

February 5th, 2024

Dear Editor and the anonymous reviewer,

Thank you so much for your positive response and effort to review our manuscript in detail. We would like to answer the reviewer's comments below;

1. "...*There are some grammatical mistakes, ...*"

We apologize for any errors that might make your review more time-consuming. Please let us know if you still find issues. We found minor errors including typos, which shall not be acceptable. On the other hand, we also found one error describing the characteristics of combretastatin. Combretastatin is an MT-destabilizing drug, not an MT-stabilizing drug.

2. "*The main content of the paper was not well written described closely with the title, and only one MT drug combretastatin was used for photo-controlled CRC treatment, ...*"

Thank you for pointing out the gap between the content and the title. It is very true that there are a few recent reports that described the development of photo-switchable epothilone and paclitaxel/docetaxel. Photoactivation of photo-switchable paclitaxel/docetaxel is more complex than simply switching the double-bond conformation (*cis*↔*trans*). Nevertheless, one recent study described a photo-isomerization of a double bond in an aromatic ring structure (spriopyrane).

We also want to note that only combretastatin is possibly the optically switchable MT-targeting drug, that is because of its chemical structure. One of the most commonly used MT-targeting drugs, such as paclitaxel, does not have the double bond that can make *cis*- versus *trans*- structural change. Optical switching is based on the rotatable double bond. (cannot be a part of an aromatic ring; R-C=C-R' [R/R' are larger groups such as aromatic rings] or R-N=N-R' in the case of photostatin).

All those are described in a new paragraph under "Development of other photo-switchable MT-targeting drugs". As a short conclusion, we also pointed out why still photostatin might be superior to taxanes or epothilone derivatives (wider potency shift upon light-induced isomerization).

Lastly, we also changed the title slightly because we discussed recent, promising clinical trials (mostly combination chemotherapy).

3. "*Moreover, the format and reference of the manuscript should be checked.*"

We did confirm the instruction provided by the publisher and it should follow the required formatting (font, citation format *etc.*).

Thank you so much for your consideration, and we are hoping that the manuscript is now acceptable.

Sincerely,

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