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INOVATYON study: Randomized phase III international study comparing trabectedin/PLD followed by platinum at progression vs carboplatin/PLD in patients with recurrent ovarian cancer progressing within 6-12 months after last platinum line

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Background

The INOVATYON trial aimed at demonstrating an improvement in overall survival (OS) for the trabectedin/PLD (TP) regimen followed, at relapse, by platinum re-challenge, over carboplatin/PLD (CP).

Methods

Patients (pts) with recurrent ovarian cancer (ROC) and a platinum-free interval (TFIp) between 6-12 months (mos) were randomized to the combination of trabectedin (1.1 mg/m^2) and PLD (30 mg/ m^2) or carboplatin (AUC 5) and PLD (30 mg/ m^2).

Results

From 2014 to 2017, we enrolled 617 pts from 117 European sites (306 CP arm, 311 TP arm). The median TFIp was 8.4 mos and 30% of pts received 2 previous platinum lines. The treatment was interrupted before the sixth cycle in 28% of pts in CP arm (70% for progression/death, 15% for toxicity and 5% for patient refusal) and in 46% in TP arm (54% for progression/death, 19% for toxicity and 13% for patient refusal). 75% and 74% of pts received a subsequent therapy (ST) in CP and TP arm respectively; in TP arm 86% of ST was platinum-based. At a median follow-up of 44 mos, 466 deaths were observed. The median OS was 21.3 and 21.5 mos in CP and TP arm (HR=1.10; 95%CI: 0.92-1.32; p=0.284). The median progression free survival (PFS) was 9.0 and 7.5 mos in CP and TP arm (HR=1.26 95%CI: 1.07-1.49; p=0.005). In pts receiving a ST, the HR for PFS from the ST was 0.84 (95%CI: 0.70-1.02, p=0.086) in favor of TP. Subgroup analyses (according to BRCA status, extent of the disease, number of previous lines, histology, ST) did not identify subsets of pts with a clear benefit from TP. Grade 3-5 (g3-5) adverse reactions (ARs) occurred in 36% and 69% of pts in CP and TP arm. G3-5 most frequent ARs were hematological (28% CP, 45% TP), gastrointestinal (7% CP, 18% TP), hepatic (1% CP, 18% TP); any grade neurotoxicity was 16% for both arms.

Conclusions

This study did not meet its primary endpoint of improving OS with the TP regimen followed by platinum over CP regimen. However, as TP reached similar OS, it can still be considered in pts who need a longer recovery time from platinum specific toxicities.

Clinical trial identification

NCT01379989.

Legal entity responsible for the study

Istituto di Ricerche Farmacologiche Mario Negri IRCCS - Milan.

Funding

PharmaMar.

Disclosure

N. Colombo: Honoraria (institution), Advisory/Consultancy: roche; Honoraria (self), Advisory/Consultancy: pharmaMar; Honoraria (self), Advisory/Consultancy: AstaZeneca; Honoraria (self), Advisory/Consultancy: Clovis; Honoraria (self), Advisory/Consultancy: Tesaro/GSK; Honoraria (self), Advisory/Consultancy: Amgen; Honoraria (self), Advisory/Consultancy: Pfizer; Honoraria (self), Advisory/Consultancy: MSD; Honoraria (self), Advisory/Consultancy: biocad; Honoraria (self), Advisory/Consultancy: Immunogen; Honoraria (self), Advisory/Consultancy: Takeda; Honoraria (self), Advisory/Consultancy: Advaxis. J. Sehouli: Honoraria (self), Advisory/Consultancy, Research grant/Funding (institution), Travel/Accommodation/Expenses: Roche; Advisory/Consultancy: Clovis; Advisory/Consultancy, Travel/Accommodation/Expenses: GSK/Tesaro; Honoraria (self), Advisory/Consultancy: AstraZeneca; Honoraria (self), Advisory/Consultancy, Research grant/Funding (institution): PharmaMar; Advisory/Consultancy: Pfizer; Advisory/Consultancy: Novocure; Advisory/Consultancy: Eisai; Advisory/Consultancy, Research grant/Funding (institution): Lilly; Advisory/Consultancy, Research grant/Funding (institution): Bayer; Research grant/Funding (institution): Roche Diagnostics; Leadership role: NOGGO; Leadership role: ESGO; Leadership role: PARSGO; Leadership role: AGO. E. Biagioli: Research grant/Funding (institution): Roche; Research grant/Funding (institution): GSK/Tesaro; Research grant/Funding (institution): AstraZeneca; Research grant/Funding (institution): PharmaMar. N. Ottevanger: Research grant/Funding (institution): PharmaMar. A.G. G. Zeimet: Honoraria (self), Speaker Bureau/Expert testimony, Travel/Accommodation/Expenses: PharmaMar; Honoraria (self), Advisory/Consultancy, Speaker Bureau/Expert testimony, Travel/Accommodation/Expenses: Roche; Honoraria (self), Honoraria (institution), Advisory/Consultancy, Speaker Bureau/Expert testimony, Research grant/Funding (institution), Travel/Accommodation/Expenses: AstraZeneca. I.B. Vergote: Advisory/Consultancy, Research grant/Funding (institution), Travel/Accommodation/Expenses: Amgen (Europe) GmBH; Advisory/Consultancy, Travel/Accommodation/Expenses: AstraZeneca; Advisory/Consultancy: Clovis; Advisory/Consultancy: Carrick Therapeutics; Advisory/Consultancy: Debiopharm International; Advisory/Consultancy, Research grant/Funding (institution), Travel/Accommodation/Expenses: Roche; Advisory/Consultancy, Contracted research: Genmab; Advisory/Consultancy: GSK; Advisory/Consultancy: Immunogen; Advisory/Consultancy: Medical University of Vienna; Advisory/Consultancy: Millenium Pharmaceuticals; Advisory/Consultancy, Travel/Accommodation/Expenses: MSD Belgium; Advisory/Consultancy: Octimet Oncology; Advisory/Consultancy, Contracted research: Oncoinvent AS; Advisory/Consultancy: PharmaMar; Advisory/Consultancy: Roche NV; Advisory/Consultancy: Sotio A.S.; Advisory/Consultancy, Travel/Accommodation/Expenses: Tesaro; Advisory/Consultancy: Deciphera Phramaceuticals; Advisory/Consultancy: Verastem Oncology; Travel/Accommodation/Expenses: MSD/Merck Zurich + USA. J. Maenpaa: Honoraria (self): Roche; Honoraria (self): GSK; Honoraria (self): AstraZeneca; Honoraria (self): Clovis; Honoraria (self): Orion Pharma. R. Fossati: Research grant/Funding (institution): Roche; Research grant/Funding (institution): AstraZeneca; Research grant/Funding (institution): GSK/Tesaro; Research grant/Funding (institution): PharmaMar. A. Poveda: Advisory/Consultancy, Research grant/Funding (self), Travel/Accommodation/Expenses: AstraZeneca; Advisory/Consultancy: Clovis; Advisory/Consultancy, Travel/Accommodation/Expenses: PharmaMar; Advisory/Consultancy: GSK. All other authors have declared no conflicts of interest.