

# Review of: "[Commentary] Implications of HPV infectivity in early diagnosis and treatment of advanced/recurrent malignancies"

Arnaud John Kombe Kombe<sup>1</sup>

<sup>1</sup> University of Science and Technology of China

Potential competing interests: No potential competing interests to declare.

**Abstract:** "Infection with HPV genotypes is a cause of cervical and pharyngeal cancer, etc. The amount of circulating HPV DNA in the blood is useful for detecting advanced/recurrent cancer earlier than the rise in tumor markers. Compared to HPV infection-negative cancer, cancer immunotherapy is more effective for HPV infection-positive cancer."

\* **Comment:** Please change to "Infection with high-risk HPV genotypes is **the main** cause of cervical and pharyngeal cancers"

\* **Comment:** Please change to "The load of circulating HPV DNA in the blood is a better marker for the early detection of advanced and recurrent cancers than the rise in tumor markers."

\* **Comment:** the following sentence should be rewritten, as it talks about and compares two different things: "Compared to HPV infection-negative cancer, cancer immunotherapy is more effective for HPV infection-positive cancer." This could be: "Cancer immunotherapy is a more effective treatment approach for HPV infection-positive cancers than for HPV infection-negative cancers."

\* **Abstract comment:** If this is the whole abstract, it does not really summarize the main idea of the manuscript. The authors should rewrite the abstract and highlight the main clue presented within this manuscript.

## Main text

\* **Comment:** "Human papillomavirus (HPV) is a virus that causes sexually transmitted diseases and skin diseases." Vague declarative sentence. Please be more precise.

\* **Comment:** "The main route of transmission of HPV is sexual intercourse (sex, oral sex, anal sex)." You have just said that HPV causes transmitted diseases in the previous sentence. So, this is a repetition.

\* **Comment:** "Latent HPV infection is established when HPV enters the basal cells from a small wound on the genitals." Please delete "latent" at the beginning of this sentence.

\* **Comment:** "In most HPV-infected people, HPV is eliminated by the host immune system, which protects the body from

foreign enemies.” **The second (underlined) proposition is redundant and rhetorical. So, no need.**

\* **Comment:** “However, in rare cases, HPV infections have been observed to persist for long periods of time without the elimination of HPV.” **The second (underlined) proposition is redundant and rhetorical. So, no need; please delete**

\* **Comment:** “HPV vaccines prevent persistent infection with certain types of HPV.” Please replace with **HPV vaccines prevent re-infections and auto-infection and mitigate persistent infection with certain types of HPV.**

\* **Comment:** “Globally, infections with HPV types 16 and 18 account for approximately 70% of all cervical cancers.” **It looks like sentences have been picked randomly from publications and added up to make paragraphs... However, there is a lack of story flow in paragraphs. Please make flow connections such that sentences bring and justify an idea in the same paragraph (specifically in the introduction part). Not only put sentences without a clear ongoing context.**

\* **Comment:** “From the results of the cancer genomic tests, it was revealed that a positive HPV16 or HPV18 infection was detected in a total of 11 cases (11/36, 30.6%) of advanced pharyngeal cancer, 37 cases (37/104, 35.6%) of advanced cervical cancer, 8 cases (8/22, 36.4%) of advanced anus cancer, and 3 cases (3/10, 30.0%) of advanced penile cancer.”

**In this sentence, are all these infections “monoinfections”? Didn't the authors find co-infections with different HPV genotypes (e.g., HPV 16 & 18, and so on)? It would be great to mention that too.**

\* **Comment:** “The results showed that nivolumab was more effective in treating 11 patients with HPV-positive throat cancer compared to 25 patients with HPV-negative throat cancer” **Do the authors mean that nivolumab could treat cancer better in the 11 patients with HPV-positive throat cancer compared to 25 patients with HPV-negative throat cancer? If that is the case, please be clear and write it that way.**

\* **Comment:** “Therefore, the infection rate of HPV16 or HPV18 in advanced cancer, as shown above, is different from the incidence of cancer due to HPV infection in Japanese people.” **How different? Would the authors be more precise by presenting the different prevalences they are referring to in this sentence?**

\* **Comment:** “Recent clinical research results show that the recurrence of various malignant tumors can be confirmed earlier by detecting circulating DNA (cDNA) in the blood derived from malignant tumor cells, rather than by increasing the tumor marker values . Therefore, it has been reported that the recurrence of HPV-infectious malignant tumors is confirmed earlier by the detection of tumor-derived circulating HPV genes in the blood rather than by increased tumor marker values ” **These two sentences describe the same thing; there is a redundancy. Please write this information and combine the two references for this same information because it is the same.**

\* **Comment:** “ Kirsten murine sarcoma virus” **is not an oncogene; it is a virus. But The v-H-ras and v-K-ras oncogene is a gene found in KRAS.**

**So this sentence** “Human oncogenes such as Kirsten murine sarcoma virus (KRAS) are well known as oncogenes derived from viral genes.” **needs to be rewritten.**

\* **Comment: This paragraph** "Human oncogenes such as Kirsten murine sarcoma virus (KRAS) are well known as oncogenes derived from viral genes. As described above, various malignant tumors caused by viral infection have been recognized. Vaccination is effective in preventing viral infection. However, unlike bacteria, mutations in viral genes easily change the structure of the viral backbone proteins and structural proteins. Therefore, it has become a problem that the preventive effect of vaccines against viral infections is reduced. Therefore, there is a need to produce vaccines that induce the production of antiviral antibodies that recognize the structural proteins of mutant virus variants." **does not convey any logical idea. Sentences are mixed up, lacking meaningful information.**

\* **Overall Comment:** Overall, there is a huge lack of precision and clarity in the entire manuscript. Also, there is a lack of flow between paragraphs; they stop abruptly with no clear information presented in a paragraph that links it to the following one. **Therefore, I recommend rejection of this article.**