**ESM Table 1.** Flow cytometry panel for T cell phenotyping

| Marker | Fluorochrome | Clone | Supplier* |
|---|---|---|---|
| CD56 | BUV 395 | NCAM16.2 | BD |
| CD45RA | BUV 737 | HI100 | BD |
| GrzmB | BV421 | GB11 | BD |
| CCR7 | BV510 | G043H7 | BL |
| CD3 | ev605 | OKT3 | eBio |
| PD1 | ev655 | J105 | eBio |
| CD127 | BV711 | A019D5 | BL |
| CD45R0 | BV786 | UCHL1 | BD |
| CD4 | BB515 | RPA-T4 | BD |
| Eomes | PE | WD1928 | eBio |
| FoxP3 | PE-CF594 | 259D | BD |
| KLRG1 | PE-vio770 | REA261 | Miltenyi |
| TIGIT | APC | MBSA43 | eBio |
| CD8 | AF700 | RPA-T8 | BL |
| CD57 | APC-vio770 | TB03 | Miltenyi |

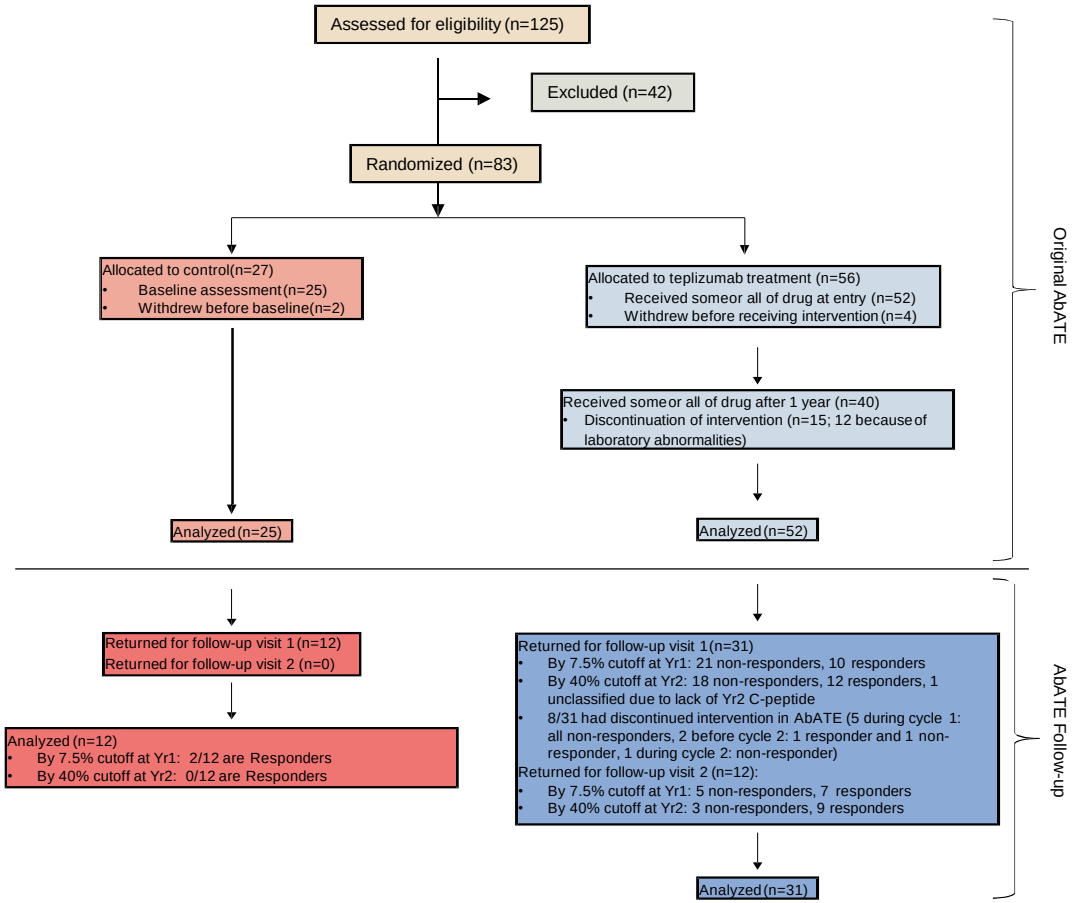
*BD Biosciences: San Jose, CA, USA. BioLegend: San Diego, CA, USA. eBiosciences: San Diego, CA, USA. Miltenyi: Auburn, CA, USA.

