2022-RA-1206-ESGO SELECTION OF PREEXISTING BRCA1/2-PROFICIENT TUMOR CELLS IN BRCA1/2-DRIVEN TUBO-OVARIAN CARCINOMAS TREATED BY NEOADJUVANT CHEMOTHERAPY

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Introduction/Background Tubo-ovarian carcinomas (OCs) are highly sensitive to platinum-based neoadjuvant chemotherapy (NACT) but almost never demonstrate complete pathologic response.

Methodology We analyzed paired primary and residual tumor tissues from 30 patients with hereditary BRCA1/2-driven OCs (BRCA1: 17; BRCA2: 13), who were treated by carboplatin/paclitaxel NACT (median number of cycles: 3, range 3–6). BRCA1/2 and TP53 genes were analyzed by the next-generation sequencing (NGS). The ratio between TP53 mutation-specific vs. wild-type reads was considered to monitor the proportion of tumor and non-tumor cells in the tissue sample. Assuming that all BRCA1/2 wild-type reads come from cells with retention of heterozygosity (ROH), one can calculate the percentage of cells with loss-of-heterozygosity (LOH). Excess of mutated vs. wild-type BRCA1/2 reads was interpreted as the LOH. We compared LOH in tumor tissues before and after NACT.

Results All 30 OCs had BRCA1/2 LOH in primary tumor and carried somatic TP53 mutation. Five (17%) tumor pairs showed transition from LOH to ROH during NACT presumably affecting all or the vast majority of residual tumor cells. Another 16 (53%) tumors demonstrated significant reduction of the percentage of tumor cells with LOH suggesting the expansion of BRCA1/2-proficient clones in the post-NACT tumor tissue. There were no signals of emergence of a second open reading frame (ORF) restoring BRCA1/2 mutation.

Conclusion Chemonaive BRCA1/2-driven carcinomas often contain a fraction of tumor cells with preserved BRCA1/2 heterozygosity. NACT can cause a selection of pre-existing BRCA1/2-proficient tumor cells, without gaining secondary reversal BRCA1/2 mutations.

2022-RA-1214-ESGO BEST OPTION TREATMENT IN FIRST LINE SETTING FOR LOW GRADE SEROUS OVARIAN CANCER:A CASE-CONTROL STUDY

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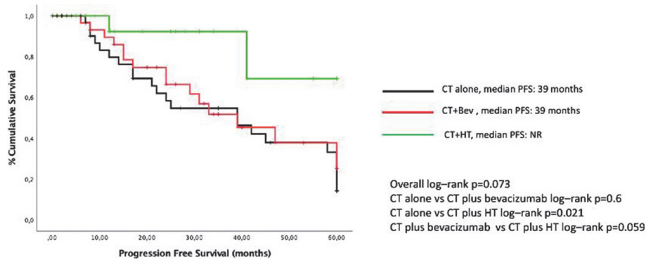
Introduction/Background Low grade serous ovarian cancer (LGSOC) is a complex disease, with reported very low response rate to standard cytotoxic agents. Despite a large retrospective study suggested a remarkable efficacy of hormone-therapy as maintenance after platinum-based chemotherapy (CT), due to its rarity very little is known about the best option treatment in the first line setting.

Methodology This is a retrospective case-control study including patients diagnosed with FIGO stage III-IV LGSOC between 2008 and 2021, aiming to assess differences in terms of efficacy between patients treated with CT alone (CT; Group 1), patients treated with CT in combination with Bevacizumab (CT+Bev; Group 2) and women receiving CT followed by hormone-therapy as maintenance (CT+HT; Group 3). Clinical data were collected, and survival analysis was performed for each study group.

Results Out of 84 patients identified, 39 (46.4%) were treated with platinum-based CT alone, 29 (34.5%) received platinum-based CT in combination with Bev and 16 (19.1%) patients received maintenance hormone-therapy after platinum-based CT. Median ages at the time of diagnosis were 49 years (range, 21–82), 47.7 years (range, 21–70) and 38 years (range, 18–60), for Group 1, 2 and 3, respectively. No statistically significant differences in FIGO stage, rate of primary or interval debulking cytoreduction, and residual tumor (gross vs absent) at upfront surgery were identified among the groups (table 1).Median PFS was 39 months in Group 1, 39 months in Group 2 and not reached in the group of patients receiving hormone-therapy as maintenance (Group 3) (log rank p=0.07), with a statistically significant advantage of Group 3 over Group 1 (p=0.021) (figure 1). Median OS was not reached in all Groups (p=0.18).

Abstract 2022-RA-1214-ESGO Table 1

Parameters	All patients n=84	CT alone (Group 1) n=39	CT+Bev (Group 2) n=29	CT+HT (Group 3) n=16	*P - value*
Age, median (IQR)	49 (18-82)	49 (21-82)	47.7 (21-70)	38 (18-60)	*0.92*
FIGO Stage, n (%)					*0.06*
III	67 (81.7)	33 (86.8)	19 (67.9)	15 (93.8)	
IV	15 (18.3)	5 (13.2)	9 (32.1)	1 (6.3)	
Upfront Surgery, n (%)					*0.13*
PDS	63 (75.9)	26 (68.4)	22 (75.9)	15 (93.8)	
NACT+IDS	20 (24.1)	12 (31.6)	7 (24.1)	1 (6.3)	
Residual Tumor, n (%)					*0.1*
0	75 (90.4)	34 (89.5)	25 (86.2)	16 (100)	
<1	8 (9.6)	4 (10.5)	4 (13.8)	-	
≥1 cm	-	-	-	-	



Abstract 2022-RA-1214-ESGO Figure 1

Conclusion Although the small simple size, these data suggest that maintenance with hormone therapy after platinum-based CT could represent the best therapeutic choice in this disease.