None - Scientific Plenary

Durvalumab plus paclitaxel/carboplatin plus bevacizumab followed by durvalumab, bevacizumab plus olaparib maintenance among patients with newly-diagnosed advanced ovarian cancer without a tumor *BRCA1*/*BRCA2* mutation: Updated results from DUO-O/ENGOT-OV46/GOG-3025 Trial

Philipp Harter, MD, PhD[1], Pauline Wimberger, MD, PhD[2], Aikou Okamoto, MD, PhD[3], Alexander Reuss, MSc[4], Myong Cheol Lim[5], Maria Jesús Rubio-Pérez, MD, PhD[6], Mehmet Ali Vardar, MD[7], Giovanni Scambia, MD[8], Olivier Trédan[9], Sakari Hietanen[10], Nicoletta Colombo, MD, PhD[11], Anita Chudecka-Glaz, MD, PhD, Associate Professor[12], Edgar Petru, MD[13], Stephanie Lheureux, MD, PhD[14], Els Van Nieuwenhuysen, MD[15], Jalid Sehouli, MD[16], Robert Wenham, MD, MSc[17], Kimio Ushijima[18], Sandra Indiviglio, PhD[19], Carol Aghajanian, MD[20]

[1]Kliniken Essen-Mitte, and AGO, Essen, Germany, [2]University Hospital Carl Gustav Carus, TU Dresden, and AGO and NOGGO, Dresden, Germany, [3]The Jikei University School of Medicine, and JGOG, Tokyo, Japan, [4]Coordinating Center for Clinical Trials of Philipps-University Marburg, and ENGOT, Marburg, Germany, [5]Center for Gynecologic Cancer, Hospital, Rare and Pediatric Cancer Branch and Immuno-oncology Branch, Research Institute, Department of Cancer Control and Policy, Graduate School of Cancer Science and Policy, National Cancer Center, Goyang, and KGOG, Goyang, Korea, Republic of, [6]Reina Sofia University Hospital, and GEICO, Córdoba, Spain, [7]University of Cukurova, and Balcalı Hospital, and TRSGO, Adana, Türkiye, [8]Fondazione Policlinico Universitario A. Gemelli IRCCS, and MITO, Rome, Italy, [9]Centre de Recherche en Cancérologie de Lyon, and GINECO, Lyon, France, [10]Turku University Hospital, and NSGO, Turku, Finland, [11]University of Milan-Bicocca and Istituto Europeo di Oncologia IRCCS, and MANGO, Milan, Italy, [12]Pomeranian Medical University, and PGOG, Szczecin, Poland, [13]Medical University of Graz, and AGO-Au, Graz, Austria, [14]Princess Margaret Hospital, and PMHC, Toronto, Canada, [15]UZ Leuven, and BGOG, Leuven, Belgium, [16]Charité Universitätsmedizin Berlin, and AGO and NOGGO, Berlin, Germany, [17]Moffitt Cancer Center, and GOG-F, Tampa, FL, United States, [18]Kurume University School of Medicine, and JGOG, Kurume, Japan, [19]Late-Stage Clinical Development, Oncology R&D, AstraZeneca, Gaithersburg, MD, United States, [20]Memorial Sloan Kettering Cancer Center, and GOG-F, New York, NY, United States

Objectives:

DUO-O (NCT03737643) met its primary endpoints at the planned interim analysis (DCO1 December 5, 2022), showing statistically significant and clinically meaningful progression-free survival (PFS) benefits in both non-t*BRCA*m HRD-positive and non-t*BRCA*m intent-to-treat (ITT) patient populations treated with paclitaxel/carboplatin + bevacizumab + durvalumab treatment followed by bevacizumab + durvalumab + olaparib maintenance versus paclitaxel/carboplatin + bevacizumab (Harter *J Clin Oncol* 2023;41:17; LBA5506). We reported updated final PFS, interim overall survival (OS), and updated safety.

