

## Peer Review File

**Article Information:** <https://dx.doi.org/10.21037/tcr-21-2864>

### Response to Reviewer A

**Comment 1:** Fludarabine in monotherapy is not a recommended regimen of chemotherapy in CLL. Should be combined with rituximab and cyclophosphamide.

**Reply 1:** Indeed, as reviewer A said, fludarabine combined with rituximab and cyclophosphamide is the standard chemotherapy regimen in CLL. However, since the patient refused intensive chemotherapy and fludarabine monotherapy was previously reported to be effective in the treatment of CLL (1-3), we only gave the patient fludarabine monotherapy in 2014.

### References

1. Janssens A, Boogaerts M, Verhoef G. Development of fludarabine formulations in the treatment of chronic lymphocytic leukemia. *Drug Des Devel Ther* 2009;3:241-52.
2. Ricci F, Tedeschi A, Morra E, et al. Fludarabine in the treatment of chronic lymphocytic leukemia: a review. *Ther Clin Risk Manag* 2009;5:187-207.
3. Keating MJ, Kantarjian H, Talpaz M, et al. Fludarabine: a new agent with major activity against chronic lymphocytic leukemia. *Blood* 1989;74:19-25.

**Comment 2:** 11th citation has to be corrected.

**Reply 2:** According to reviewer A, in the 11th citation, the authors' name "Szukalski U, Sysakiewicz-Buda M, Méciska-Jundzi K, et al" should be corrected to "Szukalski L, Sysakiewicz-Buda M, Méciska-Jundzill K, et al". We have modified our text as advised (see Page 14, line 3).

**Changes in the text:** We have corrected "Szukalski U, Sysakiewicz-Buda M,

Mêciska-Jundzi K, et al" with "Szukalski L, Sysakiewicz-Buda M, Mêciska-Jundzill K, et al" (see Page 14, line 3).

**Comment 3:** Please check my attachment and apply all corrections.

1. Raw page 2, line 4: delete the word “cells”.
2. Raw page 2, line 9: correct “of” with “diagnosed for”.
3. Raw page 3, line 21: correct “in CLL” with “in the course of CLL”.
4. Raw page 4, line 13: correct “I0” with “10”.
5. Raw page 4, line 18: the word “are” should be replaced by “were”.
6. Raw page 4, line 19: the word “support” should be replaced by “supported”.
7. Raw page 6, line 10: Has IGHV status been assessed or not?
8. Raw page 6, line 11: the word “indicate” should be replaced by “indicated”.
9. Raw page 6, line 11: the word “are” should be replaced by “were”.
10. Raw page 6, line 13: the word “is” should be replaced by “was”.
11. Raw page 6, line 21: correct the sentence “Some can be self-subsiding is its biggest characteristic”.
12. Raw page 7, line 11: Could not be diagnosed for a second time. Please delete the sentence “In summary, the patient was diagnosed with CLL (RAI stage II; Binet B) with skin infiltration”.
13. Raw page 7, line 15: Please delete the sentence “Bendamustine combined with rituximab is known as the BR regimen”.
14. Raw page 7, line 16: replace “BR” with “rituximab+bendamustine”.

15. Raw page 9, line 15: correct “leukemic cutis” with “leukemia cutis”.
16. Raw page 11, line 17: correct “his” with “her”.
17. Raw page 6, line 15: the word “can” should be replaced by “could”.
18. Raw page 6, line 22: the word “is” should be replaced by “was”.
19. Raw page 11, line 9: the word “appears” should be replaced by “appeared”.

**Reply 3:** According to reviewer A, we have fixed related errors as advised.

**Changes in the text:**

1. We have deleted the word “cells” (see Page 2, line 5).
2. We have corrected “of” with “diagnosed for” (see Page 2, line 10).
3. We have corrected “in CLL” with “in the course of CLL” (see Page 4, lines 2-3).
4. We have corrected “I0” with “10” (see Page 4, line 16).
5. We have deleted the word “are” along with the sentence it is in. (see Page 4, line 21).
6. We have replaced “support” with “supported” (see Page 5, lines 2-3).
7. We have supplemented our assessment of IGHV status (VH 3-23, homologous proportion 94.93%). During the current follow-up, there was no reassessment (see Page 6, lines 16-17).
8. We have replaced “indicate” with “indicated” (see Page 6, line 18).
9. We have replaced “are” with “were” (see Page 6, line 19).
10. We have replaced “is” with “was” (see Page 6, line 20).
11. We have corrected the sentence “Some can be self-subsiding is its biggest characteristic” with “Some could regress spontaneously without treatment was its

- unusual characteristic” to express our opinion accurately (see Page 7, lines 6-8).
12. We have deleted the sentence “In summary, the patient was diagnosed with CLL (RAI stage II; Binet B) with skin infiltration” (see Page 7, lines 20-21).
  13. We have deleted the sentence “Bendamustine combined with rituximab is known as the BR regimen” (see Page 8, lines 2-3).
  14. We have replaced “BR” with “rituximab+bendamustine” (see Page 8, line 4).
  15. We have corrected “leukemic cutis” with “leukemia cutis (LC)” (see Page 10, line 3).
  16. We have corrected “his” with “her” (see Page 12, line 7).
  17. We have replaced “can” with “could” (see Page 6, line 22).
  18. We have replaced “is” with “was” (see Page 7, line 8).
  19. We have replaced “appears” with “appeared” (see Page 11, lines 20-21).

## **Response to Reviewer B**

**Comment 1:** The laboratory findings are not well-described. For example, CLL is a small mature B-cell lymphoma, and they are not "immature monoclonal B lymphocytes", "plasma-like lymphocytes", or "immature lymphocytes".

**Reply 1:** According to reviewer B, most cells are small mature B-cell in CLL. We have modified our text as advised and redescrbed the laboratory findings accurately.

### **Changes in the text:**

1. We have corrected "immature monoclonal B lymphocytes" with "small mature B

cells" (see Page 2, lines 4-5).

2. We deleted "plasma-like lymphocytes" and "immature lymphocytes" (see Page 4, lines 18-22).
3. Importantly, we accurately redescribed the laboratory findings as “lymphocyte proliferation has significantly accounted for 53%, mainly small mature lymphocytes (47%) , occasionally prolymphocytes, larger lymphocytes, and smudge cells” (see Page 4, line 22 to page 5, line 2).

**Comment 2:** There is inconsistent use of abbreviations.

**Reply 2:** We have used abbreviations consistently and normatively as advised.

**Changes in the text:**

1. We have replaced “chronic lymphocytic leukemia” with “CLL” (see Page 2, line 10; page 3, line 6; page 4, lines 7-8; page 4, line 11; page 5, line 3; page 5, line 8).
2. We have replaced “B-CLL” with “CLL” (see Page 3, line 8; page 7, line 18; page 11, line 6).
3. We have deleted “B-CLL” (see Page 5, line 7).
4. We have replaced “leukemia cutis (LC)” with “LC” (see Page 11, line 5).