

Claims

1. Use of an anti-blood dendritic cell antigen 2 (BDCA2) antibody in the manufacture of a medicament for treating cutaneous lupus erythematosus (CLE) or systemic lupus erythematosus (SLE) in a human subject in need thereof, wherein the human subject is to be subcutaneously administered the anti-BDCA2 antibody at a dose of 225 mg every four weeks, wherein the anti-BDCA2 antibody comprises an immunoglobulin heavy chain variable domain (VH) and an immunoglobulin light chain variable domain (VL), the VH and VL, respectively, comprising:

(a) VH complementarity determining regions (CDRs) VH-CDR1, VH-CDR2, and VH-CDR3, wherein

VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:1;

VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:2; and

VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:3; and

(b) VL CDRs VL-CDR1, VL-CDR2, and VL-CDR3, wherein

VL-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:4;

VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:5; and

VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:6.

2. The use of claim 1, wherein the human subject is to be administered a loading dose of the anti-BDCA2 antibody two weeks after the first administration of the anti-BDCA2 antibody.

3. Use of an anti-blood dendritic cell antigen 2 (BDCA2) antibody in the manufacture of a medicament for treating cutaneous lupus erythematosus (CLE) or systemic lupus erythematosus (SLE) in a human subject in need thereof, wherein the human subject is to be subcutaneously administered the anti-BDCA2 antibody at a dose of 225 mg every four weeks, wherein the human subject is to be administered a loading dose of 225 mg of the anti-BDCA2 antibody two weeks after the first administration of the anti-BDCA2 antibody, wherein the anti-BDCA2 antibody comprises an immunoglobulin heavy chain variable domain (VH) and an immunoglobulin light chain variable domain (VL), the VH and VL, respectively, comprising:

(a) VH complementarity determining regions (CDRs) VH-CDR1, VH-CDR2, and VH-CDR3, wherein

VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:1;

VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:2; and
VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:3; and
(b) VL CDRs VL-CDR1, VL-CDR2, and VL-CDR3, wherein
VL-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:4;
VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:5; and
VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:6.

4. The use of any one of claims 1 to 3, wherein the human subject is to be administered a second loading dose of the anti-BDCA2 antibody.
5. The use of claim 4, wherein the second loading dose is 225 mg.
6. The use of any one of claims 1 to 3, wherein the anti-BDCA2 antibody is to be administered at a dose of 225 mg every four weeks over at least 16 weeks.
7. The use of any one of claims 1 to 6, wherein the anti-BDCA2 antibody is to be administered at a dose of 225 mg every four weeks over at least 52 weeks.
8. The use of any one of claims 1 to 5, wherein at least four doses of the anti-BDCA2 antibody are to be administered to the human subject.
9. The use of any one of claims 1 to 5, wherein at least twelve doses of the anti-BDCA2 antibody are to be administered to the human subject.
10. The use of any one of claims 1 to 5, wherein at least fourteen doses of the anti-BDCA2 antibody are to be administered to the human subject.
11. The use of any one of claims 1 to 5, wherein at least sixteen doses of the anti-BDCA2 antibody are to be administered to the human subject.
12. The use of any one of claims 1 to 11, wherein the use is for treating moderate CLE.

13. The use of any one of claims 1 to 11, wherein the use is for treating severe CLE.
14. The use of any one of claims 1 to 11, wherein the use is for treating acute CLE (ACLE).
15. The use of any one of claims 1 to 11, wherein the use is for treating subacute CLE (SCLE).
16. The use of any one of claims 1 to 11, wherein the use is for treating chronic CLE (CCLE).
17. The use of claim 16, wherein the CCLE is discoid lupus erythematosus (DLE).
18. The use of any one of claims 1 to 11, wherein the use is for treating active CLE.
19. The use of claim 18, wherein the active CLE is with systemic manifestations of lupus and the human subject is intolerant or refractory to antimalarial therapy.
20. The use of claim 18, wherein the active CLE is without systemic manifestations of lupus and the human subject is intolerant or refractory to antimalarial therapy.
21. The use of any one of claims 1 to 20, wherein the use is for treating CLE, wherein the human subject achieves clinically meaningful reduction in Cutaneous Lupus Erythematosus Disease Area and Severity Index-A (CLASI-A) score from baseline about sixteen weeks to about 24 weeks after the first administration of the anti-BDCA2 antibody.
22. The use of any one of claims 1 to 20, wherein the use is for treating CLE, wherein the human subject achieves a clinically meaningful reduction from baseline in disease activity on an CLA-IGA-R specific for CLE about sixteen weeks to about 24 weeks after the first administration of the anti-BDCA2 antibody.
23. The use of any one of claims 1 to 11, wherein the use is for treating active SLE.

