SUPPLEMENTARY MATERIAL

Inclusion/Exclusion Criteria

Inclusion Criteria

Subjects who meet the following criteria will be considered eligible to participate in the clinical study if they:

1. Are male or female 18 years of age or older
2. Meet the ACR/EULAR 2018 Classification Criteria for IgG4-RD (see appendix G)
3. Have active disease based on an IgG4-RD RI ≥2 at screening with disease manifestation in at least one organ system excluding lymph nodes and isolated retroperitoneal fibrosis at screening
4. May or may not have received prior IgG4-RD therapy
5. Must be willing to taper off any systemic corticosteroid therapy within 8 weeks of first dose of trial drug.
6. Must be able and willing to discontinue any immunosuppressive agent at screening (e.g. methotrexate, mycophenolate mofetil, 6-mercaptopurine, tacrolimus, cyclophosphamide or azathioprine).
7. No history of severe allergic reactions to monoclonal antibodies.
8. Are able and willing to complete the entire study per the study schedule.
9. Are willing to forego other forms of experimental treatment during the study.
10. can provide written informed consent.

Exclusion Criteria

Subjects who meet one or more of the following criteria will not be considered eligible to participate in the clinical study:

1. History or evidence of a clinically unstable/uncontrolled disorder, condition or disease (including but not limited to cardiopulmonary, oncologic, renal, hepatic, metabolic, hematologic or psychiatric) other than IgG4-RD that, in the opinion of the Investigator, would pose a risk to patient safety or interfere with the study evaluation, procedures or completion.
2. Malignancy within 5 years (except successfully treated in situ cervical cancer, resected squamous cell or basal cell carcinoma of the skin, or prostate cancer with no recurrence ≥3 years following prostatectomy).
3. Liver disease: Acute or chronic non-IgG4-related liver disease deemed sufficiently severe to impair their ability to participate in the trial.
4. Uncontrolled disease: evidence of another uncontrolled condition, including drug and alcohol abuse, which could interfere with participation in the trial according to the protocol.
5. Presence of recurrent or chronic infections, defined as ≥3 infections requiring antimicrobials over the past 6 months prior to screening.
6. Active infection requiring hospitalization or treatment with parenteral antimicrobials within the 30 days prior to randomization.
7. Prior use of rituximab (or other B cell depleting agents) within 6 months of enrollment unless B cells have been demonstrated to have repopulated.
8. Use of any investigational agent within 5 half-lives of the agent (or 6 months if the half-life is unknown) prior to enrollment.
9. White blood cell count < 2.5 x 103/µL.
10. Absolute neutrophil count (ANC) < 1.0 x 103/µL.
11. IgG4-related renal disease with serum creatinine >2.0 mg/dL.
12. Hemoglobin < 10 g/dL.
13. Platelet count < 75 x 109/L.

