Session PO.IM02.04 - Immune Monitoring / Clinical Correlates

5705 / 11 - The key role of kynurenine in anti-PD-1 failure

Add To My Itinerary

April 18, 2018, 8:00 AM - 12:00 PM | Section 32

Presenter/Authors

Andrea Botticelli[1], Bruna Cerbelli[2], Luana Lionetto[1], Ilaria Zizzari[2], Annalina Pisano[2], Michela Roberto[1], Elisa Onesti[1], Francesca Romana DI Pietro[1], Chiara Napoletano[2], Laura Pizzuti[3], Patrizia Vici[3], Giulia D'Amati[2], Federica Mazzuca[1], Maurizio Simmaco[1], Marianna Nuti[2], Paolo Marchetti[1]. [1]Sant'Andrea Hospital, Sapienza University of Rome, Rome, Italy; [2]Sapienza University of Rome, Rome, Italy; [3]Division of Medical Oncology 2, Regina Elena National Cancer Institute, Rome, Italy, Rome, Italy

Disclosures

A. Botticelli: None. **B. Cerbelli:** None. **L. Lionetto:** None. **I. Zizzari:** None. **A. Pisano:** None. **M. Roberto:** None. **E. Onesti:** None. **F. DI Pietro:** None. **C. Napoletano:** None. **L. Pizzuti:** None. **P. Vici:** None. **G. D'Amati:** None. **F. Mazzuca:** None. **M. Simmaco:** None. **M. Nuti:** None. **P. Marchetti:** None.

Abstract

Background: Immune checkpoint inhibitors have revolutionized treatment and outcome of severe and often fatal disease, as metastatic lung cancer, demonstrating long-term tumor control and extended patient survival. Unfortunately, only 25-30% of patients have a long-term benefit from immunotherapy, while the remaining 70-75% demonstrate primary or acquired resistance. Recently, indoleamine 2,3-dioxygenase (IDO) has been proposed as a possible mechanism of resistance to anti-PD1 treatment. Indeed, IDO catalyzes the degradation of tryptophan (Trp) into kynurenine (Kyn), which seems to enhance the activity of Treg, leading to an immunosuppressive microenvironment.

Methods: The serum concentrations of Trp and Kyn were measured by high-performance liquid chromatography tandem mass spectrometry in 26 patients affected by non-small cell lung cancer (NCLSC) before the start of the second-line therapy with nivolumab. The IDO activity was expressed with Kyn/Trp ratio. The associations between Kyn/Trip ratio and early progression, PS, age, sex, brain metastases and pleural effusion were analyzed using Spearman test and Mann Whitney test.

Results: 14 out of 26 patients (54%) presented early progression (defined as progression of the disease within 6 months from the beginning of nivolumab treatment). The median value of Kyn/Trp ratio was 0.073 (0.024-0.18). We found a significant association between Kyn/Trp ratio and early progression (p= 0.009), while no statistical associations were found between Kyn/Trp ratio and PS, age, sex, brain metastases and pleural effusion. Indeed, patients with early progressive disease presented a median value of Kyn/Trp ratio significantly higher than other patients (0.094 vs 0.052; p= 0.01).

Conclusion: The pretreatment evaluation of IDO activity, expressed as Kyn/Trp ratio, seems to be associated with response to immunotherapy. In particular, higher Kyn/Trp ratio could predict resistance to anti-PD-1 treatment. These preliminary results suggest the possibility of using anti-PD-1 plus IDO inhibitor in patients with high level of Kyn/Trp ratio.