Nature Reviews Clinical Oncology **11**, 442 (2014); published online 8 July 2014; doi:10.1038/nrclinonc.2014.118

OVARIAN CANCER

TRINOVA-1, beyond VEGF inhibition

Whereas the benefit of antiangiogenic agents in several solid tumour has been debatable, their efficacy in the treatment of epithelial ovarian cancer is unquestionable, with the inhibitor of VEGF, bevacizumab, showing notable results in this setting. Now, the team led by Bradley Monk, at the University of Arizona Cancer Center, has provided us with a new antiangiogenic strategy for the treatment of epithelial ovarian cancer.

Unlike bevacizumab, trebananib inhibits angiogenesis through the angiopoietin axis—involved in vascular growth, remodelling, and stabilization—by preventing the interaction of the ligands angiopoietin 1 and 2 (ANG1 and ANG2) with the Tie2 receptor. The agent had shown antiangiogenic activity in preclinical models of ovarian cancer, and prolonged progression-free survival (PFS) in a randomized phase II trial in patients with recurrent epithelial ovarian cancer. Encouraged by these results, Monk and colleagues launched the TRINOVA-1 study, a randomized phase III trial that investigated the addition of trebananib to paclitaxel administered weekly as single-agent in patients with platinum-resistant and partially platinum-sensitive relapsed ovarian cancer. "Weekly paclitaxel was chosen as the chemotherapy backbone for this clinical trial because it is an accepted standard-of-care option, and because both drugs are dosed every week", explains Monk.

> "...has provided us with a new anti-angiogenic strategy for the treatment of epithelial ovarian cancer"

The study enrolled 919 women with recurrent epithelial ovarian cancer from 32 countries who were randomly assigned to receive weekly intravenous paclitaxel plus either weekly masked intravenous placebo ($n = 458$) or trebananib ($n = 461$). The primary endpoint was PFS assessed in the intention-to-treat population. Median PFS was significantly longer in the trebananib group (7.2 months) than in the placebo group (5.4 months). Trebananib was associated with more adverse event-related treatment discontinuations than was placebo, and with higher incidences of oedema (64% patients had oedema in the trebananib group compared with 28% patients in the placebo group); however, the incidence of grade 3 or higher adverse events was similar between the two groups.

Although the weekly scheduling of trebananib lends itself to combination with paclitaxel, trebananib might also be effective in combination with other antiangiogenic agents. Future trials will address this questions but, so far, this is a good start.

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Original article Monk, B. J. *et al.* Anti-angiopoietin therapy with trebananib for recurrent ovarian cancer (TRINOVA-1): a randomised, multicentre, double-blind, placebo-controlled phase 3 trial. *Lancet Oncol.* **15**, 799–808 (2014)