6. Ovarian cancer

**ICON8B: GCIG PHASE III RANDOMISED TRIAL COMPARING WEEKLY DOSE-DENSE CHEMOTHERAPY + BEVACIZUMAB TO THREE-WEEKLY CHEMOTHERAPY + BEVACIZUMAB IN FIRST-LINE HIGH-RISK STAGE III-IV EPITHELIAL OVARIAN CANCER TREATMENT: PRIMARY PROGRESSION-FREE SURVIVAL ANALYSIS**

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**Introduction/Background** First-line phase III trials in stage III/IV Epithelial Ovarian Cancer (EOC) have shown improved survival both with addition of bevacizumab (BEV) to three-weekly (q3w) carboplatin (C)-paclitaxel (T) and integration of weekly dose-dense paclitaxel (ddwT) with carboplatin compared to q3wCT alone. ICON8B, a 3-arm trial, compared BEV+q3wCT versus (vs) BEV+q3wCddwT vs q3wCddwT in high-risk stage III (residual disease >1cm diameter after primary surgery or requirement for primary chemotherapy) and stage IV EOC.

**Methodology** Eligible patients were randomised 1:1:1 to Arm B1 (standard- q3w C AUC5/6+q3w T 175mg/m2+ q3w BEV 7.5mg/kg); Arm B2- q3w C AUC5/6+ddwT 80mg/m2; Arm B3- q3w C AUC5/6+ddwT 80mg/m2+ q3w BEV 7.5mg/kg. Up to six cycles chemotherapy and 18 BEV cycles were administered. Arm B2 recruitment discontinued after ICON8 saw no evidence of progression-free survival (PFS) improvement with q3wCddwT vs q3wCT. The consolidated Arm B1 vs B3 trial targeted 509 PFS events to detect B3vB1 HR=0.75 with 90% power.

**Results** 707 patients randomised from 07/2015 – 03/2020 (B1=292, B2=129, B3=286), median age 64 years, 94% ECOG Performance Status 0-1, 53% stage IIIIC, 40% stage IV, 91% High Grade Serous histology. 14% upfront surgery, 84% planned Delayed Primary Surgery, 2% no surgery planned. 88%/83%/82% completed 6 cycles carboplatin-based chemotherapy and 45%/51%/58% experienced ≥grade 3 toxicities in B1:B2:B3. 49%/61% completed 18 cycles bevacizumab in B1: B3. Median 59.0 months follow-up (07/2023-B1 and B3). Given slow additional event rate, the study committee concluded 465 progression events were sufficient for primary analysis, giving 87% power for the targeted effect size of 0.75. PFS was better in B3 compared to B1. Median PFS 16.7 months B1 vs 22.2 months B3 (HR=0.75, 95% CI=0.62-0.90, p=0.002). Median OS; 40.9 months B1 vs 51.1 months B3 (HR=0.77, 95% CI=0.62-0.96, p=0.020).

**Conclusion** In primary treatment of high-risk stage IIIIC/IV EOC, BEV+q3wCddwT improves median PFS by 5.5 months compared to BEV+q3wCT.

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