

CORRESPONDENCE

Response to letter re: Benefit from maintenance with PARP inhibitor in newly diagnosed ovarian cancer according to *BRCA1/2* mutation type and site: a multicenter real-world study



We would like to express our gratitude to Dr Kim and Dr Lim et al. for their valuable insights and feedback regarding our study on the effectiveness of olaparib maintenance therapy for newly diagnosed *BRCA*-mutant ovarian cancer, categorized by mutation site and type.¹ Our research indicates that patients with *BRCA1/2* mutations benefit from olaparib, with notable differences linked to the specific mutation types and functional domains (FDs). In particular, patients with *BRCA1* mutations located in the RING or BRCT FDs and those with *BRCA2* mutations in the RAD51-binding (BD) FD experience the most significant benefits. Patients with missense mutations, especially p.(Ala1708Glu), show the most significant advantage of olaparib maintenance therapy.

In contrast, Kim et al.² observed that the most common BRCT domain mutation identified in their research was p.Leu1780Pro (c.5339T>C), while p.(Ala1708Glu) was notably absent, underscoring significant disparities in mutation domains among the Asian (mainly Korean) population, compared with the Caucasian population.

Interestingly, the PAOLA1 study, which focuses on a primarily European cohort similar to ours, reported that among patients with missense mutation in the BRCT FD, only 3 out of 10 had the p.(Ala1708Glu) mutation,³ compared with 9 out of 11 in our research.¹

Additionally, as highlighted in the supplementary material of the PAOLA1 study, none of the patients presented the BRCT domain mutation p.Leu1780Pro (c.5339T>C).³

This evidence further emphasizes the potential ethnic differences in *BRCA* FDs, and even within the same ethnic category, which may influence treatment responses and ovarian cancer prevalence.

Numerous studies have highlighted this issue, especially the research by Qin et al.,⁴ which examined the distinct ethnic-specific traits of *BRCA* variations in Asian populations. Furthermore, Bhaskaran et al.⁵ pointed out that *BRCA* data gathered from Caucasian groups might not effectively represent the *BRCA* status in non-Caucasian populations, particularly in Chinese individuals.

Consequently, we concur with Dr Kim and Dr Lim et al. that a *BRCA* FD-based interpretation would benefit from integrating ethnic-specific variant data. This approach could enhance therapeutic predictions and enable more tailored clinical decision-making.

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