**METHODS**

**Patient characteristics**

Patients were recruited and samples were obtained at the Department of Gynecology and Obstetrics at the Technische Universität Dresden, Germany with inclusion criteria as described before [1]. Overall, 79 consecutive patients with histologically confirmed primary epithelial ovarian cancer with a primary diagnosis from 2013-2017 were included into our retrospective study. According to national guidelines, patients received cytoreductive surgery with the aim of macroscopic complete tumor resection, which was followed by platinum-based adjuvant chemotherapy. Patients treated with primary or neoadjuvant chemotherapy followed by interval debulking surgery were excluded from the study. Participation in clinical trials did not result in exclusion of a patient. Overall survival (OS) and progression-free survival (PFS) was calculated from the date of primary diagnosis. The study had been approved by the Local Research Ethics Committee at the Technische Universität Dresden, Germany (file number: EK74032013) and was performed in accordance with good clinical practice guidelines, the Declaration of Helsinki and national laws. All study participants gave written informed consent. Patients' clinical data are summarized in **Supplementary Table 1**. Ovarian cancer was reported in agreement with the WHO‐classification of tumors derived from female genital tract and staging was documented according to the FIGO classification [2], revised in 2014 [3]. FIGO-stage was reported according to the revised version for all patients who underwent primary surgery from 2014 onwards. In the case of no contraindications, patients with a tumor stage of FIGO III-IV were additionally treated with the antiangiogenic antibody bevacizumab in parallel to chemotherapy, which was followed by bevacizumab maintenance therapy. Surgical outcome was reported dichotomously (“macroscopically complete tumor resection”: no macroscopically visible tumor after primary debulking surgery *vs.* “any residual tumor”: any macroscopically visible residual tumor, left after primary debulking surgery (R≠0)).

**Ethic Statement**

This study strictly adheres to good clinical practice guidelines, national laws and the Declaration of Helsinki. Informed written consent was obtained from all patients and the study had been approved by the Local Research Ethics Committee in Dresden, Germany (reference number; EK74032013; EK236082012).

**Serum preparation and RNA isolation**

Following blood withdrawal with a 7.5 ml S-Monovette® (Sarstedt AG & Co., Nuembrecht, Germany), obtained blood samples were incubated at room temperature for at least 30 min to allow complete blood coagulation. Within 1 h post blood drawing, serum was prepared by centrifugation for 8 min at 1800 x g at room temperature. The obtained cell free serum fraction was immediately frozen at -80°C until further processing. Unnecessary freeze-thaw cycles were avoided. Samples were blinded so that neither time of blood drawing nor any other information was disclosed during analysis. Samples were thawed on ice and were immediately processed after complete thawing. For isolation of total RNA, the High Pure Viral RNA Kit (Roche Diagnostics, Mannheim, Germany) was used according to the manufacturer’s instruction as described previously by us [4-9]. Briefly, 350 µl serum was mixed with binding buffer and supplemented with Poly (A) carrier RNA (50 µg/ml). After RNA binding to the columns and washing steps, RNA was eluted in nuclease-free water.

**Blood-based detection of cfABCB1tx**

cfABCB1tx were quantified using a Bio-Rad QX200 Droplet Digital PCR System (Bio-Rad Laboratories GmbH, Munich, Germany) and the ddPCRTM Supermix for Probes (Bio-Rad), according to the manufacturer's instructions. Briefly, 1x master mix was supplemented with primer probe mix (https://www.bio-rad.com/digital-assays/assay-detail/dHsaCPE5045426) and complementary DNA (cDNA). Droplet generation for ddPCR was performed following manufacturer's instructions using the QX200 droplet generator. Briefly, 20 μl PCR mix and 70 μl droplet generator oil was given in the respective cavities of the droplet generator cartridges (Bio-Rad). Thereafter, 40 μl droplet suspension was pipetted into twin.tec 96-well PCR plates (Eppendorf, Hamburg, Germany). PCR was carried out (95°C for 10 min followed by 39x 95°C for 30 s and 60°C for 60 s and 98°C for 10 min) using a T100 thermal cycler. Droplet quantification was performed in the QX200 droplet reader. The system counts all generated droplets and detects the amount of PCR product-positive (fluorescent) droplets. Poisson correction of generated droplet amount and data analysis was done using the quanta life (Bio-Rad) software.

