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Principal results of the EORTC-1508 trial: A phase II randomised, multicentre study of bevacizumab vs atezolizumab and bevacizumab with acetylsalicylic acid or placebo in recurrent platinum-resistant ovarian, fallopian tube or primary peritoneal adenocarcinoma

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Background

Anti-PD-1/L1 therapy alone has limited activity in ovarian cancer. We hypothesised that blockade of VEGF and prostaglandin E2 (PGE2) can reverse the endothelial barrier allowing T cell infiltration and subsequent T cell activation by PD-L1 blockade. This is the first trial combining an anti-PD-L1 antibody, atezolizumab (ATE), with bevacizumab (BEV) and the irreversible COX1/2 inhibitor acetylsalicylic acid (ASA).

Methods

Patients with platinum-resistant ovarian cancer (PROC) were randomised to 1) BEV(15mg/kg q3w) 2) ATE(1200mg q3w)+placebo(P) 3) ATE(1200mg q3w)+ASA(320mg/d) 4) BEV(15mg/kg q3w)+ATE(1200mg q3w)+P or 5) BEV(15mg/kg q3w)+ATE(1200mg q3w)+ASA(320mg/d) and treated until progression or unacceptable toxicity. Arms 2 and 3 were closed early following phase III results indicating insufficient activity of PD-L1 inhibitor monotherapy. Mandatory biopsies (pre-treatment and pre-cycle 3) and serial blood samples were collected. The primary endpoint was progression-free survival rate at 6 months (PFS-6). Secondary endpoints included tolerability, PFS, response rate (RR) and time to first subsequent therapy (TFST).

Results

122 patients were randomised: BEV(33); ATE+P(11); ATE+ASA(13); BEV+ATE+P(32); BEV+ATE+ASA(33). Median age 63 (36-82); 84% ≥3 prior therapies. 39/52 (75%) patients treated (Arms 1-3) crossed over at progression to BEV+ATE. PFS-6 rates (ITT) were 22%, 9%, 23%, 25% and 25% respectively. Median PFS were 2.3, 2.1 (HR 1.78, 0.89-3.58); 2.2 (HR 0.95, 0.49-1.85), 4.1 (0.84, 0.50-1.38), and 4.0 months (0.81, 0.49-1.34). RR: 10%, 0%, 9%, 19% and 15% respectively. Median TFST was longest in BEV+ATE containing arms (3.0, 2.4, 1.8, 5.3 and 5.8 months; P<0.001). Grade 3/4 treatment-related adverse events were 48%,10%, 36%, 32% and 30% respectively.

Conclusions

The addition of ASA to BEV+ATE did not improve efficacy. Relative to BEV or ATE(+/-ASA) arms, the BEV+ATE combinations numerically improved PFS and TFST and merits further exploration. Translational analyses are ongoing to identify biomarkers of clinical benefit.

Clinical trial identification

EudraCT 2015-004601-17 / NCT02659384.

Legal entity responsible for the study

European Organisation for Research and Treatment of Cancer - EORTC.

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Disclosure

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