24. The use of any one of claims 1 to 11, wherein the use is for treating active, autoantibody-positive SLE.
25. The use of any one of claims 1 to 11, wherein the use is for treating active, autoantibody-positive SLE, and wherein the human subject is receiving a standard of care therapy for SLE.
26. The use of any one of claims 1 to 11, wherein the use is for treating moderate SLE.
27. The use of any one of claims 1 to 11, wherein the use is for severe SLE.
28. The use of any one of claims 1 to 11, wherein the use is for treating SLE, wherein the human subject has a modified SLEDAI-2K ≥ 6 excluding alopecia, fever, lupus-related headache, and organic brain syndrome at initiation of treatment with the anti-BDCA2 antibody.
29. The use of any one of claims 1 to 11, wherein the use is for treating SLE, wherein the human subject has a clinical SLEDAI-2K ≥ 4 excluding alopecia, lupus-related headache and organic brain disease, anti-ds DNA, low complement C3 and/or C4, or fever, at initiation of treatment with the anti-BDCA2 antibody.
30. The use of any one of claims 1 to 11, wherein the use is for treating SLE, wherein the human subject has BILAG-2004 grade A in ≥ 1 organ system or BILAG-2004 grade B in ≥ 2 organ systems at initiation of treatment with the anti-BDCA2 antibody.
31. The use of any one of claims 1 to 11, wherein the human subject is treated with an antimalarial, an oral corticosteroid, and/or an immunosuppressant prior to initiation of treatment with the anti-BDCA2 antibody.
32. The use of any one of claims 1 to 31, wherein the anti-BDCA2 antibody is formulated as a sterile, liquid pharmaceutical composition comprising:
the anti-BDCA2 antibody at a concentration of 150 mg/ml;
sucrose at an a concentration of 3%;

L-histidine at a concentration of 20 mM;
L-Arginine HCl at a concentration of 100 mM;
glutathione at a concentration of 0.4 mM; and
polysorbate 80 (PS80) at a concentration of 0.05%,
wherein the pharmaceutical composition has a pH of 5.7.

33. The use of any one of claim 1 to 32, wherein:
the VH comprises a sequence at least 80% identical to the amino acid sequence of SEQ ID NO:7 and the VL comprises a sequence at least 80% identical to the amino acid sequence of SEQ ID NO:8.

34. The use of any one of claim 1 to 32, wherein:
the VH comprises a sequence at least 90% identical to the amino acid sequence of SEQ ID NO:7 and the VL comprises a sequence at least 90% identical to the amino acid sequence of SEQ ID NO:8.

35. The use of any one of claim 1 to 32, wherein:
the VH comprises the amino acid sequence set forth in SEQ ID NO:7 and the VL comprises the amino acid sequence set forth in SEQ ID NO:8.

36. The use of any one of claims 1 to 35, wherein the anti-BDCA2 antibody comprises an immunoglobulin heavy chain and an immunoglobulin light chain, wherein:
the immunoglobulin heavy chain comprises a sequence at least 80% identical to the amino acid sequence of SEQ ID NO:9 and the immunoglobulin light chain comprises a sequence at least 80% identical to the amino acid sequence of SEQ ID NO:10.

37. The use of any one of claims 1 to 35, wherein the anti-BDCA2 antibody comprises an immunoglobulin heavy chain and an immunoglobulin light chain, wherein:
the immunoglobulin heavy chain comprises a sequence at least 90% identical to the amino acid sequence of SEQ ID NO:9 and the immunoglobulin light chain comprises a sequence at least 90% identical to the amino acid sequence of SEQ ID NO:10.