**Detection of disseminated tumor cells (DTCs) in the bone marrow**

The entire DTC detection procedure was performed as described previously [10] and in line with the recommendations for standardized tumor cell detection, published by the German Consensus Group of Senology [11, 12]. Bone marrow was bilaterally aspirated from the anterior iliac crests (between 5-10 ml per site) under local anesthesia, heparinized (5000 U/ml) and processed within 24 h. Bone marrow mononuclear cells (MNCs) were isolated from heparinized bone marrow (5000 U/ml) by Ficoll-Hypaque density gradient centrifugation (density 1.077 g/mol; Pharmacia, Freiburg, Germany) at 400 x g for 30 min. Interphase cells were washed (400 x g for 15 min) and re-suspended in phosphate buffered saline (PBS). A total of 1.5 x 106 MNCs per area of 240 mm2 were directly spun onto glass slides (400 x g for 5 min) coatedwith poly-L-lysine (Sigma, Deisenhofen, Germany) using a Hettich cytocentrifuge (Tuttlingen, Germany). In total, 8 x 106 MNCs per patient were analyzed. The slides were air-dried overnight at room temperature. Immunocytochemical detection of cytokeratin (CK)-positive DTCs was performed using the murine monoclonal antibody A45-B/B3 (Micromet, Germany), directed against a common epitope of CK polypeptides including the CK heterodimers 8/18 and 8/19. The protocol has already been described in detail elsewhere [11, 12]. Briefly, the method includes permeabilization of the cells with a detergent (5 min), fixation with a formaldehyde-based solution (10 min), binding of a A45-B/B3-alkaline phosphatase conjugate to cytoskeletal CKs (45 min) and formation of an insoluble red reaction product at the site of binding of the specific conjugate (15 min) using the DAKO-APAAP detection kit (DakoCytomation, Denmark). Subsequently, the cells were mounted with Kaiser’s glycerol/gelatin (Merck, Darmstadt, Germany) in Tris-EDTA buffer (Sigma, Deisenhofen, Germany). A Fab-fragment-alkaline phosphatase conjugate (Micromet, Munich, Germany) served as negative control and did not show relevant background staining in human bone marrow samples. Furthermore, a positive control using the A45-B/B3-alkaline phosphatase conjugate and CK-expressing MCF-7 breast cancer cells (ATCC, Rockville, MD) was stained in parallel to each batch of patient samples under identical experimental conditions.Microscopic evaluation of the CK-stained slides for DTC-detection was carried out using the ARIOL system (Applied Imaging). The software was specifically trained for the automated detection of CK-positive cells, based on particular color, intensity, size, pattern, and shape. Each detected cell was reviewed and classified according to the International Society for Haematotherapy and Graft Engineering (ISHAGE) evaluation criteria and the DTC consensus [11, 12]. A patient was categorically considered DTC-positive, if at least one CK-positive cell was detectable in at least one of the two bone marrow aspirates.

**Statistical analysis**

Statistical analysis was performed using GraphPad Prism version 10 for Windows (GraphPad Software, La Jolla California USA) and RStudio based on R-3.2.3 ([Free Software Foundation](http://www.gnu.org/)’s [GNU General Public License](https://www.r-project.org/COPYING)). P-values <0.05 were considered statistically significant. Predictive capacity of the cfABCB1tx level to predict surgical outcome was assessed by receiver operating characteristic (ROC) curve analysis. The correlation of cfABCB1tx with cfMACC1tx or CA125 was performed using Pearson correlation (raw values) and/or linear regression analysis (logarithmicvalues). Longitudinal cfABCB1tx levels were analyzed by the mixed effects model with Dunnet correction. Associations of cfABCB1tx levels with clinicopathological parameters were analyzed by the logrank test, non-parametric two-sided Mann-Whitney-U test for two groups and Kruskal-Wallis test with Dunn’s correction for three or more groups for continuous variables or the chi-square test for variables expressed in percentages. The prognostic relevance of cfABCB1tx was assessed using univariate Cox regression (logarithmic values) and continuous PFS/OS values. Kaplan-Meier analyses were performed using cfABCB1tx levels either dichotomized by the optimal cut-off determined by bootstrapping using the logrank-statistics or by their progression pattern under chemotherapy (*cfABCB1tx-induction-pattern* vs. *cfABCB1tx-decline-pattern*). Statistical significance between the survival curves was assessed using the Log-Rank (Mantel-Cox) and Mantel-Haenszel test.

