DOI:
10.1016/S0140-6736(20)30167-7

Document Version
Peer reviewed version

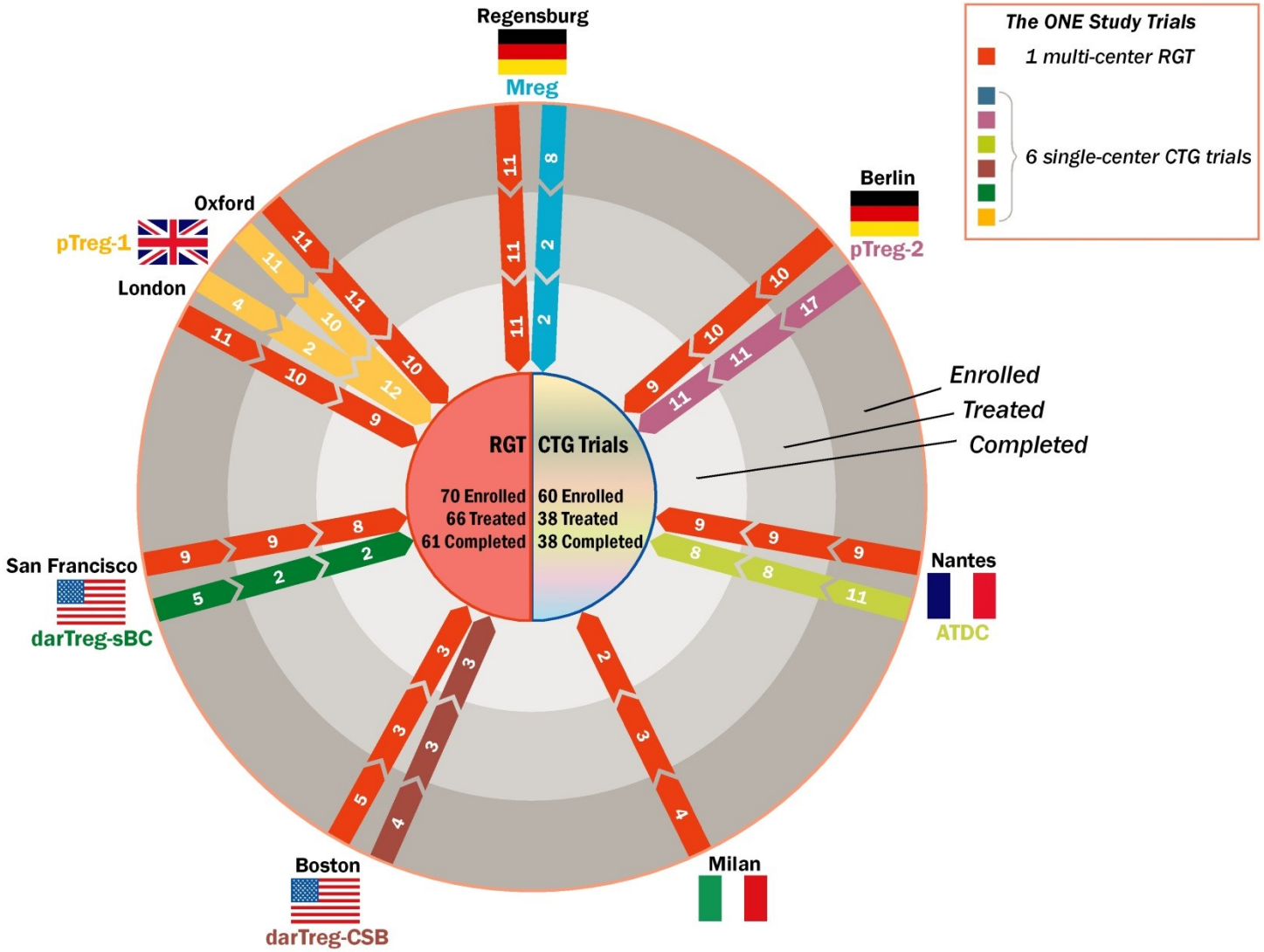
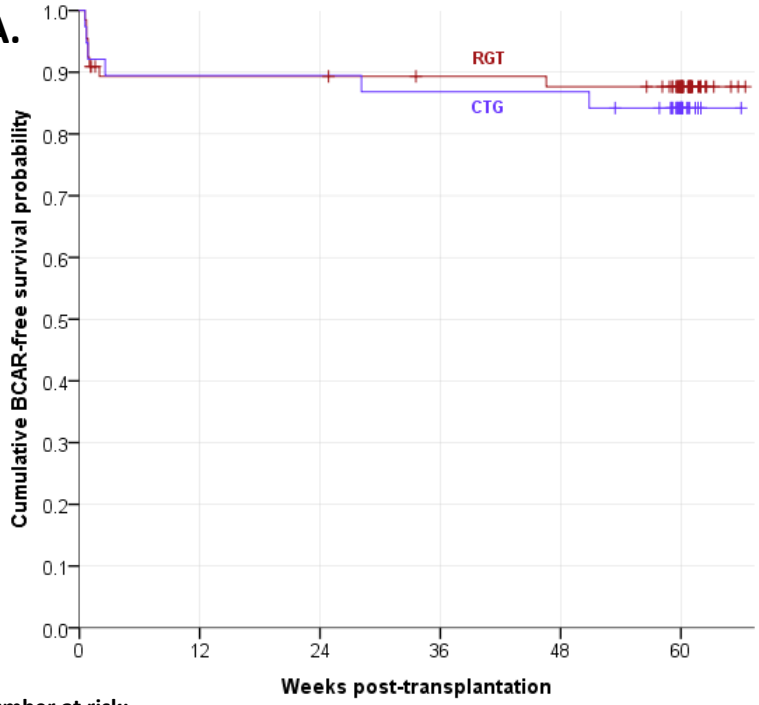