**ESM Table 2.** Characteristics of study participants at study enrollment

| | **Control group (n=12)** | **Drug-treated Non-responders (n=21)** | **Drug-treated Responders (n=10)** | ***p* value** |
|---|---|---|---|---|
| Age at baseline (years) | 12.27+/-0.86 | 12.20+/-0.75 | 11.39+/-0.84 | 0.77 |
| Duration of diabetes at enrollment (days) | 37.33+/-2.86 | 38.48+/-1.93 | 41.80+/-2.06 | 0.47 |
| Male (%) | 66.7% | 61.9% | 50% | 0.72 |
| White (%) | 100% | 85.7% | 90% | 0.40 |
| Minority (%) | 0% | 9.5% | 10% | 0.54 |
| BMI ($kg/m^2$) | 19.60+/-0.78 | 18.56+/-0.73 | 19.64+/-1.11 | 0.56 |
| Insulin use (units/kg/day) | 0.40+/-0.04 | 0.39+/-0.06 | 0.29+/-0.09 | 0.50 |
| $HbA_{1C}$ (mmol/mol) | 60.15+/-4.56 | 59.87+/-2.56 | 52.78+/-2.96 | 0.28 |
| $HbA_{1C}$ (%) | 7.66+/-0.42 | 7.63+/-0.23 | 6.98+/-0.27 | 0.28 |
| C-peptide AUC (nmol/l) | 0.50+/-0.05 | 0.49+/-0.03 | 0.57+/-0.07 | 0.43 |

**ESM Table 3.** Safety data. At the time of the follow-up visit the participants were queried about significant adverse events occurring since the study period was over. The Table shows the number of individuals (%) with the indicated adverse events (n=12 control, 21 drug-treated non-responders, 10= drug-treated responder). Adverse events were graded as per the original AbATE [9] and only grade 2 and above adverse events are shown. The adverse events were all considered unrelated or unlikely related to study drug.

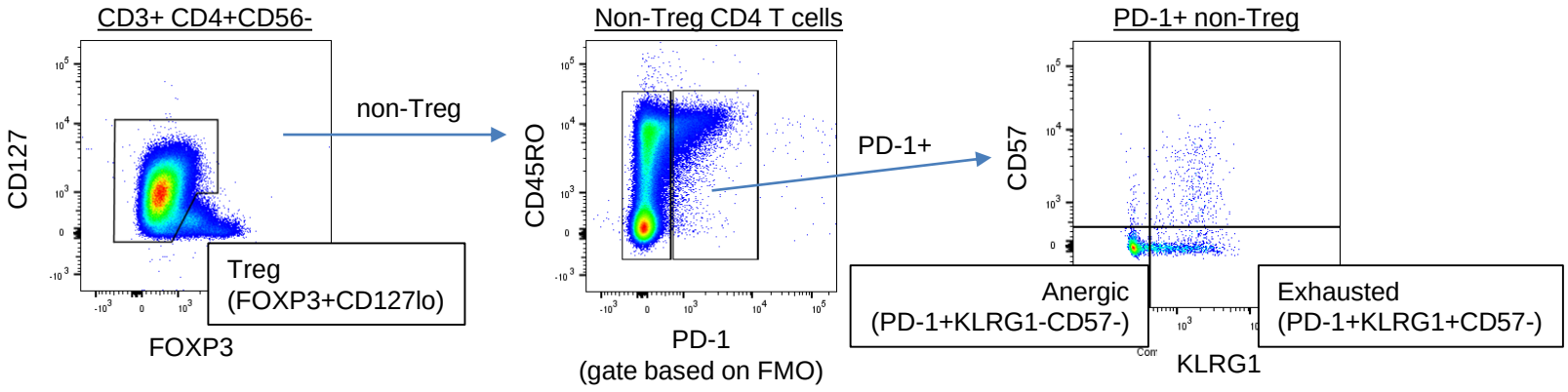
| Term | Control (%) | Drug treated Non-responder (%) | Drug treated Responder (%) |
|---|---|---|---|
| Severe hypoglycemia | 2(18%) | 6(28.6%) | 1 (10%) |
| Diabetic ketoacidosis | 1 (8.3%) | 1 (4.8%) | 1 (10%) |
| Acquired hypothyroidism | 2 (16.7%) | | 1 (10%) |
| Other | | Neuropathic syndrome treated with IVIG | |



