Reviewer’s report

Title: The genomic landscape of chronic lymphocytic leukemia: clinical implications

Version: 1 Date: 14 March 2013

Reviewer: Gianluca Gaidano

Reviewer’s report:

In this review, the authors aim at discussing the clinical implications of the genomic landscape of chronic lymphocytic leukemia. The review is well written and of certain interest for the general readership as well as for hematologists and oncologists. I have only a few minor suggestions for improvement, as detailed below.

MiNOR REVISIONS

1. In the abstract, the authors state that “This means that a large percentage of cases do not display clear tumor-driving mutations, or show candidate driving mutations with no obvious biochemical relationship to the more frequently mutated genes”. This statement is certainly valid when referring specifically to point mutations, but it is not totally correct when expanding to genetic lesions in general. In fact, a substantial fraction of CLL do harbor genetic lesions that are considered as initiating/driving alterations (eg del13q14, trisomy 12). The authors should clarify this issue.

2. Since the authors’ submission of the current manuscript, Landau et al have reported on the clonal evolution of CLL. These novel and very important findings should be adequately discussed.

3. Two independent reports of the CLL genome appeared simultaneously in the literature (Puente et al on June 5, 2011; Fabbri et al on June 13, 2011). The authors should acknowledge this fact and should revise the statement “Subsequent studies have confirmed these findings” (p. 5, l. 21).

4. Because the title of this review expicitely refers to the clinical implications of the CLL genomic landscape, the authors should discuss in detail the prognostic meaningfulness of novel CLL mutations, that has been assessed not only in retrospective series, but also in prospective clinical trials (eg: Oscier et al, Blood. 2013 Jan 17;121:468-75; Epub 2012 Oct 18). Alternatively, the authors may choose to remove “clinical implications” from the title of the manuscript.

5. p. 3: “high overall survival” should be “extended or prolonged overall survival”

DISCRETIONARY REVISIONS

1. p. 3: the statement “However, the genomic events that dictate the initiation and heterogeneous evolution of CLL remained unknown” is not totally correct, and
should rather read as “However, the genomic events that dictate the initiation and heterogeneous evolution of CLL remained partially unknown

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that i have no competing interests