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**SUPPLEMENTARY TABLES**

**Supplementary Table 1A: Clinical characteristics of study patients according to the total study cohort and defined subgroups.**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Total cohort** | **cfABCB1tx-low** | **cfABCB1tx-high** | **P-value** | **DTC negative** | **DTC positive** | **P-value** | **cfABCB1tx-decline-pattern** | **cfABCB1tx-increase-pattern** | **P-value** |
| **n** |  |  |  |  |  |  |  |  |  |  |
|  | 79 | 33 | 44 |  | 47 | 17 |  | 45 | 14 |  |
| **Age** |  |  |  |  |  |  |  |  |  |  |
| (median [IQR]) | 60.0  [52.5, 70.0] | 60.0  [51, 73] | 60.0  [53.0, 68.5] | 0.925 | 60.0  [50.5, 65.0] | 59.0 [51.0, 68.0] | 0.955 | 60.0  [53.0, 68.0] | 57.5  [51.0, 73.0] | 0.637 |
| **FIGO** |  |  |  |  |  |  |  |  |  |  |
| FIGO I/II (%) | 16 (20.3) | 11 (68.75) | 5 (31.25) | **0.019** | 10 (76.9) | 3 (23.1) | 0.750 | 9 (75.0) | 3 (25.0) | 0.908 |
| FIGO III/IV (%) | 63 (79.7) | 22 (36.1) | 39 (63.9) |  | 37 (72.6) | 14 (82.4) |  | 36 (76.6) | 11 (23.4) |  |
| **Surgical debulking (%)** |  |  |  |  |  |  |  |  |  |  |
| Macroscopic complete resection | 36 (45.6) | 19 (54.3) | 16 (45.7) | 0.064 | 22 (78.6) | 6 (21.4) | 0.412 | 22 (84.6) | 4 (15.4) | 0.181 |
| Any residual tumor | 43 (54.4) | 14 (33.3) | 28 (66.7) |  | 25 (69.4) | 11 (30.6) |  | 23 (69.7) | 10 (30.3) |  |
| **Histology (%)** |  |  |  |  |  |  |  |  |  |  |
| Serous | 67 (84.8) | 26 (40.0) | 39 (60.0) | 0.219 | 41 (74.5) | 14 (25.5) | 0.778 | 39 (78.0) | 11 (22.0) | 0.665 |
| Mucinous | 5 (6.3) | 4 (80.0) | 1 (20.0) |  | 3 (75.0) | 1 (25.0) |  | 3 (75.0) | 1 (25.0) |  |
| Endometrioid | 7 (8.9) | 3 (42.9) | 4 (57.1) |  | 3 (60.0) | 2 (40.0) |  | 3 (60.0) | 2 (40.0) |  |
| **Grading (%)** |  |  |  |  |  |  |  |  |  |  |
| Grade 1 | 3 (3.8) | 3 (100.0) | 0 (0.0) | 0.106 | 2 (66.7) | 1 (33.3) | 0.884 | 1 (50.0) | 1 (50.0) | 0.626 |
| Grade 2 | 8 (10.1) | 4 (50.0) | 4 (50.0) |  | 4 (66.7) | 2 (33.3) |  | 5 (71.4) | 2 (28.6) |  |
| Grade 3 | 68 (86.1) | 26 (39.4) | 40 (60.6) |  | 41 (74.5) | 14 (25.5) |  | 39 (78.0) | 11 (22.0) |  |
| High-grade serous | 67 (100.0) | 26 (40.0) | 39 (60.0) | N/A | 41 (74.5) | 14 (25.5) | N/A | 39 (78.0) | 11 (22.0) | N/A |
| Low-grade serous | 0 (0) | 0 (0) | 0 (0) |  | 0 (0) | 0 (0) |  | 0 (0) | 0 (0) |  |
| High-grade mucinous | 0 (0) | 0 (0) | 0 (0) | N/A | 0 (0) | 0 (0) | N/A | 0 (0) | 0 (0) | N/A |
| Low-grade mucinous | 5 (100) | 4 (80.0) | 1 (20.0) |  | 3 (75.0) | 1 (25.0) |  | 3 (75.0) | 1 (25.0) |  |
| High-grade endometrioid | 1 (14.2) | 0 (0) | 1 (100) | N/A | 0 (0) | 0 (0) | N/A | 0 (0) | 0 (0) | N/A |
| Low-grade endometroid | 6 (85.7) | 3 (50.0) | 3 (50.0) |  | 3 (60.0) | 2 (40.0) |  | 3 (60.0) | 2 (40.0) |  |
| **BRCA1/2 mutational status (%)** |  |  |  |  |  |  |  |  |  |  |
| *BRCA1/2wt* | 24 (30.4) | 9 (40.9) | 13 (59.1) | 0.482 | 13 (72.2) | 6 (33.3) | 0.833 | 12 (66.7) | 6 (33.3) | 0.248 |
| *BRCA1/2mut* | 16 (20.3) | 5 (31.25) | 11 (68.75) |  | 10 (76.9) | 3 (23.1) |  | 12 (92.3) | 1 (7.7) |  |
| Unknown | 39 (49.4) | 19 (48.7) | 20 (51.3) |  | 24 (75.0) | 8 (25.0) |  | 21 (75.0) | 7 (25.0) |  |
| **Progression-free survival (months)** |  |  |  |  |  |  |  |  |  |  |
