

CLAIMS

What is claimed is:

1. A method of treating a patient having AL amyloidosis associated with the deposition of misfolded immunoglobulin light chain proteins having the amino acid sequence GD at positions 81-82 (Kabat numbering), comprising administering an effective dosage of a chimeric or humanized version of antibody 2A4 (ATCC Accession Number 9662) to the patient.
2. The method of claim 1, wherein the antibody is a humanized version of antibody 2A4.
3. The method of claim 1, wherein the antibody comprises a light chain variable region comprising three complementarity determining regions set forth as SEQ ID NOs: 1, 2, and 3, and a heavy chain variable region comprising three complementarity determining regions set forth as SEQ ID NOs: 4, 5, and 6.
4. The method of claim 1, wherein the antibody comprises a light chain variable region comprising an amino acid sequence set forth as SEQ ID NO: 7, 8, or 9 and a heavy chain variable region comprising an amino acid sequence set forth as SEQ ID NO: 10, 11, or 12.
5. The method of claim 1, wherein the antibody comprises a light chain variable region comprising an amino acid sequence set forth as SEQ ID NO: 9 and a heavy chain variable region comprising an amino acid sequence set forth as SEQ ID NO: 12.
6. The method of claim 1, wherein the antibody comprises a light chain comprising an amino acid sequence set forth as SEQ ID NO: 13 and a heavy chain comprising an amino acid sequence set forth as SEQ ID NO: 14.
7. The method of claim 1, wherein the antibody is an antigen-binding fragment of an antibody selected from the group consisting of Fab, Fab', F(ab')₂, F(ab)c, Dab, nanobody or Fv fragment.

8. The method of claim 1, wherein the effective dosage of the antibody is administered as a pharmaceutical formulation comprising:

- a) the antibody at a concentration within the range from about 1 mg/mL to about 100 mg/mL;
- b) histidine buffer at a concentration within the range from about 20 mM to about 30 mM;
- c) trehalose at a concentration within the range from about 210 mM to about 250 mM; and
- d) polysorbate 20 at a concentration within the range from about 0.005% to about 0.05% by weight; and

wherein the pharmaceutical formulation is characterized by a pH within the range from about 6 to about 7.

9. The method of claim 8, wherein:

- a) the antibody is present at a concentration of about 50 mg/mL;
 - b) the histidine buffer is present at a concentration of about 25 mM;
 - c) the trehalose is present at a concentration of about 230 mM;
 - d) the polysorbate 20 is present at a concentration of about 0.2 g/L; and
- wherein the pH is about 6.5.

10. The method of claim 1, wherein the effective dosage is from about 0.5 mg/kg to about 30 mg/kg and the antibody is administered intravenously or subcutaneously at a frequency from about weekly to about quarterly.

11. The method of claim 1, wherein the effective dosage is about 24 mg/kg and the antibody is administered intravenously every 28 days.

12. The method of claim 10, wherein the duration of the treatment is the length of time necessary to achieve a treatment benefit.

13. The method of claim 11, wherein the duration of the treatment is the length of time necessary to achieve a treatment benefit.

14. Use of a chimeric or humanized version of antibody 2A4 (ATCC Accession Number 9662) for the treatment AL amyloidosis associated with the deposition of misfolded immunoglobulin light chain proteins having the amino acid sequence GD at positions 81-82 (Kabat numbering).

15. The use of claim 14, wherein the antibody is a humanized version of antibody 2A4.

16. The use of claim 14, wherein the antibody comprises a light chain variable region comprising three complementarity determining regions set forth as SEQ ID NOs: 1, 2, and 3, and a heavy chain variable region comprising three complementarity determining regions set forth as SEQ ID NOs: 4, 5, and 6.

17. The use of claim 14, wherein the antibody comprises a light chain variable region comprising an amino acid sequence set forth as SEQ ID NO: 7, 8, or 9 and a heavy chain variable region comprising an amino acid sequence set forth as SEQ ID NO: 10, 11, or 12.