38. The use of any one of claims 1 to 35, wherein the anti-BDCA2 antibody comprises an immunoglobulin heavy chain and an immunoglobulin light chain, wherein:

the immunoglobulin heavy chain comprises the amino acid sequence set forth in SEQ ID NO:9 and the immunoglobulin light chain comprises the amino acid sequence set forth in SEQ ID NO:10.

39. A pre-filled syringe comprising a sterile preparation of an anti-blood dendritic cell antigen 2 (BDCA2) antibody, wherein the pre-filled syringe is adapted for subcutaneous administration of the anti-BDCA2 antibody at a fixed dose of 225 mg, and wherein the anti-BDCA2 antibody comprises an immunoglobulin heavy chain variable domain (VH) and an immunoglobulin light chain variable domain (VL), the VH and VL, respectively, comprising:

(a) VH complementarity determining regions (CDRs) VH-CDR1, VH-CDR2, and VH-CDR3, wherein

VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:1;

VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:2; and

VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:3; and

(b) VL CDRs VL-CDR1, VL-CDR2, and VL-CDR3, wherein

VL-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:4;

VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:5; and

VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:6.

40. The pre-filled syringe of claim 39, wherein:

the VH comprises a sequence at least 80% identical to the amino acid sequence of SEQ ID NO:7 and the VL comprises a sequence at least 80% identical to the amino acid sequence of SEQ ID NO:8.

41. The pre-filled syringe of claim 39, wherein:

the VH comprises a sequence at least 90% identical to the amino acid sequence of SEQ ID NO:7 and the VL comprises a sequence at least 90% identical to the amino acid sequence of SEQ ID NO:8.

42. The pre-filled syringe of claim 39, wherein:

the VH comprises the amino acid sequence set forth in SEQ ID NO:7 and the VL comprises the amino acid sequence set forth in SEQ ID NO:8.

43. The pre-filled syringe of any one of claims 39 to 42, wherein the anti-BDCA2 antibody comprises an immunoglobulin heavy chain and an immunoglobulin light chain, wherein:

the immunoglobulin heavy chain comprises a sequence at least 80% identical to the amino acid sequence of SEQ ID NO:9 and the immunoglobulin light chain comprises a sequence at least 80% identical to the amino acid sequence of SEQ ID NO:10.

44. The pre-filled syringe of any one of claims 39 to 42, wherein the anti-BDCA2 antibody comprises an immunoglobulin heavy chain and an immunoglobulin light chain, wherein:

the immunoglobulin heavy chain comprises a sequence at least 90% identical to the amino acid sequence of SEQ ID NO:9 and the immunoglobulin light chain comprises a sequence at least 90% identical to the amino acid sequence of SEQ ID NO:10.

45. The pre-filled syringe of any one of claims 39 to 42, wherein the anti-BDCA2 antibody comprises an immunoglobulin heavy chain and an immunoglobulin light chain, wherein:

the immunoglobulin heavy chain comprises the amino acid sequence set forth in SEQ ID NO:9 and the immunoglobulin light chain comprises the amino acid sequence set forth in SEQ ID NO:10.

46. The pre-filled syringe of any one of claims 39 to 45, wherein the anti-BDCA2 antibody is formulated as a sterile, liquid pharmaceutical composition comprising:

the anti-BDCA2 antibody at a concentration of 150 mg/ml;

sucrose at an a concentration of 3%;

L-histidine at a concentration of 20 mM;

L-Arginine HCl at a concentration of 100 mM;

glutathione at a concentration of 0.4 mM; and

polysorbate 80 (PS80) at a concentration of 0.05%,

wherein the pharmaceutical composition has a pH of 5.7.

47. The pre-filled syringe of any one of claims 39 to 46, wherein the pre-filled syringe is a United States Pharmacopeia or European Pharmacopeia, Type 1, clear glass vial that is stoppered with a rubber stopper.