| (median [IQR]) | 23.7  [14.6, 62.8] | 45.5  [20.2, 94.2] | 19.7  [13.2, 28.0] | **0.002** | 21.1  [14.93, 81.9] | 31.5  [13.3, 64.0] | 0.768 | 23.1  [15.7, 46.0] | 21.4  [11.1, 30.8] | 0.429 |
| No progression/death (%) | 19 (24.1) | 12 (66.7) | 6 (33.3) | **0.012** | 12 (70.6) | 5 (29.4) | 0.756 | 10 (83.3) | 2 (16.7) | 0.519 |
| Progression/death (%) | 60 (75.9) | 21 (35.6) | 38 (64.4) |  | 35 (74.5) | 12 (25.5) |  | 35 (74.5) | 12 (25.5) |  |
| **Overall survival (months)** |  |  |  |  |  |  |  |  |  |  |
| (median [IQR]) | 50.1  [25.5, 84.8] | 71.9  [36.7, 97.7] | 36.3  [23.8, 64.0] | **0.01** | 51.7  [28.9, 91.2] | 50.1  [23.4, 86.0] | 0.657 | 52.6  [30.7, 89.4] | 26.4  [19.3, 54.6] | **0.024** |
| Alive (%) | 26 (32.9) | 15 (60.0) | 10 (40.0) | **0.035** | 17 (77.3) | 5 (22.7) | 0.615 | 16 (88.9) | 2 (11.1) | 0.131 |
| Dead (%) | 53 (67.1) | 18 (34.6) | 34 (65.4) |  | 30 (71.4) | 12 (28.6) |  | 29 (70.7) | 12 (29.3) |  |
| **DTCs (%)** |  |  |  |  |  |  |  |  |  |  |
| DTC negative | 47 (59.5) | 20 (43.5) | 26 (56.5) | 0.057 | 47 (100) | 0 (0) | N/A | 33 (91.7) | 3 (8.3) | **0.001** |
| DTC positive | 17 (21.5) | 10 (62.5) | 6 (37.5) |  | 0 (0) | 17 (100) |  | 5 (41.7) | 7 (58.3) |  |
| Unknown | 15 (19.0) | 3 (20.0) | 12 (80.0) |  | 0 (0) | 0 (0) |  | 7 (63.6) | 4 (36.4) |  |
| **Dynamics (%)** |  |  |  |  |  |  |  |  |  |  |
| cfABCB1tx-decline-pattern | 45 (57.0) | 19 (42.2) | 26 (57.8) | 0.116 | 33 (86.8) | 5 (13.2) | **0.001** | 45 (100) | 0 (0) | N/A |
| cfABCB1tx-increase-pattern | 14 (17.7) | 9 (64.3) | 5 (35.7) |  | 3 (30.0) | 7 (70.0) |  | 0 (0) | 14 (100) |  |
| X | 20 (25.3) | 5 (27.8) | 13 (72.2) |  | 11 (68.75) | 5 (31.25) |  | 0 (0) | 0 (0) |  |
| **cfABCB1tx (n; median [IQR])** |  |  |  |  |  |  |  |  |  |  |
| preoperative | 77; 354 [172 – 730] | 33; 150 [116 – 220] | 44; 639 [433.5 – 1318.5] | NA | 46; 352 [184 – 849.5] | 16; 236 [95.5 – 624] | NA | 45; 350 [150 – 730] | 14; 254 [170.5 – 448] | N/A |
| postoperative | 72; 892 [495.5 – 1500] | 30; 631 [421.5 – 1266] | 40; 1107 [592.5 – 1810] |  | 43; 912 [486 – 1570] | 15; 596 [486 – 1150] |  | 43; 944 [500 – 1473] | 11; 596 [433 – 1191] |  |
| before chemotherapy | 64; 372 [221.5 – 676.5] | 26; 320 [209.5 – 517] | 36; 445 [255 – 835] |  | 37; 392 [258 – 732] | 13; 378 [170 – 590] |  | 34; 406 [249 – 766] | 13; 258 [208 – 378] |  |
| during chemotherapy | 50; 125 [95.5 – 221.5] | 22; 115 [92.5 – 146] | 26; 126 [100 – 229] |  | 31; 146 [101 – 288] | 10; 115 [82.5 – 144] |  | 32; 132 [108 – 240] | 11; 102 [93 – 129] |  |
| after chemotherapy | 55; 132 [77 – 273] | 27; 140 [88 – 254] | 28; 126 [75.5 – 281.5] |  | 33; 110 [76 – 192] | 12; 260 [133 – 465] |  | 41; 110 [74 – 190] | 14; 281 [209 – 471] |  |
| **Chemotherapy cycles (n; %)** |  |  |  |  |  |  |  |  |  |  |
| no chemotherapy | 2 (2.5) |  |  |  |  |  |  |  |  |  |
| 1 cycle | 1 (1.3) |  |  |  |  |  |  |  |  |  |
| 2 cycles | 0 (0.0) |  |  |  |  |  |  |  |  |  |
| 3 cycles | 0 (0.0) |  |  |  |  |  |  |  |  |  |
| 4 cycles | 0 (0.0) |  |  |  |  |  |  |  |  |  |
| 5 cycles | 3 (3.8) |  |  |  |  |  |  |  |  |  |
| 6 cycles | 68 (86.1) |  |  |  |  |  |  |  |  |  |
| 7 cycles | 2 (2.5) |  |  |  |  |  |  |  |  |  |
| 8 cycles | 3 (3.8) |  |  |  |  |  |  |  |  |  |

