PTK2 expression and immunochemotherapy outcome in chronic lymphocytic leukemia.

Abstract:
Addition of rituximab (R) to fludarabine and cyclophosphamide (FC) has significantly improved patient outcomes in chronic lymphocytic leukemia (CLL). Whether baseline gene expression can identify patients who will benefit from immunochemotherapy over chemotherapy alone has not been determined. We assessed genome-wide expression of 300 pretreatment specimens from a subset of 552 patients in REACH, a study of FC or R-FC in relapsed CLL. An independent test set was derived from 282 pretreatment specimens from CLL8, a study of FC or R-FC in treatment-naive patients. Genes specific for benefit from R-FC were determined by assessing treatment-gene interactions in Cox proportional hazards models. REACH patients with higher pretreatment protein tyrosine kinase 2 (PTK2)
messenger RNA levels derived greater benefit from R-FC, with significant improvements in progression-free survival, independent of known prognostic factors in a multivariate model. Examination of PTK2 gene expression in CLL8 patients yielded similar results. Furthermore, PTK2 inhibition blunted R-dependent cell death in vitro. This retrospective analysis from 2 independent trials revealed that increased PTK2 expression is associated with improved outcomes for CLL patients treated with R-FC vs FC. PTK2 expression may be a useful biomarker for patient selection in future trials. These trials were registered at www.clinicaltrials.gov as #NCT00090051 (REACH) and #NCT00281918 (CLL8).