Can circulating PD-1, PD-L1, BTN3A1, pan-BTN3As, BTN2A1 and BTLA levels enhance prognostic power of CA125 in patients with advanced High-Grade Serous Ovarian Cancer?

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Background: The most common subtype of ovarian cancer (OC) is the high-grade serous ovarian carcinoma (HGSOC), accounting for 70-80% of all OC deaths. Although HGSOC is a potentially immunogenic tumor, clinical studies assessing the effectiveness of inhibitors of programmed death protein and its ligand (PD-1/PD-L1) in OC patients so far showed only response rates <15%. However, recent studies revealed an interesting prognostic role of plasma PD-1/PD-L1 and other circulating immunoregulatory molecules, such as the B and T lymphocyte attenuator (BTLA), butyrophilin sub-family 3A/CD277 receptors (BTN3A), and butyrophilin sub-family 2 member A1 (BTN2A1) in several solid tumors. Since evidence showed the prognostic relevance of pretreatment serum CA125 levels in OC, the aim of our study was to investigate if soluble forms of inhibitory immune checkpoints can enhance prognostic power of CA125 in advanced HGSOC women.

Material and methods: Using specific ELISA tests, we examined the circulating PD-1, PD-L1, pan-BTN3As, BTN3A1, BTN2A1 and BTLA levels in 100 pretreated advanced HGSOC patients, correlating them with baseline CA125, age at diagnosis, BMI and peritoneal carcinomatosis. Univariate and multivariate Cox proportional hazard regression models were built to identify significant prognostic factors for Progression-free Survival (PFS).

Results: A multivariate analysis revealed that plasma BTN3A1≤4.75 ng/mL (HR: 1.94; 95% CI: 1.23 to 3.07; p=0.004), age at diagnosis ≤60 years (HR: 1.65; 95% CI: 1.05 to 2.59; p=0.03) and absence of peritoneal carcinomatosis (HR: 2.65; 95% CI: 1.66 to 4.22; p<0.0001) were independent prognostic factors for a longer PFS (≥30 months) in advanced HGSOC women. However, further analyses showed that each circulating immune checkpoints (PD-1>2.48 ng/mL, PD-L1>0.42 ng/mL, pan-BTN3As>13.06 ng/mL, BTN3A1>4.75 ng/mL, BTN2A1>5.59 ng/mL, BTLA>2.78 ng/mL) individually correlated in a statistically significant way with serum CA125>401 U/mL levels, suggesting shorter PFS (<30 months) and poor prognosis.

Conclusions:
Plasma PD-L1, PD-1, BTN3A1, pan-sBTN3As, BTN2A1 or BTLA levels could be helpful biomarkers to increase prognostic value of CA125.

Bibliography:
1.Fanale D.et al., Can circulating PD-1, PD-L1, BTN3A1, pan-BTN3As, BTN2A1 and BTLA levels enhance prognostic power of CA125 in patients with advanced High-Grade Serous Ovarian Cancer? Frontiers in Oncology (2022) In press
2. Fanale d. et al., Prognostic Role of Plasma PD-1, PD-L1, pan-BTN3As and BTN3A1 in Patients Affected by Metastatic Gastrointestinal Stromal Tumors: Can Immune Checkpoints Act as a Sentinel for Short-Term Survival? Cancers (2021)
3. Bian, B., et al. Prognostic significance of circulating PD-1, PD-L1, pan-BTN3As, BTN3A1 and BTLA in patients with pancreatic adenocarcinoma. OncoImmunology

Characteristic	No. of Patients (%)
Total patients	100
Age at diagnosis (y):	
Median: 61	
Mean: 60	
Range: 27-79	
Age groups (y)	
≤ 60	48 (48)
> 60	52 (52)
FIGO stage [a]	
IIIB	23 (23)
IIIC	52 (52)
IV	25 (25)
Histological grade	
G1/2	0 (0)
G3	100 (100)
Histological subtype	
Serous	100 (100)
Other	0 (0)
OC	
Unilateral	64 (64)
Bilateral	36 (36)
Surgery	
Surgical staging	52 (52)
Cytoreductive surgery	48 (48)
Serum CA125 levels	
≤ 401	50 (50)
> 401	50 (50)
Peritoneal carcinomatosis	
Yes	43 (43)
No	57 (57)
BMI	
≤ 25	59 (59)
> 25	41 (41)
Smoker	
Yes	23 (23)
No	77 (77)

Table 1. Clinical and pathological characteristics of advanced HGSOC patients.

