

European Respiratory Society Annual Congress 2013

Abstract Number: 4398

Publication Number: P2683

Abstract Group: 8.2. Transplantation

Keyword 1: Transplantation **Keyword 2:** Bronchiolitis **Keyword 3:** No keyword

Title: De novo anti-HLA immunization after lung transplantation: Immunological monitoring and clinical significance

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Body: Introduction: Development of de novo (DN) anti-HLA antibodies (Abs) leads to chronic graft dysfunction and lower survival in most solid organ transplant but still stays elusive in lung transplantation (LTx). This study assesses the influence of DN anti-HLA immunization on occurrence and severity of bronchiolitis obliterans syndrome (BOS), and survival after LTx. Methods: Retrospective study including 66 LTx patients. We determined 3 groups: patients with DN anti-HLA donor specific Abs (DSA) (group 1, n=17), patients with DN anti-HLA non-donor specific (NDS) Abs (group 2, n=7), and non-anti-HLA immunized patients (group 3, n=42). After immunological analysis, we compared FEV1 monitoring curves, survival with and without BOS (Kaplan-Meier, log rank), and incidences of acute cellular rejection (ACR), lower respiratory infection (LRI) and bronchial stenosis (BS) (Fischer's Test, Chi-2, ANOVA). Results: Anti-HLA DSA and NDS Ab were diagnosed 25 (5-156) and 36 (13-50) days after LTx and were detected during 136 (7-462) and 76 (1-458) days respectively. Mean and maximum Abs rates increased in group 1 compared to group 2 (p<0,05). FEV1 decreased soon 4 post-LTx months in group 2, 10 months in group 1, and 12 months in group 3. FEV1 decreased in group 1 compared to group 3 (p = 0,03). Mean delays between LTx and BOS diagnosis in group 1 and group 3 were 12 (2-22) and 19 (6-30) months respectively. BOS incidences (BOS 0p and BOS 1) increased in group 1 compared to group 3 (p < 0,05). DN anti-HLA Abs affects neither survival nor the incidences of ACR, LRI and BS. Conclusion: DN anti-HLA immunization is related to early onset of FEV1 decline. DN anti-HLA DSA lead to humoral rejection.