

Review of: "Monitoring of Cell-free Human Papillomavirus DNA in Metastatic or Recurrent Cervical Cancer: Clinical Significance and Treatment Implications"

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The manuscript entitled "Monitoring of Cell-free Human Papillomavirus DNA in Metastatic or Recurrent Cervical Cancer: Clinical Significance and Treatment Implications" has been thoroughly studied and evaluated. This work highlights the significance of monitoring circulating HPV DNA in metastatic and recurrent cervical cancer, demonstrating its potential as a strong predictor for treatment response and disease progression, ultimately improving clinical management.

Here are the comments outlined below:

- 1- It would be better to include the conclusion section under a separate heading in the text and expand it a bit further.
- 2- While the introduction highlights the potential of circulating HPV cfDNA as a biomarker for treatment monitoring, could the authors further clarify how cfDNA levels might differentiate between various metastatic patterns or treatment responses, and how these distinctions would directly influence clinical decision-making in real-time?
- 3- It would be better if the title is changed to: "Monitoring Circulating Cell-free HPV DNA in Metastatic and Recurrent Cervical Cancer: Clinical Importance and Implications for Treatment."
- 4- Regarding the correlation between HPV cfDNA levels and metastasis patterns: The study mentions a significant difference in baseline HPV cfDNA levels between single-metastasis and multiple-metastasis pattern groups. Could the authors clarify whether they observed any specific trends or predictive value in using HPV cfDNA levels to anticipate the transition from single to multiple metastasis patterns over time in patients?
- 5- Regarding the use of SCC-Ag as a comparison marker: The study finds that HPV cfDNA provides superior monitoring over SCC-Ag for squamous cell cervical cancer. Could the authors further discuss potential reasons for the lack of correlation between SCC-Ag levels and HPV cfDNA levels, and whether they suggest alternative or additional biomarkers for better comprehensive monitoring?
- 6- It would be better to very briefly discuss the following two articles and reference them in the introduction.



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Regards