

[0007] As such, a need exists for methods and compositions for the treatment of lupus.

SUMMARY

[0008] Disclosed herein, ~~in one aspect~~, is a method of treating B cell driven autoimmune and/or allergic diseases, such as lupus, comprising administering to a subject in need thereof a B cell inhibitor that is non-depletional. In some embodimentsexamples, the subject has reduced CD32B signaling compared to a healthy subject, wherein the B cell inhibitor is capable of agonizing CD32B despite the reduced CD32B signaling.

[0009] Also disclosed herein is a composition for use as a medicament for the treatment of B cell driven autoimmune and/or allergic diseases, such as lupus, comprising a B cell inhibitor that is non-depletional. In some embodimentsexamples, the composition can be used to treat a subject that has reduced CD32B signaling compared to a healthy subject, wherein the B cell inhibitor is capable of agonizing CD32B despite the reduced CD32B signaling.

[0010] Further disclosed herein is use of a composition for the manufacture of a medicament for the treatment of B cell driven autoimmune and/or allergic diseases, such as lupus, wherein the composition includes a B cell inhibitor that is non-depletional. In some embodimentsexamples, the composition can be used to treat a subject that has reduced CD32B signaling compared to a healthy subject, wherein the B cell inhibitor is capable of agonizing CD32B despite the reduced CD32B signaling.

[0010a] In one aspect, disclosed herein is use of a composition in the manufacture of a medicament for the treatment of B cell driven autoimmune and/or allergic diseases, wherein the composition comprises a B cell inhibitor that is non-depletional, wherein the disease is characterized by reduced CD32B signaling compared to a healthy subject, and wherein the B cell inhibitor is capable of agonizing CD32B despite the reduced CD32B signaling.

[0011] In some embodimentsexamples, the B cell inhibitor is a CD32B×CD79B bi-specific antibody capable of immunospecifically binding an epitope of CD32B and an epitope of CD79B. In some embodimentsexamples, the CD32B×CD79B bi-specific antibody comprises:

- (A) a VL_{CD32B} domain that comprises the amino acid sequence of SEQ ID NO: 1;
- (B) a VH_{CD32B} domain that comprises the amino acid sequence of SEQ ID NO: 2;
- (C) a VL_{CD79B} domain that comprises the amino acid sequence of SEQ ID NO: 3; and
- (D) a VH_{CD79B} domain that comprises the amino acid sequence of SEQ ID NO: 4.

[0012] In some embodimentsexamples, the CD32B x CD79B bi-specific antibody is an Fc diabody comprising:

- (A) a first polypeptide chain that comprises the amino acid sequence of SEQ ID NO: 5;
- (B) a second polypeptide chain that comprises the amino acid sequence of SEQ ID NO: 6; and
- (C) a third polypeptide chain that comprises the amino acid sequence of SEQ ID NO: 7.

[0013] In some [embodimentsexamples](#), the Fc diabody can be administered at a dose of between about 5 mg/kg and about 40 mg/kg, and at a dosage regimen of between one dose per 2 to 8 weeks, for a total of 2 to 20 doses. In some [embodimentsexamples](#), the Fc diabody can be administered at a dose of about 5 to 20 mg/kg, and at a dosage regimen of one dose every 2 to 6 weeks for a total of 5 to 10 doses. In some [embodimentsexamples](#), the Fc diabody can be administered at a dose of about 10 mg/kg and at a dosage regimen of one dose per 2 to 4 weeks for a total of 6 to 8 doses. In some [embodimentsexamples](#), the Fc diabody can be administered at a dose of about 10 mg/kg and at a dosage regimen of one dose every 4 weeks for a total of 6 doses.

[0014] In some [embodimentsexamples](#), the Fc diabody can be administered via an intravenous infusion. In some [embodimentsexamples](#), the Fc diabody can be administered over a period of about 1-10 hours, or about 2-4 hours, or about 2 hours.

[0015] In some [embodimentsexamples](#), the Fc diabody can be administered 10 mg/kg IV or SC equivalent once every 4 weeks, indefinitely (e.g., chronic therapy).

[0016] In some [embodimentsexamples](#), the disease can be selected from Systemic Lupus Erythematosus (SLE), Multiple Sclerosis (MS), Rheumatoid Arthritis (RA), Psoriasis, Dermatomyositis/Polymyositis, Sjogren's Syndrome (SS), Primary Vasculitis (e.g. Polymyalgia rheumatica/Giant cell arteritis/Behçets), Graft vs. Host Disease (GVHD), Myasthenia Gravis, Pemphigus, Neuromyelitis Optica, Anti-NMDA receptor encephalitis, Guillain-Barré syndrome, Chronic inflammatory demyelinating polyneuropathy (CIDP), Grave's ophthalmopathy, IgG4 Related Disease (IgG4-RD), Idiopathic thrombocytopenic purpura (ITP), Inflammatory Bowel Disease (IBD), and Crohn's Disease. In some [embodimentsexamples](#), the disease is Systemic Lupus Erythematosus.

