Letter to the Editor

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Advanced cervical cancer: how to interpret the new standard of care

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Dear Editor,

As pivotal practice-changing studies, the KEYNOTE-826 (KN-826) and BEATcc trials provided the opportunity to add immune checkpoint inhibitors (ICPIs) to the combination of platinum-taxane doublet chemotherapy and bevacizumab, which has been the standard of care for advanced cervical cancer for many years.[1-3] Based on subgroup analysis of KN-826, adding pembrolizumab to chemotherapy provided clinically meaningful progression-free survival (PFS) and overall survival (OS) benefit in programmed death-ligand 1 (PD-L1) combined positive score (CPS) ≥1 tumors and independent of concomitant bevacizumab use. The BEATcc study was initiated at approximately the same time as KN-826 and its results were announced very recently. The addition of atezolizumab to platinum-based doublet chemotherapy plus bevacizumab significantly improved PFS and OS in a cohort of patients included independently of PD-L1. Combination with ICPI represents the current benchmark for the first-line treatment of advanced cervical cancer. However, there are still issues that need to be questioned in terms of precision medicine.

In the KN-826 study, the proportion of PD-L1 negative patients was only 11.4%, whereas the patients with a PD-L1 CPS ≥10 represented more than half (51.3%). On the other side, the PD-L1 rate was not stated in the BEATcc study. Advanced cervical cancer has been reported to have lower PD-L1 positivity rates in real life.[4] Therefore, PD-L1 negative patients who are more likely to be encountered in real life, appear to be relatively underrepresented in studies.

These two randomized trials suggest nuances of benefit in certain patient groups. According to the subgroup analysis, age of the women (cut off of 65), stage of the disease at diagnosis (denovo metastatic or recurrent disease), previous exposure to chemoradiotherapy may influence the extent of benefit. The proportion of patients aged ≥65 years was less than 20% in both studies. Women over the age of 65 are more likely to present with advanced disease at diagnosis and have higher rates of comorbidities compared with younger women.[5] The proportion of patients achieving a complet response (CR) was found to be approximately 30% in both studies. It may be considered to evaluate whether local treatment would be beneficial in these patients.

To summarize briefly, we believe that studies that are not limited by the selection criteria of randomized clinical trials, reflect real-life practices, and measure outcomes for larger patient groups with more balanced representation of different subgroups would be valuable.

ETHICAL DECLARATIONS

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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