High circulating CD4+CD25[hi]FOXP3+ T cell subpopulation early after lung transplantation is associated with development of BOS

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Context

Chronic Bronchiolitis Obliterans Syndrome (BOS) remains a major limitation for long-term survival after lung transplantation. The immune mechanisms involved and predictive biomarkers have still to be identified.

The purpose of this study was to assess whether the peripheral blood T-lymphocyte profile could predict BOS in lung transplant recipients.

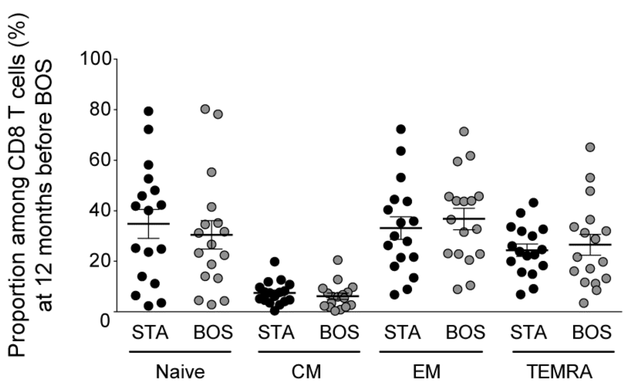
Material

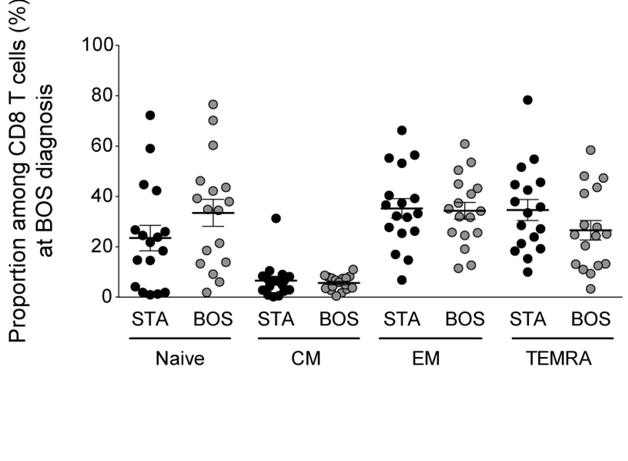
An in-depth profiling of CD4 and CD8 T cells was prospectively performed on blood cells from stable and BOS patients from the COLT cohort with a longitudinal follow-up. Samples were analyzed at 1 and 6 months after transplantation, at the time of BOS diagnosis, and at an intermediate time point at 6 to 12 months before BOS diagnosis.

Results

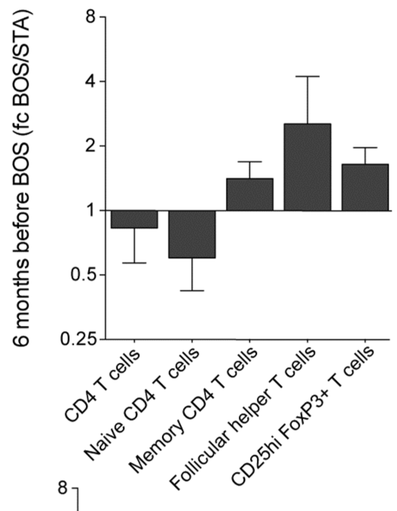
No difference in the CD4 and CD8 T cells profile at the BOS diagnosis and months before.