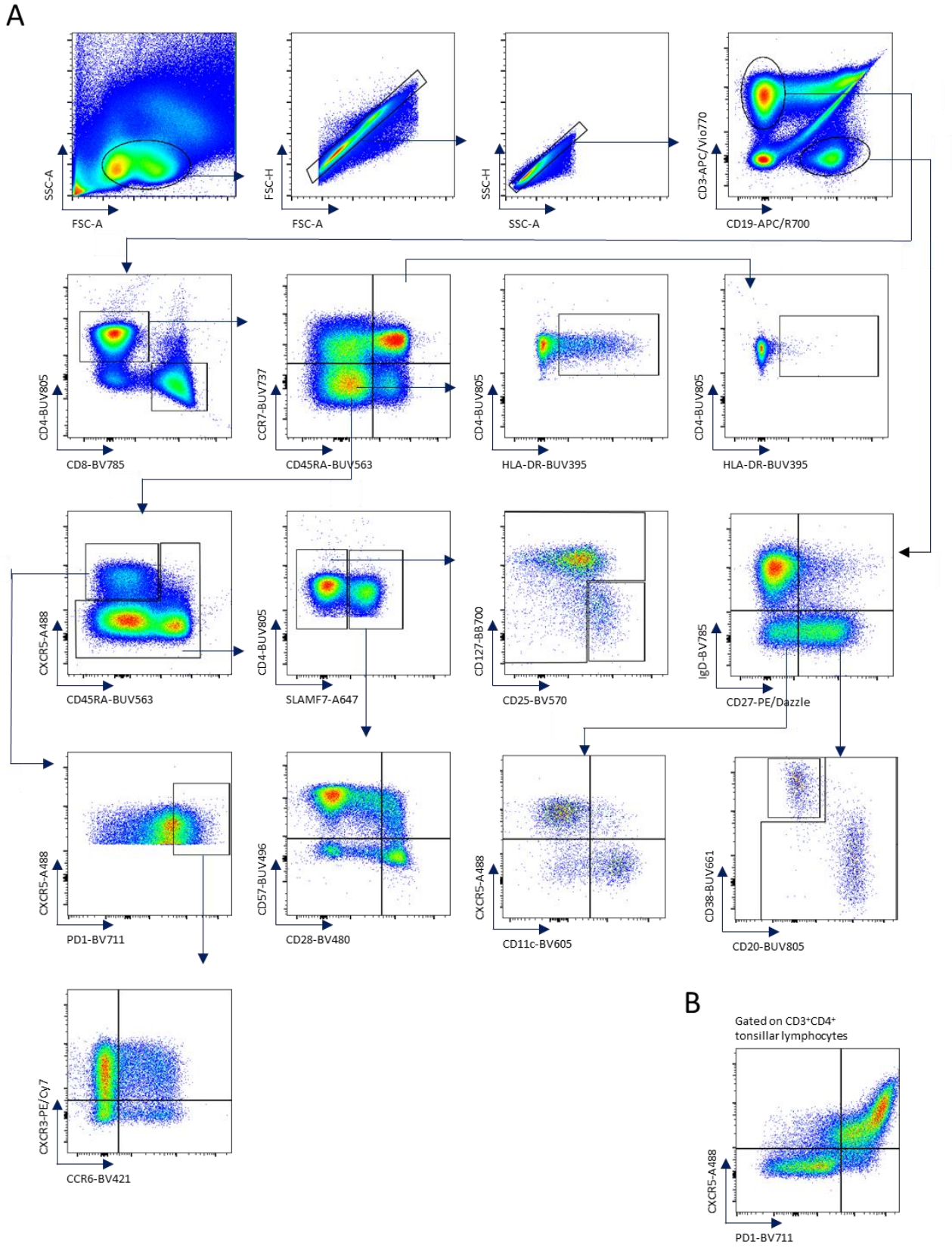
14. Known positive result for HIV I or II antibody, hepatitis B surface antigen, hepatitis B core antibody or hepatitis C antibody.
15. Has received live vaccines within 4 weeks' ok enrollment.
16. Inability to communicate reliably with the investigator.
17. Patient is pregnant or breast feeding or planning to become pregnant while enrolled in the study, up to EOS visit.
18. Positive pregnancy test at screening or during the study.
19. Subjects of childbearing potential who do not agree to use medically acceptable methods of contraception.
20. Known or suspected sensitivity to mammalian cell-derived products or any components of the study drug.
21. History of alcohol and/or substance abuse within 12 months prior to screening.
22. Unable or unwilling to partake in follow-up assessments or required protocol procedures.

