NEUTROPHIL-TO-EOSINOPHIL RATIO AS A BIOMARKER FOR CLINICAL OUTCOMES IN ADVANCED STAGE MELANOMA PATIENTS TREATED WITH ANTI-PD-1 THERAPY

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Background An association between lower neutrophil-to-eosinophil ratios (NER) and improved clinical outcomes in patients with metastatic renal cell carcinoma treated with combination ipilimumab/nivolumab (I/N) was recently reported.1 While neutrophil-to-lymphocyte ratios (NLR) and eosinophil counts have been associated with improved survival in melanoma patients treated with immunotherapy, no studies have investigated NER as a predictor of outcomes in advanced melanoma patients receiving anti-PD-1 therapy.

Methods We conducted a single-center, retrospective review of unresectable stage III and IV melanoma patients treated with anti-PD-1 monotherapy (nivolumab or pembrolizumab) or I/N between 2011 and 2022. Overall survival (OS) and progression-free survival (PFS) were measured from the first dose of treatment to date of death and clinical or radiographic progression, respectively. Treatment-related adverse events (trAEs) of grade ≥3 were also assessed. Baseline NLR and NER were measured relative to anti-PD-1 treatment start date. Change in NLR and NER from baseline were measured at 3-months follow up. Patients were divided into groups by median NLR and NER at baseline (<mNER vs ≥mNER) and analyzed for OS and PFS using univariate and multivariate analyses with Cox proportional hazard (CPH) models. Logistic regression models were used to evaluate risk differences for trAEs. The multivariate analyses accounted for the following covariates: Age, gender, anti-PD-1 therapy type, primary melanoma type, pre-treatment LDH, BRAF status, presence of brain or liver metastasis, and prior adjuvant or non-anti-PD-1 treatment for advanced-stage melanoma.

Results 190 patients were identified. Lower NER at baseline, relative to the mNER of 30.7, was associated with improved OS [HR: 0.330, 95% CI: 0.175–0.623, p=0.0006] but not PFS (table 1). Both PFS and OS differed between groups relative to the mNER and an explicit NER cut-off of 35 on univariate analysis (figure 1). Neither PFS nor OS differed between groups based on baseline NLR. A trend towards decreased grade ≥3 trAEs was associated with lower NER at baseline [OR: 0.411, 95% CI: 0.157–1.022, p=0.061]. Baseline NLR was not associated with trAEs. Change in the NLR and NER at three months relative to baseline was not associated with clinical outcomes.

Conclusions Lower pre-treatment NER is associated with improved OS in patients with advanced-stage melanoma treated with anti-PD-1 base regimens. Survival outcomes may differ with an explicit NER cut-off of 35. Higher baseline NER may be associated with high-grade trAEs. Further validation is warranted to evaluate NER as a predictive marker for clinical outcomes in melanoma patients treated with immune checkpoint inhibitors.

REFERENCES

Ethics Approval The study was approved by the University of Wisconsin institutional ethical guidelines and patients’ consents were waived following Institutional Review Board protocol review (UW21110).