for specific neurologic conditions was observed in LMB compared to non-LMB survivors: epilepsy (RR 15.2, 95% CI:3.1-73.4), balance problems (RR 8.9, 95% CI:2.3-34.8), tremors (RR 7.5, 95% CI:1.9-29.9), weakness in legs (RR 8.1, 95% CI:2.5-26.4), severe headaches (RR 3.2, 95% CI:1.6-6.3), and prolonged arm, leg, or back pain (RR 4.0, 95% CI:2.2-7.1). LMB risk group Group C (n=50) survivors were at the highest risk for these conditions; however, except for worse functional status (OR 2.7, 95% CI:1.2-5.8), they were not at increased risk for other adverse health status or socioeconomic outcomes compared to non-LMB survivors.

CONCLUSION: Survivors treated with LMB and non-LMB regimens are largely comparable in late health outcomes except for excess neurotoxicity among LMB survivors. These data inform treatment efforts seeking to optimize disease control while minimizing toxicity.