Mechanistic Study Procedures

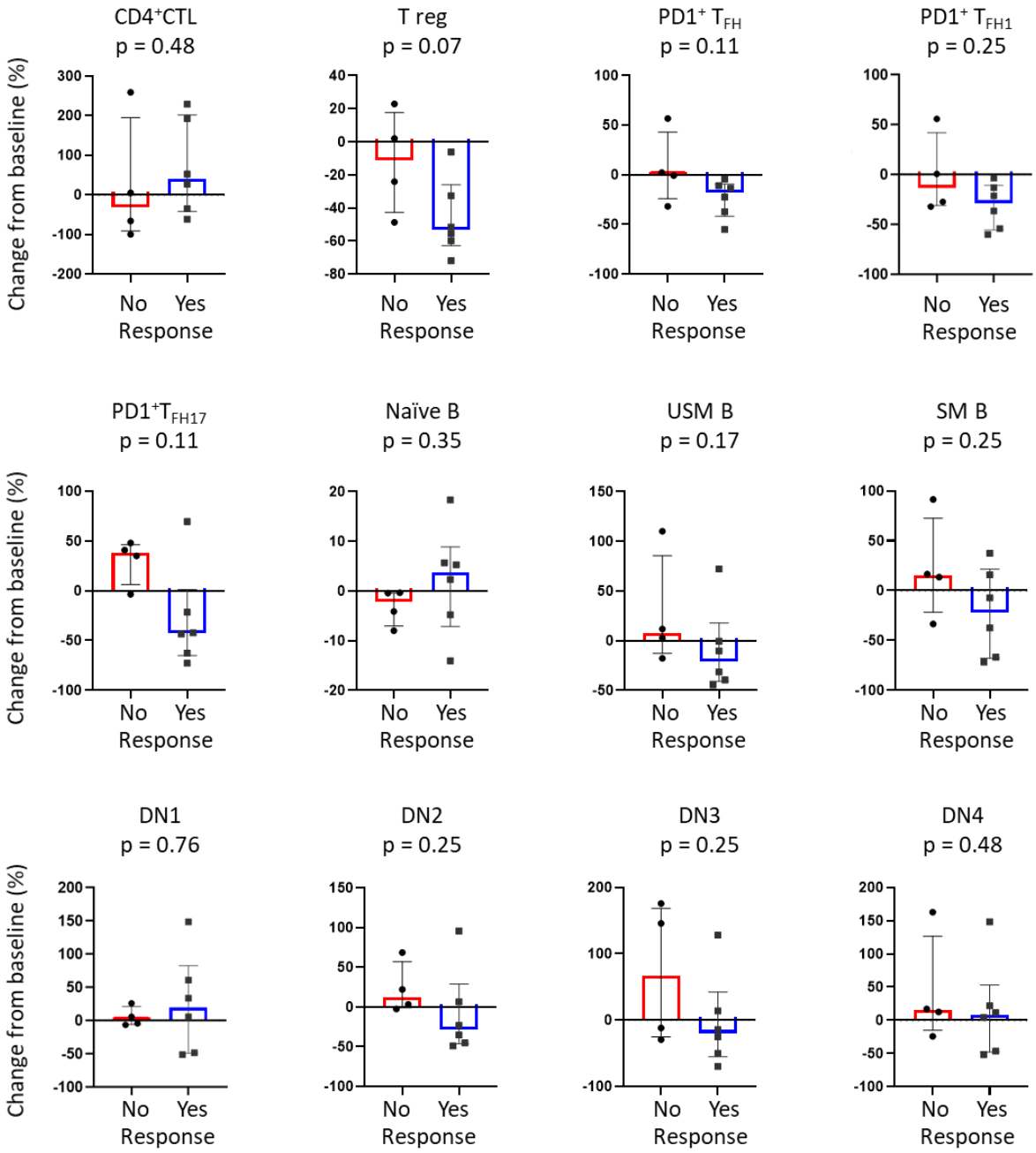
Frozen PBMCs were thawed and washed in complete DMEM. Prior to antibody staining, Fc receptors were blocked using Human TruStain FcX (BioLegend, 422302) at a concentration of 1:20 on ice for 15 minutes. Cells were stained at 37C for 20 minutes, protected from light, at a concentration of approximately 20 million cells/mL using the following antibody panel (manufacturer, clone, concentration used): anti-human CCR7-BUV737 (BD Biosciences, Clone 3D12, 1:200), anti-human CD20-BUV805 (BD Biosciences, Clone 2H7, 1:100), anti-human CCR6-BV421 (BioLegend, Clone G034E3, 1:100), anti-human CD28-BV480 (BD Biosciences, Clone CD28.2, 1:100), anti-human CD21-BV480 (BD Biosciences, Clone B-ly4, 1:100), anti-human CD25-biotin (BioLegend, Clone BC96, 1:100), anti-human PD1-BV711 (BD Biosciences, Clone EH12.1, 1:100), anti-human CD86-BV750 (BD Biosciences, Clone FUN-1, 1:100), anti-human CXCR5-A488 (BD Biosciences, Clone RF8B2, 1:100), anti-human CD127-BB700 (BD Biosciences, Clone HIL-7R-M21, 1:50), anti-human CXCR3-PE-Cy7 (BioLegend, Clone G025H7, 1:50), anti-human SLAMF7-A648 (BD Biosciences, Clone 235614, 1:10). Cells were washed with 1% BSA in PBS after staining, centrifuged and stained for 30 minutes on ice, protected from light, at a concentration of approximately 20 million cells/mL using the following antibody panel: anti-human HLA-DR-BUV395 (BD Biosciences, Clone Tu39, 1:400), anti-human CD45RA-BUV563 (BD Biosciences, Clone HI100, 1:600), anti-human CD57-BUV496 (BD Bioscience, Clone NK-1, 1:400), anti-human CD38-BUV661 (BD Biosciences, Clone HIT2, 1:400), anti-human CD4-BUV805 (BD Biosciences, Clone SK3, 1:100), streptavidin-BV570 (BioLegend, catalogue #405227), anti-human CD11c-BV605 (BD Biosciences, Clone B-ly6, 1:100), anti-human CD8-BV785 (BioLegend, Clone SK1, 1:400), anti-human IgD-BV785 (BioLegend, Clone 1A6-2, 1:100), anti-human CCR4-PE (BioLegend, Clone L291H4, 1:50), anti-human CD27-PE-Dazzle (BioLegend, Clone M-T271, 1:100), anti-human CD19-APC-R700 (BD Biosciences, Clone SJ25C1, 1:25), anti-human CD3-APC-Vio770 (Milltenyi, Clone BW264/56, 1:200). Cells were washed with 1% BSA in PBS after staining, centrifuged and resuspended in 1% BSA in PBS. Just prior to flow cytometry, dead cells were stained with SYTOX AADvanced Dead Cell Stain (Thermo Fisher Scientific, S10274) at a dilution of 1:1000. Flow cytometry was performed on a BD FACS Symphony cytometer (BD Biosciences, San Jose, CA) and rainbow tracking beads were used to ensure consistent signals between flow cytometry batches. FCS files were analyzed using FlowJo software (version 10.7.2). Non-viable cells were determined by dual emission in APC-Vio770 and APC-R700 channels (as per expected emission spectra of DRAQ7 dye). To draw a positive gate on PD1 expression, a single cell suspension of human tonsil cells was stained as part of each batch of flow cytometry. Human tonsil T cells are predominantly composed of $PD1^{+}CXCR5^{+}CD4^{+}$ T cells with a lesser contribution from $PD1^{-}CXCR5^{-}CD4^{+}$ T cells. These two populations, as demonstrated in **Supplemental Figure 1B**, provide a framework for defining PD1 expression as a categorical positive or negative variable.