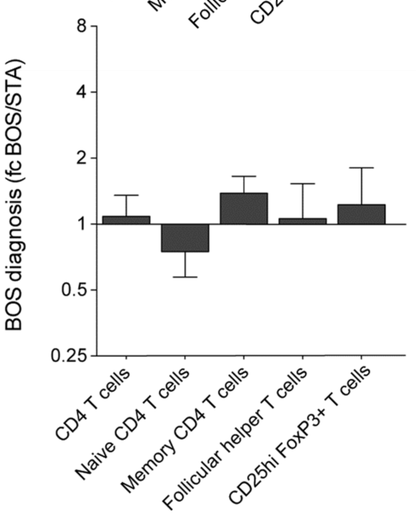
CD8 T cell profile





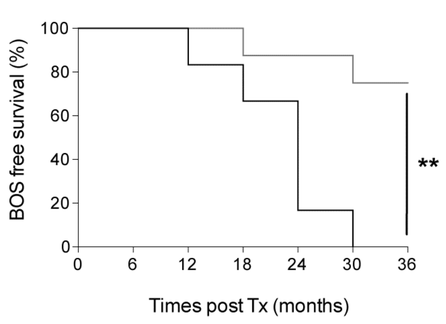
CD4 T cell profile

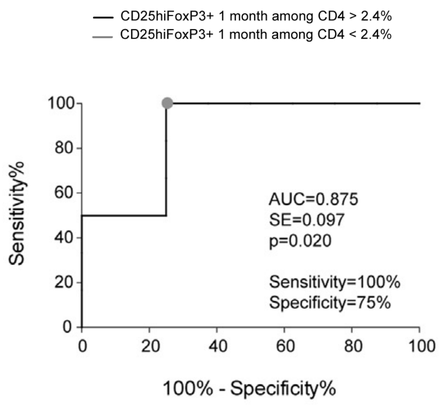




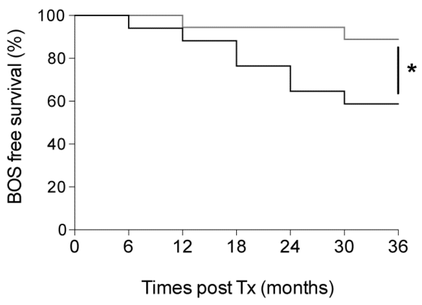
Tregs proportion > 2.4% in the 6 months post-transplantation is an independent risk factor of BOS development

1 month post-transplantation





6 months post-transplantation

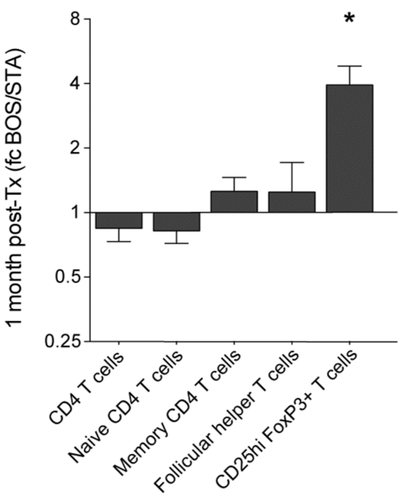


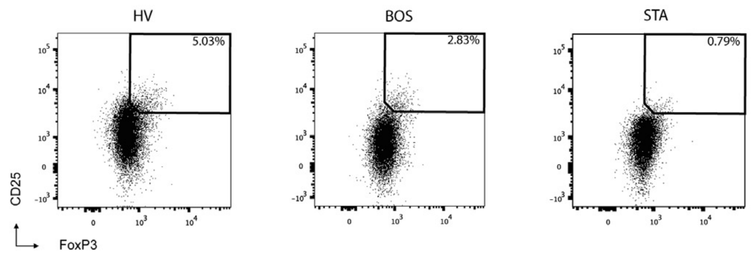
Multivariate analysis

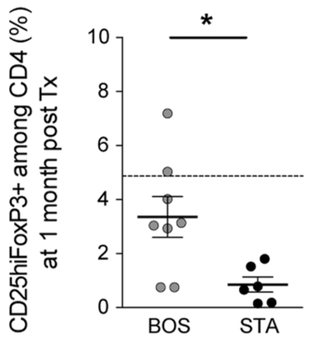
Parameters	*Wald test p. Value*	*Hazard ratio*
	Multivariate Analysis	
CD4+ CD25hi FoxP3+ T cells proportion up to 2.4 %	**0.0012**	**0.17**
Time post-transplantation	**0.016**	**0.99**

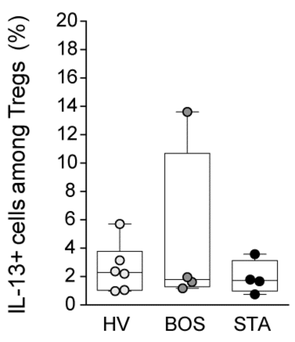
Early modification at 1 month and 6 months post-transplantation of circulating CD4+CD25hiFoxP3+ T cells proportion in BOS patients.

