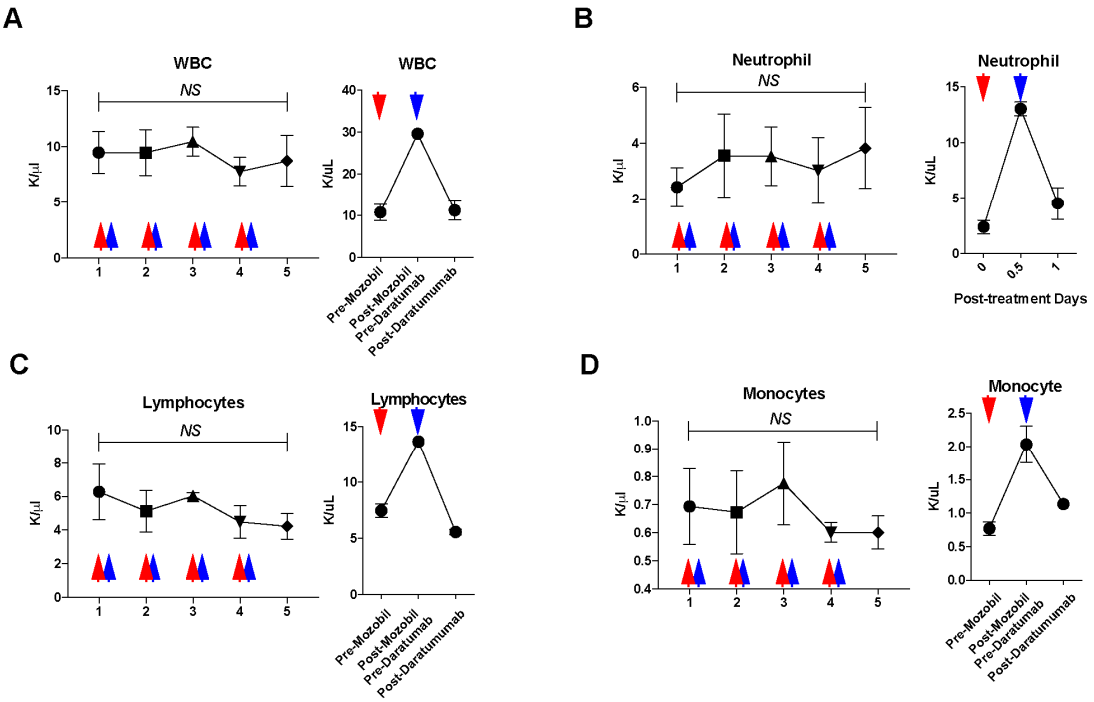
Supplemental clinical description

Heart allograft transplantation after daratumumab

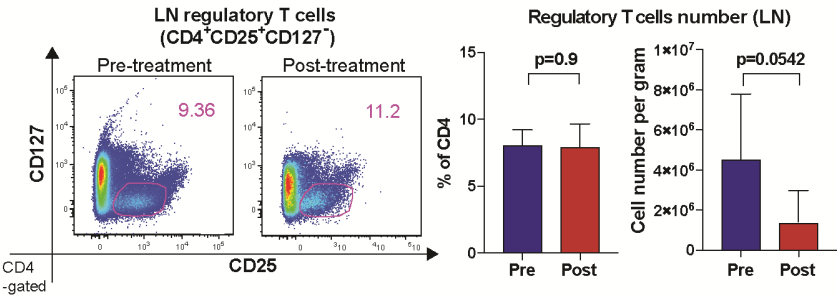
Despite maximum medical treatment and a triple chamber pacemaker, she had several episodes of cardiac decompensation and remained symptomatic in NYHA class III heart failure (New York Heart Association functional classification).Despite maximum medical treatment and a triple chamber pacemaker, she had several episodes of cardiac decompensation and remained symptomatic in NYHA class III heart failure (New York Heart Association functional classification). She was registered on the cardiac transplant waiting list in December 2016. Initial immunological evaluation showed that up to 80% of heart allografts from deceased donors were incompatible due to the patient's broad sensitization. In our center patients with HLA specificities of MFI > 3000 are excluded for heart transplantation. Luminex assay analysis showed 35 class I alloantibody specificities and five class II specificities. Initial desensitization included plasmapheresis, high dose IVIG (2 g/kg), and rituximab (1 gram). No significant changes were observed with 74% cPRA. A second course of desensitization included high doses of IVIG, rituximab, and 24 sessions of plasmapheresis, but no effect was observed on class I immunization with N=35 class I anti-HLA antibodies with MFI > 3000 and no class II. cPRA was 98%. She was therefore considered as non-responsive to classic desensitization. At the same time, the clinical condition deteriorated