Chemotherapy-free strategy for platinum-sensitive recurrent ovarian cancer

We read with great interest the study by Mansoor Raza Mirza and colleagues in *The Lancet Oncology*,[1] in which niraparib plus bevacizumab combination therapy significantly improved progression-free survival (PFS; hazard ratio [HR] 0·35, 95% CI 0·21–0·57) compared with niraparib alone in patients with platinum-sensitive recurrent ovarian cancer, irrespective of *BRCA* mutation or homologous recombination deficiency status. The efficacy observed with this chemotherapy-free strategy in patients with platinum-sensitive recurrent ovarian cancer warrants further evaluation in phase 3 trials; however, a few points first require consideration.

For patients with platinum-sensitive recurrent ovarian cancer with a germline *BRCA* (g*BRCA*) mutation or who have homologous recombination deficiency-positive tumours, we believe that platinum-based chemotherapy plus poly(ADP-ribose) polymerase maintenance treatment will continue to be the first choice, irrespective of response to the last platinum-based therapy. A phase 3 randomised trial[2] showed that niraparib maintenance therapy after standard platinum-based treatment (with or without bevacizumab) significantly extended PFS, especially in patients with a g*BRCA* mutation (median PFS 21·0 months [95% CI 12·9–not estimable]) or in those who had homologous recombination deficiency-positive tumours (12·9 months [8·1–15·9]). The PFS was calculated from the day of randomisation to disease progression in the NOVA study.[3] If PFS was calculated from the day of receiving platinum-based regimens to disease progression, as was the case in Mirza and colleagues' study, the total PFS benefit should be extended by an average 6 months, which would be longer than the chemotherapy-free strategy for patients with homologous recombination deficiency-positive tumours (median PFS 11·9 months [8·5–16·7]). Future studies should use a head-to-head design, in which platinum-based chemotherapy plus niraparib maintenance therapy is compared with bevacizumab plus niraparib.

For patients with platinum-sensitive recurrent ovarian cancer who do not have g*BRCA* mutation or whose tumours are homologous recombination deficiency negative, the PFS benefit of the chemotherapy-free strategy (median PFS 11·3 months [95% CI 5·9–16·7]) seems to be similar to standard platinum-based treatment (average 6 months) after niraparib maintenance therapy (median PFS 6·9 months [5·6–9·6]). Considering the chemotherapy-free regimen avoided the substantial cumulative toxicities and had better tolerability than platinum-based treatment, the chemotherapy-free strategy seems to be promising in this population.

We found it remarkable that PFS was not improved with niraparib plus bevacizumab versus niraparib alone in patients who had been previously treated with bevacizumab. Whether a different anti-angiogenic agent (such as cediranib, brivanib) than bevacizumab will improve the situation needs to be further explored.

In conclusion, although all patients with platinum-sensitive recurrent ovarian cancer might benefit from chemotherapy-free regimen, *BRCA* mutation or homologous recombination deficiency status and previous use of bevacizumab should be considered when decisions about the best treatment choice are being made.

We declare no competing interests.

*Qi Zhou, Dongling Zou, Xingtao Long
drqizhou9128@126.com

Department of Gynecologic Oncology, Chongqing Cancer Hospital, Chongqing, China (QZ, DZ, XL)

1 Mirza MR, Lundqvist EÅ, Birrer MJ, et al. Niraparib plus bevacizumab versus niraparib alone for platinum-sensitive recurrent ovarian cancer (NSGO-AVANOVA2/ENGOT-ov24): a randomised, phase 2, superiority trial. *Lancet Oncol* 2019; **20:** 1409–19.

2 Mirza M, Monk B, Herrstedt J, et al. Niraparib maintenance therapy in platinum-sensitive, recurrent ovarian cancer. *N Engl J Med* 2016; **375:** 2154–64.

3 Mirza MR, Benigno B, Dørum A et al. Long-term safety of niraparib in patients with recurrent ovarian cancer (ROC): results from the ENGOT-OV16/NOVA trial. *Int J Gyn Cancer* 2018; **28:** 21–22.