

SUPPLEMENTAL TABLE 1. Characteristics of the Subgroups at Inclusion

Total study population	INR (n=21)	IR (n=21)	INR vs IR P-value
Age, (IQR)	49.9 (41.6-57.6)	45.0 (39.3-53.8)	NS
Male gender, n (%)	17 (81.0)	16 (76.2)	NS
Ethnicity, n (%)			
Caucasian	14 (66.7)	14 (66.7)	NS
Risk group, n (%)			
MSM	8 (38.1)	11 (52.4)	NS
Other ¹	13 (61.9)	10 (47.6)	NS
Smoking, n (%)			
Current smoking	4 (19.0)	9 (42.9)	NS
Comorbid diseases, n (%)			
Cardiovascular	1 (4.8)	1 (4.8)	NS
Hypertension	2 (9.5)	1 (4.8)	NS
Previous cancer	1 (4.8)	0 (0)	NS
Previous TBC	3(14.3)	0 (0)	NS
Any comorbidity ²	7 (33.3)	5 (23.8)	NS
CMV IgG pos	21 (100)	21 (100)	NS
HIV characteristics, (IQR)			
Years since HIV diagnosis	7.6 (5.4-12.4)	9.0 (7.5-14.3)	NS
Years of continuous ART	5.3 (3.4-6.1)	6.6 (4.9-8.6)	P = 0.03
Viral load at ART initiation, cop/mL	33000 (12675-87000)	140000 (50000-460000)	P = 0.01
Time to viral suppression, months	8.0 (3.7-14.5)	6.7 (4.4-8.6)	NS
Duration of viral suppression, years	3.5 (2.6-5.5)	6.1 (4.2-7.6)	P = 0.01
Viral blip ³	6 (31.6)	11 (52.4)	NS
Viral rebound ⁴	1 (5.3)	8 (38.1)	P = 0.02
Current use of PI	7 (33.3)	14 (66.6)	NS
Current use of INSTI	5 (23.8)	0 (0)	P = 0.05
Experience of ≥ 2 ART regimens	17 (81)	17 (81)	NS

Previous use of ART	5 (23.8)	5 (23.8)	NS
CD4 count nadir, cells/ μ L	120 (80-165)	174 (94-200)	NS
Years since nadir	5.5 (3.9-7.4)	6.8 (5.0-10.2)	NS
CD4 count, cells/ μ L	308 (233-350)	792 (732-848)	P < 0.001
CD8 count, cells/ μ L	581 (482-820)	992 (796-1443)	P < 0.001
CD4/CD8	0.52(0.35-0.59)	0.75 (0.55-0.99)	P < 0.01

Data are presented as no. (%) of patients or median (interquartile range (IQR)) values.

¹Other. Heterosexual and unknown. There were no Intravenous drug abusers.

²One or more of the following comorbidities; cardiovascular disease, hypertension, diabetes, renal disease, osteoporosis, chronic obstructive pulmonary disease, neurodegenerative disease, previous cancer or TBC.

³Isolated measurement of HIV RNA 50-500 copies/mL, preceded and followed by another value with full viral suppression.

⁴Either a HIV RNA value >50 copies/mL at 2 consecutive visits, or one HIV RNA value >500 copies/mL.

Mann-Whitney U Test, Pearson Chi-Square and Fischer's Exact Test.

