Qeios

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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This study demonstrates the dynamic changes in ctDNA according to the clinical course of patients, a distinction from previous reports. A key strength is the direct comparison of ctDNA with SCC-Ag, highlighting the superior utility of ctDNA as a biomarker for treatment monitoring and disease progression in HPV-positive cervical cancer.

Comments

1. Clarity in Figure 3 Description: The descriptions below the x-axis in Figure 3, such as 'progression of disease' and 'chemotherapy response,' are unclear. Please either provide additional clarification or remove them.

2. Median Time Calculation in Figure 3A1: The statement, "The median time from detection of elevated plasma HPV cfDNA to imaging confirmation of disease progression was 4.2 months (range 1.9-16.9; Figure 3A1)," is unclear. The data points (104D, 109D, 507D) in 3A1 do not seem to support this range. An explanation of how the median and range were calculated is needed.

3. Interpretation of SCC-Ag Reduction in Figure 3B: In Figure 3B, SCC-Ag appears to show a more significant reduction during cytotoxic chemotherapy compared to ctDNA. The authors should address this observation and discuss the implications in the context of biomarker comparison.

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4. Imaging Measurement Criteria: The study claims that ctDNA reflects disease progression earlier than imaging. However, the imaging criteria and schedules are not adequately detailed. If the imaging intervals were significantly longer than the blood sampling intervals, the advantage of ctDNA may be overestimated. Harmonization of imaging and blood collection timelines should be clarified.

Statistical Methodology for Concordance:

5. The statement, "For patients with squamous cell CC who had longitudinal monitoring (n=20), the concordance with disease change was 90% for HPV cfDNA and 50% for SCC-Ag (P=0.014, 95% CI, 0.022-0.621)," requires elaboration. Details on the statistical method used to derive this concordance are essential for reproducibility and transparency.

6. Mismatch in Description of Figure 3E1 and 3E2: The description, "matched serum HPV cfDNA showed fluctuating changes above normal values at some time points," is not supported by Figure 3E1, which shows no fluctuation. This fluctuation is observed only in 3E2. The inconsistency should be corrected.

7. Survival Analysis and Cohort Heterogeneity: The heterogeneity of the patient cohort in the survival analysis diminishes the strength of the conclusions.

Declarations

Potential competing interests: No potential competing interests to declare.