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CpG simulated karyotypic analysis of chronic lymphocytic leukemia (CLL) is a significant prognostic factor and should be performed on all patients

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CLL has a variable clinical course and prognostic factors are vital. Metaphase cytogenetics have been minimally informative as CLL cells do not respond to traditional mitogens. CpG stimulates CLL cells to divide in <80% cases. Investigation of karyotypic abnormalities within one year of diagnosis in untreated CLL patients using CpG-stimulation identified complex karyotype (CK) (>3 unrelated abnormalities) that predicted a shorter time to first treatment (TFT) compared to non-CK (NCK, 12 months estimates 45% and 15%, respectively, p=0.0005). Despite a strong correlation of del(17p) with CK, CK predicted TFT independent of del(17p), a known poor prognosticator. Additionally, in patients with either balanced or unbalanced translocation, the good prognosis of mutated IGHV was negated (mutated IGHV translocation present vs absent, HR 3.59, p<0.001; unmutated IGHV translocation present vs absent, HR 1.03, p=0.92, interaction p=0.002). Independent of IGHV and translocation, CK (HR 1.70, p=0.037) remained statistically significant. Patients with Richter's transformation (RT), an aggressive lymphoma in some CLL patients, exhibited higher risk for death with CK (HR 2.72, p=0.025) than in patients with NCK after R-EPOCH treatment. CK was independently associated with ibrutinib discontinuation due to progression. Although a low percentage of patients treated with ibrutinib experience RT, 6/9 patients with near-tetraploidy detected prior to ibrutinib treatment developed RT. In a multivariable model, both near-tetraploidy (HR 8.66, p<0.0001) and CK (HR 4.78, p=0.01) were independent risk factors for discontinuing ibrutinib due to transformation. In conclusion, CpG-stimulated karyotypes should be performed in CLL patients to identify karyotypic abnormalities that are significant for prognostication.

Biography

Nyla A Heerema is a professor in the Department of Pathology at The Ohio State University Wexner Medical Center. She is the Director of the Cancer Cytogenetics Laboratory there, as well as conducts an active research program. Her areas of research are the cytogenetics of chronic lymphocytic leukemia (CLL) and of pediatric acute lymphoblastic leukemia. She is a member of the CLL Research Consortium, and is the Chairperson of the Cytogenetics Discipline for the Children's Oncology Group. She has published over 300 articles.

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