**Supplementary Table 1B: Clinical characteristics of study patients with available longitudinal serum samples (n=59).**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Total cohort** | **Patients with  longitudinal  serum samples** | **P-value** |
| **n** |  |  |  |
|  | 79 | 59 |  |
| **Age** |  |  |  |
| (median [IQR]) | 60.0  [52.5, 70.0] | 60.0  [51.5, 70.0] | 0.773 |
| **FIGO** |  |  |  |
| FIGO I/II (%) | 16 (20.3) | 12 (20.3) | 0.990 |
| FIGO III/IV (%) | 63 (79.7) | 47 (79.7) |  |
| **Surgical debulking (%)** |  |  |  |
| Macroscopic complete resection | 36 (45.6) | 26 (44.1) | 0.861 |
| Any residual tumor | 43 (54.4) | 33 (55.9) |  |
| **Histology (%)** |  |  |  |
| Serous | 67 (84.8) | 50 (84.7) | 0.992 |
| Mucinous | 5 (6.3) | 4 (6.8) |  |
| Endometrioid | 7 (8.9) | 5 (8.5) |  |
| **Grading (%)** |  |  |  |
| Grade 1 | 3 (3.8) | 2 (3.4) | 0.944 |
| Grade 2 | 8 (10.1) | 7 (11.9) |  |
| Grade 3 | 68 (86.1) | 50 (84.7) |  |
| High-grade serous | 67 (100.0) | 50 (100.0) | N/A |
| Low-grade serous | 0 (0) | 0 (0) |  |
| High-grade mucinous | 0 (0) | 0 (0) | N/A |
| Low-grade mucinous | 5 (100) | 4 (100) |  |
| High-grade endometrioid | 1 (14.2) | 0 (0) | N/A |
| Low-grade endometroid | 6 (85.7) | 5 (100) |  |
| **BRCA1/2 mutational status (%)** |  |  |  |
| *BRCA1/2wt* | 24 (30.4) | 18 (30.5) | 0.963 |
| *BRCA1/2mut* | 16 (20.3) | 13 (22.0) |  |
| Unknown | 39 (49.4) | 28 (47.5) |  |
| **Progression-free survival (months)** |  |  |  |
| (median [IQR]) | 23.7  [14.6, 62.8] | 22.6  [14.5, 43.7] | 0.626 |
| No progression/death (%) | 19 (24.1) | 12 (20.3) | 0.605 |
| Progression/death (%) | 60 (75.9) | 47 (79.7) |  |
| **Overall survival (months)** |  |  |  |
| (median [IQR]) | 50.1  [25.5, 84.8] | 46.4  [25.8, 86.4] | 0.745 |
| Alive (%) | 26 (32.9) | 18 (30.5) | 0.764 |
| Dead (%) | 53 (67.1) | 41 (69.5) |  |
| **DTCs (%)** |  |  |  |
| DTC negative | 47 (59.5) | 36 (61.0) | 0.981 |
| DTC positive | 17 (21.5) | 12 (20.3) |  |
| Unknown | 15 (19.0) | 11 (18.6) |  |
| **Dynamics (%)** |  |  |  |
| cfABCB1tx-decline-pattern | 45 (57.0) | 45 (76.3) | N/A |
| cfABCB1tx-increase-pattern | 14 (17.7) | 14 (23.7) |  |
| X | 20 (25.3) | 0 (0.0) |  |
| **cfABCB1tx (n; median [IQR])** |  |  |  |
| preoperative | 77; 354 [172 – 730] | 59; 320 [152 – 639] | N/A |
| postoperative | 72; 892 [495.5 – 1500] | 54; 892 [490.5 – 1463.5] |  |
| before chemotherapy | 64; 372 [221.5 – 676.5] | 47; 364 [227 – 663] |  |
| during chemotherapy | 50; 125 [95.5 – 221.5] | 43; 124 [100 – 169] |  |
| after chemotherapy | 55; 132 [77 – 273] | 55; 132 [77 – 273] |  |