Fig. 1: *ONE Study design and patient disposition for the multicenter RGT and six monocenter CTG trials.* RGT = Reference Group Trial; CTG = Cell Therapy Group trials; Mreg: regulatory macrophages; ATDC: autologous tolerogenic dendritic cells; pTreg-1 / pTreg-2: polyclonal regulatory T cells; darTreg-sBC: donor-alloantigen reactive Treg; darTreg-CSB: costimulatory blockade generated Treg.

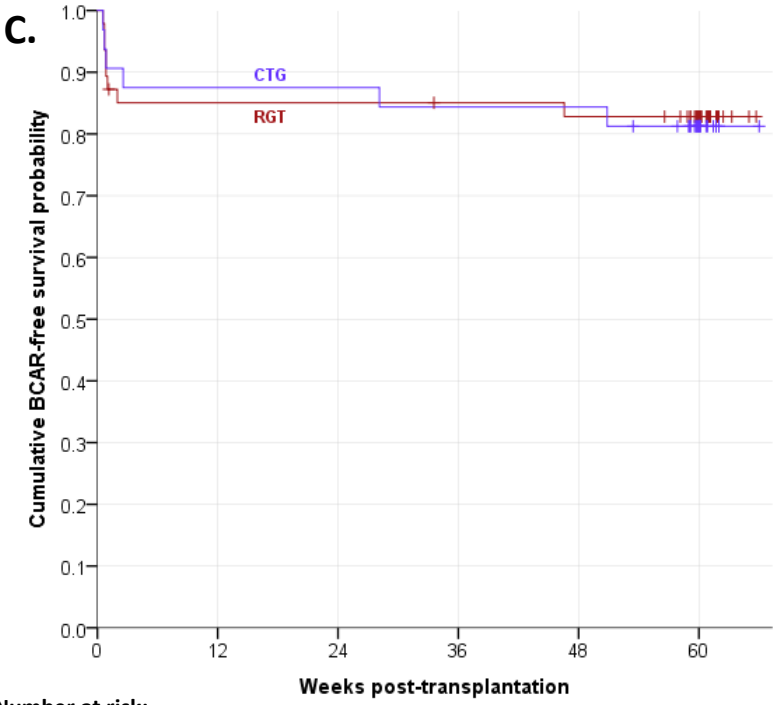
A.



