

In this manuscript, Balakrishnan and coll present a perspective concerning the potential use of pharmacological cyclin dependent kinase inhibitors for the treatment of colorectal cancer. Overall, I found this to be a good review.

Here are a few suggestions and/or corrections which would improve the article:

- 1- Title: I think the term "pharmacological" should be specified in the title as follows: "Pharmacological cyclin dependent kinase inhibitors: Implications for colorectal cancer" and elsewhere in the text to distinguish them from cellular inhibitors.

*Title altered to reflect that the focus on the article is on the pharmacological aspects.*

- 2- The "Conflict-of-interest statement" should be completed.

*Conflict of interest statement was completed*

- 3- Page 4, 2nd para.: Rewrite "(...) the battle against cancer is combatted and (...)")

*Sentence deleted because it was repetitive.*

- 4- Page 6, 2nd para.: It would seem pertinent to identify the main cellular forms of CDK inhibitors of the two classes.

*Included more information on the differences between the two classes*

- 5- Page 6, 2nd para.: The relatively abundant literature reporting the effects of cellular CDK inhibitors on growth arrest and tissue specific gene expression in colorectal cancer cell lines should be considered in the "theorization" that the use of pharmacological CDK inhibitors can be used as anti-cancer drugs.

*Added "This cell cycle attenuating effect documented in the literature of cellular CDK inhibitors implicate the use of pharmacological CDK inhibitors as an anti-cancer drug."*

- 6- Page 6, 2nd para.: The beginning of the last sentence of this paragraph: (...) testing of the first CDK inhibitor, Flavopiridol, several (...) should be rewritten as : (...) testing of this first CDK pharmacological inhibitor, several other (...) for more clarity.

*Sentence altered to reflect this change*

- 7- Page 6, last line: the title should be "pharmacological CDK inhibitors"

*Title changed to emphasize the focus on pharmacological CDK inhibitors*

- 8- Page 8, last sentence: It should be specified that these clinical studies are phase I as: Phase i clinical studies (...).

*Sentence was altered to specify that these were phase I studies.*

- 9- The Fig 1 is somewhat redundant to Table 1. One way to improve its usefulness would be to complete the Fig by adding the cellular CDK inhibitors.

*Table focuses more on the pharmacological drugs while the Figure emphasizes how the drugs fit to regulate the cell cycle.*

10- Page 9, end of 1st para.: the beginning of the sentence "For example, in flavopiridol, the first ever CDK-inhibitor tested in clinical trials has (...)" is redundant to the previous page. The sentence should begin like "For example, flavopiridol has (...)".

*Sentence has been altered to reduce the redundancy*

11- Page 11, third line: the sentence "(...) on CDK inhibitors, it wise to investigate (...)" should be completed (would be wise?)

*Sentence completed*