

Real-world longitudinal Tissue Microarray Platform within clinical routine for Ovarian Cancer: from Primary Surgery through Recurrence in a large Tertiary-Center Cohort

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Real-world longitudinal Tissue Microarray Platform within clinical routine for Ovarian Cancer: from Primary Surgery through Recurrence in a large Tertiary-Center Cohort

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What does this study add to the clinical work?

This study establishes a longitudinal platform linking a detailed, systematically curated clinical database to primary and recurrent ovarian cancer tissue and patient-derived organoids. Reproduction of established prognostic associations, together with exploratory analyses across successive recurrence landmarks, demonstrates the platform's potential for clinically anchored biomarker research.

Abstract

Purpose

To establish a tissue microarray-linked clinical platform for epithelial ovarian cancer, benchmark it against established prognostic associations, and evaluate surgical outcome across recurrence landmarks.

Methods

This retrospective single-center cohort included 524 consecutive patients with epithelial ovarian cancer. Clinicopathologic, surgical, treatment, and time-to-event data were linked to tumor tissue, including recurrent samples from 50 patients, and to a patient-derived organoid biobank. Survival was estimated using Kaplan-Meier methods and analyzed using log-rank tests and Cox proportional hazards models.

Results

High-grade serous carcinoma accounted for 415/524 cases (79.2%). In the overall cohort, 411/524 patients (78.4%) had FIGO stage III–IV disease. Of these, 374/411 (91.0%) underwent primary surgery, with complete gross tumor resection achieved in 225/374 (60.2%). In this cohort, median progression-free survival was 26.4 months after complete gross tumor resection compared to 13.6 months after postoperative residual disease ($p < 0.001$), and median overall survival was 70.7 versus 21.9 months, respectively ($p < 0.001$). First-line platinum-based chemotherapy and bevacizumab maintenance were associated with improved outcome. Complete gross tumor resection at primary surgery remained associated with longer survival across the first, second, and third recurrence landmarks, and complete gross tumor resection at secondary cytoreductive surgery was also associated with longer survival after recurrence.

Conclusion

The platform integrates longitudinal clinical outcomes with systematically curated tumor tissue and functional models. Although the recurrence-landmark analyses are exploratory, this resource provides a detailed and clinically anchored foundation for biomarker research.

Keywords: ovarian cancer; precision medicine; clinical database; patient-derived organoids; biomarker research

Introduction

Clinical outcomes in epithelial ovarian cancer (EOC) are determined by surgical cytoreduction, systemic treatment, and tumor biology. However, integrating translational research across these dimensions into routine practice and identifying clinically relevant biomarkers and therapeutic targets remain challenging.

EOC comprises biologically distinct subtypes, dominated by high-grade serous ovarian cancer (OC), while rarer histologies have distinct biological and clinical features. Because effective screening is unavailable and symptoms are nonspecific, most patients present with advanced disease. Five-year survival decreases from 86% in International Federation of Gynecology and Obstetrics (FIGO) stage I to 26% in stage IV [1], and approximately 85% of patients experience recurrence within ten years [2]. Despite this heterogeneity, first-line treatment remains largely uniform and consists of cytoreductive surgery and platinum-based chemotherapy [3].

Based on the established value of complete gross tumor resection at primary surgery [4], LION (AGO-OVAR OP.3) showed no survival benefit from systematic lymphadenectomy in patients with clinically negative lymph nodes after complete gross tumor resection [5]. In recurrent disease, DESKTOP III (AGO-OVAR OP.4) showed that complete gross tumor resection at secondary cytoreductive surgery improved OS, with a median of 53.7 versus 46.0 months [6]. TRUST (ENGOT ov33 / AGO-OVAR OP.7) recently underscored the importance of surgical quality metrics and center expertise in advanced EOC [7].

Targeted maintenance therapies have expanded first-line systemic treatment. Bevacizumab, administered with chemotherapy and continued as maintenance, prolonged progression-free survival (PFS) in the phase III GOG-0218 and AGO-OVAR 11/ICON7 trials, while PARP inhibitors benefited biomarker-defined populations [8-12]. Antibody-drug conjugates and immune checkpoint inhibitors are further shifting treatment toward molecularly defined strategies [13, 14]. However, evidence predominantly concerns later treatment lines; first-line use remains limited, and validated target populations are lacking [15].

Standardized tissue resources linked to deeply annotated longitudinal data across successive disease stages remain scarce. To address this gap, we established a tissue microarray (TMA) platform comprising 524 patients with OC surgically treated at our institution between 01/2011 and 12/2020. The cohort includes 415 (79.2%) high-grade serous, 26 (5.0%) low-grade serous, and 83 (15.9%) less frequent histologic subtypes. Each case is linked to a curated database of clinicopathologic characteristics, detailed surgical parameters, systemic and maintenance treatment, and time-to-event endpoints with available matched tissue for a subset of cases. Additionally, further systematic biobanking of tumor material to establish a patient-derived

organoid (PDO) bank as a functional translational resource is also part of scientific routine, as previously described [16, 17].

As a quality assurance metric, we validated the cohort by reproducing landmark findings from practice-changing prospective trials. The integrated TMA and clinical database thereby provide a reliable resource for contextual biomarker evaluation, clinical hypothesis testing, and future precision-oncology research.

Material and Methods

Tissue Microarray and Patient Cohort

Tumor samples were collected from 524 consecutive patients with EOC undergoing primary surgery at the Department of Obstetrics and Gynecology, University Hospital, LMU Munich, Munich, Germany, between 01/2011 and 12/2020. Tissue was formalin-fixed and paraffin-embedded, and the histopathologic diagnosis was confirmed by board-certified gynecologic pathologists at the Institute of Pathology, LMU Munich. Two representative tumor areas per patient were incorporated into the TMA.

The TMA comprises 415 (79.2%) high-grade serous, 26 (5.0%) low-grade serous, 24 (4.6%) endometrioid, 22 (4.2%) clear cell, 15 (2.9%) mucinous, and 22 (4.2%) rare ovarian carcinomas, including undifferentiated, transitional cell, and carcinosarcoma subtypes. Grading followed World Health Organization criteria. Serous carcinomas were classified as high- or low-grade and clear cell carcinomas as grade 3. Additional tissue from recurrent-disease surgery was available and included for 50 patients.

All patients received standard-of-care treatment according to national and international guidelines [18, 19]. Clinical, pathologic, and treatment data were extracted from institutional records, and follow-up was supplemented by the Munich Cancer Registry. Median follow-up was 35.0 months, and the data cutoff was June 3, 2025.

Ethical approval

Tissue collected during cytoreductive surgery was stored in the archives of the Institute of Pathology, LMU Munich, and corresponding patient data were anonymized before analysis. The local ethics committee waived specific informed consent in accordance with local regulations and approved the study protocol (LMU Munich reference 22-0257).

