

BACKGROUND and PURPOSE of the STUDY

- Ovarian cancer (OC) still has the highest mortality rate of all gynecological malignancies, diagnosed mostly at advanced stages, resulting in a generally poor outcome. Radical tumor debulking, followed by platinum-based chemotherapy with/without bevacizumab and with/without PARP inhibitors is the standard of care in advanced OC.
- Nevertheless, the majority of patients will ultimately relapse due to the development of platinum resistance. Efforts to apply immunotherapy has been less successful, however, immunologic processes play an important role in tumorigenesis and therapy response.

In view of biomarker research to identify patients at high risk for relapse,

we here determined cytokine/chemokine/immune-related marker levels in blood samples of primary, non-metastatic, high grade serous (HGS) OC patients before and after platinum-based chemotherapy to estimate their value with regard to overall survival (OS), progression-free survival (PFS), and platinum resistance.

PATIENTS and METHODS

- Plasma samples of 53 primary HGSOC patients, the majority of them diagnosed between 2019 and 2022, were collected prior (n=53) and following platinum-based chemotherapy (n=27) with/without bevacizumab.
- Cytokine/chemokine/immune-related marker levels were quantified using the Olink Target 48 Cytokine panel and Immune Surveillance Panel (LuminoDx, San Diego, USA), which includes a total of 89 immune-related proteins and requires only 1 µL of sample.
- Correlation between cytokine/chemokine/immune-related marker levels and OS as well as PFS was assessed using the Cox proportional hazards model and Log-rank test, and platinum resistance was evaluated using the student's t-test.

FIGURE 1. Patient Cohort

53 primary, non-metastatic HGSOC patients were enrolled.

Exclusion criteria:

- Non-serous histology,
- Metastatic disease
- Insufficient sample quality
- Missing follow-up data

Final cohort:
53 patients included
Baseline samples: n=53
Post-therapy samples: n=27

SUMMARY and CONCLUSION

Plasma cytokine profiling in HGSOC patients demonstrates prognostic value for OS, PFS and platinum resistance.

- Baseline Associations:**
OS: Lower IL17A, IL19, VEGFA, and IL27 levels, as well as higher FASLG levels, were significantly associated with a longer OS ($p < 0.01$), [FIGURE 2](#).
PFS: Lower IL19 levels and higher FASLG and CEACAM5 levels were significantly associated with an improved PFS ($p < 0.01$), [FIGURE 3](#).
- Platinum Response:**
Higher baseline IL19 and IL6 levels were associated with *platinum resistance* ($p < 0.05$). Higher baseline CXCL12 and IL18 levels were associated with *platinum sensitivity* ($p < 0.05$), [FIGURE 4](#).
- Longitudinal (Follow-up) Associations:**
Increasing VEGFA levels over time were significantly associated with a longer OS, [TABLE 1](#).
Declining FASLG and CEACAM5 levels over the course of treatment correlated with a longer PFS, [TABLE2](#).

Overall Conclusion

IL19 is the only marker demonstrating statistical significance for both, PFS and platinum resistance, highlighting its potential as a key prognostic and predictive biomarker in HGSOC.

RESULTS for Baseline Associations and Platinum Resistance

FIGURE 2. Cytokine/Chemokine/Immune-related marker that significantly correlate with OS

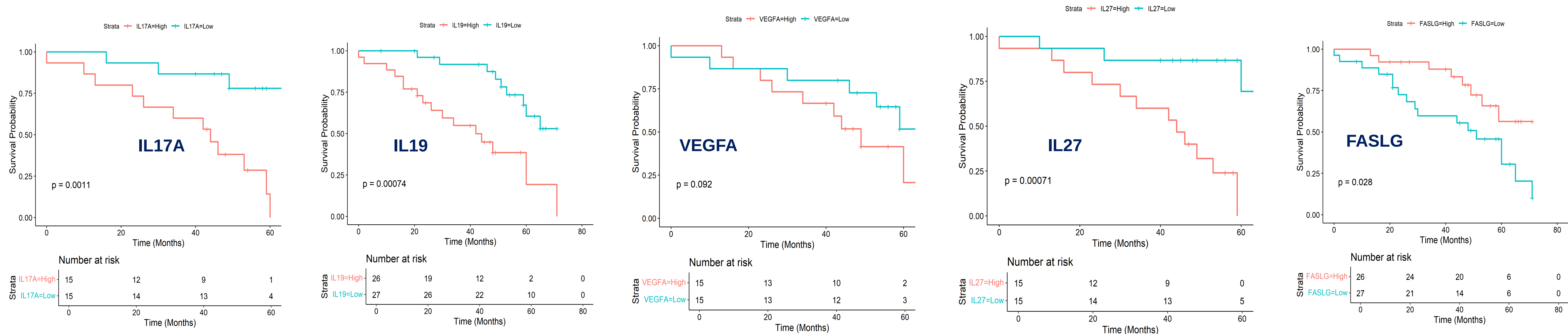


FIGURE 3. Cytokine/Chemokine/Immune-related marker that significantly correlate with PFS