Number at risk:

RGT	66	56	56	54	53	33
CTG	38	34	34	33	33	12

C.



Number at risk:

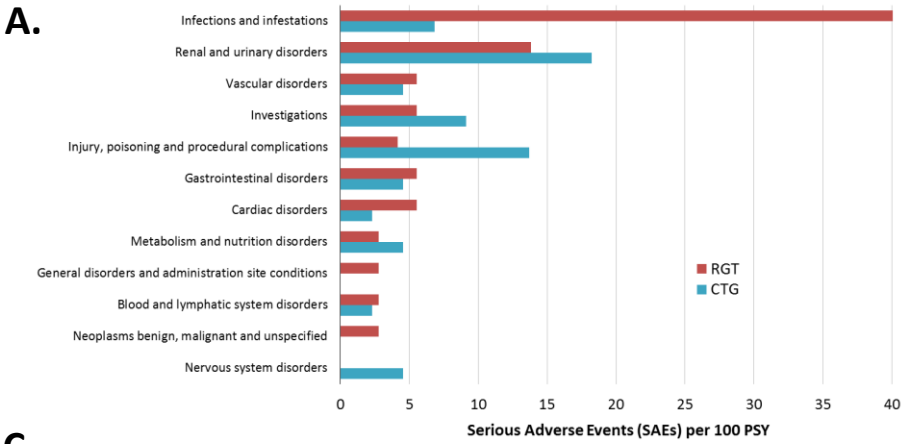
RGT	47	39	39	38	37	23
CTG	32	28	28	27	27	10

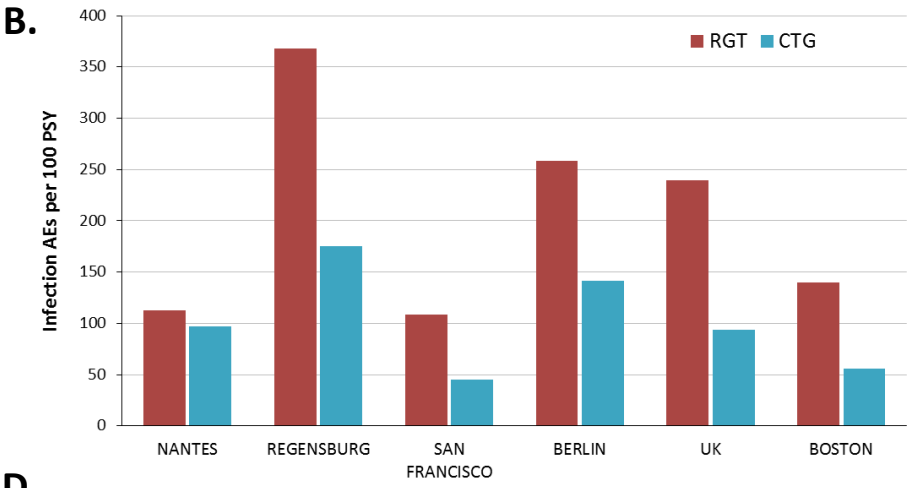
B.

