Claims

1. A method for monitoring efficacy of treatment of an autoantibody-mediated disease in a subject following treatment with a first FcRn antagonist, the method comprising:

(a) measuring in vitro the frequency of B cells in a blood sample taken from the subject; and

(b) comparing the frequency of B cells to a reference value associated with the autoantibody-mediated disease in the subject,

wherein the treatment is not effective if the frequency of B cells in the sample is greater than or equal to the reference value, and wherein the treatment is effective if the frequency of B cells is less than the reference value.

2. Use of a second FcRn antagonist in the manufacture of a medicament for treating an autoantibody-mediated disease in a subject that has received a first FcRn antagonist and is receiving a corticosteroid dosing regimen, wherein:

(a) a therapeutically effective amount of the second FcRn antagonist is administered to the subject;

(b) the frequency of B cells in a blood sample taken from the subject is measured in vitro; and

(c) the frequency of B cells is compared to a reference value associated with the autoantibody-mediated disease in the subject,

wherein the corticosteroid dosing regimen is maintained if the frequency of B cells in the sample is greater than or equal to the reference value, and wherein the corticosteroid dosing regimen is tapered if the frequency of B cells is less than the reference value.

3. Use of an FcRn antagonist in the manufacture of a medicament for treating an autoantibody-mediated disease in a subject, wherein:

(a) one or more initial doses of a therapeutically effective amount of a first FcRn antagonist is administered to the subject, and

(b) one or more further doses of a therapeutically effective amount of a second FcRn antagonist is administered to the subject if the frequency of B cells in the subject after step (a) is greater than or equal to a reference value associated with the autoantibody-mediated disease in the subject or the first FcRn antagonist is discontinued if the frequency of B cells

in the subject after step (a) is less than a reference value associated with the autoantibody-mediated disease in the subject.

4. A method for determining if a subject that has previously been treated for an autoantibody-mediated disease using a first FcRn antagonist requires further treatment with a second FcRn antagonist, the method comprising:

(a) measuring in vitro the frequency of B cells in a blood sample taken from the subject; and

(b) comparing the frequency of B cells to a reference value associated with the autoantibody-mediated disease in the subject,

wherein if the frequency of B cells in the sample is greater than or equal to the reference value, then the subject is in need of further treatment with the second FcRn antagonist.

5. Use of a second FcRn antagonist in the manufacture of a medicament for treating an autoantibody-mediated disease in a subject, wherein the autoantibody-mediated disease has relapsed in the subject following prior therapy with a first FcRn antagonist and wherein the subject has a frequency of B cells that is greater than or equal to a reference value associated with the autoantibody-mediated disease in the subject, and wherein a therapeutically effective amount of the second FcRn antagonist is administered to the subject.

6. Use of a second FcRn antagonist in the manufacture of a medicament for treating an autoantibody-mediated disease in a subject, wherein the autoantibody-mediated disease has relapsed in the subject following prior therapy with a first FcRn antagonist, wherein a therapeutically effective amount of the second FcRn antagonist is administered to the subject, and wherein the therapeutically effective amount is determined based on the frequency of B cells in a blood sample taken from the subject.

7. A method for monitoring remission of an autoantibody-mediated disease in a subject following treatment with a first FcRn antagonist, the method comprising:

(a) measuring in vitro the frequency of B cells in a blood sample taken from the subject; and

(b) comparing the frequency of B cells to a reference value associated with the autoantibody-mediated disease in the subject,

wherein the subject is in remission from the autoantibody-mediated disease if the frequency of B cells in the sample is lower than the reference value.

8. The method or use according to any one of claims 1-5 or 7, wherein the reference value is:

(a) about 1.5-fold, 2-fold, 3-fold, 4-fold, 5-fold, 6-fold, or 7-fold times a normal frequency of B cells; and optionally wherein the normal frequency of B cells is about 3%, 5%, 10%, 15%, 20%, 25%, or 30% of lymphocytes; or

(b) about 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, or 90% of the maximum frequency of B cells measured in the subject prior to receiving any treatment for the autoantibody-mediated disease; or

(c) about 2-fold, 3-fold, 4-fold, 5-fold, or 6-fold times the lowest frequency of B cells measured in the subject following treatment with the first FcRn antagonist for the autoantibody-mediated disease.