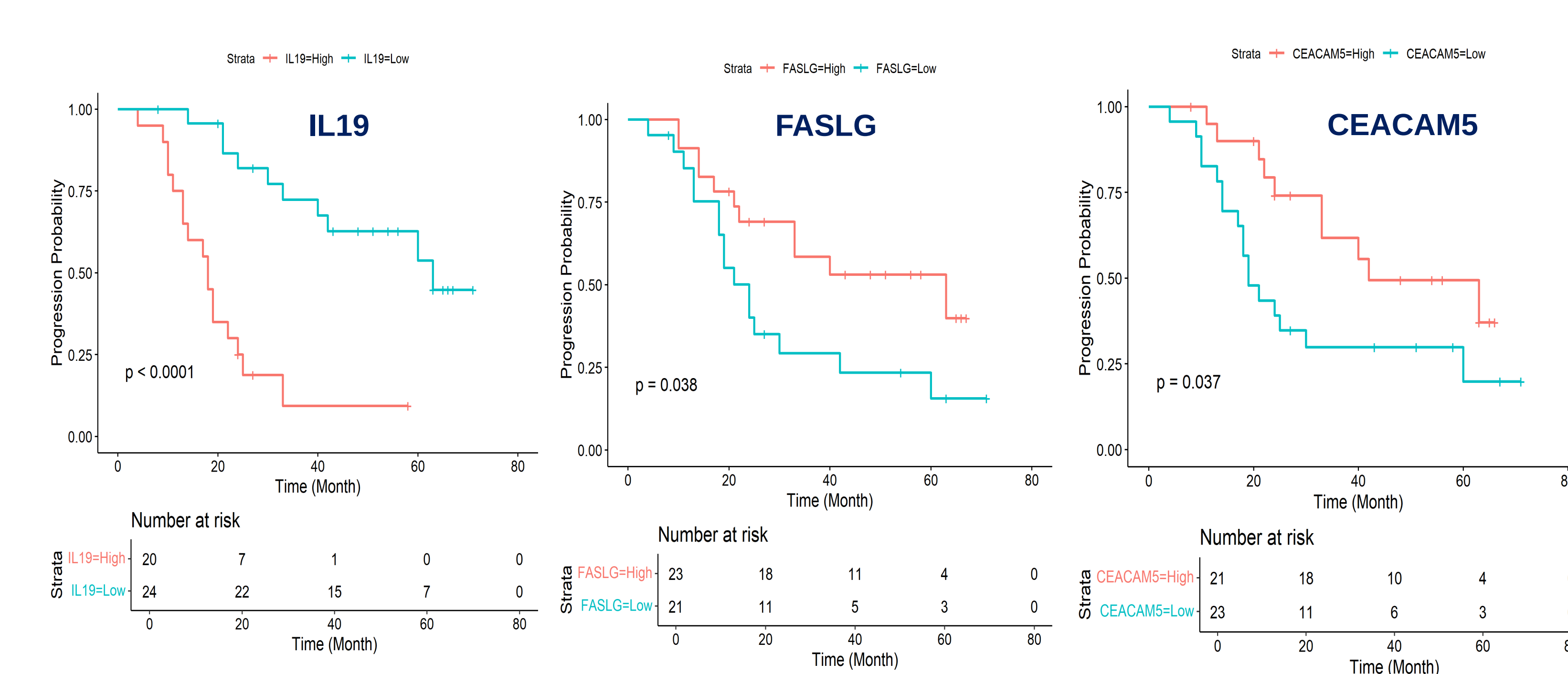
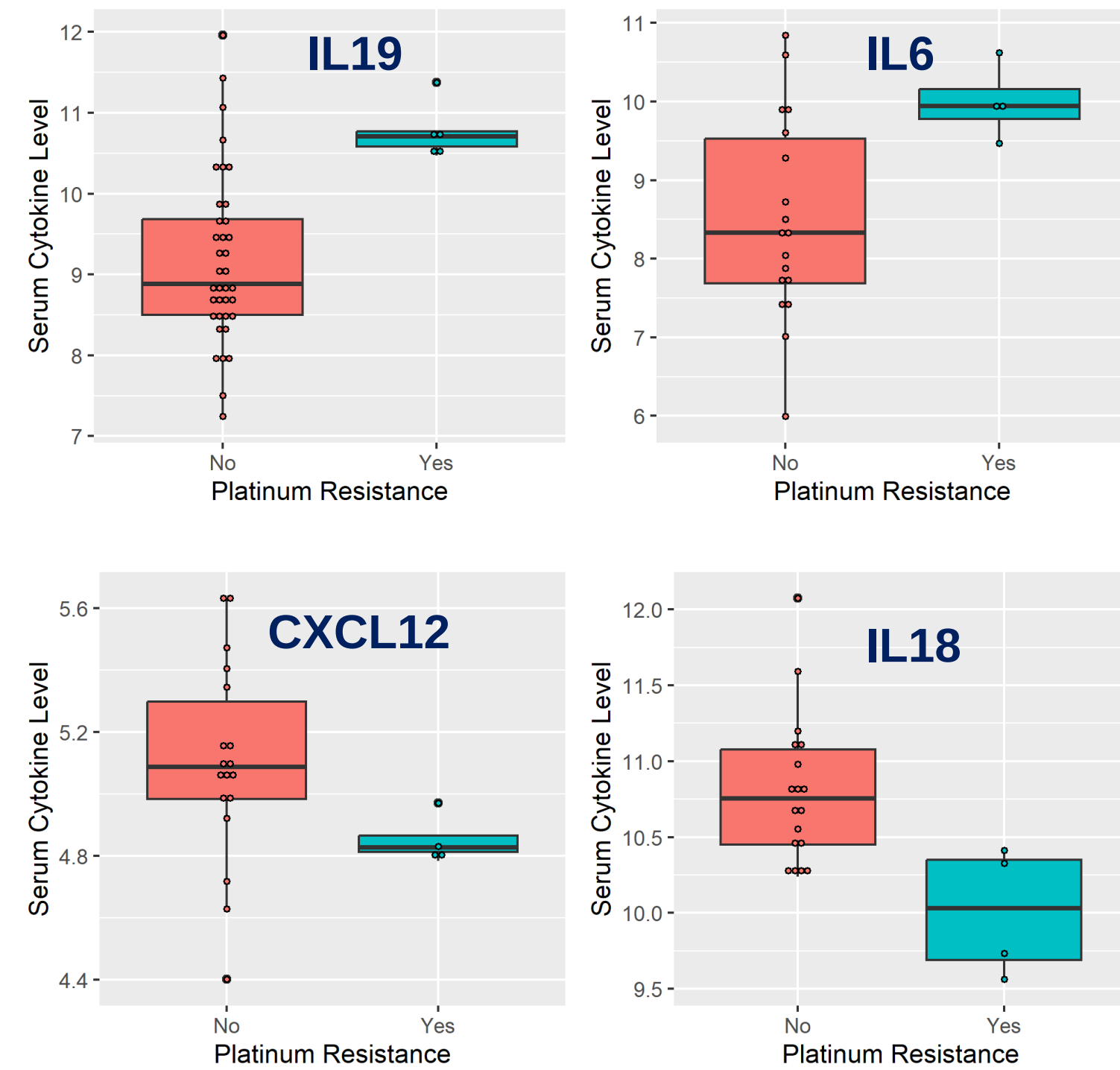


