Veliparib for advanced ovarian cancer

Veliparib plus chemotherapy followed by veliparib maintenance therapy significantly improves progression-free survival in patients with advanced ovarian cancer, according to new research.

In the phase 3 trial, Robert Coleman (MD Anderson Cancer Center, Houston, TX, USA) and colleagues enrolled patients with previously untreated stage 3 or 4, high-grade serous ovarian carcinoma. 1140 patients were randomly assigned to receive first-line induction chemotherapy with carboplatin and paclitaxel plus placebo, followed by maintenance with the placebo (control group; n=375); chemotherapy plus the poly-ADP ribose polymerase (PARP) inhibitor veliparib, followed by placebo maintenance (n=383); or chemotherapy plus veliparib, followed by veliparib maintenance (veliparib throughout group; n=382). The primary endpoint was investigator-assessed progression-free survival in the veliparib throughout group compared with the control group.

In patients with *BRCA* mutations (n=298), median progression-free survival was 34·7 months for the veliparib throughout group versus 22·0 months in the control group (hazard ratio [HR] 0·44 [95% CI 0·28–0·68]; p<0·01). In patients with homologous recombination deficient (HRD) tumours (n=627), median progression-free survival was 31·9 months in the veliparib throughout group versus 20·5 months in the control group (HR 0·57 [95% CI 0·43–0·76]; p<0·001). In the intention-to-treat population, progression-free survival was 23·5 months (95% CI 19·3–26·3) for the veliparib throughout group versus 17·3 months (15·1–19·1) in the control group (HR 0·68 [95% CI 0·56–0·83]; p<0·001).

Jonathan Ledermann (Cancer Research UK and UCL Cancer Trials Centre, London, UK) welcomed the results. "There is clear evidence that the patient population that benefits from the PARP inhibitor goes beyond those with *BRCA* mutations", he commented. "The drawback of this trial is that it did not include a fourth arm, where veliparib was given as maintenance-only."

Coleman noted that future challenges will be to develop combinations that can augment the effect of the PARP inhibitors, produce clinically meaningful responses in patients with non-HRD tumours, and overcome PARP inhibitor resistance. "This is the next big thing and will incorporate anti-angiogenesis agents, immune and DNA checkpoint inhibitors and DNA damage response inhibitors", he said.

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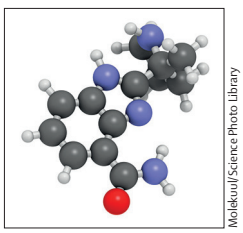

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For the **trial by Coleman and colleagues** see *N Engl J Med* 2019; published online Sept 28. DOI:10.1056/NEJMoa1909707