Methods:

Patients had newly diagnosed FIGO stage III or IV high-grade epithelial, non-t*BRCA*m advanced ovarian cancer; primary or planned interval debulking surgery; and 1 cycle of paclitaxel/carboplatin ± bevacizumab. At cycle 2, patients were randomized 1:1:1 to Arm 1 (control): paclitaxel/carboplatin + bevacizumab + durvalumab placebo (PBO) (up to 6 cycles) followed by bevacizumab (total 15 months) + durvalumab PBO (total 24 months) + olaparib PBO (total 24 months) maintenance; Arm 2: paclitaxel/carboplatin + bevacizumab + durvalumab followed by bevacizumab + durvalumab + olaparib PBO maintenance; or Arm 3: paclitaxel/carboplatin + bevacizumab + durvalumab followed by bevacizumab + durvalumab + olaparib maintenance. The final descriptive PFS analyses (RECIST 1.1 per investigator) compared Arm 3 versus Arm 1 in the non-t*BRCA*m HRD-positive and non-t*BRCA*m ITT populations. Secondary endpoints of PFS in Arm 2 versus Arm 1 (non-t*BRCA*m ITT) and OS were formally tested per the pre-defined multiple testing procedure (MTP).

Results:

A total of 1,130 patients were randomized: 378 Arm 1, 374 Arm 2, and 378 Arm 3. At this updated PFS analysis (DCO2 September 18, 2023), a sustained improvement was observed for Arm 3 versus Arm 1 in the non-t*BRCA*m HRD-positive population: HR 0.46 (95% CI: 0.33–0.65), with a median (m)PFS of 45.1 versus 23.3 months, and PFS rate at 24 months of 72.9% versus 46.5%, respectively, and for Arm 3 versus Arm 1 in the non-t*BRCA*m ITT population: HR 0.61 (95% CI: 0.51–0.73), with mPFS of 25.1 versus 19.3 months, and PFS rate at 24 months of 53.0% versus 33.2%, respectively. A PFS benefit continued to be observed for Arm 3 versus Arm 1 in the HRD-negative population (HR: 0.68; 95% CI: 0.54–0.85). Similar to DCO1, a numerical improvement in PFS was shown for Arm 2 versus Arm 1 (non-t*BRCA*m ITT), but statistical significance was not reached in this final PFS analysis (Table). The interim OS analysis for Arm 3 versus Arm 1 was not statistically significant in the non-t*BRCA*m ITT population (HR: 0.95; 95% CI: 0.76–1.20; *P*=0.68; 39% maturity); however, a positive OS trend was noted in the non-t*BRCA*m HRD-positive population (23% maturity); no further testing was performed per MTP (Table). Safety was broadly consistent between DCO1 and DCO2.

Conclusions:

Paclitaxel/carboplatin + bevacizumab + durvalumab treatment followed by bevacizumab + durvalumab + olaparib maintenance continued to demonstrate improvement in PFS in the non-t*BRCA*m ITT, and both HRD subgroups versus control, with the longest mPFS of 45.1 months seen in the non-t*BRCA*m HRD-positive population, and an associated favorable OS trend. Safety was generally consistent with the known profiles of each agent.

	Arm 1 (control arm) PC + B	Arm 2 (durvalumab arm) PC + B + D	Arm 3 (durvalumab + olaparib arm) PC + B + D + O mtx
Non-tBRCAm HRD-positive*			
PFS events, n/N (%)	94/143 (65.7)	89/148 (60.1)	57/140 (40.7)
Median PFS, mo	23.3	25.1	45.1
HR (95% CI)†‡		0.89 (0.67–1.19)	0.46 (0.33–0.65)
24 mo PFS, %	46.5	50.9	72.9
OS events, n/N (%)	35/143 (24.5)	24/148 (16.2)	30/140 (21.4)
Median OS, mo	NR	NR	NR
HR (95% CI)†‡		0.69 (0.41–1.15)	0.84 (0.51–1.37)
24 mo OS, %	88.6	91.7	96.4
Non-tBRCAm ITT			
PFS events, n/N (%)	283/378 (74.9)	257/374 (68.7)	221/378 (58.5)
Median PFS, mo	19.3	20.6	25.1
HR (95% CI)†‡		0.87 (0.74–1.03) *P*=0.11§	0.61 (0.51–0.73)
24 mo PFS, %	33.2	38.7	53.0
OS events, n/N (%)	150/378 (39.7)	137/374 (36.6)	145/378 (38.4)
Median OS, mo	48.0	NR	48.5
HR (95% CI)†¶		0.92 (0.73–1.16)	0.95 (0.76–1.20) *P*=0.68¶
24 mo OS, %	79.8	81.2	83.3
HRD-negative*			
PFS events, n/N (%)	173/216 (80.1)	152/199 (76.4)	144/211 (68.2)
Median PFS, mo	17.5	15.4	21.1
HR (95% CI)†¶		0.92 (0.74–1.14)	0.68 (0.54–0.85)
24 mo PFS, %	26.1	30.9	41.1
OS events, n/N (%)	103/216 (47.7)	103/199 (51.8)	101/211 (47.9)
Median OS, mo	39.6	37.9	41.1
HR (95% CI)†¶		1.05 (0.80–1.38)	0.99 (0.76–1.31)
24 mo OS, %	76.9	73.0	76.4

