CLAIMS

1. A pharmaceutical composition for treating an autoimmune disease comprising a pharmaceutically acceptable carrier and an agent capable of activating CD4+CD25+ regulatory T cells, wherein the composition is to be administered to a subject in a dose of the agent from 0.2 mg to 30 mg.

2. A pharmaceutical composition according to claim 1 wherein the agent is to be administered to a subject in an amount from 0.2 to 20 mg.

3. A pharmaceutical composition according to claim 2 wherein the agent is to be administered to a subject in an amount from 0.3 to 5 mg.

4. A pharmaceutical composition according to claim 3 wherein the agent is to be administered to a subject in an amount from 0.3 to 1 mg.

5. A pharmaceutical composition for treating an autoimmune disease comprising a pharmaceutically acceptable carrier and an agent capable of activating CD4+CD25+ regulatory T cells, wherein the composition is to be administered to a subject in a dose of the agent from 0.10 to 20 mg/m^2 body surface area of the subject.

6. A pharmaceutical composition according to claim 5 wherein the composition is to be administered to a subject in a dose of the agent from 0.12 to 15 mg/m^2.

7. A pharmaceutical composition according to claim 6 wherein the composition is to be administered to a subject in a dose of the agent from 0.20 to 10 mg/m^2.

8. A pharmaceutical composition according to claim 7 wherein the composition is to be administered to a subject in a dose of the agent from 0.30 to 0.50 mg/m^2.

9. A pharmaceutical composition for treating an autoimmune disease comprising a pharmaceutically acceptable carrier and an agent capable of activating CD4+CD25+

regulatory T cells, wherein the composition is to be administered to a subject in a dose of the agent from 1 to 500 μg/kg.

10. A pharmaceutical composition according to claim 9 wherein the composition is to be administered to a subject in a dose of the agent from 2 to 400 μg/kg.

11. A pharmaceutical composition according to claim 10 wherein the composition is to be administered to a subject in a dose of the agent from 2 to 250 μg/kg.

12. A pharmaceutical composition according to claim 11 wherein the composition is to be administered to a subject in a dose of the agent from 2.5 to 20 μg/kg.

13. A pharmaceutical composition according to any preceding claim wherein the autoimmune disease is selected from psoriasis, rheumatoid arthritis, multiple sclerosis, type-1 diabetes, inflammatory bowel diseases, Crohn's disease, autoimmune thyreoiditis, autoimmune myasthenia gravis, systemic lupus erythematosus and transplantation-related diseases such as graft-versus-host or general organ tolerance issues.

14. A pharmaceutical composition according to claim 13 wherein the disease is psoriasis.

15. A pharmaceutical composition according to claim 14 wherein the composition is capable of treating psoriasis by providing at least a 40% improvement in the Psoriasis Area and Severity Index (PASI) score of the patient.

16. A pharmaceutical composition according to claim 15 wherein the composition is capable of treating psoriasis by providing at least a 50% improvement in the Psoriasis Area and Severity Index (PASI) score of the patient.

17. A pharmaceutical composition according to claim 13 wherein the disease is rheumatoid arthritis.

18. A pharmaceutical composition according to any preceding claim wherein the composition is for parenteral administration.

19. A pharmaceutical composition according to claim 18, wherein the composition is for intramuscular administration, intravenous administration or subcutaneous administration.

20. A pharmaceutical composition according to claim 19 wherein the composition is for intravenous administration and is provided in a dosage volume of 0.5 to 500 ml or in a form for dilution to the dosage volume of 0.5 to 500 ml.

21. A pharmaceutical composition according to claim 20 wherein the dosage volume is 15 to 25 ml.

22. A pharmaceutical composition according to claim 19 wherein the composition is for subcutaneous administration and is provided in a dosage volume of 0.1 to 3 ml.

23. A pharmaceutical composition according to claim 22 wherein the dosage volume is 0.5 to 1.5ml.

24. A pharmaceutical composition according to claim 19 wherein the composition is for intramuscular administration and is provided in a dosage volume of 0.1 to 3 ml.

25. A pharmaceutical composition according to claim 24 wherein the composition is provided in a dosage volume of 0.5 to 1.5 ml.

26. A pharmaceutical composition according to any preceding claim which is for use as a single dose or as part of a plurality of doses.