Definition of endpoints

OS was measured from primary surgery or the respective recurrence landmark to death from any cause or last follow-up. PFS was measured from surgery to the first documented recurrence, progression, or death, whichever occurred first. Available dates of first, second, and later recurrences defined recurrence-specific survival landmarks for exploratory analyses. Survival analyses included only patients undergoing primary surgery followed by postoperative chemotherapy; patients receiving neoadjuvant chemotherapy were excluded because preoperative treatment would have limited the comparability of surgery-based survival estimates. *Statistical Analysis*

Analyses used IBM SPSS Statistics version 30.0 (IBM Corp., Armonk, NY, USA) and R version 4.5.0 (R Foundation for Statistical Computing, Vienna, Austria) in RStudio version 2025.09.1+401. Survival analyses used *survival* [20] and were visualized with *survminer* [21] and *ggplot2* [22].

Prespecified survival analyses evaluated established prognostic and treatment-related variables, including PFS and OS by FIGO stage and surgical outcome at primary cytoreductive surgery.

Survival was estimated by Kaplan-Meier analysis and compared by the log-rank test. Hazard ratios (HRs) and 95% confidence intervals (CIs) were derived from univariable Cox proportional hazards models. Tests were two-sided, and $p < 0.05$ was considered statistically significant.

Multivariable Cox proportional hazards models identified independent predictors of PFS and OS. Covariates included primary resection status; surgery for first recurrence, where applicable; age at diagnosis as a continuous variable; first-line platinum-based chemotherapy; bevacizumab-based first-line maintenance; American Society of Anesthesiologists (ASA) score; and FIGO stage. HRs, 95% CIs, and p-values were reported.

Results

Patient Cohort and Clinicopathologic Characteristics

The TMA included 524 consecutive patients (**Table 1**), with a median age of 64.0 years (range, 25-93 years). High-grade serous ovarian carcinoma accounted for 415 cases (79.2%), low-grade serous tumors for 26 (5.0%), and other histologies for 15.9%. Overall, 411 patients (78.4%) had advanced FIGO stage III-IV disease, while 12.4% had FIGO stage I disease.

Patient characteristics (total number of TMA cases)	Patient numbers (n = 524)
Age (median; range)	64 (25 - 93)
BMI (median; range)	24.5 (16.4 - 53.91)
Histology, n (%)	
High-grade serous	415 (79.2 %)
Low-grade serous	26 (5.0 %)
Mucinous	15 (2.9 %)
Endometrioid	24 (4.6 %)
Clear cell	22 (4.2 %)
Others	22 (4.2 %)
FIGO stage, n (%)	
I	65 (12.4 %)
II	25 (4.8 %)
III	317 (60.5 %)
IV	94 (17.9 %)
Grading (for serous histologies, n = 441), n (%)	
High-grade	415 (94.1 %)
Low-grade	26 (5.9 %)
Grading (for all non-serous histologies), n (%)	
1	12 (2.3%)
2	17 (3.2%)
3	48 (9.2%)

Table 1. Baseline clinicopathologic characteristics of the TMA cohort. The table summarizes demographic and tumor-related characteristics of 524 consecutive patients with epithelial ovarian cancer who underwent primary cytoreductive surgery between 2011-2020. Only patients with complete documentation were included in this analysis.

Surgical outcomes and first-line chemotherapy data for the 411 patients with FIGO stage III-IV disease are shown in Table 2. Primary surgery was performed in 374 patients (91.0%), while 37 (9.0%) underwent interval cytoreductive surgery. Complete gross tumor resection was achieved in 225 of the 374 patients undergoing upfront surgery (60.2%; **Table 2A**).

Among all OC patients meeting European Medicines Agency (EMA) approval criteria, 402 (88.7%) received platinum-based chemotherapy and 158 (44.9%) received bevacizumab. The main reasons for omitting platinum-based chemotherapy despite treatment eligibility were

patient death and comorbidities (**Table 2B**). Bevacizumab was mainly omitted because of thromboembolic events, impaired wound healing, bowel surgery complications, diagnosis before regulatory approval, or a decision favoring single-agent PARP inhibitor therapy in 10 patients.

2A

Patient characteristics (only FIGO III/IV)	Patient numbers (n = 411)
Cytoreductive surgery	
Upfront, n (%)	374 (91.0 %)
Complete cytoreduction, n/upfront n (%)	225 (60.2 %)
Incomplete cytoreduction, n/upfront n (%)	149 (39.8 %)
Interval, n (%)	37 (9.0 %)
Complete cytoreduction, n/interval n (%)	28 (75.7 %)
Incomplete cytoreduction, n/interval n (%)	9 (24.3 %)

2B

First-line platinum-based chemotherapy, n (%) (Platinum indication)	Patient numbers (n = 453)
Administered	402 (88.7 %)
Not administered	51 (11.3 %)
Platinum contraindication	17 (3.8 %)
Renal impairment (N17-N19)	13 (2.9 %)
Neuropathy (G62/G63)	0 (0.0 %)
Hearing loss (H90/H91)	1 (0.2 %)
Thrombocytopenia/Neutropenia (D69/D70)	4 (0.9 %)
Death within 4 weeks after surgery	8 (1.8 %)
With Platinum contraindication	4 (0.9 %)
No Platinum contraindication	4 (0.9 %)

Table 2. Surgical outcome and clinical information on first-line chemotherapy in the TMA cohort. **Table 2A** summarizes the surgical approach and resection status in patients with FIGO stage III-IV disease (n = 411). **Table 2B** details the use of platinum-based chemotherapy in patients with an indication for platinum therapy (FIGO IA-IB with G3 tumors and FIGO IC-IV; n = 453). Contraindications or death within four weeks after surgery were the most common reasons for omitting platinum-based chemotherapy despite treatment eligibility according to EMA approval criteria. Several patients had more than one contraindication, and only those with complete follow-up data were included in the analysis. Percentages refer to the total patient cohort unless indicated otherwise.

Survival Analysis for Cohort Validation

Survival analyses excluded patients receiving neoadjuvant chemotherapy to ensure cohort homogeneity.

Progression-free and overall survival according to FIGO stage and resection status

Stage-based survival analyses included all histologic subtypes receiving first-line platinum-based chemotherapy. PFS and OS decreased with advancing FIGO stage. Patients with FIGO stage I disease had a 5-year PFS rate of 86%, compared with 70% for stage II disease ($p = 0.04$), and a 5-year OS rate of 78%, compared with 63% ($p = 0.08$). Median PFS and OS were not reached (NR) in either subgroup. Median PFS was 19.9 (17.8-25.7) months in FIGO stage III and 15.5 (14.0-20.3) months in stage IV disease ($p = 0.06$; **Figure 1A**). Median OS was 46.1 (39.5-60.5) and 28.6 (22.4-36.4) months, respectively ($p = 0.003$; **Figure 1B**).