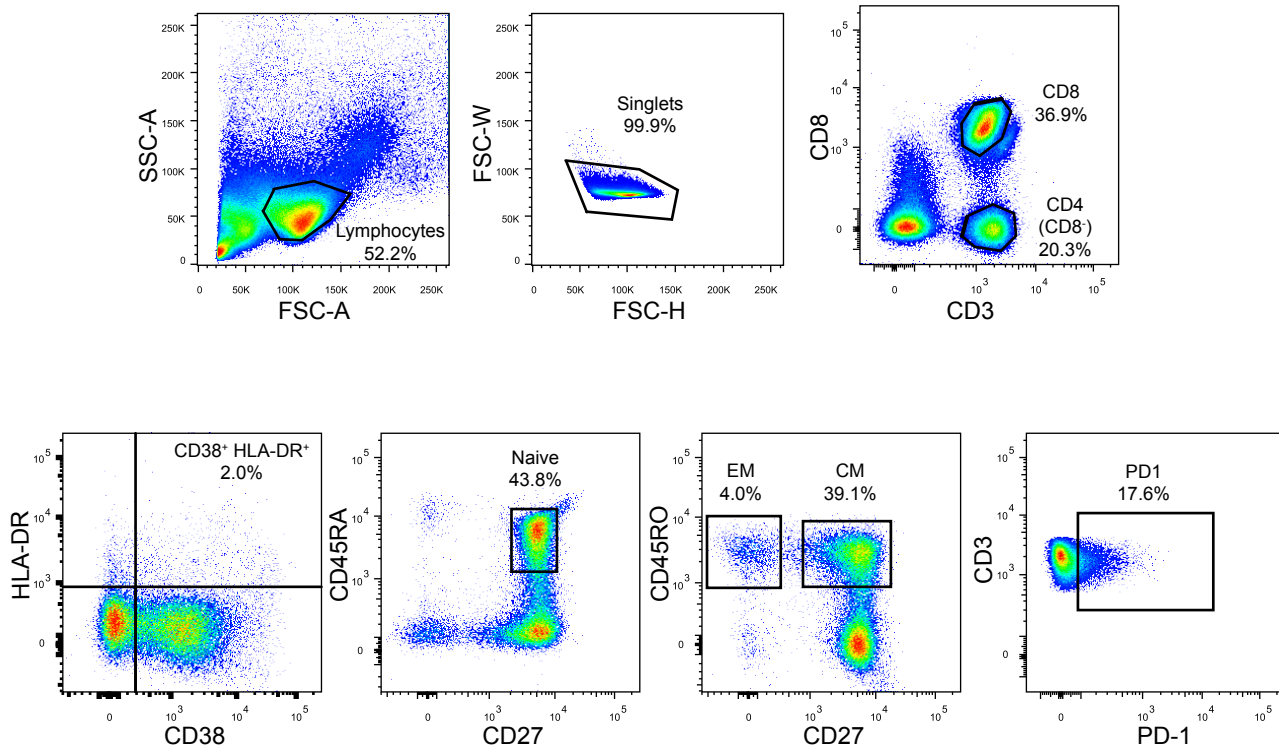
INR, Immunological non-responders; IR, Immunological responders; MSM, Men who have sex with men; TBC, Mycobacterium tuberculosis infection; CMV, Cytomegalovirus; ART, Antiretroviral therapy; PI, Protease inhibitor; INSTI, Integrase strand transfer inhibitor.

Supplemental Table S2. Correlation between IP-10 and inflammation markers, both cohorts combined

	β2-microglobulin		IL-6		sCD14		Neopterin		Kynurenine		KTR	
	Correlation coefficient	p-value	Correlation coefficient	p-value	Correlation coefficient	p-value	Correlation coefficient	p-value	Correlation coefficient	p-value	Correlation coefficient	p-value
IP-10	0.47	< 0.01	0.37	< 0.01	0.26	0.04	0.42	< 0.001	0.30	0.01	0.37	< 0.01

KTR, Kynurenine / tryptophan ratio. Spearman's rank order correlation.

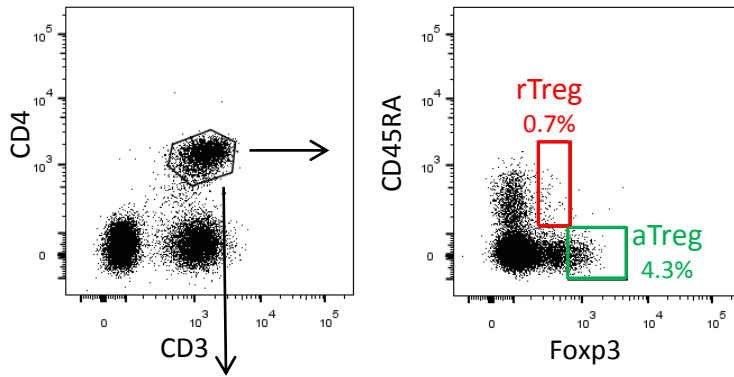
Supplemental Figure S1



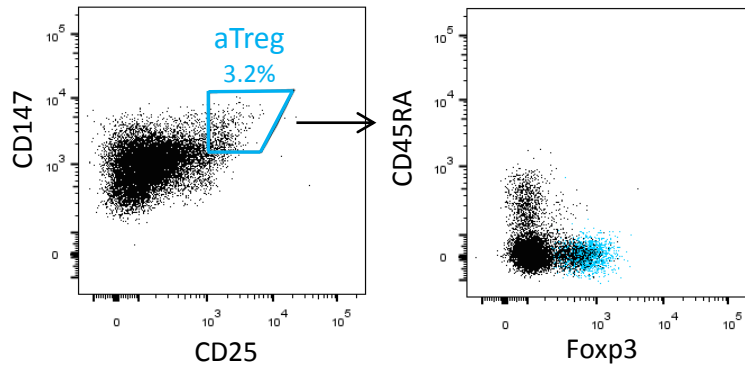
Supplemental Figure S1. Gating strategy for activated and differentiated T cells. PBMCs were stained for surface markers and analyzed by flow cytometry. Activation and differentiation, as indicated in the lower panels, were studied on both CD3⁺CD8⁺ and CD3⁺CD8⁻ (CD4) T cells. The figure shows one representative sample gated on the CD8⁺ population.