with several cardiac decompensations, and it was decided not to offer long-term ventricular assistance because of the bi-ventricular dysfunction and mechanical valves. We decided after a multidisciplinary meeting to introduce daratumumab as anti-PC therapy, with a potential action on anti-HLA MFI. The first daratumumab dose was in October 2018. She received eight weekly injections of 16mg/kg each. The drug was tolerated without side effects. After eight doses, we observed a significant decrease of anti-HLA antibodies MFI (Figure 6C). PRA decreased to 62% in January 2018, allowing heart transplantation in March 2018, with only two DSA (one class I and one class II). Heart allograft HLA included B8 and DQ6 antigens. Before treatment MFI of both were > 3000 (6255 and 3258) prohibiting transplantation. In January, after treatment, MFIs were lower than 3000 (2497 and 1814 respectively) allowing heart transplantation. She unfortunately died four days after transplant because of hemorrhagic shock secondary to surgical technique problem (large artery wound). This event is not reported as possibly linked to daratumumab treatment.

Supplemental FIgure 1



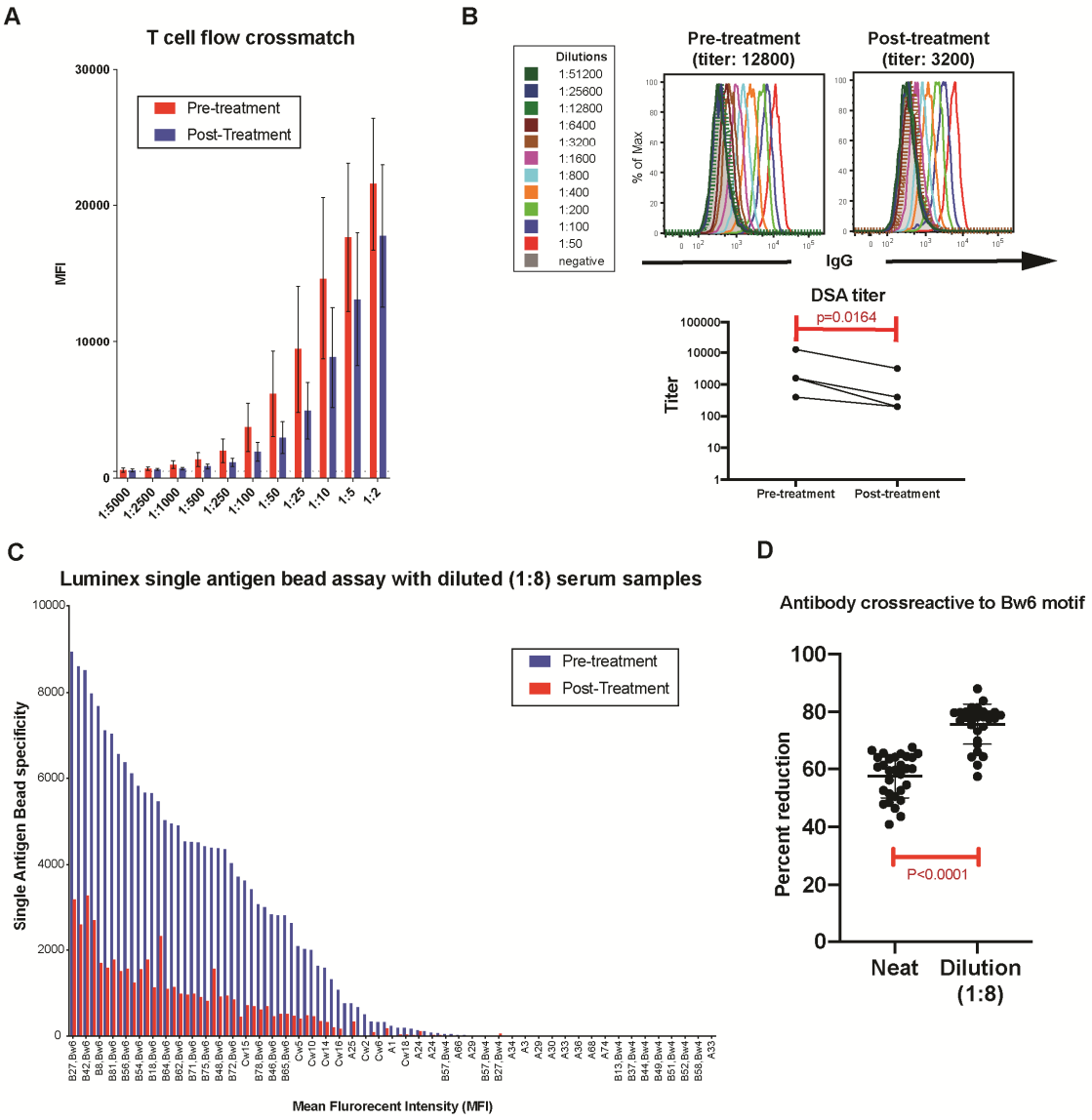
Supplemental Figure 1. Longitudinal and transient changes of circulating leukocyte populations during daratumumab and plerixafor treatment. Administration of daratumumab and plerixafor induced transient fluctuation of total WBC **(A)**, neutrophil **(B)**, lymphocytes **(C)**, and monocyte **(D)** populations, however, overall longitudinal kinetics were not significantly changed.