27. A pharmaceutical composition according to claim 26 wherein the composition is part of a plurality of doses and each dose is to be administered daily, every two days, weekly, every two weeks, every four weeks, every eight weeks, every twelve weeks, every twenty-four weeks, every forty-eight weeks, every six months or every year.

28. A pharmaceutical composition according to claim 27 wherein the autoimmune disease is psoriasis and the dose is to be administered once every two weeks.

29. A pharmaceutical composition according to claim 27 wherein the autoimmune disease is psoriasis and the dose is to be administered once every four weeks.

30 A pharmaceutical composition according to claim 27 wherein the autoimmune disease is rheumatoid arthritis and the dose is to be administered once every two weeks.

31. A pharmaceutical composition according to claim 27 wherein the autoimmune disease is rheumatoid arthritis and the dose is to be administered once every four weeks.

32. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and an agent capable of activating CD4+CD25+ regulatory T cells, wherein the agent is present in a concentration of from 10 μg/ml to 150 mg/ml.

33. A pharmaceutical composition according to claim 32 wherein the agent is present in a concentration of 0.5 mg/ml to 75 mg/ml.

34. A pharmaceutical composition according to claim 32 or 33 wherein the volume of the composition is from 0.5 to 500 ml.

35. A pharmaceutical composition according to claim 34 wherein the volume of the composition is from 15 to 25 ml.

36. A pharmaceutical composition according to claim 32 wherein the agent is present in a concentration of from 10 to 28 mg/ml.

37. A pharmaceutical composition according to claim 36 wherein the volume of the composition is 0.1 to 3 ml.

38. A pharmaceutical composition according to claim 37 wherein the volume of the composition is 0.5 to 1.5 ml.

39. A pharmaceutical composition according to any preceding claim wherein within the period of 10 minutes after the beginning of administration to 96 hours after the completion of administration the level of a cytokine in the subject's blood plasma is less than a 20 fold increase of the level immediately prior to administration, and wherein the cytokine is selected from IFN-γ, TNF-α, IL-6 and IL-2.

40. A pharmaceutical composition according to any one of claims 1 to 38 wherein within the period of 10 minutes after the beginning of administration to 96 hours after the completion of administration the level of a cytokine in the subject's blood plasma is less than a 20 fold increase of the upper limit of normal (ULN) value, wherein the cytokine is selected from IFN-γ, TNF-α, IL-6 and IL-2, and wherein the ULN value is 3.8, 2.8, 4.4, and 19.4 pg/ml respectively.

41. A pharmaceutical composition according to any preceding claim wherein within the period of 72 to 96 hours after administration the cell count of CD4+ lymphocytes in the subject's blood plasma is at least 250 cells/μl.

42. A pharmaceutical composition according to any preceding claim wherein the agent is a humanized monoclonal antibody or fragment or derivative thereof.

43. A pharmaceutical composition according to claim 42 wherein the agent is an anti-CD4 antibody or fragment or derivative thereof.

44. A pharmaceutical composition according to any preceding claim wherein the agent is a humanized anti-CD4 antibody, or fragment or derivative thereof having V domains defined by the following polypeptide sequences:

- H chain V domain:

EEQLVESGGGLVKPGGSLRLSCAASGFSFSDCRMYWLRQAPGKGLEWIGVISVKSEN YGANYAESVRGRFTISRDDSKNTVYLQMNSLKTEDTAVYYCSASYYRYDVGAWFA YWGQGTLVTVSS (SEQ ID NO: 1)

- L chain V domain:

DIVMTQSPDSLAVSLGERATINCRASKSVSTSGYSYIYWYQQKPGQPPKLLIYLASILE SGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQHSRELPWTFGQGTKVEIK (SEQ ID NO: 2).

or V domains comprising polypeptide sequences having at least 80% sequence identity with SEQ ID NO: 1 and SEQ ID NO: 2.

45. A pharmaceutical composition according to any preceding claim wherein the agent is a humanized anti-CD4 antibody derived from the mouse monoclonal anti-CD4 antibody B-F5.

46. A method of treatment of an autoimmune disease, which method comprises administering a pharmaceutical composition to a subject, wherein the composition comprises an agent capable of activating CD4+CD25+ regulatory T cells, and wherein the agent is administered to the subject in a dose as defined in any one of claims 1 to 12.

47. A method of treatment according to claim 46 wherein the autoimmune disease is as defined in claims 13, claim 14 or claim 17.