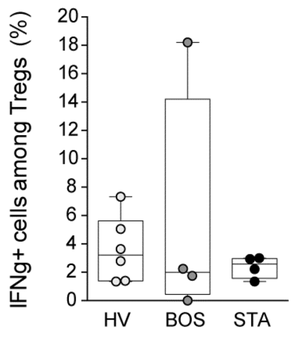
1 month post-transplantation

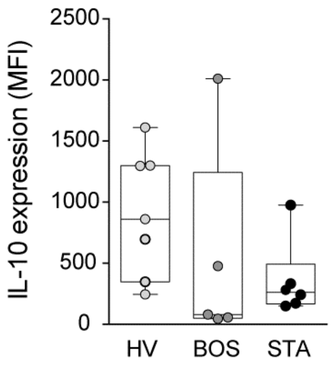


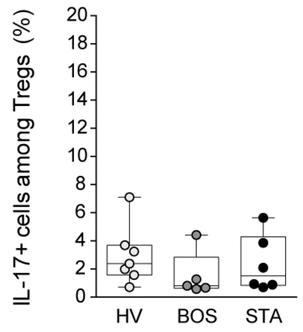


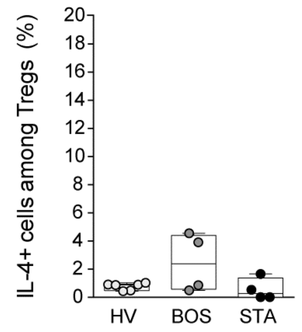




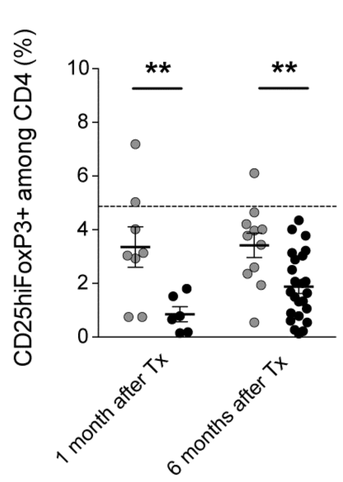


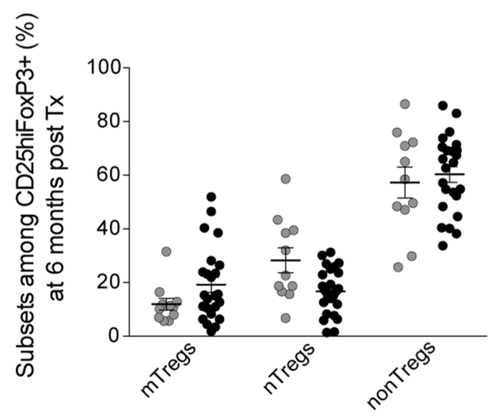






6 months post-transplantation





Conclusion & long-term prospects

Whereas no significant difference was found for T cell compartments at BOS diagnosis or several months before, we report an increase in the CD4+CD25hiFoxP3+ T cell subpopulation in BOS patients at 1 and 6 months after transplantation. A CD4+CD25hiFoxP3+ T cell threshold of 2.4% discriminated BOS and stable patients at 1 month post-transplantation. This was validated on a second set of patients at 6 months post-transplantation. Patients with a proportion of CD4+CD25hiFoxP3+ T cells up to 2.4% in the 6 months following transplantation had a 2-fold higher risk of developing BOS.

This study is the first to report an increased proportion of circulating CD4+CD25hiFoxP3+ T cells early post-transplantation in lung recipients who will develop BOS within 3 years, and support for its use as a BOS predictive biomarker.