42 IL-6 AS PROGNOSTIC FACTOR IN ADJUVANT OR METASTATIC SKIN CANCER PATIENTS TREATED WITH IMMUNOTHERAPY – A DEEP BIOMARKER ANALYSIS

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Background The immune checkpoint inhibitors (ICIs) revolutionized cancer therapeutic landscape and substantially improved the survival of patients (pts) with advanced malignancies, especially in skin cancer pts.[1–5] IL-6 is a key inflammatory molecule secreted by M2 macrophages after polarization, mediating the progression of pancreatic and colorectal cancer.[6 7] The purpose of this study is to retrospectively investigate the relationships between IL-6 and outcome in skin cancer patients treated with immunotherapy.

Methods IL-6 levels were analyzed in two independent cohorts, in cohort 1 serum IL-6 were evaluated from 386 consecutive skin cancer pts before start ICIs. We included pts with unresectable/metastatic cutaneous squamous cell carcinoma (cSCC) treated with cemiplimab (n=47); pts with resected stage III/IV melanoma (n=98) treated with anti-PD1; pts with metastatic melanoma treated with anti-PD1 (n=139), combo ipi+nivo (n=65) and ipilimumab alone (n=37). IL-6 was measured by Electrochemiluminescence immunoassays (ECLIA) from Cobas C6000 (Roche). In cohort 2 we conducted a gene profile analysis with Nanostring from PBMCs of 121 metastatic melanoma pts. All pts signed informed consent. Patient's characteristics are listed in table 1. ROC curves were used to determine the best cut off. Survival rates were analyzed using the Kaplan-Meier method. Hazard Ratios (HR) and their 95% confidence intervals (CI) were estimated using a Cox regression model.

Results Among 507 pts, in cohort 1 lower serum IL-6 was associated with a better Progression Free Survival (PFS) 18.67 months (95% CI 16.6–20.7) versus 10.31 months (95% CI 8.5–12.0), HR = 0.45 (CI 0,3–0,5, p<0.0001); Overall Survival (OS) (27.59 months (95% CI 25.9–29.2) versus 20.12 months (95% CI 17.7–22.4), HR = 0.32 (CI 0,23–0,47, p<0.0001) and Overall Response Rate (ORR) (p<0.001). Similarly, IL-6 and previous therapy are associated with OS and PFS in multivariate analysis (p <0.01). We also confirmed the association between IL-6 and outcomes in all subgroups. In cohort 2 we observed a similar trend in pts with lower IL-6 expression. Moreover, higher IL-6 was associated to MAP3K12, EGFR, SELL,FPR1 genes.

Conclusions We found that lower levels of both serum and gene expression of IL-6 are associated with better OS, PFS and ORR. Furthermore, IL-6 is associated to higher expression of genes relate to cell cycle, proliferation and metastasis. Further investigations are needed to get additional information.

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Ethics Approval This study was approved by the Ethics Committee of National Cancer Institute—IRCCS—Fondazione "G. Pascale", Naples, Italy, protocol number 32/22 oss. All patients provided their written informed consent to participate in this study.

Consent Written informed consent was obtained from the patient for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

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Patient characteristics	Cohort 1 N = 386	Cohort 2 N = 121
Median age	62 (range 23-96)	62 (range 27-91)
Gender: female/male , n (%)	146/240 (38/62)	53/68 (38/62)
BRAF Status, Mutation, n (%)	126 (32)	22 (32)
Line of treatment in mtx pts	N = 288	
1st line treatment, anti-PD1	145 (38)	88 (73)
1st line treatment, anti-CTLA4	15 (4)	33 (27)
1st line treatment, ipi+nivo	28 (7)	36 (30)
1st line treatment, CSCC	40 (10)	
ORR, n (%)	48 (64)	
Adjuvant setting	N = 98	
Progression disease, n (%)	26 (27)	

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