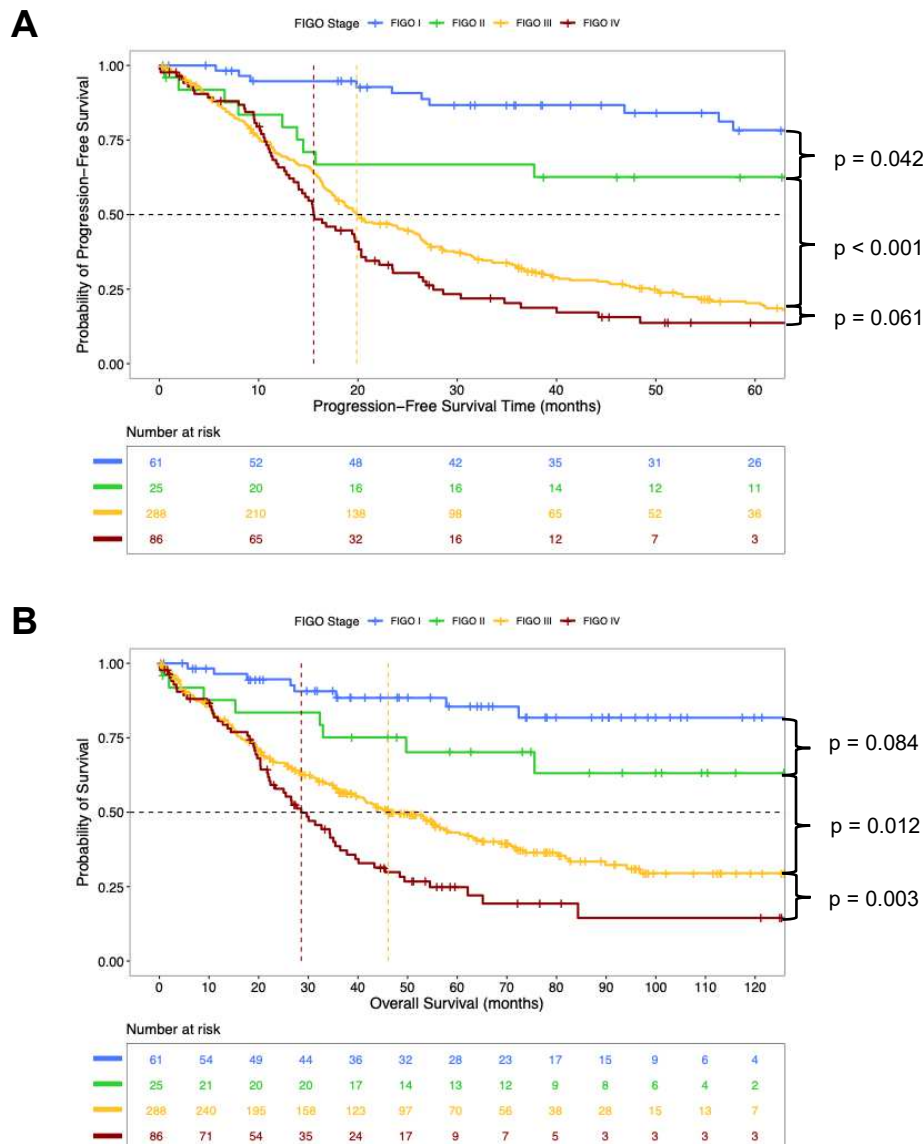


Fig. 1 Progression-free and overall survival stratified by FIGO stage. Increasing FIGO stage is associated with shorter PFS (**A**) and OS (**B**).

Among 374 patients with FIGO stage III-IV tumors undergoing primary cytoreductive surgery, complete gross tumor resection was achieved in 225 and postoperative residual disease remained in 149. Median PFS was 26.4 (20.8-31.9) months after complete gross tumor resection and 13.6 (10.8-16.3) months with residual disease ($p < 0.001$; **Figure 2 A1**). Median

OS was 70.7 (51.4-90.0) and 21.9 (15.4-28.4) months, respectively ($p < 0.001$; **Figure 2 All**). Among the 149 patients with residual disease, median PFS was 13.8 months for residual tumor <1 cm and 12.2 months for residual tumor >1 cm ($p = 0.3$). Median OS was 25.3 and 20.4 months, respectively ($p = 0.3$).

This pattern persisted when FIGO stages III and IV were analyzed separately (**Figure 2 BI-CII**). In stage III disease, complete gross tumor resection was associated with a median PFS of 26.9 months, compared with 13.6 months for residual disease ($p < 0.001$), and a median OS of 72.0 versus 20.6 months ($p < 0.001$). In stage IV disease, median PFS was 20.1 versus 13.5 months ($p = 0.02$), and median OS was 45.5 versus 22.4 months ($p = 0.002$).

At last follow-up, 153 of 374 patients (40.9%) with FIGO stage III–IV disease who underwent primary surgery between January 2011 and December 2020 were alive, including 123 of 225 (54.7%) with complete gross tumor resection versus 30 of 149 with residual gross disease ($p < 0.0001$).

