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Peer Review

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 aim of this study is to assess the clinical potential of HPV cfDNA as a tumor marker in patients with cervical cancer. The subject is very interesting because it is important to define new biomarkers to monitor potentially disease progression, recurrence, and treatment efficacy.

The aim is clear, but there are some revisions that require attention.

Methods: HPV “subtypes” should be replaced with HPV “genotypes” throughout the text. Exclusion criteria should be better described in the Study Design section.

The sample used for HPV detection in the cervix should be described in more detail. The device for cervical cell collection used, the medium and volume of resuspension, and the starting sample volume for the analysis should be included in the HPV diagnostics and typing section.

Results: I suggest including in Table 1 which specific HPV genotypes have been detected in squamous cell carcinoma (SCC), adenocarcinoma, and large cell neuroendocrine carcinoma.

Genotype-specific viral loads are reported in Figure 2A. The graph showed different amounts of HPV cfDNA based on the genotype detected. The analysis comparing each specific HPV genotype viral load according to the metastatic status could enrich the data obtained, in particular for HPV16, which is the prevalent genotype detected.

Discussion: In the discussion, the author reported that the MMP group had a higher median HPV cfDNA copy number at baseline than the SMP group. This analysis was performed without considering the

doi.org/10.32388/9VMF6T

specific HPV genotype detected. This should be better explained in the Discussion section.

Declarations

Potential competing interests: No potential competing interests to declare.