*Determined using the Myriad MyChoice® CDx assay: non-tBRCA HRD-positive defined as a GIS ≥42; HRD-negative defined as a GIS <42.
†Vs Arm 1.
‡HR and CI were estimated from a stratified Cox proportional hazards model (stratified by the timing and outcome of cytoreductive surgery [non-tBRCAm HRD-positive population] or by the timing and outcome of cytoreductive surgery and geographic region [non-tBRCAm ITT population]).
§Testing boundary: two-sided *P*<0.0248.
¶HR and CI were estimated from an unstratified Cox proportional hazards model.
¶Testing boundary: two-sided *P*<0.0104.
B, bevacizumab; CI, confidence interval; D, durvalumab; GIS, genomic instability score; HR, hazard ratio; HRD, homologous recombination repair deficiency; ITT, intent to treat; mo, months; mtx, maintenance; NR, not reached; O, olaparib; OS, overall survival; PC, paclitaxel/carboplatin; PFS, progression-free survival; tBRCAm, tumor *BRCA1/BRCA2* mutation.

None - Scientific Plenary

Overall survival with camrelizumab plus famitinib versus camrelizumab alone and investigator's choice of chemotherapy for recurrent or metastatic cervical cancer

Xiaohua Wu, MD[1], Jianqing Zhu[2], Rutie Yin[3], Jiaxin Yang[4], Jihong Liu[5], Jing Wang[6], Lingying Wu[7], Ziling Liu[8], Yunong Gao[9], Danbo Wang[10], Ge Lou[11], Hongying Yang[12], Qi Zhou[13], Beihua Kong, phD[14], Yi Huang[15], Zhao Huang[16], Juan Dong[16], Charlie Zhang[16], Jianmei Hou[16], Mansoor Mirza, MD[17]

[1]Fudan University Shanghai Cancer Center, Shanghai, China, [2]Zhejiang Cancer Hospital, Hangzhou, China, [3]West China Second University Hospital, Sichuan University, Chengdu, China, [4]Peking Union Medical College Hospital, Beijing, China, [5]Sun Yat-sen University Cancer Center, Guangzhou, China, [6]Hunan Cancer Hospital, Changsha, China, [7]National Cancer Center/Cancer Hospital, Chinese Academy of Medical Sciences, Beijing, China, [8]The First Hospital of Jilin University, Changchun, China, [9]Peking University Cancer Hospital & Institute, Beijing, China, [10]Cancer Hospital of Dalian University of Technology, Liaoning Cancer Hospital & Institute, Shenyang, China, [11]Harbin Medical University Cancer Hospital, Harbin, China, [12]Yunnan Cancer Hospital, Kunming, China, [13]Chongqing University Cancer Hospital, Chongqing, China, [14]Qilu Hospital of Shandong University, Jinan, China, [15]Hubei Cancer Hospital, Wuhan, China, [16]Zai Lab (Shanghai) Co., Ltd, Shanghai, China, [17]Rigshospitalet–Copenhagen University Hospital, Copenhagen, Denmark

Objectives:

In the randomized, double-blind, placebo-controlled phase III NORA trial (NCT03705156) among patients with platinum-sensitive recurrent ovarian cancer (PSROC), niraparib maintenance therapy using an individualized starting dose (ISD) demonstrated a significant improvement in progression-free survival (PFS) at the primary analysis and a favorable trend in overall survival (OS) at an interim analysis, irrespective of germline *BRCA* mutation (g*BRCA*m) status. In contrast, an inconsistent OS trend was observed among patients without