Supplemental Table 1: Surface Markers

Subset	Defining surface markers
Naive CD4+	CD3+CD4+CD8-CCR7+CD45RA+
Activated CD4+	CD3+CD4+CD8-CCR7-CD45RA-HLADR+
Effector-memory CD4+	CD3+CD4+CD8-CCR7-CD45RA-
Follicular helper T cells	CD3+CD4+CD8-CCR7-CD45RA-CXCR5+
Type 1 follicular helper T cells	CD3+CD4+CD8-CCR7-CD45RA-CXCR5+CXCR3+CCR6-
Type 2 follicular helper T cells	CD3+CD4+CD8-CCR7-CD45RA-CXCR5+CXCR3-CCR6-
Type 17 follicular helper T cells	CD3+CD4+CD8-CCR7-CD45RA-CXCR5+CXCR3-CCR6+
CD4+ cytotoxic T lymphocytes	CD3+CD4+CD8-CCR7-CD45RA-CXCR5-SLAMF7+CD28-CD57+
Regulatory T cells	CD3+CD4+CD8-CCR7-CD45RA-SLAMF7-CXCR5-CD127^{Lo}CD25^{Hi}
Naïve B cells	CD3-CD19+IgD+CD27-
Unswitched memory B cells	CD3-CD19+IgD+CD27+
Switched memory B cells	CD3-CD19+IgD-CD27+CD20+CD38lo/int
Double negative (DN) B cells	CD3-CD19+IgD-CD27-
DN1	CD3-CD19+IgD-CD27-CXCR5+CD11c-
DN2	CD3-CD19+IgD-CD27-CXCR5-CD11c+
DN3	CD3-CD19+IgD-CD27-CXCR5-CD11c-
DN4	CD3-CD19+IgD-CD27-CXCR5+CD11c+
Plasmablasts	CD3-CD19+IgD-CD27+CD20-CD38hi



Supplemental Figure 1: Flow cytometry gating strategy. A) Pseudocolor plots display the comprehensive gating strategy used for flow cytometric analyses of patient PBMCs. B) Pseudocolor plot of human tonsil cells displaying the cut-off gate for defining PD1 positivity.



Supplemental Figure 2: Immunologic effects of abatacept on B and T cells. Dot plots of flow cytometry data displaying changes in relative proportions of respective T and B cell subsets from pre- to post-treatment time points. Blood samples from week 12 (or the latest time point prior to withdrawal if withdrawn prior to week 12) were used as post-treatment samples. Subjects were stratified based on clinical response to abatacept with 'Yes' indicating either a partial or complete clinical response. Each dot plot is labeled with the respective cell population and corresponding statistic. All p-values were calculated using the Mann-Whitney test. Bars represent medians and inter-quartile ranges. p-values <0.05 were considered significant.