2021 ESMO congress

LBA68

Clinical value of pre-treatment T-cell receptors (TCR) repertoire in non-small cell lung cancer (NSCLC) patients treated with single agent immunotherapy

A. Abed[1], L. Calapre[1], S. Bowyer[2], M. Millward[3], E.S. Gray[1]

[1] School of Medical and Health Sciences, Edith Cowan University, Joondalup, WA, Australia, [2] Department of Medical Oncology, Sir Charles Gairdner Hospital, Perth, WA, Australia[3] School of Medicine, University of Western Australia, Perth, WA, Australia

Background

Reduced Shannon diversity, increased clonality and increased convergence of TCRs have been suggested to reflect clonal expansion of antigen-specific T-cells in the tumour microenvironment and correlated with improved response rate (RR), progression free survival (PFS) and overall survival (OS). Moreover, increased clonality has been linked with increased risk of developing immune related toxicity. We aim to correlate TCR repertoire features with overall response rate RR, PFS, OS and adverse events in peripheral blood of NSCLC patients (with PDL1≥50%) treated with first line single agent pembrolizumab.

Methods

We prospectively collected baseline blood from 50 NSCLC patients treated with pembrolizumab. High quality DNA was extracted and TCR sequencing was performed. TCR repertoir variables were correlated with RR, PFS, OS and immune related toxicity.

Results

Our data matured for 29 patients with a follow-up of at least 18 months. We found that reduced number of unique clones and reduced Shannon diversity was associated with improved RR to pembrolizumab (P = 0.038, 0.021 respectively). 3 TCR families (TRBV6-4, TRBV10-2 and TRBV10-3) were observed to occur more frequently among non-responders comparing to responders (P=0.018, 0.046 and 0.018 respectively). Moreover, there was a significantly longer PFS in patients with reduced number of unique clones (HR = 0.40, P = 0.040), reduced Shannon diversity (HR = 0.44, P = 0.044), reduced Evenness (HR = 0.31, P = 0.033) and elevated clonality (HR = 2.45, P = 0.044). None of these parameters were statically significant in relation to OS. On the other hand, reduced evenness was associated with increased risk of immune related toxicity (P=0.017).

Conclusions

Increased pre-treatment TCR clonality and reduced diversity are associated with improved RR and PFS, but not OS in NSCLC patients with high PD-L1 treated with pembrolizumab monotherapy. Reduced eveness and increased clonality was correlated with increased risk of immune related adverse events. Further maturation of this cohort will demonstrate whether the circulating pre-treatment TCR repertoire is a prognostic factor for immune checkpoint inhibition.

Legal entity responsible for the study

The authors.

Funding

The Australasian Lung Cancer Trials Group.

Disclosure

All authors have declared no conflicts of interest.