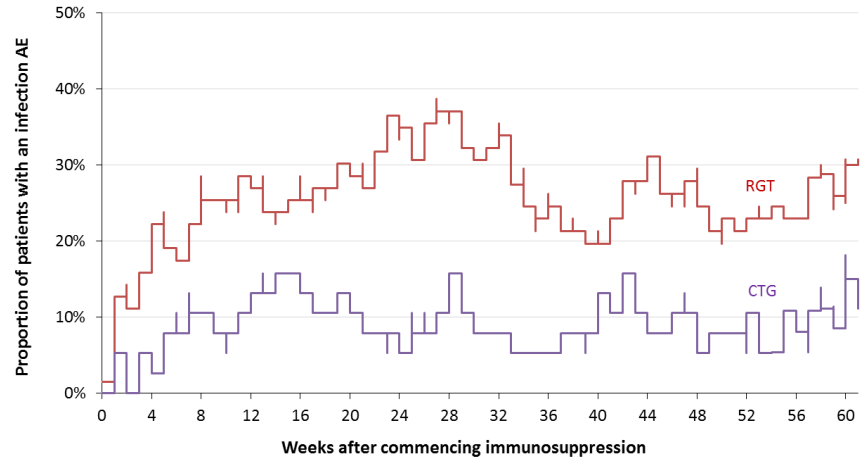
Severity of 1st BCAR episode	**RGT (N=8)**	**CTG (N=6)**
Central pathological diagnosis		
Acute TCMR IA	1 (12.5 %)	1 (16.7 %)
Acute TCMR IIA	3 (37.5 %)	2 (33.3 %)
Acute TCMR IB	1 (12.5 %)	1 (16.7 %)
Acute TCMR IIB	0 (0.0 %)	2 (33.3 %)
Borderline changes	3 (37.5 %)	0 (0.0 %)
ABMR diagnosed locally?		
Yes	1 (12.5 %)	2 (33.3 %)
No	7 (87.5 %)	4 (66.7 %)
Response to treatment		
Glucocorticoid-responsive	4 (50.0 %)	3 (50.0 %)
Responsive to depleting antibody treatment	3 (37.5 %)	3 (50.0 %)
Not applicable*	1 (12.5 %)	0 (0.0 %)

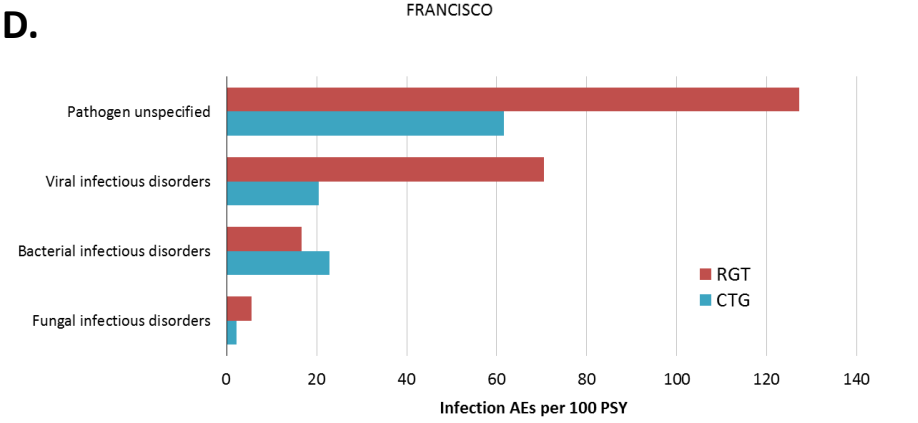
Fig. 2: *Primary endpoint (BCAR) data.* 2A). Kaplan-Meier estimates of the cumulative BCAR-free survival probability in the RGT (N=66) and CTG (N=38) intention-to-treat analysis sets (87.7 % vs. 84.2 % at 60 weeks). Censored patients marked with ticks. 2B). Severity of first BCAR episode by central pathological diagnosis and response to treatment. * Patient treated with low-dose oral steroids and by not tapering immunosuppression. 2C). Kaplan-Meier estimates of the cumulative BCAR-free survival probability in the RGT (N=47) and CTG (N=32) per-protocol analysis sets (82.8 % vs. 81.3 % at 60 weeks). Censored patients marked with ticks.

RGT = Reference Group Trial; CTG = Cell Therapy Group trials; BCAR = biopsy-confirmed acute rejection; TCMR = T cell-mediated rejection; ABMR = antibody-mediated rejection.