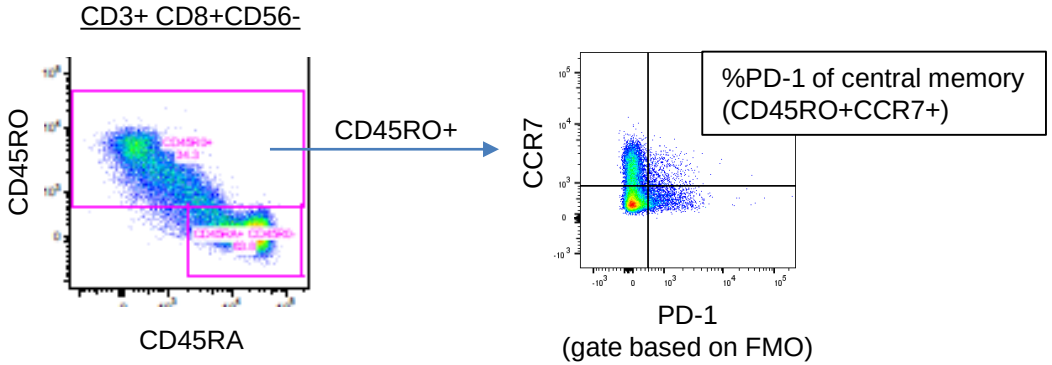

**ESM Fig. 1.** Enrollment, randomization, and participation in the original AbATE study and follow-up. The original randomization and participation were described previously [9]. Of the 83 individuals initially randomized, 77 were included in the AbATE ITT analysis, 25 in the control group and 52 in the treated group. A total of 15 patients discontinued the intervention in the original AbATE, 6 during cycle 1, 6 prior to initiation of cycle 2, and 3 during cycle 3. Of the 77 individuals that participated in AbATE, 43 were analyzed for follow-up. Thirty-one drug-treated participants returned for follow-up, including 21 drug-treated non-responders and 10 drug-treated responders.

Eight of the follow-up participants had discontinued therapy during AbATE, 5 during cycle 1(all drug-treated non-responders), 2 prior to starting cycle 2 (a responder and a non-responder) and 1 during cycle 2 (a non-responder). By the original AbATE criteria (<40% decline in C-peptide at Yr2), the individuals who followed up were classified as 18 drug-treated non-responders, 12 drug-treated responders and 1 unclassified due to lack of C-peptide at Yr2. Twelve treated participants returned for follow-up visit 2, 5 drug-treated non-responders and 7 drug-treated responders (3 drug-treated non-responders and 9 drug-treated responders by the original AbATE criteria). Twelve control individuals were analyzed for follow-up. All of the control participants were drug-treated non-responders per the original response criteria and 2 were drug-treated responders by the current criteria. None of the controls returned for follow-up visit 2.

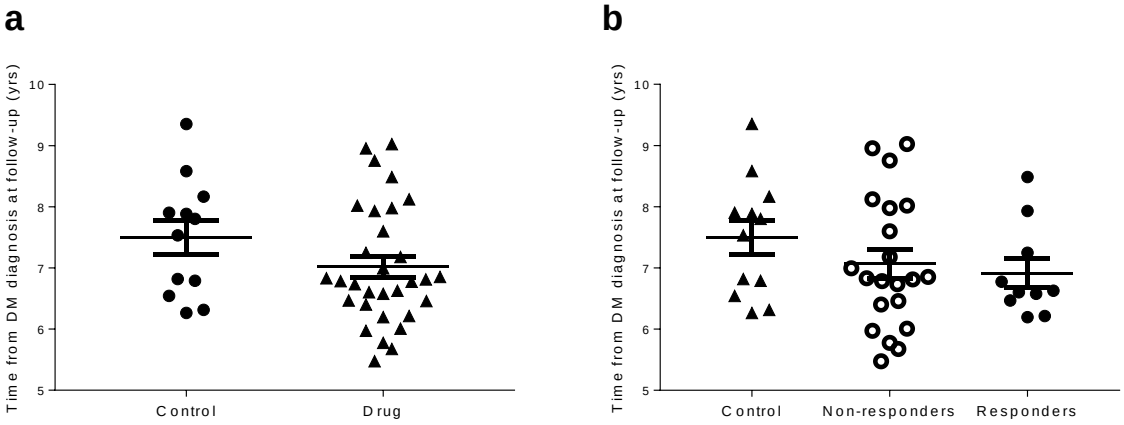
**a**. Treg, anergic and exhausted CD4 and CD8 (shown for CD4)