48. A method of treatment according to claim 46 or claim 47 wherein the agent is a humanized anti-CD4 antibody or fragment or derivative thereof derived from the mouse monoclonal anti-CD4 antibody B-F5.

49. A method of treatment according to any one of claims 46 to 48 wherein the agent is a humanized anti-CD4 antibody or fragment or derivative thereof having V domains defined by the following peptide sequences:

- H chain V domain:

EEQLVESGGGLVKPGGSLRLSCAASGFSFSDCRMYWLRQAPGKGLEWIGVISVKSEN YGANYAESVRGRFTISRDDSKNTVYLQMNSLKTEDTAVYYCSASYYRYDVGAWFA YWGQGTLVTVSS (SEQ ID NO: 1)

- L chain V domain:

DIVMTQSPDSLAVSLGERATINCRASKSVSTSGYSYIYWYQQKPGQPPKLLIYLASILE SGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQHSRELPWTFGQGTKVEIK (SEQ ID NO: 2).

or V domains comprising polypeptide sequences having at least 80% sequence identity with SEQ ID NO: 1 and SEQ ID NO: 2.

50. A pharmaceutical composition according to claim 27 wherein the autoimmune disease is psoriasis and the dose is to be administered once every week.

51. A pharmaceutical composition according to claim 27 wherein the autoimmune disease is rheumatoid arthritis and the dose is to be administered once every week.

52. A pharmaceutical composition according to any preceding claim wherein within the period of 3 to 6 hours after administration the cell count of CD4+ lymphocytes in the subject's blood plasma is below 250 cells/µl.

53. A pharmaceutical composition according to any one of claims 1 to 52 wherein within the period of 72 to 96 hours after administration the cell count of CD4+ lymphocytes in the subject's blood plasma is equal to or higher than 50% of the cell count of the subject immediately prior to administration.

54. A pharmaceutical composition according to claim 15 or claim 16 wherein the improvement is seen at 56 days after administration of a single dose of the composition.

55. A pharmaceutical composition according to claim 15 or 16 wherein the improvement is seen at 75 days after administration of a single dose of the composition.

56. A pharmaceutical composition according to any one of claims 15, 16, 54 or 55 wherein the dose of the agent is 0.5 mg.

57. A pharmaceutical composition according to any one of claims 15, 16, 54 or 55 wherein the dose of the agent is 2.5 mg.

Claims

1. Use of a humanized anti-CD4 antibody capable of activating CD4+CD25+ regulatory T cells for the manufacture of a medicament for treating an autoimmune disease in a subject, wherein the humanized anti-CD4 antibody comprises an H chain V domain, an L chain V domain and an IgG1 constant domain wherein:

(a) the H chain V domain comprises the sequences DCRMY, VISVKSENYGANYAESVRG and SYYRYDVGAWFAY, and the L chain V domain comprises the sequences RASKSVSTSGYSYIY, LASILES and QHSRELPWT; and/or

(b) the H chain V domain has at least 80% sequence identity with SEQ ID No: 1 and the L chain V domain has at least 80% sequence identity with SEQ ID No: 2,

wherein the medicament is to be administered to the subject intravenously in a dose of the humanized anti-CD4 antibody from 0.2 mg to 5 mg,

and wherein the medicament is to be administered weekly, every two weeks, every four weeks, every calendar month or every six weeks.

2. Use of a humanized anti-CD4 antibody capable of activating CD4+CD25+ regulatory T cells for the manufacture of a medicament for treating an autoimmune disease in a subject, wherein the humanized anti-CD4 antibody comprises an H chain V domain, an L chain V domain and an IgG1 constant domain wherein:

(a) the H chain V domain comprises the sequences DCRMY, VISVKSENYGANYAESVRG and SYYRYDVGAWFAY, and the L chain V domain comprises the sequences RASKSVSTSGYSYIY, LASILES and QHSRELPWT; and/or

(b) the H chain V domain has at least 80% sequence identity with SEQ ID No: 1 and the L chain V domain has at least 80% sequence identity with SEQ ID No: 2,

wherein the medicament is to be administered to the subject intravenously in a dose of the humanized anti-CD4 antibody from 2.5 to 20 µg/kg of body mass of the subject,

and wherein the medicament is to be administered weekly, every two weeks, every four weeks, every calendar month or every six weeks.