[0017] Also provided herein are pharmaceutical compositions comprising the B cell inhibitors disclosed herein, provided (e.g., packaged) at therapeutically effective unit doses. Instructions for dosage regimens as disclosed herein can also be provided.

BRIEF DESCRIPTION OF THE DRAWINGS

[0018] The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) can be provided by the Office upon request and payment of the necessary fee.

[0019] Figure 1: Dose proportional PK upon repeat dosing.

[0020] Figures 2A-2B: No sustained reduction in % (Figure 2A) or total (Figure 2B) B cells after

CLAIMS

1. Use of a composition ~~for~~in the manufacture of a medicament for the treatment of B cell driven autoimmune and/or allergic diseases, wherein the composition comprises a B cell inhibitor that is non-depletional, wherein the disease is characterized by reduced CD32B signaling compared to a healthy subject, and wherein the B cell inhibitor is capable of agonizing CD32B despite the reduced CD32B signaling.
2. The use of claim 1, wherein the B cell inhibitor is a CD32B×CD79B bi-specific antibody capable of immunospecifically binding an epitope of CD32B and an epitope of CD79B.
3. The ~~method-use~~ of claim 2, wherein the CD32B×CD79B bi-specific antibody comprises:
 - (A) a VL_{CD32B} domain that comprises the amino acid sequence of SEQ ID NO: 1;
 - (B) a VH_{CD32B} domain that comprises the amino acid sequence of SEQ ID NO: 2;
 - (C) a VL_{CD79B} domain that comprises the amino acid sequence of SEQ ID NO: 3; and
 - (D) a VH_{CD79B} domain that comprises the amino acid sequence of SEQ ID NO: 4.
4. The use of claim 3, wherein said CD32B x CD79B bi-specific antibody is an Fc diabody comprising:
 - (A) a first polypeptide chain that comprises the amino acid sequence of SEQ ID NO: 5;
 - (B) a second polypeptide chain that comprises the amino acid sequence of SEQ ID NO: 6; and
 - (C) a third polypeptide chain that comprises the amino acid sequence of SEQ ID NO: 7.
5. The use of claim 4, wherein the Fc diabody is to be administered at a dose of between about 5 mg/kg and about 40 mg/kg, and at a dosage regimen of between one dose per 2 to 8 weeks, for a total of 2 to 20 doses.
6. The use of claim 4, wherein the Fc diabody is to be administered at a dose of about 5 to 20 mg/kg, and at a dosage regimen of one dose every 2 to 6 weeks for a total of 5 to 10 doses.
7. The use of claim 4, wherein the Fc diabody is to be administered at a dose of about 10 mg/kg and at a dosage regimen of one dose per 2 to 4 weeks for a total of 6 to 8 doses.
8. The use of claim 4, wherein the Fc diabody is to be administered at a dose of about 10 mg/kg and at a dosage regimen of one dose every 4 weeks for a total of 6 doses.
9. The use of claim 4, wherein the Fc diabody is to be administered via an intravenous infusion.
10. The use of claim 9, wherein the Fc diabody is to be administered over a period of about

1-10 hours, or about 2-4 hours, or about 2 hours.

11. The use of claim 8, wherein the Fc diabody is to be administered via an intravenous infusion.

12. The use of claim 11, wherein the Fc diabody is to be administered over a period of about 1-10 hours, or about 2-4 hours, or about 2 hours.

13. The use of any one of claims 1-13, wherein the disease is selected from Systemic Lupus Erythematosus (SLE), Multiple Sclerosis (MS), Rheumatoid Arthritis (RA), Psoriasis, Dermatomyositis/Polymyositis, Sjogren's Syndrome (SS), Primary Vasculitis (e.g. Polymyalgia rheumatica/Giant cell arteritis/Behçets), Graft vs. Host Disease (GVHD), Myasthenia Gravis, Pemphigus, Neuromyelitis Optica, Anti-NMDA receptor encephalitis, Guillain-Barré syndrome, Chronic inflammatory demyelinating polyneuropathy (CIDP), Grave's ophthalmopathy, IgG4 Related Disease (IgG4-RD), Idiopathic thrombocytopenic purpura (ITP), Inflammatory Bowel Disease (IBD), and Crohn's Disease.

14. The use of any one of claims 1-13, wherein the disease is Systemic Lupus Erythematosus.

15. The use of any one of claims 1-13, wherein the disease is chronic Systemic Lupus Erythematosus.