18. The use of claim 14, wherein the antibody comprises a light chain variable region comprising an amino acid sequence set forth as SEQ ID NO: 9 and a heavy chain variable region comprising an amino acid sequence set forth as SEQ ID NO: 12.

19. The use of claim 14, wherein the antibody comprises a light chain comprising an amino acid sequence set forth as SEQ ID NO: 13 and a heavy chain comprising an amino acid sequence set forth as SEQ ID NO: 14.

20. The use of claim 14, wherein the antibody is an antigen-binding fragment of an antibody selected from the group consisting of Fab, Fab', F(ab')₂, F(ab)c, Dab, nanobody or Fv fragment.

21. The use of claim 14, wherein the effective dosage of the antibody is administered as a pharmaceutical formulation comprising:

- a) the antibody at a concentration within the range from about 1 mg/mL to about 100 mg/mL;
- b) histidine buffer at a concentration within the range from about 20 mM to about 30 mM;
- c) trehalose at a concentration within the range from about 210 mM to about 250 mM; and
- d) polysorbate 20 at a concentration within the range from about 0.005% to about 0.05% by weight; and

wherein the pharmaceutical formulation is characterized by a pH within the range from about 6 to about 7.

22. The use of claim 21, wherein:

- a) the antibody is present at a concentration of about 50 mg/mL;
 - b) the histidine buffer is present at a concentration of about 25 mM;
 - c) the trehalose is present at a concentration of about 230 mM;
 - d) the polysorbate 20 is present at a concentration of about 0.2 g/L; and
- wherein the pH is about 6.5.

23. The use of claim 14, wherein the antibody is intravenously or subcutaneously administrable to a patient in an amount from about 0.5 mg/kg to about 30 mg/kg at a frequency from about weekly to about quarterly.

24. The use of claim 14, wherein the antibody is intravenously administrable to a patient in an amount of about 24 mg/kg every 28 days.

25. The use of claim 23, wherein the antibody is administrable for a length of time necessary to achieve a treatment benefit.

26. The use of claim 24, wherein the antibody is administrable for a length of time necessary to achieve a treatment benefit.

27. Use of a chimeric or humanized version of antibody 2A4 (ATCC Accession Number 9662) in the manufacture of a medicament for the treatment of AL amyloidosis associated with the deposition of misfolded immunoglobulin light chain proteins having the amino acid sequence GD at positions 81-82 (Kabat numbering).

28. The use of claim 27, wherein the antibody is a humanized version of antibody 2A4.

29. The use of claim 27, wherein the antibody comprises a light chain variable region comprising three complementarity determining regions set forth as SEQ ID NOs: 1, 2, and 3, and a heavy chain variable region comprising three complementarity determining regions set forth as SEQ ID NOs: 4, 5, and 6.

30. The use of claim 27, wherein the antibody comprises a light chain variable region comprising an amino acid sequence set forth as SEQ ID NO: 7, 8, or 9 and a heavy chain variable region comprising an amino acid sequence set forth as SEQ ID NO: 10, 11, or 12.

31. The use of claim 27, wherein the antibody comprises a light chain variable region comprising an amino acid sequence set forth as SEQ ID NO: 9 and a heavy chain variable region comprising an amino acid sequence set forth as SEQ ID NO: 12.

32. The use of claim 27, wherein the antibody comprises a light chain comprising an amino acid sequence set forth as SEQ ID NO: 13 and a heavy chain comprising an amino acid sequence set forth as SEQ ID NO: 14.

33. The use of claim 27, wherein the antibody is an antigen-binding fragment of an antibody selected from the group consisting of Fab, Fab', F(ab')₂, F(ab)₂c, Dab, nanobody or Fv fragment.

34. The use of claim 27, wherein the effective dosage of the antibody is administered as a pharmaceutical formulation comprising:

- a) the antibody at a concentration within the range from about 1 mg/mL to about 100 mg/mL;
- b) histidine buffer at a concentration within the range from about 20 mM to about 30 mM;
- c) trehalose at a concentration within the range from about 210 mM to about 250 mM; and
- d) polysorbate 20 at a concentration within the range from about 0.005% to about 0.05% by weight; and

wherein the pharmaceutical formulation is characterized by a pH within the range from about 6 to about 7.

