

CD39 AFFECT THE PROGNOSTIC ROLE OF NLR VIA N2 NEUTROPHILS IN METASTATIC MELANOMA PATIENTS TREATED WITH IMMUNOTHERAPY

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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. Several predictive biomarkers are under evaluation, in order to identify patients who can benefit from ICI. Recently, elevated NLR, calculated from absolute neutrophil count and white cell count, were found to be independent predictors of reduced survival and increased risk of progression in melanoma patients receiving ICI. The purpose of this study is to retrospectively investigate relationship of NLR with inflammation-immune mediators.

Methods Gene profiling analysis was performed from 78 basal PBMCs of metastatic melanoma pts treated in first line with anti-PD1 using NanoString IO360 panel. Patient's characteristics are listed in table 1. To identify the best genes signature the Sparse Partial Least Squares Discriminant Analysis (sPLS-DA) was applied.

Results Overall, 78 patients were included in the analysis. Pts with high NLR at baseline (ratio >5.57) had a poorer PFS (HR=7.27, 95% CI = 3.57–14.8; p < 0.0001) and OS (HR=3.98; 95% CI = 2.0–7.9) than the pts with low NLR. Brain metastases were present in a higher proportion of pts with high NLR compared to those with low NLR (p=0.01). In the transcriptomic analysis, NLR was associated with SH2D1A, CD3, ZAP70, CD45RA genes, while a high NLR with CCNA1, LDHA, IL18R1, CD39, PTEN, MYD88 and MMP9 genes (ROC curve, AUC=0.97, p<0001). The signatures are also associated to response. In addition, CD39 expression is higher in NLR high and is associate with increase of N2 neutrophils. NLR increase on treatment is also associated to worse outcome and a specific genetic signature.

Conclusions NLR high is related with immunosuppressive, inflammatory and tumor related genes; in particular with N2 neutrophils associate to adenosine pathway activation. This could explain the prognostic role of NLR. Further investigations are needed to get additional information.

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Ethics Approval This study was approved by the Ethics Committee of Istituto Nazionale Tumori—IRCCS—Fondazione 'G. Pascale', Naples, Italy, protocol number 17/17 oss. All patients released informed consent to participate.

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.

Abstract 41 Table 1

Patient characteristics	N = 78
Median age	61 (range 27-91)
Gender: female/male, n (%)	41 (53)/37 (47)
Melanoma AJCC VII Stage	
Stage IV, n (%)	74 (94)
Stage IIIC	4 (5)
Stage IIIB	1 (1)
CNS metastases at baseline, n (%)	18 (23)
BRAF Status	
Wilde type, n (%)	59 (76)
Mutation, n (%)	16 (21)
NA, n (%)	3 (3)
Response rate at 1st assessment	
Complete response, n (%)	9 (11)
Partial response, n (%)	16 (21)
Stable disease, n (%)	17 (22)
Progression disease, n (%)	36 (46)
ORR, n (%)	39 (50)
DCR, n (%)	25 (32)
LDH	
High	26 (33)
Normal	34 (44)
NA	18 (23)

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