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Session MINI ORAL 15 - Cellular and Molecular Pathways to CLAD

355 - Immune Checkpoint Espression Associates with Rejection in Lung Transplant Recipients

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Authors

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Disclosures

I. Righi: None. **V. Vaira:** None. **L. Rosso:** None. **L. Morlacchi:** None. **M. Cattaneo:** None. **S. Ferrero:** None. **F. Blasi:** None. **M. Nosotti:** None. **M. Clerici:** None.

Abstract or Presentation Description

Purpose: The outcome of lung transplantion (LuTx) suffers from a high rejection rate, and there are still huge gaps of knowledge about immune-mediated rejection mechanisms. Acute rejection (AR) can lead to chronic lung allograft dysfunction (CLAD), the main cause of poor survival and low quality of life. The standardized morphologic evaluation of rejection is based on histopathologic diagnostic criteria at a given time-point, but it has a limited prognostic value towards clinical outcome and the likelihood to develop CLAD. We analyzed immune-check point proteins in lung tissues of patients who received a LuTx and who were or were not undergoing rejection in the attempt to define novel immunological markers that could predict rejection.

Methods: We conducted an observational retrospective study on eight consecutive explanted grafts for chronic rejection and on transbronchial cryobiopsies (TCB) obtained from 24 consecutive patients during the first year LuTx follow-up. A broad spectrum of immunohistochemical analysis was carried out (PD1/CD279, PDL1/CD274, CTLA4/CD152, CD4, CD8, hFoxp3, TIGIT, TOX, B-Cell-Specific Activator Protein). Of those TCB-patients we recorded at least 1 year follow up of survival, infections and rejections (acute and chronic) rate.

Results: Exhausted (PD1+/TOX+) as well as Treg (PD1+/FOXP3+) lymphocytes were significantly reduced in restrictive allograft syndrome (RAS)-compared to bronchiolitis-obliterans-syndrome (BOS)-rejected lungs. PD1-expressing T-lymphocytes in TCBs correlated (sensitivity 0.69; specificity 1) with the presence of AR and were highly suggestive of CLAD development (sensitivity 0.86; specificity 0.82; overall 10 times higher risk of developing CLAD) at one-year follow-up.

Conclusion: Results herein for the first time show the importance of immunological checkpoints in the setting of LuTx rejection and indicate that the evaluation of the expression of such proteins could offer a distinct prognostic advantage in monitoring the onset of AR in patients who underwent LuTx. Longitudinal analyses in ampler cohorts will be needed to confirm these data.