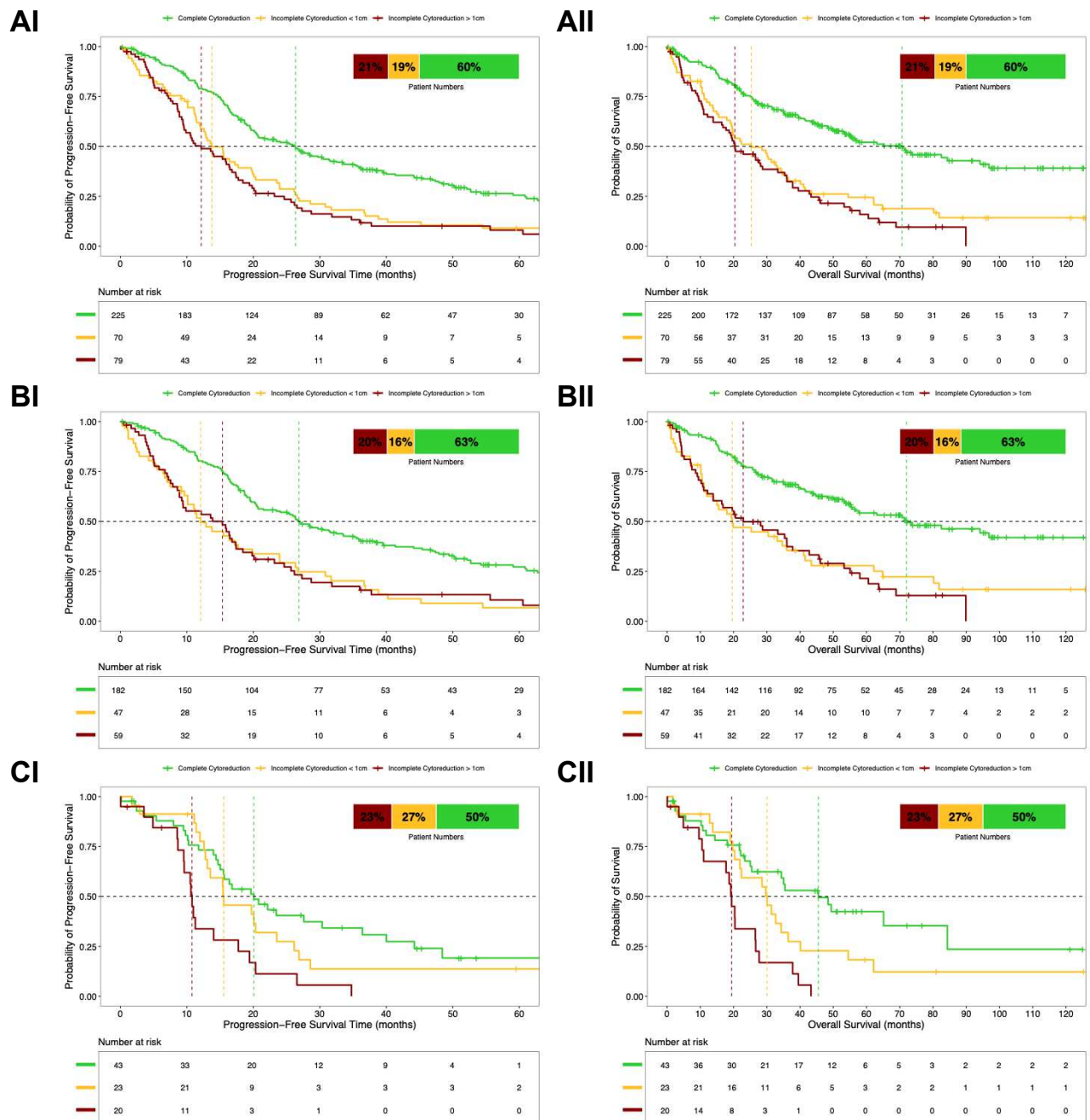


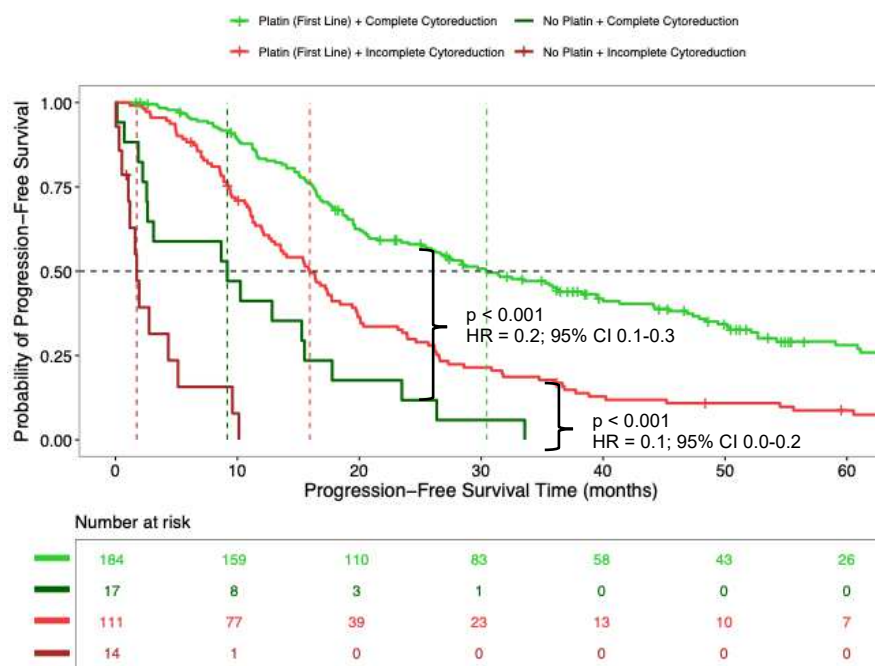
Fig. 2 Progression-free and overall survival according to resection status. Patients with FIGO stage III-IV disease who achieved complete gross tumor resection demonstrated significantly improved PFS (**AI**) and OS (**AII**) compared to patients with incomplete cyto-reduction. No survival difference was observed between patients with residual tumor <1 cm and >1 cm. Similar survival patterns were observed when patients with FIGO stage III (**BI**, **BII**) and FIGO stage IV disease (**CI**, **CII**) were analyzed separately.

Association of first-line platinum-based chemotherapy and bevacizumab maintenance with PFS and OS

PFS and OS were analyzed according to first-line platinum administration and primary surgical outcome. The cohort was restricted to patients with FIGO stage III-IV disease to allow meaningful stratification.

Platinum-based chemotherapy was associated with longer PFS and OS regardless of resection status. After complete gross tumor resection, median PFS was 30.5 months among 184 patients receiving platinum and 9.2 months among 17 patients who did not ($p < 0.001$). Median OS was 84.3 versus 15.7 months ($p < 0.001$). Among patients with residual disease, median PFS was 15.9 months in 111 platinum-treated patients and 1.7 months in 14 patients who did not receive a platinum-based therapy ($p < 0.001$). Median OS was 30.4 versus 1.7 months ($p < 0.001$; **Figure 3A, B**).

A



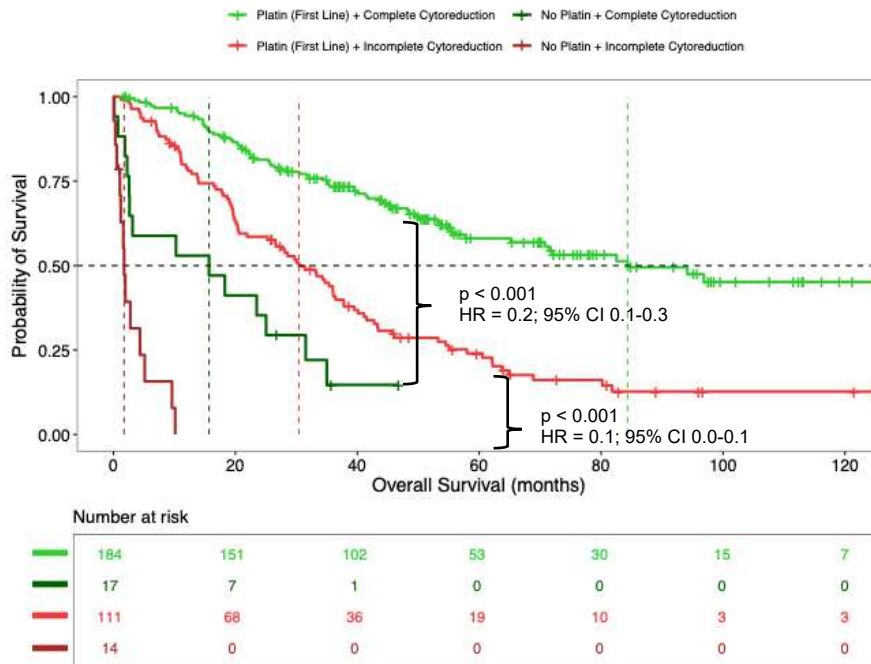
B

Fig. 3 Progression-free and overall survival according to platinum-based first-line chemotherapy, stratified by resection status. Platinum-based chemotherapy was associated with significantly improved PFS (A) and OS (B) in patients with FIGO stage III-IV disease, irrespective of resection status at primary surgery (complete or incomplete cytoreduction).

