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Front-line Bevacizumab (BEV) Combined With Weekly Paclitaxel (wPAC) and Carboplatin (C) for Ovarian Cancer (OC): Safety Results From the Concurrent Chemotherapy (CT) Phase of the OCTAVIa Study

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Background: In two randomised phase III trials in OC (GOG218 and ICON7), front-line BEV + q3w PAC + C followed by BEV alone significantly improved progression-free survival (PFS) vs CT. In the Japanese NOVEL trial, wPAC + C was more effective than q3w PAC + C, but toxicity limited CT delivery. There are no published safety data for BEV + wPAC + C in OC.
Materials and Methods: In the single-arm OCTAVIA study, patients (pts) received 6−8 cycles of BEV (7.5 mg/kg, d1) + wPAC (80 mg/m^2 d1, 8, 15) + C (AUC6, d1) iv q3w, followed by single-agent BEV q3w for up to a total of 1 year as front-line therapy for newly diagnosed OC (FIGO stage I−IIa [grade 3/clear cell] or stage IIb−IV [any grade]). The primary endpoint was PFS. To assess safety of concurrent BEV + wPAC + C, we analysed data from the first CT dose to 28d after the last CT dose.
Results: Between Jun 2009 and Jun 2010, 189 eligible pts were enrolled. Baseline characteristics: median age 55 years (range 24−79); ECOG 0 73%; FIGO stage I/II/III/IV 10%/10%/63%/17%; serous/clear cell 71%/7%; 71% optimally debulked. Pts received a median of 6 CT cycles (range 1−8); 90% and 95% of pts completed $\geqslant$6 cycles of wPAC and C, respectively. In 170 pts who completed $\geqslant$6 wPAC cycles, 92% of planned wPAC doses were delivered. The most common reasons for discontinuing CT were adverse events (AEs; wPAC 25% of pts, C 7%) and disease progression (both 3%). wPAC and C were delayed for AEs in 51% and 59% of pts, respectively. AEs led to wPAC dose reduction in 30% and a switch from C to cisplatin in 7%. The most common grade $\geqslant$3 AEs were neutropenia (56%); thrombocytopenia (8%); anaemia (8%); peripheral neuropathy (6%); leucopenia (6%); and fatigue/asthenia (6%). 36% of pts received G-CSF. Typical BEV AEs were no more common than in phase III OC trials. 9 pts (5%) had grade $\geqslant$2 hypertension during the CT phase (single-agent BEV period excluded in this analysis), 1 pt (0.5%) had GI perforation and 11 (6%) had thromboembolic events (any grade). There were no treatment-related deaths.
Conclusions: We observed a high CT completion rate in OCTAVIA, unlike NOVEL. BEV AEs during CT were no more frequent with wPAC than q3w PAC in GOG218. Safety and efficacy from all treatment periods will be reported in 2012. OCTAVIA (NCT00937560, sponsored by Roche) has completed accrual.

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Experience With Bevacizumab in the Management of Relapsed Ovarian Cancer − a Retrospective Observational Study in Five French Hospitals

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Background: We report the largest series of patients receiving bevacizumab (bev) for relapsed ovarian cancer (rOC) and describe the safety profile and efficacy of bev in real-life clinical practice conditions.
Methods: This was a retrospective, multicentre, observational study including patients from five French institutions. Women with rOC who received bev between January 2006 and June 2009 were included. The following data were collected from patient files: baseline patient and disease characteristics, bev treatment use, progression-free survival (PFS), overall survival (OS) and safety.
Results: 156 patients were included. Mean age was 55$\pm$12 years at initial diagnosis and 93% had FIGO stage 3 or 4. Before bev initiation, patients received at least 1st-line chemotherapy (99%) based on a paclitaxel+platinum regimen (92%); 35% were platinum-resistant and 65% sensitive. 24% of patients received Bev as 2nd-line therapy. Bev dose was 5 mg/kg/week in 51%, combined with chemotherapy in 98% and was not continued beyond progression in 88%. The most commonly reported adverse effects (AEs) were hypertension (AHT 42%, grade 3: 12%) and proteinuria (27%, grade 3/4: 5%). Severe intestinal AEs were reported for 6 patients (1 intestinal perforation, 5 fistulae) and were related to bulky disease at the time of bev initiation (OR 2.78, 95% CI 1.02–7.56, p = 0.045). Patients at greatest risk of developing severe AHT were those with AHT at baseline (OR 3.96, 95% CI 1.48–10.58, p = 0.006). Bev dose was not associated with severe AEs (p = 0.84). Median PFS was 8.3 months (95% CI 6.5–10.1). Factors favouring longer PFS were: platinum sensitivity (HR 0.53, 95% CI 0.56–0.77, p = 0.001); bev use in combination with chemotherapy (HR = 0.52, 95% CI 0.31–0.86, p = 0.011); and initiation of bev before the 3rd relapse (HR 0.67, 95% CI 0.46–0.99, p = 0.042). Median OS was 23.4 months (95% CI 17.7–29.7). Factors favouring longer OS were: platinum sensitivity (HR 0.44, 95% CI 0.27–0.73, p = 0.002); and bev initiation before the 3rd relapse (HR 0.37, 95% CI 0.21–0.65, p < 0.001).
Conclusions: This study reports the routine practice use of bev in the management of rOC across multiple centres in France. Its safety profile seems acceptable but caution is warranted for patients presenting with hypertension or bulky disease. Treatment with bev appears to show efficacy for patients suffering from platinum-sensitive OC at the time of 1st or 2nd relapse.

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Safety and Efficacy Outcomes in Heavily and Non-heavily Pretreated Patients With Recurrent Ovarian Cancer (ROC) After Single-agent Trabectedin Treatment − Pooled Analysis of Phase II Trials

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Background: Three phase II trials (one randomized) of single-agent trabectedin in ROC patients (pts) previously treated with at least 1 or >1 chemotherapy lines were performed using three different schedules: two every 3 weeks (q3w; A: 1.3 mg/m^2 3-h and B: 1.5 mg/m^2 24-h) and one weekly (C: 0.58 mg/m^2 3-h, during 3 weeks, followed by one rest week). The q3w schedules showed no difference between 3-h and 24-h administration with respect to efficacy and had higher efficacy with manageable and non-cumulative toxicities than the weekly treatment.
Methods: 295 pts were enrolled in the three above mentioned studies. The data was retrospectively analyzed from 148 pts, who were assigned to one of the two trabectedin q3w regimen (schedules A or B), and who had significantly superior efficacy than pts treated with the weekly schedule (schedule C). The aim of this analysis is to evaluate relationship between early grade (G) 3/4 increases of alanine aminotransferase (ALT) in Cycle 1−2 with progression-free survival (PFS) and duration of response (DR) in pts who received 1 and >1 lines of prior platinum.
Results: Ninety-six (64.9%) and 52 (35.1%) pts had received 1 and >1 lines of platinum-based chemotherapy, respectively. G 3/4 ALT increase occurred in 56% and 57% of patients in schedules A and B.
Conclusions: Although trabectedin treatment is associated with transient transaminase elevations, this retrospective analysis demonstrates that early G 3/4 ALT increase in Cycle 1−2 in patients, that have been previously treated with 1 and >1 platinum-based regimen, does not worsen efficacy outcomes (PFS and DR). This analysis supports the activity of trabectedin given in a q3w schedule for the treatment of patients with relapsed ovarian cancer.