Reviewer's report

Title: Panobinostat synergizes with bortezomib to induce endoplasmic reticulum stress and ubiquitinated protein accumulation in renal cancer cells

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Reviewer: TAKASHI KARASHIMA

Reviewer's report:

March 1, 2014 Review

Comments

This original article entitled “Panobinostat synergizes with bortezomib to induce endoplasmic reticulum stress and ubiquitinated protein accumulation in renal cancer cells” describes the therapy with panobinostat has synergistically enhanced tumor suppression by the therapy with bortezomib in human renal cell carcinoma (RCC) cell lines. The novel combination therapy with histone deacetylase (HDAC) inhibitor and proteasome inhibitor may be a potent to contribute the patient with advanced RCC.

Author could consider the following comments.

Major Revisions
1. The article could be corrected by native speakers.
2. Figures are too busy. Author should submit essential figures. The Figure 1, 2A and photos of colony assay in Figure 2B may be omitted, leading to be clearly expressed.
   The FACS data could be changed to bar graphs in Figure 3, leading to be clearly expressed.
3. When author present the data, author should explain it using suitable expression.
4. Author should discuss clinical information such as efficacy and adverse events of the therapy with HDAC inhibitor and proteasome inhibitor for patients with malignant neoplasm in the section of DISCUSSION.
5. An animal monitoring and tolerability should be described in Materials and Methods. Also, typical adverse events should be described if there are.

Minor Revisions
1. Line 25: Background: Inducing endoplasmic reticulum stress
   #Background: Inducing endoplasmic reticulum (ER) stress

2. Line 73: accumulation, and kills cancer cells effectively in vitro and in vivo.
   #accumulation, and kills cancer cells effectively in vitro and in vivo.
3. Line 149-150: Colony formation assay showed that the combination suppressed colony formation significantly (Figure 2B).

#ex) Colony formation assay demonstrated the combination therapy significantly suppressed colony formation compared to control vehicle, panobinostat or bortezomib alone (Figure 2B, *p = 0.0495; **p = 0.0463).


#combination therapy in vivo.

5. Line 156: group. The average tumor size at day 15 was 520 ± 175 mm3 (mean ± SE)

#group. The average tumor size at day 15 was 520 ± 175 mm3 (mean ± SD)


#renal cancer growth both in vitro and in vivo.

Discretionary Revisions

1. When author describes significance of data, author should state the comparative group.

Line 162: The combination increased the annexin-V fluorescence intensity (up to 19.4-fold)

#ex) up to 19.4-fold compared to control vehicle.

Line 163-164: (Figure 4A) and also increased the number of the cells in the sub-G1 fraction (up to 70.5%)

#ex) 70.5% compared to control vehicle.

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

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