PFS and OS were further analyzed according to bevacizumab exposure and primary surgical outcome in FIGO stage III-IV disease. After complete gross tumor resection, the 72 patients receiving bevacizumab maintenance had a median PFS of 39.5 (30.4-52.7) months, compared with 17.0 (15.3-19.5) months among 111 patients who did not receive bevacizumab ($p < 0.001$; **Figure 4A**). Median OS was NR in the bevacizumab group and 48.2 (32.1-57.7) months in the non-bevacizumab group ($p < 0.001$; **Figure 4B**).

Among patients with postoperative residual disease, median PFS was 18.4 (16.4-25.7) months in 57 patients receiving bevacizumab and 7.6 (6.7-11.5) months in 56 patients who did not ($p < 0.001$; **Figure 4A**). Median OS was 37.8 (30.1-54.5) and 12.2 (7.2-28.1) months, respectively ($p < 0.001$; **Figure 4B**).

The approval-period analysis compared 31 patients treated before bevacizumab approval, none of whom received bevacizumab, with patients treated after approval. Among 127 post-approval patients receiving bevacizumab, median PFS was 27.6 months, compared with 13.6 months in the pre-approval cohort ($p < 0.001$), and median OS was 65.1 versus 43.4 months ($p = 0.04$). Outcomes among post-approval patients not receiving bevacizumab did not differ significantly from those in the pre-approval cohort (**Figure S1**).

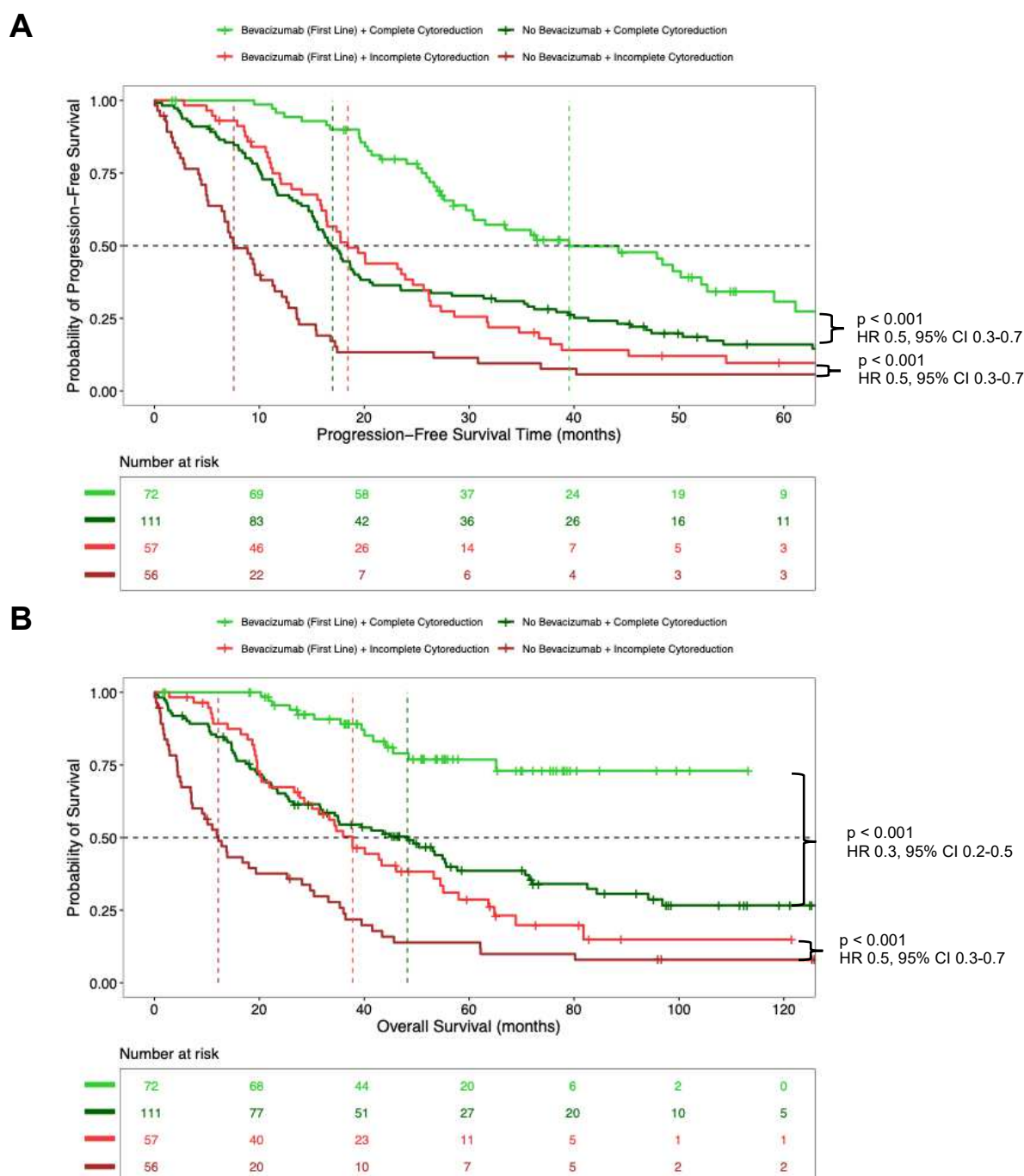


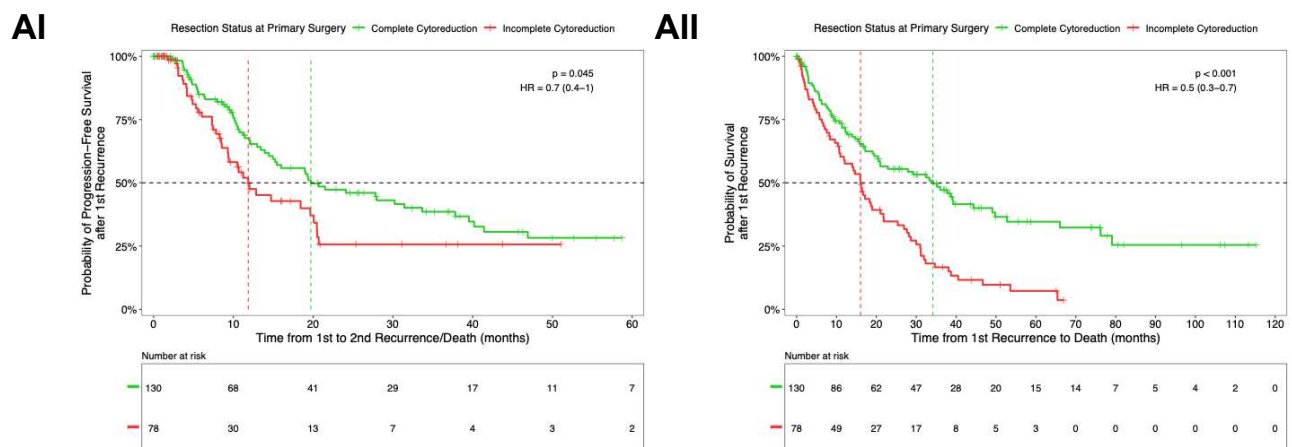
Fig. 4 Progression-free and overall survival in patients with FIGO stage III-IV disease according to bevacizumab maintenance therapy, stratified by resection status. Bevacizumab maintenance therapy was associated with significantly improved PFS (**A**) and OS (**B**), irrespective of resection status at primary surgery (complete or incomplete cytoreduction).

