Reviewer's report

Title: Notch1 mutations influence survival in B-cell chronic lymphocytic leukemia patients

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Reviewer: valter VG gattei

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The manuscript characterizes the NOTCH1, NOTCH2 and mutational status in a cohort of 209 CLL previously characterized for TP53 and IGHV mutational status. Authors define a short overall survival for NOTCH1 mutated CLL when compared with NOTCH1 wild type CLL. An association with IGHV mutational status and a more aggressive disease is also found. Finally, Authors define significant shorter survivals for CLL cases carrying either TP53 or NOTCH1 mutations when compared with cases wild type for both the two genes.

Major points:
1) The main problem regarding this study is the lack of FISH analyses that represent the gold standard in the prognostic stratification of CLL patients.

2) The study lacks of multivariate regression models with NOTCH1 mutations and the other clinical and biological features of CLL.

Minor points:
1) Significant associations between clinical and biological features and presence of NOTCH1 mutations in the 209 CLL cases should be added in Table 2. Relative sentences should be added in text, in particular for IGHV status and Binet staging.

2) The background section is not focused and sentences regarding genes that are not investigated in this study should be deleted or, alternatively, heavily reduced.