**Supplementary Table 2: Prognostic value of cfABCB1tx levels at primary diagnosis (univariate Cox regression).**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| ***Outcome*** | ***β*** | ***exp(β)/HR*** | ***Lower bound 95%CI*** | ***Upper bound 95%CI*** | ***z*** | ***P-value*** |
| ***PFS*** | 0.3016 | 1.3521 | 1.045 | 1.749 | 2.295 | **0.0217** |
| ***OS*** | 0.2795 | 1.3224 | 1.002 | 1.746 | 1.972 | **0.0486** |

**Supplementary Table 3: Prognostic value of induction of increased cfABCB1tx levels during chemotherapy (univariate Cox regression).**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| ***Outcome*** | ***β*** | ***exp(β)/HR*** | ***Lower bound 95%CI*** | ***Upper bound 95%CI*** | ***z*** | ***P-value*** |
| ***OS*** | 0.7646 | 2.1482 | 1.089 | 4.237 | 2.207 | **0.0273** |

**Supplementary Table 4: Prognostic value of induction of increased cfABCB1tx levels during chemotherapy (multivariate Cox regression).**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| ***Outcome*** | ***Variable*** | ***β*** | ***exp(β)/HR*** | ***Lower bound 95%CI*** | ***Upper bound 95%CI*** | ***z*** | ***P-value*** |
| ***OS*** | Induction | 0.9544 | 2.5972 | 1.2181 | 5.538 | 2.471 | **0.01349** |
| FIGO status | 0.8981 | 2.4549 | 1.3544 | 4.45 | 2.96 | **0.00308** |
| Surgical debulking | 0.4864 | 1.6265 | 0.6524 | 4.055 | 1.044 | 0.2967 |