Prognostic Impact of Surgical Outcome Across Successive Recurrence Landmarks

We next evaluated whether primary surgical outcome remained prognostic across up to four subsequent treatment lines. Complete gross tumor resection at primary surgery was associated with longer PFS (**Figure 2 AI, BI, CI**) and OS (**Figure 2 AII, BII, CII**) from initial surgery, and survival differences remained detectable after recurrence.

Patients who achieved complete gross tumor resection at primary surgery had a median PFS from first recurrence of 19.7 (15.2-37.8) months, compared with 11.9 (9.4-20.5) months after residual disease ($p = 0.045$; **Figure 5 AI**). After first recurrence, median OS was 34.2 (20.9-49.8) months in patients with complete gross tumor resection at primary surgery, compared to 16.0 (11.9-21.8) months in patients with postoperative residual disease ($p < 0.001$; **Figure 5 AII**). This difference persisted after second recurrence, with a median OS of 22.7 (12.8-29.8) versus 9.0 (8.4-16.4) months, respectively ($p = 0.002$; **Figure 5 AIII**), and after third recurrence, with a median OS of 14.7 (9.3-26.6) versus 6.3 (3.8-9.9) months, respectively ($p < 0.001$; **Figure 5 AIV**).

A similar pattern was observed after secondary cytoreductive surgery. Patients who achieved complete gross tumor resection had a median PFS from subsequent recurrence of 46.9 (33.67-NR) months, compared with 17.3 (11.43-NR) months after residual disease ($p < 0.001$; **Figure 5 BI**). OS from first recurrence followed the same pattern: median OS was NR in patients with complete gross tumor resection at secondary cytoreductive surgery, compared to 20.4 (4.4-NR) months in patients with postoperative residual disease ($p < 0.001$; **Figure 5 BII**). Among patients who experienced a second recurrence, complete gross tumor resection at secondary cytoreductive surgery was also associated with longer OS calculated from the time of second recurrence, with a median OS of 58.1 (58.1-NR) months compared to 14.2 (8.5-NR) months in patients with postoperative residual disease ($p = 0.002$; **Figure 5 BIII**).



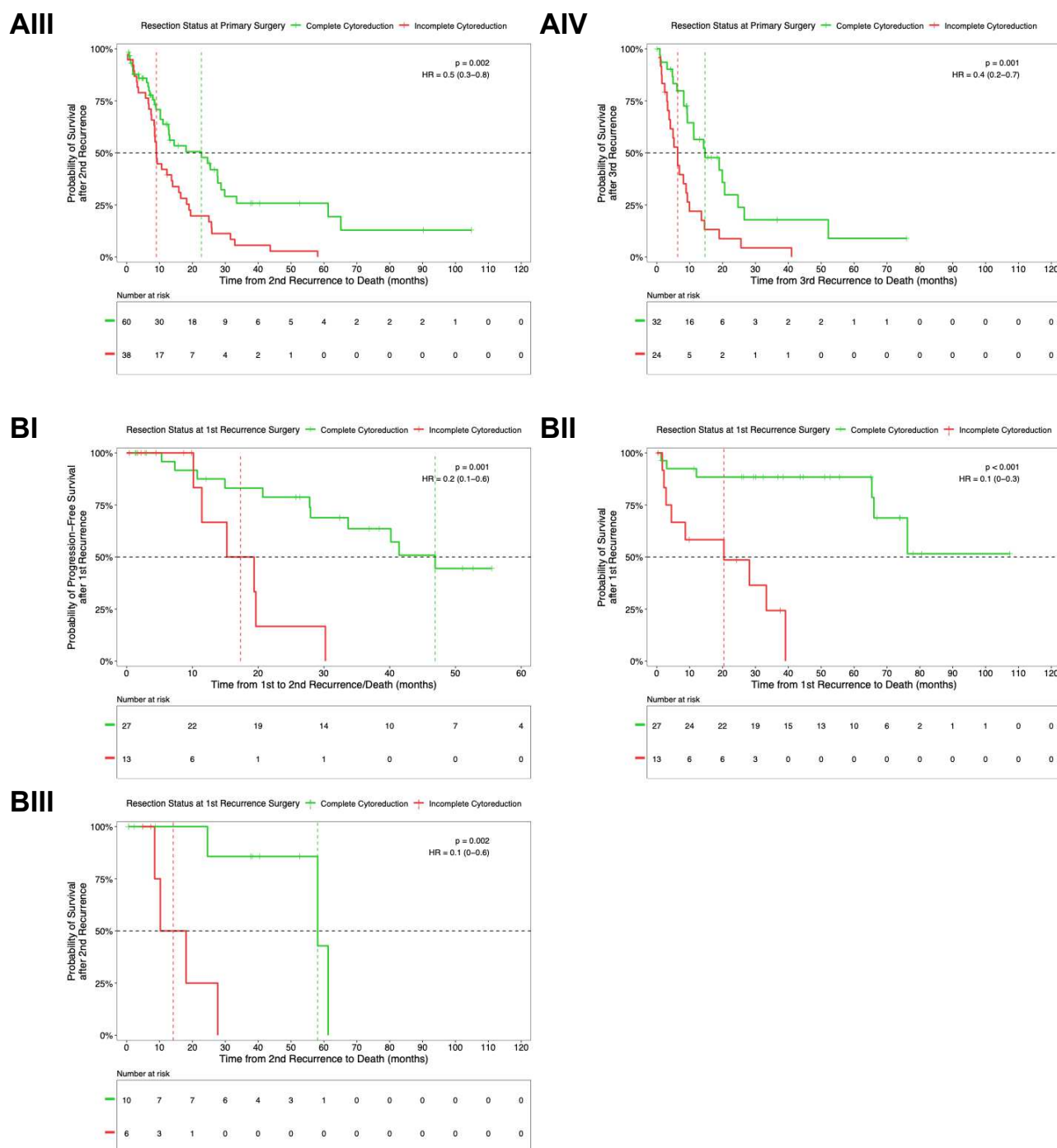


Fig. 5 Prognostic relevance of resection status for survival across recurrence landmarks. Complete gross tumor resection at primary surgery (**A**) was associated with longer PFS calculated from first recurrence (**I**) and longer OS calculated from first (**II**), second (**III**), and third recurrence (**IV**). Complete gross tumor resection at secondary cytoreductive surgery (**B**) was associated with longer PFS (**I**) and OS (**II**) calculated from first recurrence, as well as longer OS calculated from second recurrence (**III**).