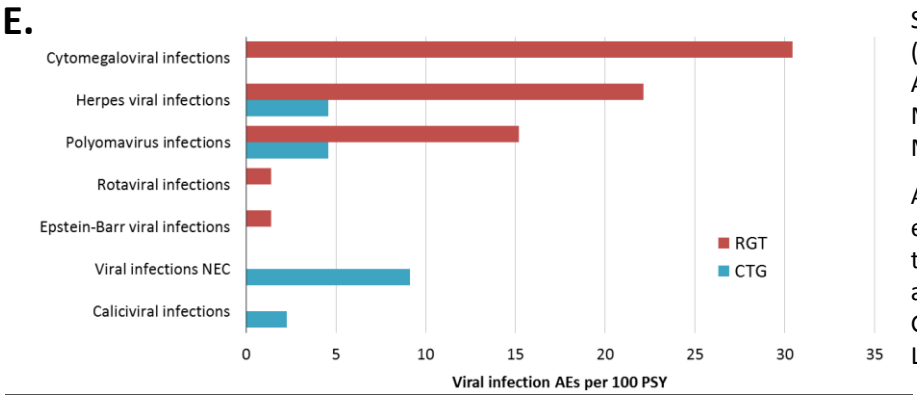


Fig. 3: *ONE Study safety data (normalized).* 3A) Incidence rate of treatment-emergent SAEs by MedDRA primary SOC. 3B) Incidence rate of treatment-emergent infections (all AEs) by study site. 3C) Incidence proportion of treatment-emergent infections (all AEs) over time. 3D) Incidence rate of treatment-emergent infections (all AEs) by MedDRA HLGT. 3E) Incidence rate of treatment-emergent viral infections (all AEs) by MedDRA HLT.

All adverse events coded using MedDRA version 20.1. Treatment-emergent (S)AEs are events with onset date equal to or after first dose of any study drug. All events coded to the MedDRA PT: "Transplant rejection" are excluded, since rejection was measured as the primary efficacy endpoint. RGT = Reference Group Trial; CTG = Cell Therapy Group trials; SOC = System Organ Class; HLGT = High Level Group Term; HLT = High Level Term; PSY = Patient study years; NEC = Not elsewhere classified.