35. The use of claim 34, wherein:

- a) the antibody is present at a concentration of about 50 mg/mL;
 - b) the histidine buffer is present at a concentration of about 25 mM;
 - c) the trehalose is present at a concentration of about 230 mM;
 - d) the polysorbate 20 is present at a concentration of about 0.2 g/L; and
- wherein the pH is about 6.5.

36. The use of claim 27, wherein the antibody is intravenously or subcutaneously administrable to a patient in an amount from about 0.5 mg/kg to about 30 mg/kg at a frequency from about weekly to about quarterly.

37. The use of claim 27, wherein the antibody is intravenously administrable to a patient in an amount of about 24 mg/kg every 28 days.

38. The use of claim 37, wherein the antibody is administrable for a length of time necessary to achieve a treatment benefit.

39. The use of claim 36, wherein the antibody is administrable for a length of time necessary to achieve a treatment benefit.

40. A chimeric or humanized version of antibody 2A4 (ATCC Accession Number 9662) for use in the treatment of AL amyloidosis associated with the deposition of misfolded immunoglobulin light chain proteins having the amino acid sequence GD at positions 81-82 (Kabat numbering).

41. The antibody for use of claim 40, wherein the antibody is a humanized version of antibody 2A4.

42. The antibody for use of claim 40, wherein the antibody comprises a light chain variable region comprising three complementarity determining regions set forth as SEQ ID NOs: 1, 2, and 3, and a heavy chain variable region comprising three complementarity determining regions set forth as SEQ ID NOs: 4, 5, and 6.

43. The antibody for use of claim 40, wherein the antibody comprises a light chain variable region comprising an amino acid sequence set forth as SEQ ID NO: 7, 8, or 9 and a heavy chain variable region comprising an amino acid sequence set forth as SEQ ID NO: 10, 11, or 12.

44. The antibody for use of claim 40, wherein the antibody comprises a light chain variable region comprising an amino acid sequence set forth as SEQ ID NO: 9 and a heavy chain variable region comprising an amino acid sequence set forth as SEQ ID NO: 12.

45. The antibody for use of claim 40, wherein the antibody comprises a light chain comprising an amino acid sequence set forth as SEQ ID NO: 13 and a heavy chain comprising an amino acid sequence set forth as SEQ ID NO: 14.

46. The antibody for use of claim 40, wherein the antibody is an antigen-binding fragment of an antibody selected from the group consisting of Fab, Fab', F(ab')₂, F(ab)_c, Dab, nanobody or Fv fragment.

47. The antibody for use of claim 40, wherein the effective dosage of the antibody is administered as a pharmaceutical formulation comprising:

- a) the antibody at a concentration within the range from about 1 mg/mL to about 100 mg/mL;
- b) histidine buffer at a concentration within the range from about 20 mM to about 30 mM;
- c) trehalose at a concentration within the range from about 210 mM to about 250 mM; and
- d) polysorbate 20 at a concentration within the range from about 0.005% to about 0.05% by weight; and

wherein the pharmaceutical formulation is characterized by a pH within the range from about 6 to about 7.

48. The antibody for use of claim 47, wherein:

- a) the antibody is present at a concentration of about 50 mg/mL;
 - b) the histidine buffer is present at a concentration of about 25 mM;
 - c) the trehalose is present at a concentration of about 230 mM;
 - d) the polysorbate 20 is present at a concentration of about 0.2 g/L; and
- wherein the pH is about 6.5.

49. The antibody for use of claim 40, wherein the antibody is intravenously or subcutaneously administrable to a patient in an amount from about 0.5 mg/kg to about 30 mg/kg at a frequency from about weekly to about quarterly.

50. The antibody for use of claim 40, wherein the antibody is intravenously administrable to a patient in an amount of about 24 mg/kg every 28 days.

51. The antibody for use of claim 49, wherein the antibody is administrable for a length of time necessary to achieve a treatment benefit.

52. The antibody for use of claim 50, wherein the antibody is administrable for a length of time necessary to achieve a treatment benefit.