In multivariable Cox regression analysis, complete cytoreduction in primary surgery was confirmed to be an independent predictor of prolonged PFS from the time of primary surgery ($p < 0.001$; **Table S1**). It was also independently associated with improved OS calculated from

the time of primary surgery ($p < 0.001$; **Table S2**), as well as from first recurrence ($p = 0.02$; **Table S3**).

Discussion

We established a clinically annotated TMA platform of 524 consecutive patients with EOC treated at a large tertiary gynecologic oncology center. It integrates clinicopathologic characteristics, detailed surgical and systemic treatment data, and longitudinal outcomes with matched tumor tissue, including recurrent samples, and an extensive PDO biobank. The cohort reproduced expected prognostic patterns for FIGO stage, complete gross tumor resection, and first-line treatment. It also demonstrated that surgical outcome can be analyzed across recurrence-specific survival landmarks.

The cohort's clinicopathologic composition supports its translational relevance. High-grade serous ovarian carcinoma accounted for 79.2% of tumors, consistent with its expected distribution [23]. Low-grade serous, endometrioid, and clear cell carcinomas accounted for 5.0%, 4.6%, and 4.2%, respectively, consistent with their minority contribution [1]. FIGO stage III and IV disease accounted for 60.5% and 17.9%, broadly comparable with the 51% and 29% reported for serous ovarian carcinomas by Torre et al. [1].

Surgical characteristics also support dataset quality. Complete gross tumor resection in this unselected real-world cohort was achieved in 60.2% of patients with FIGO stage III–IV disease undergoing upfront surgery, in line with reported resection rates like the TRUST study (ENGOT ov33 / AGO-OVAR OP.7). The same holds true for the median operating time, which was 384 minutes in our cohort. Because TRUST required predefined surgical quality and accreditation standards for advanced OC surgery, our real-world observation is encouragingly consistent with these benchmarks [7, 24].

Survival also followed expected stage-dependent patterns. Median OS was 46.1 months in FIGO stage III and 28.6 months in stage IV disease, consistent with the corresponding medians of 43 and 29 months reported by Westin et al. in a US real-world cohort [25].

Complete gross tumor resection at primary surgery was strongly associated with survival in FIGO stage III–IV disease. Median OS was 70.7 months after complete gross tumor resection and 21.9 months with residual disease. Similarly, the pooled AGO-OVAR/GINECO analysis from prospective randomized trials by du Bois et al. reported a median OS of 99.1 months after complete resection, 36.2 months with residual disease of 0.1–1 cm, and 29.6 months with residual disease >1 cm. The absence of a significant difference between residual tumor <1 cm and >1 cm in our cohort further supports the concept of complete gross resection as the clinically relevant surgical goal [4].

Systemic treatment analyses provided additional internal validation. First-line platinum-based chemotherapy was associated with longer PFS and OS irrespective of surgical outcome, while bevacizumab maintenance was associated with longer PFS and OS in both surgical strata. Median PFS with versus without bevacizumab was 39.5 versus 17.0 months after complete gross tumor resection and 18.4 versus 7.6 months with residual disease. These differences exceeded those reported in ICON7, where median PFS was 19.0 versus 17.3 months [26], and GOG-0218, which showed an approximately 4-month extension with bevacizumab continuation [10]. The larger apparent effect in our cohort likely reflects treatment-selection and guarantee-time bias because maintenance requires progression-free completion of induction and is preferentially administered to fitter patients without contraindications, such as thromboembolic events, impaired wound healing or bowel surgery complications. The PFS and OS advantage persisted relative to the pre-approval cohort, which was not selected for bevacizumab eligibility, but this comparison does not address guarantee-time bias; residual confounding remains likely.

Beyond benchmark validation, we confirmed that surgical outcome remained prognostic across successive recurrences. DESKTOP III (AGO-OVAR OP.4) established the clinical relevance of recurrence surgery by showing longer OS with secondary cytoreductive surgery followed by chemotherapy than with chemotherapy alone in appropriately selected patients [6].

In our cohort, complete gross tumor resection at primary surgery remained associated with longer OS from the first, second, and third recurrences. Complete gross tumor resection at secondary cytoreductive surgery was associated with longer PFS and OS from the first recurrence and longer OS from the second. It is important to note that these recurrence-landmark analyses may be distorted because subgroup sizes decreased at later landmarks, some CIs were wide, and the relevance of repeated surgery on subsequent treatment could not be assessed independently because surgical outcomes across successive procedures were interrelated. Furthermore, incomplete ASA documentation resulted in the exclusion of some patients from the Cox regression analyses. Nevertheless, the consistent associations across landmarks support this platform for hypothesis generation across longitudinal disease states.

Strengths include the consecutive patient cohort from a center with defined surgical quality metrics, detailed longitudinal annotation across treatment lines and recurrence stages, and a complete gross tumor resection rate (60.2%) at benchmark [27]. The platform also links real-world outcomes to systematically curated tumor tissue, including paired primary and recurrent samples in a subset, and an extensive PDO biobank.

This TMA and clinical database platform extends beyond a static tissue resource by longitudinally linking surgical quality, systemic treatment, survival, and tumor biology throughout the ovarian cancer course. It provides a strong foundation for translational research, biomarker discovery, and clinically anchored hypothesis generation.

Supplements

Figure S1:

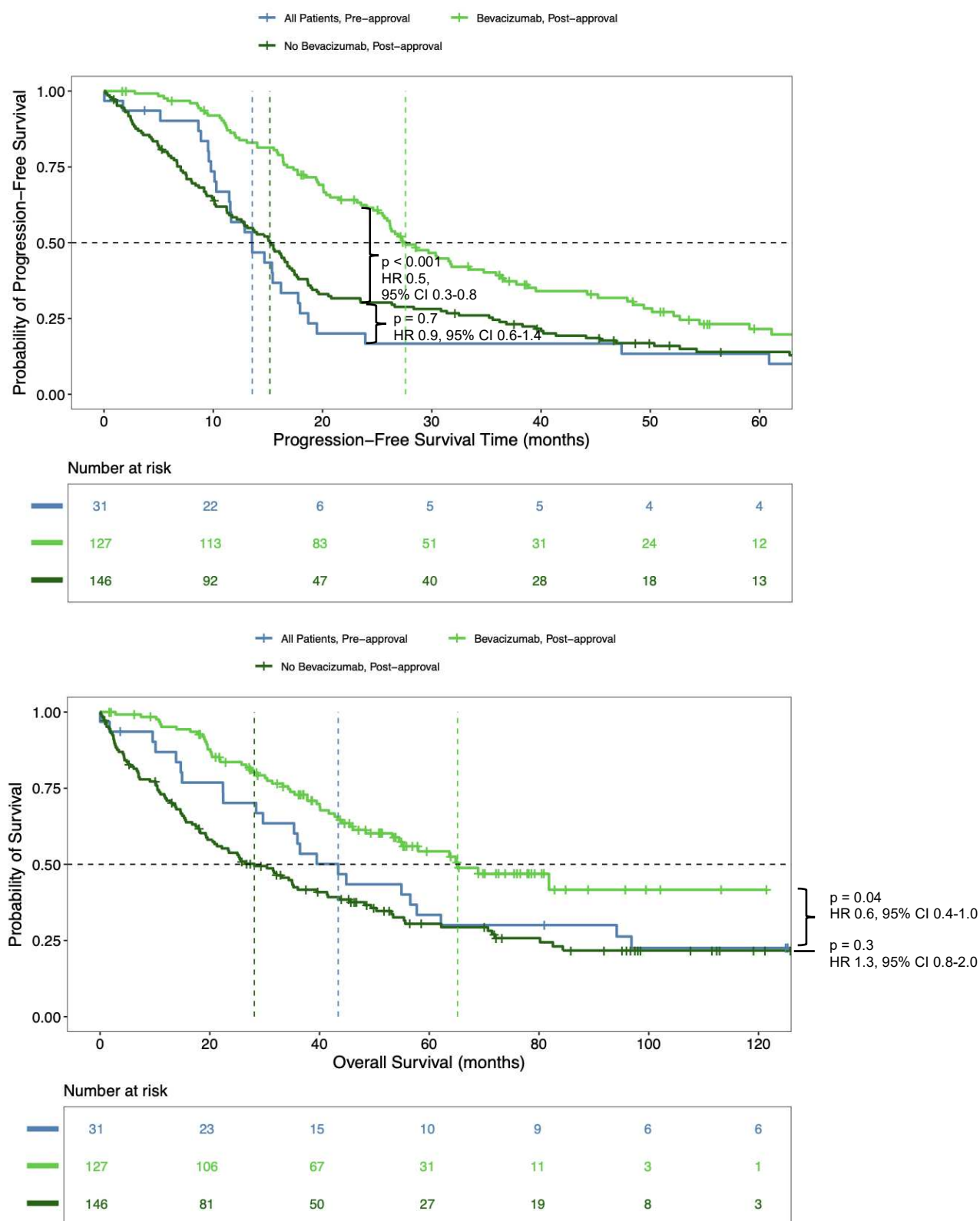


Fig. S1 Kaplan-Meier estimates of (A) progression-free and (B) overall survival by treatment period. Patients treated before bevacizumab approval (none bevacizumab-exposed) and post-approval patients with and without bevacizumab maintenance.

Table S1:

Variable	HR	95% CI		p value
		Lower	Upper	
Resection Status at Primary Surgery (<i>Ref: Incomplete gross tumor resection</i>)	0.47	0.34	0.65	<0.001
Age at Primary Diagnosis (continuous)	1.02	1.00	1.03	0.021
Platinum (First Line)	0.26	0.15	0.43	<0.001
Bevacizumab (First Line)	0.5	0.36	0.69	<0.001
FIGO Stage (<i>Ref: FIGO III</i>)				
FIGO IV	1.49	1.05	2.11	0.026
ASA (continuous)	1.37	1.04	1.80	0.024

Table S1: Multivariable Cox regression analysis for PFS in patients with FIGO stage III-IV disease identified primary resection status, age at diagnosis, platinum-based chemotherapy, bevacizumab treatment, FIGO stage and ASA Score as independent predictors of progression to first recurrence or death.

Table S2:

Variable	HR	95% CI		p value
		Lower	Upper	
Resection Status at Primary Surgery (<i>Ref: Incomplete gross tumor resection</i>)	0.35	0.25	0.51	<0.001
Age at Primary Diagnosis (continuous)	1.03	1.01	1.05	0.003
Platinum (First Line)	0.22	0.13	0.39	<0.001
Bevacizumab (First Line)	0.37	0.25	0.54	<0.001
FIGO Stage (<i>Ref: FIGO III</i>)				
FIGO IV	2.00	1.36	2.92	<0.001
ASA (continuous)	1.61	1.17	2.20	0.003

Table S2: Multivariable Cox regression analysis for OS from primary surgery in patients with FIGO stage III-IV disease identified primary resection status, age at diagnosis, platinum-based chemotherapy, bevacizumab treatment, FIGO stage and ASA score as independent predictors of survival.

Table S3:

Variable	HR	95% CI		p value
		Lower	Upper	
Resection Status at Primary Surgery (<i>Ref: Complete Cytoreduction</i>)	0.05	0.00	0.57	0.017
Resection Status at Secondary Surgery (<i>Ref: Complete Cytoreduction</i>)	0.06	0.01	0.36	0.002
Age at Primary Diagnosis	0.98	0.91	1.05	0.540
Platinum (First Line)	0.28	0.01	6.34	0.423
Bevacizumab (First Line)	0.71	0.16	3.25	0.664
FIGO Stage (<i>Ref: FIGO III</i>)				
FIGO IV	11.0	1.84	65.6	0.009
ASA (continuous)	0.56	0.08	3.77	0.55

Table S3: Multivariable Cox regression analysis for OS following secondary surgery for first recurrence identified complete gross tumor resection at primary and secondary surgery and FIGO stage as independent predictors.

Author Contribution

FBT Kraus: Data collection and management, Data analysis, Manuscript writing and editing

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Statements and Declarations

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Competing Interests

Financial interest: FBTK participated in the GynOnco Barcamp hosted by AstraZeneca. AB has participated in advisory boards and received honoraria from AstraZeneca, Roche, and Tesaro/GSK. BC has received speaker and advisory board honoraria from AbbVie, AstraZeneca, and MSD. SM has received lecture fees, research grants, honoraria, and congress and travel support from AbbVie, AstraZeneca, Clovis, Daiichi, Eisai,

GlaxoSmithKline, Hubro, ImmunoGen, Medac, MEDiSTRAVA (an Inizio company), MSD, Novartis, Nykode, Olympus, PharmaMar, Pfizer, Roche, Seagen, Sensor Kinesis, Teva, and Tesaro. FT has received research support from AstraZeneca and SAGA Diagnostics and honoraria from AbbVie, AstraZeneca, Eisai, GSK, ImmunoGen, and MSD. All reported relationships were outside the submitted work. The remaining authors declare that they have no relevant financial or non-financial interests to disclose.

Author Contributions

FBTK: Protocol/project development, data collection and management, data analysis, manuscript writing/editing. CS: Data collection and management, data analysis. LK: Data management, data analysis. DdB: Data management, data analysis. CVT: Data collection and management. NET: Data collection and management. AV: Data collection and management. MK: Manuscript writing/editing. FK: Manuscript writing/editing. AB: Data collection and management. DM: Data collection and management. BC: Data collection and management. SM: Protocol/project development, data management, data analysis, manuscript writing and editing. FT: Protocol/project development, data management, data analysis, manuscript writing and editing. All authors reviewed and approved the final manuscript.

Ethics approval

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of the Ludwig-Maximilians-University (No 22-0257).

Consent to participate

The requirement for individual informed consent was waived by the Ethics Committee of the Ludwig-Maximilians-University (No 22-0257).

Data availability statement

The data used in this study are available from the corresponding author upon reasonable request, subject to approval by the responsible institution.