Reviewer's report

Title: A new non-invasive approach based on polyhexamethylene biguanide increases the regression rate of HPV infection

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Reviewer: Makoto Kunisada

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Authors carried out the clinical trial with polyhexamethylene biguanide (PHMB) for the patients who are positive for HPV and found significant effects in term of clearance of HPV, suggesting that PHMB is effective and safe agents for the HPV-positive patients.

The design of study itself is fair and the plausible mechanisms of PHMB in Discussion are informative. However, authors will need to be clarified following points.

Major points:

1. Authors evaluated only or exclusively matters of clearance of HPV infections. If the logic of in this study is prophylactic effects of PHMB, preventing cervical dysplasia infecting HPV from development to the cervical cancer, definitely cytological or histopathological evaluation for smear samples should have been performed in every time points (before, T1 and T2). This is quite important because those evaluations would give us clues how PHMB is functioning at the cervical epithelium and whether PHMB is effective for inhibition of progress to cervical cancer, not solely by clear HPV. If it is highly unlike to perform reevaluation for those by not taking histopathological samples during the trail study, authors at least should state about this consideration in Discussion.

2. The one of most concerning points of this trial study is the credibility of methods of sampling, meaning the possibility of false negative cases by not taking appropriate parts of examination. Did authors perform sampling as duplicate or triplicate for each patient? It needs to be stated in Material and Methods.

3. If hybrid capture system (Qiagen) is not the system in which specific HPV type is not able to identify, why did authors choose this kit? It also is important to know what specific types of HPV were detected, especially for cervical tissue which is assumingly high positive rate of HPV-16 and -18. The evaluation of HC2 system is sensitive but not specific for providing information aimed at prevention of cervical cancer. It would have been more sophisticated data once HPV-16 or -18 specifically were followed.

Minor points;

1. Are there any other reports that PHMB showed effectiveness to other types of
HPV infected lesions such as common warts in the skin, oral squamous cell carcinoma, verrucous carcinoma, etc?

2. It stated no significant side effects were observed. Was there really nothing of complaints from patients including the irritation?

3. In abstract, it should show the abbreviation of PHMB.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**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.