3. Use according to claim 1 or claim 2 wherein the medicament is to be administered to the subject in a dose of the humanized anti-CD4 antibody from: (i) 0.3 to 5 mg; or (ii) 20 µg/kg.

4. Use of a humanized anti-CD4 antibody capable of activating CD4+CD25+ regulatory T cells for the manufacture of a medicament for treating an autoimmune disease in a subject, wherein the humanized anti-CD4 antibody comprises an H chain V domain, an L chain V domain and an IgG1 constant domain wherein:

(a) the H chain V domain comprises the sequences DCRMY, VISVKSENYGANYAESVRG and SYYRYDVGAWFAY, and the L chain V domain comprises the sequences RASKSVSTSGYSYIY, LASILES and QHSRELPWT; and/or

(b) the H chain V domain has at least 80% sequence identity with SEQ ID No: 1 and the L chain V domain has at least 80% sequence identity with SEQ ID No: 2,

wherein the medicament is to be administered to a subject intravenously in a dose of the humanized anti-CD4 antibody over a period of 10 days of between 0.2 to 7.5 mg, wherein the subject is to receive a plurality of doses.

5. Use according to any preceding claim wherein the humanized anti-CD4 antibody comprises V domains defined by the following polypeptide sequences:

- H chain V domain:

EEQLVESGGGLVKPGGSLRLSCAASGFSFSDCRMYWLRQAPGKGLEWIGVISVKSEN YGANYAESVRGRFTISRDDSKNTVYLQMNSLKTEDTAVYYCSASYYRYDVGAWFA YWGQGTLVTVSS (SEQ ID NO: 1)

- L chain V domain:

DIVMTQSPDSLAVSLGERATINCRASKSVSTSGYSYIYWYQQKPGQPPKLLIYLASILE SGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQHSRELPWTFGQGTKVEIK (SEQ ID NO: 2),

or V domains comprising polypeptide sequences having at least 90% sequence identity with SEQ ID NO: 1 and SEQ ID NO: 2.

6. Use of a humanized anti-CD4 antibody for the manufacture of a medicament for treating an autoimmune disease in a subject, wherein the humanized anti-CD4 antibody

comprises an H chain V domain, an L chain V domain, and an IgG1 constant domain, wherein the H chain V domain has SEQ ID No: 1, and the L chain V domain has SEQ ID NO: 2, wherein the humanized anti-CD4 antibody is to be administered intravenously to the subject in a dose of the humanized anti-CD4 antibody from 0.2 mg to 5 mg,
wherein the medicament is to be administered weekly, every two weeks, every four weeks, every calendar month or every six weeks.

7. Use of a humanized anti-CD4 antibody for the manufacture of a medicament for treating an autoimmune disease in a subject, wherein the humanized anti-CD4 antibody comprises an H chain V domain, an L chain V domain, and an IgG1 constant domain, wherein the H chain V domain has SEQ ID No: 1, and the L chain V domain has SEQ ID NO: 2, wherein the humanized anti-CD4 antibody is to be administered intravenously to the subject in a dose of the humanized anti-CD4 antibody from 2.5 to 20 μg/kg of body mass of the subject,
wherein the medicament is to be administered weekly, every two weeks, every four weeks, every calendar month or every six weeks.

8. Use of a humanized anti-CD4 antibody for the manufacture of a medicament for treating an autoimmune disease in a subject, wherein the humanized anti-CD4 antibody comprises an H chain V domain, an L chain V domain, and an IgG1 constant domain, wherein the H chain V domain has SEQ ID No: 1, and the L chain V domain has SEQ ID NO: 2, wherein the medicament is to be administered to a subject intravenously in a dose of the humanized anti-CD4 antibody over a period of 10 days of between 0.2 to 7.5 mg, wherein the subject is to receive a plurality of doses.

9. Use according to any preceding claim wherein the autoimmune disease is selected from psoriasis, rheumatoid arthritis, multiple sclerosis, type-1 diabetes, inflammatory bowel diseases, Crohn's disease, autoimmune thyreoiditis, autoimmune myasthenia gravis, systemic lupus erythematosus and transplantation-related diseases.

10. Use according to claim 9, wherein the transplantation-related disease is graft-versus-host or general organ tolerance issues.

11. Use according to claim 9 wherein the disease is psoriasis or rheumatoid arthritis.