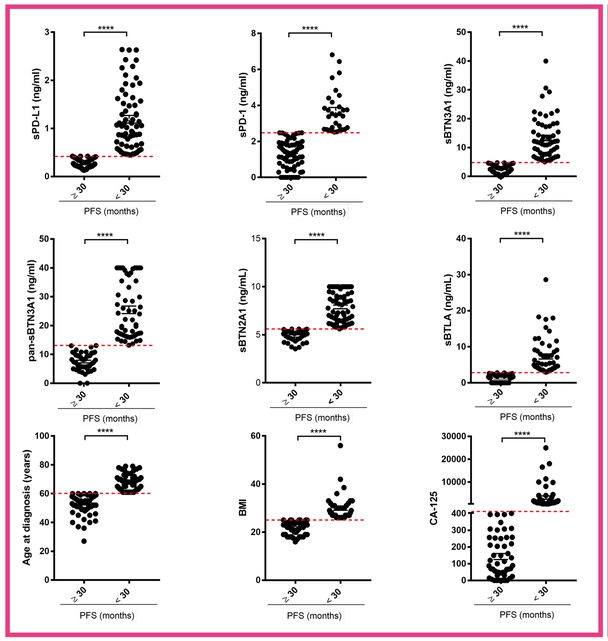

Figure 1. Scatter plots by group discriminating advanced HGSOC patients based on long versus short PFS for each examined factor.

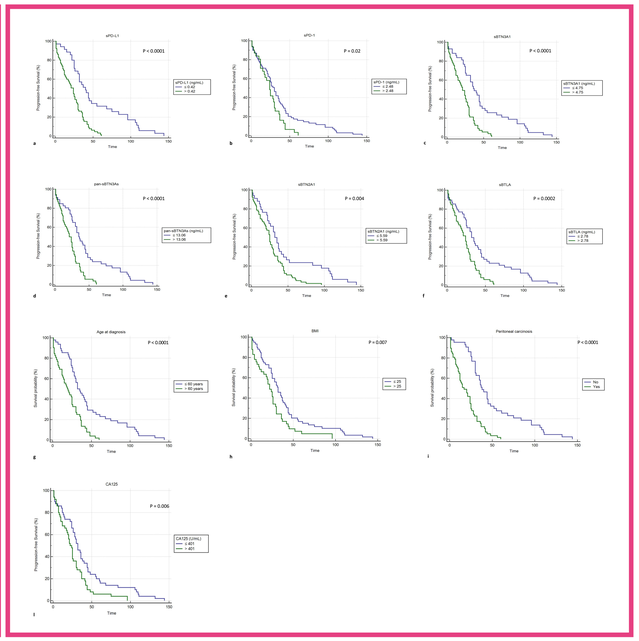

Figure 2. Kaplan-Meier analysis of progression-free survival in one-hundred advanced HGSOC patients with high and low plasma levels of a) sPD-L1, b) sPD-1, c) sBTN3A1, d) pan-sBTN3As, e) sBTN2A1 and f) sBTLA

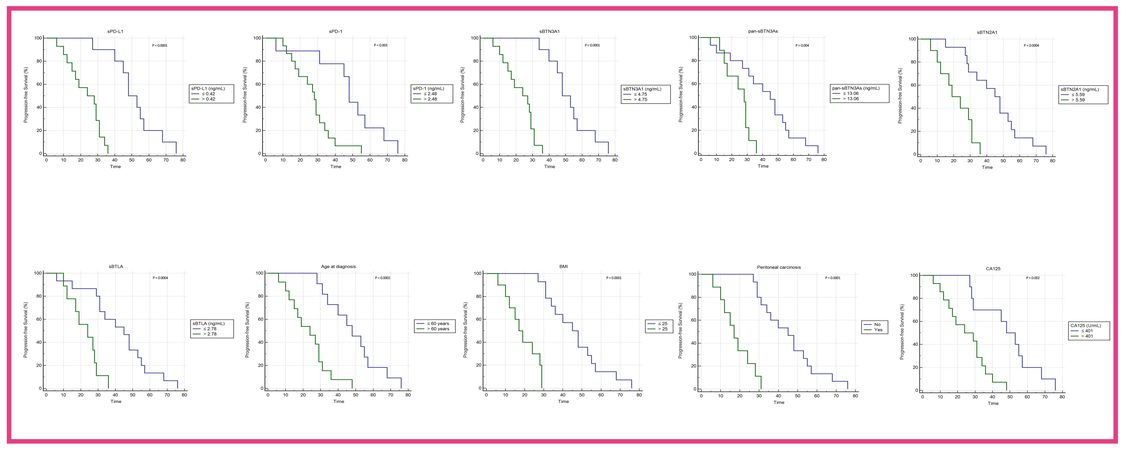

Figure 3. Kaplan-Meier analysis of progression-free survival in twenty-four advanced HGSOC patients from validation cohort.

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DISCLOSURE

The authors declare no conflict of interest