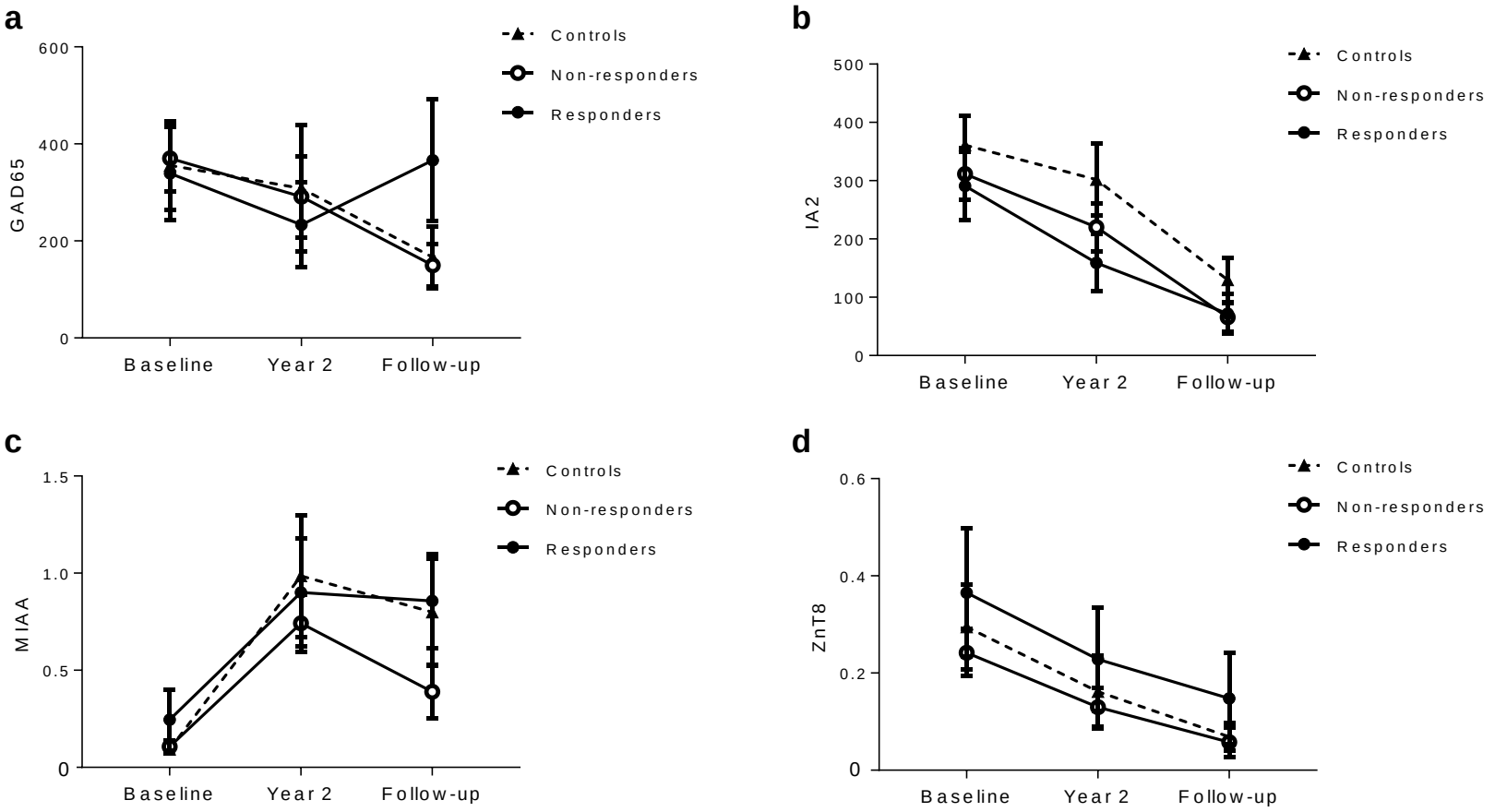

**b**. PD-1 on central memory CD8




**ESM Fig. 2**. Representative electronic gating for T cell subsets. **(a)** Forward and side scatter gates were placed around lymphocytes. On CD3+Foxp3- cells, gates were placed on PD-1+CD45RO+ cells. These were further identified on the basis of KLRG1 and CD57 staining as anergic (PD-1+CD57-KLRG1- or exhausted PD-1+KLRG1+CD57-). **(b)** Central memory cells were identified as CD45RO+CCR7+.




**ESM Fig. 3.** Time from diabetes diagnosis to follow-up. The time from diabetes diagnosis to follow-up was similar between **(a)** controls and treated participants (7.50±0.28 and 7.02±0.17 respectively, difference not statistically significant by Student's t test) and **(b)** response groups (7.50±0.28 for controls, 7.07±0.23 for drug-treated non-responders, 6.91±0.24 for drug-treated responders, difference not statistically significant by one-way ANOVA). (mean±SEM)




**ESM Fig. 4.** Changes in autoantibody titers over time and between groups. Autoantibody titers are shown at baseline, 2 years, and follow-up for controls and response groups. **(a)** GAD65 autoantibody **(b)** IA-2 autoantibody **(c)** MIAA autoantibody **(d)** ZnT8 autoantibody. There was a significant decline in anti-ZnT8 ($p<0.01$, two-way ANOVA) and anti-IA-2 ($p<0.001$, two-way ANOVA) and a significant increase in MIAA ($p<0.001$, two-way ANOVA) over time. The anti-GAD65 titers did not change significantly. There were no overall differences between groups. (mean±SEM)