9. The method or use according to any one of claims 1, 2, or 4-8, wherein the subject was previously treated with the first FcRn antagonist at a dose of:

(a) about 10 mg/kg to about 30 mg/kg, administered intravenously; or

(b) about 750 mg to about 3000 mg, administered subcutaneously.

10. The method or use according to any one of the preceding claims, wherein the subject was previously treated with a corticosteroid or an immunosuppressive agent.

11. The method or use according to any one of claims 2, 3, 5, 6, or 8-10, wherein the effective amount of the second FcRn antagonist is:

(a) (i) a higher dose than the previous treatment with the first FcRn antagonist; or

(ii) a lower dose than the previous treatment with the first FcRn antagonist; or

(b) (i) administered more frequently compared to the previous treatment with the first FcRn antagonist; or

(ii) administered less frequently compared to the previous treatment with the first FcRn antagonist; or

(c) (i) administered intravenously at a dose of about 10 mg/kg to about 30 mg/kg once weekly, every two weeks, every three weeks, every four weeks, or every six weeks; or

(ii) administered intravenously at a dose of 10 mg/kg once weekly, every two weeks, every three weeks, every four weeks, or every six weeks; or

(iii) administered intravenously at a dose of 25 mg/kg once weekly, every two weeks, every three weeks, every four weeks, or every six weeks; or

(iv) administered subcutaneously at a fixed dose of about 750 mg to about 3000 mg once weekly, every two weeks, every three weeks, every four weeks, or every six weeks; or

(v) administered subcutaneously at a fixed dose of 1000 mg or 2000 mg once weekly, every two weeks, every three weeks, every four weeks, or every six weeks.

12. The method or use according to any one of claims 3, 5, 6, or 8-11, further comprising administering to the subject an effective amount of a corticosteroid or an immunosuppressive agent; and optionally wherein the effective amount of the corticosteroid is administered at a dose of about 0.25 mg/kg per day; about 0.5 mg/kg per day; about 10 mg per day; or about 20 mg per day.

13. The method or use according to any one of the preceding claims, wherein the frequency of B cells is measured with flow cytometry; and/or wherein the B cells are CD19+ B cells.

14. The method or use according to any one of claims 2-6 or 8-13 wherein the first FcRn antagonist and the second FcRn antagonist are each the same FcRn antagonist; and optionally wherein the FcRn antagonist:

(a) is an anti-FcRn antibody that is further optionally selected from: rozanolixizumab (UCB7665), nipocalimab (M281), orilanolimab (ALXN1830/SYNT001), or batoclimab (IMVT-1401/RVT1401/HBM9161); or

(b) is efgartigimod; or

(c) comprises the amino acid sequence of SEQ ID NO: 1, 2, or 3.

15. The method or use according to any one of claims 2-6 or 8-13, wherein the first FcRn antagonist and the second FcRn antagonist are each a different FcRn antagonist; and optionally wherein:

(a) the first FcRn antagonist and/or the second FcRn antagonist is an anti-FcRn antibody that is further optionally selected from: rozanolixizumab (UCB7665), nipocalimab (M281), orilanolimab (ALXN1830/SYNT001), or batoclimab (IMVT-1401/RVT1401/HBM9161); or

(b) the first FcRn antagonist or the second FcRn antagonist is efgartigimod; or

(c) the first FcRn antagonist or the second FcRn antagonist comprises the amino acid sequence of SEQ ID NO: 1, 2, or 3; or

(d) the first FcRn antagonist is an anti-FcRn antibody that is further optionally selected from rozanolixizumab (UCB7665), nipocalimab (M281), orilanolimab (ALXN1830/SYNT001), or batoclimab (IMVT-1401/RVT1401/HBM9161) and the second FcRn antagonist is efgartigimod; or

(e) the first FcRn antagonist is an anti-FcRn antibody that is further optionally selected from rozanolixizumab (UCB7665), nipocalimab (M281), orilanolimab (ALXN1830/SYNT001), or batoclimab (IMVT-1401/RVT1401/HBM9161) and the second FcRn antagonist comprises the amino acid sequence of SEQ ID NO: 1, 2, or 3.

