PERIPHERAL LOW DENSITY NEUTROPHILS IDENTIFY A SUBSET OF NSCLC PATIENTS WITH HIGH PD-L1 TUMOR EXPRESSION THAT CAN BENEFIT FROM CHEMO-IMMUNOTHERAPY


BACKGROUND

Single agent immunotherapy (IO) has been accepted as standard frontline treatment for NSCLC with high PD-L1 expression, however most of the patients do not respond and some of them could benefit from chemothermunotherapy (CT+IT). Low-density neutrophils (LDNs) are cells with immunosuppressive activities enriched in peripheral blood of cancer patients. We have studied the association between baseline LDNs and response to IO in NSCLC.

METHODS

PBMCs from 31 patients treated with IO and 21 treated with CT+IT were purified from fresh peripheral blood. Baseline LDNs were quantified through flow cytometry, and the proportions were correlated with clinical outcomes. Plasma from patients was compared through quantitative proteomics.

RESULTS

A threshold of 7.09% LDN identified patients with DC < 6 months with a sensitivity of 83.3% and a specificity of 92.2% (ROC analysis AUC 0.895, p = 0.001). Patients with LDNs levels over this threshold had significantly shorter PFS (6.1 vs 68.1 weeks, p < 0.001). A threshold of 7.09% LDN identified patients with DC < 6 months with a sensitivity of 83.3% and a specificity of 92.2% (ROC analysis AUC 0.895, p = 0.001). Patients with LDNs levels over this threshold had significantly shorter PFS (6.1 vs 68.1 weeks, p < 0.001).

A depletion of LDNs was observed in all the patients with high LDNs levels who responded to CT+IT.

CONCLUSIONS

High baseline LDN levels are associated with primary resistance to IO monotherapy in patients with NSCLC. These patients can respond to CT+IT, thus identifying a subgroup whom should be offered this treatment regardless of high PD-L1 tumor expression. The upregulation of HGF/c-MET suggests that targeting this pathway could have synergistic effect.

D) Quantitative proteomics suggest a key role for the HGF/c-MET pathway.

Quantitative proteomics were performed comparing the plasma from patients with NSCLC and high LDNs levels and patients with NSCLC and normal LDNs proportions. A distinct proteome with upregulation of some proteins associated with the HGF/c-MET pathway were detected.

FUNDING

With the support of the “Clínico Junior 2019” Grant from AECC (Spanish Society Against Cancer)