FIGURE 4. Cytokine/Chemokine/Immune-related marker that significantly correlate with platinum resistance



RESULTS for Longitudinal (Follow-up) Associations

TABLE 1. Association of Longitudinal Changes in Cytokine, Chemokine, and Immune-Related Markers with OS

Top six genes ($p < 0.05$) identified by Cox proportional hazards model

Gene Symbol	Hazard Ratio	p
FLT1	2.50	0.013
LTA	4.40	0.013
VEGFA	0.37	0.022
LAG3	3.07	0.034
CCL19	2.07	0.042
IL4R	0.53	0.048

Increasing plasma levels of FLT1, LTA, LAG3, and CCL19 levels during therapy were associated with a shorter OS, whereas increasing VEGFA and IL4R levels were associated with a longer OS.

TABLE 2. Association of Longitudinal Changes in Cytokine, Chemokine, and Immune-Related Markers with PFS

Top seven genes ($p < 0.05$) identified by Cox proportional hazards model

Gene Symbol	Hazard Ratio	p
LAG3	4.22	0.004
FASLG	3.31	0.029
IL25	1.78	0.029
LTA	3.38	0.030
IL17F	2.52	0.040
CSF2	3.50	0.045
CEACAM5	2.68	0.047

Increasing plasma levels of LAG3, FASLG, IL25, LTA, IL17F, CSF2, and CEACAM5 during therapy were associated with a shorter PFS.