Supplemental Figure 2



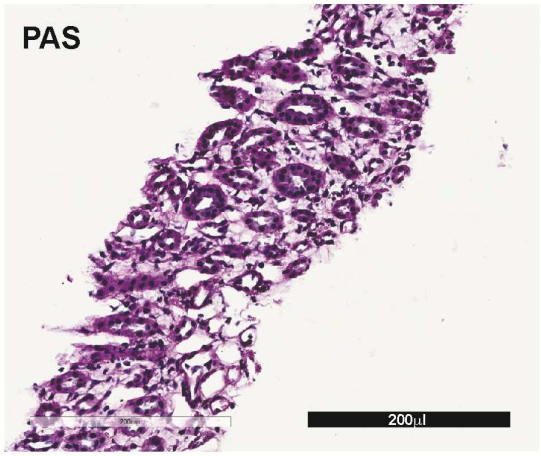
Supplemental Figure 2. Effect of daratumumab and plerixafor on lymph node Treg cells. Although the frequency of Treg cell population (CD4+CD25+CD127-) was not affected by daratumumab and plerixafor treatment, the quantity of Tregs is reduced in the lymph nodes after desensitization.

Supplemental Figure 3



Supplemental Figure 3. No profound prozone but some saturation effect were shown in serial diluted samples. (A) serial dilution of recipients' serum samples did not show profound prozone effect with flow crossmatch assay. (B) evaluated titer based on serial dilution showed a significant reduction after plerixafor and daratumumab treatment. (C) Diluted serum samples (1:8) did not show profound evidence of prozone effect with luminex single antigen bead assay. (D) Diluted serum samples showed a significant reduction of Bw6 motif binding antibodies.

Supplemental Figure 4



Treatment		t	v	i	ti	g	ci	ct	cg	mm	cv	ah	ptc	Interstitial Plasma cells	Interstitial Neutrophils	Interstitial Eosinophils	Tubular Injury	Glomerular fibrin	Inclusions	Edema	PTC fibrin	C4d	Arteriole fibrin	Diagnosis
Daratumumab + Plerixafor	POD6	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0	Tubular injury No AR

Supplemental Figure 4. Early renal biopsy after daratumumab and plerixafor treatment. A renal biopsy at post-operation day 6 showed no sign of cell-mediated rejection or antibody-mediated rejection.