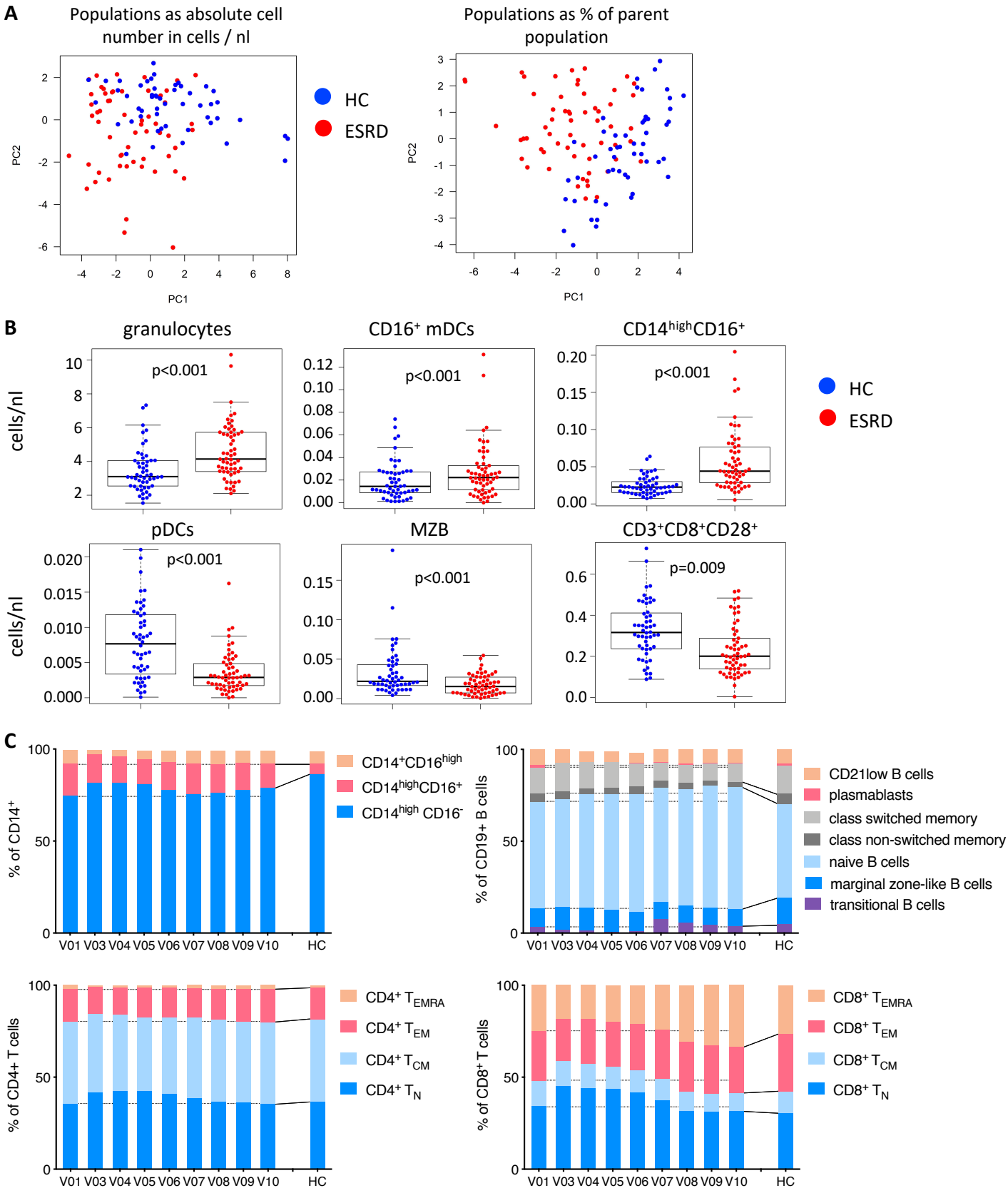


Fig. 4: *Leukocyte subset alterations in ESRD patients and time-dependent changes after kidney transplantation.* A) Principal component analysis revealing the differences in leukocyte subset between whole blood samples from end stage renal renal disease (ESRD, n= 70) and healthy controls (HC, n= 98). B) Box-and-whiskers plots of absolute numbers from leukocyte subpopulations with highest influence at the PCA shown in A. C) Time-dependent changes from visit 1 prior to transplantation (V01) to visit 10 at 60 weeks post-transplant (V10) of monocyte, B cell, CD4⁺ and CD8⁺ T cell subset composition (stacked bars of mean proportions) in whole blood samples of RGT patients (n=59). Statistical analysis by Kruskal-Wallis-Test. * p<0.05, ** p<0.01