16. The method or use according to any one of the preceding claims, wherein the subject has not been previously treated with efgartigimod.

17. The method or use according to any one of the preceding claims, wherein the subject has:

(a) one or more physical symptoms of an autoantibody-mediated disease following treatment with the first FcRn antagonist; and/or

(b) a serum level of a pathogenic IgG autoantibody that is associated with relapse of the autoantibody-mediated disease; and optionally wherein the pathogenic IgG autoantibody is an anti-Dsg-3 antibody or an anti-Dsg-1 antibody.

18. The method or use according to any one of the preceding claims, wherein the autoantibody-mediated disease is selected from the group consisting of: allogenic islet graft rejection, alopecia areata, ankylosing spondylitis, antiphospholipid syndrome (APS), autoimmune Addison’s disease, Alzheimer’s disease, antibody-mediated allograft rejection

(AMR), antineutrophil cytoplasmic autoantibodies (ANCA), ANCA vasculitis, autoimmune diseases of the adrenal gland, autoimmune encephalitis, autoimmune hemolytic anemia, autoimmune hepatitis, autoimmune myocarditis, autoimmune neutropenia, autoimmune oophoritis and orchitis, immune thrombocytopenia (ITP or idiopathic thrombocytopenic purpura or idiopathic thrombocytopenia purpura or immune-mediated thrombocytopenia), autoimmune urticaria, Behcet's disease, bullous pemphigoid (BP), cardiomyopathy, Castleman syndrome, celiac sprue-dermatitis, chronic fatigue immune dysfunction syndrome, chronic inflammatory demyelinating polyneuropathy (CIDP), Churg-Strauss syndrome, cicatricial pemphigoid, CREST syndrome, cold agglutinin disease, COVID-19 mediated postural orthostatic tachycardia syndrome (POTS), Crohn's disease, delayed graft function after kidney transplant, dilated cardiomyopathy, discoid lupus, epidermolysis bullosa acquisita, essential mixed cryoglobulinemia, factor VIII deficiency, fibromyalgia-fibromyositis, glomerulonephritis, Grave's disease, Guillain- Barre syndrome (GBS), Goodpasture syndrome, graft-versus-host disease (GVHD), Hashimoto's thyroiditis, hemophilia A, hemolytic disease of the fetus and newborn (HDFN), idiopathic membranous neuropathy, idiopathic pulmonary fibrosis, IgA neuropathy, IgM polyneuropathies, juvenile arthritis, Kawasaki disease, lichen planus, lichen sclerosus, lupus erythematosus, lupus nephritis, membranous neuropathy, membranous nephropathy, Ménière's disease, mixed connective tissue disease, mucous membrane pemphigoid, multiple sclerosis, Type 1 diabetes mellitus, multifocal motor neuropathy (MMN), myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD), myasthenia gravis (MG), generalized myasthenia gravis (gMG), ocular myasthenia gravis (OMG), myositis, neuromyelitis optica (NMO), paraneoplastic bullous pemphigoid, pemphigoid gestationis, pemphigus vulgaris (PV), pemphigus foliaceus (PF), pernicious anemia, polyarteritis nodosa, polychondritis, polyglandular syndromes, polymyalgia rheumatica, polymyositis, dermatomyositis (DM), necrotizing autoimmune myopathy (NAM), antisynthetase syndrome (ASyS), primary agammaglobulinemia, primary biliary cirrhosis, psoriasis, psoriatic arthritis, relapsing polychondritis, Raynaud's phenomenon, Reiter's syndrome, rheumatoid arthritis (RA), sarcoidosis, scleroderma, Sjögren's syndrome, solid organ transplant rejection, stiff-man syndrome, systemic lupus erythematosus (SLE), Takayasu's arteritis, toxic epidermal necrolysis (TEN), Stevens-Johnson syndrome (SJS), temporal arteritis/giant cell arteritis, thrombotic thrombocytopenia purpura (TTP), thyroid eye disease, ulcerative colitis, uveitis, warm autoimmune hemolytic anemia (wAIHA), dermatitis herpetiformis vasculitis, anti-

neutrophil cytoplasmic antibody-associated vasculitides, vitiligo, and Wegener's granulomatosis.