Supplemental Figure S2

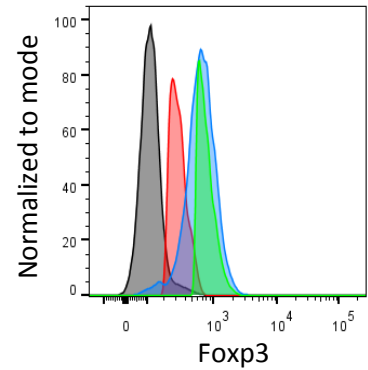
(a) Traditional gating strategy of resting and activated Treg



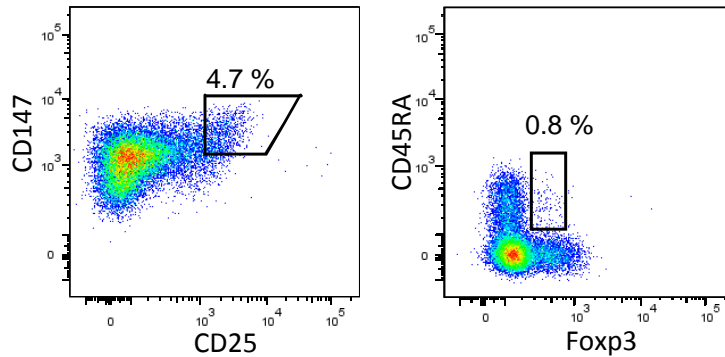
(b) Alternative gating strategy with CD147 for identification of activated Treg



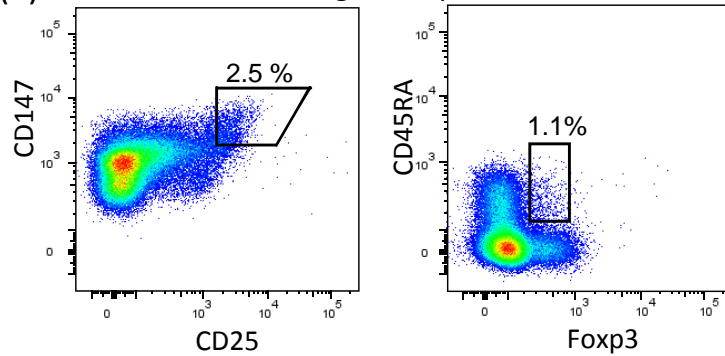
(c) Histogram of Foxp3 expression



(d) Immunological non-responder



(e) Immunological responder



Supplemental Figure S2. Gating strategy for activated and resting Tregs and examples of resting and activated Treg distributions in INR and IR. (a) All of the Tregs were gated from the CD3⁺CD4⁺ T cell population (left plot). The resting Tregs (rTreg) were defined as CD45RA⁺FoxP3⁺ according to standard gating strategies (red gate, right plot). The green gate illustrates the traditional method of defining activated Tregs (aTreg) (CD45RA⁻FoxP3^{high}). (b) aTreg defined by the alternative method. The blue gate displays aTreg defined as CD147^{high}CD25^{high} (left panel). The dot plot at the right shows that the CD147^{high} aTreg are CD45RA⁻Foxp3^{high} (blue dots, right plot) in contrast to the rest of the CD4⁺ T cells. (c) Overlay showing Foxp3 expression. The black histogram represents CD45RA⁺/⁻ CD25^{low} conventional CD4⁺ T cells (gating not shown), the red histogram represents the rTreg, whereas the green and blue histograms indicates aTreg identified by the traditional or alternative gating strategy, respectively. (d-e) Representative flow cytometry analysis of one INR (d) and one IR (e) displaying the amounts of resting (left) and CD147^{high} activated (right) Tregs. The Treg subsets are given as percentages of CD4⁺ T cells. Tregs; regulatory T cells; rTreg; resting Tregs; aTreg, activated Tregs. IR, immunological responders; INR, immunological non-responders.