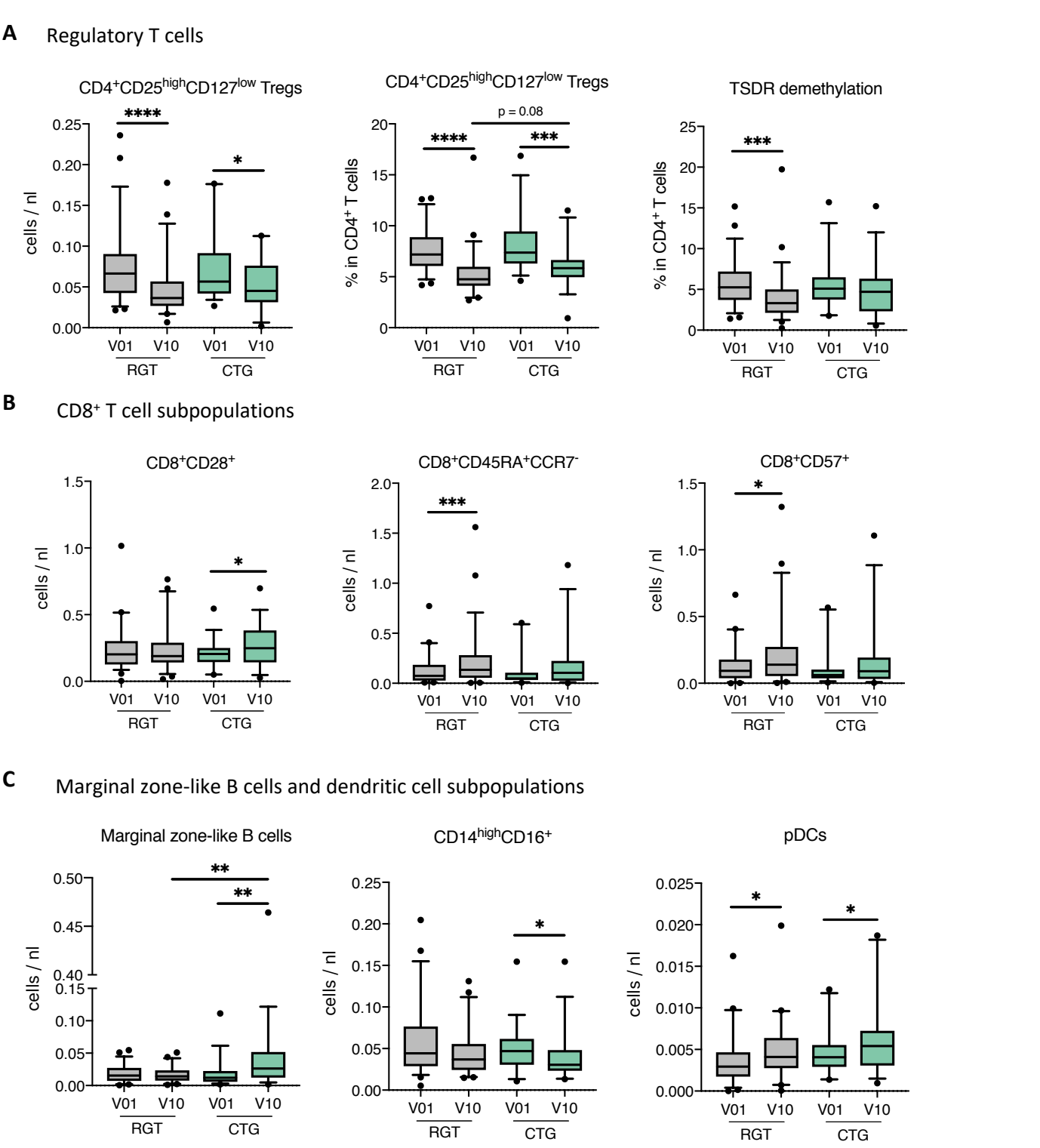


Fig. 5: *Differences in post-transplant changes between RGT and CTG patients.* A) Differences in post-transplant changes in regulatory T cells. Box and whisker plots of absolute numbers and proportions of $CD4^+CD25^{high}CD127^{low}$ Tregs as well as % $CD4^+$ T cells with demethylated TSDR in whole blood samples collected pre-transplant (V01) and at the end of the observation period (15 months post-transplant, V10) from RGT (n=59) and CTG patients (n=38) measured as described in material and methods. B) Differences in post-transplant changes in $CD8^+$ T cell subpopulations. Box and whisker plots of absolute numbers of $CD8^+CD28^+$, $CD8^+CD45RA^+CCR7^-$ T_{EMRA} and $CD8^+CD57^+$ chronically activated cells in whole blood samples collected pre-transplant (V01) and at the end of the observation period (15 months post-transplant, V10) from RGT (n=59) and CTG patients (n=38). C) Differences in post-transplant changes in marginal zone-like B cells and dendritic cell subpopulation. Box and whisker plots of absolute numbers and proportions of marginal zone-like B cells, $CD16^+$ mDCs and pDCs in whole blood samples collected pre-transplant (V01) and at the end of the observation period (15 months post-transplant, V10) from RGT (n=59) and CTG patients (n=38). Statistical analysis by by Wilcoxon matched-pairs signed rank and Dunn's multiple comparison test. * p<0.05, ** p<0.01, *** p<0.001, **** p<0.0001