Level of evidence.

1. What type of study was performed? (1 mark)

A comprehensive analysis was performed using a dataset from three phase I and II studies regarding Venetoclax monotherapy done on relapsed/refractory chronic lymphatic leukaemia.

Quality of evidence

2. Was the study blinded and if so was it single- or double? (1 mark)

No, the study was not a blinded study

3. How were the subjects allocated to treatments? (1 mark)

If the patients were participants in either a specific phase 1 study or two other specific phase II studies between June, 2011 and November, 2016, they were included in the analysis. How subjects were allocated to treatments in the three studies this article is analysing about it not included.

4. What possible confounding factors are accounted for in this study? (1 mark)

Deletion of chromosome 17p or TP53 mutation, disease progression due to prior BCRi therapy such as ibrutinib, idelalisib, and investigational BCR-targeting agents, baseline neutropenia and tumour lysis syndrome,

5. What was measured as an outcome? Is it objective or subjective? (1 mark)

Adverse events associated with the dose-ramp up during the Venetoclax treatment.

It is Objective

6. Were patients lost to follow-up? How many (% of starting sample) and is this acceptable? (2 marks)

As this is only a comprehensive analysis it doesn’t specifically mention if there has been any loss of follow-up in the original three early-phase clinical trials.

Strength of evidence

7. How large was the effect? Consider both statistical and clinical effects. (2 marks)

Most patients (343 out of 350 patients in the main group) in the considered 3 clinical trials developed and adverse effect of some sort during the dose ramp-up. However, the onset and severity of these adverse effects decreasing over time except for in patients who had a low-grade gastrointestinal toxicity at baseline.

The most common grade 3/4 adverse effect was neutropenia during the dose ramp-up with 141 out of 350 affected participants while other effects such as anaemia and thrombocytopenia being popular adverse effects as well. The most common low-grade adverse effects were diarrhea and nausea with 145 and 109 affected patients respectively.

8. Overall how would you rate the quality of this study. (1 mark)

The article presents facts of three early-phase clinical studies in a rather non-comparative way. I find it a little confusing to read through the article knowing that the data comes from three different studies. I would’ve preferred a more comparative type of analysis.

However, comprehensive analysis is helpful to make general sense of certain streams and this article is written in a well-researched manner with an inclusion of the limitations of the analysed studies in general as well. I would say that it’s an informative study, but it would’ve been better if there was a comparison across the three studies going on.