CLAIMS

1. Use of an effective amount of methotrexate for the manufacture of a medicament for inducing immune tolerance in a subject in need of treatment with a therapeutic, wherein the methotrexate is administered in a single cycle thereby inducing immune tolerance toward the therapeutic in the subject, wherein the single cycle of methotrexate consists of 1 day of methotrexate administration or 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 consecutive days of methotrexate administration.

2. Use of an effective amount of methotrexate for the manufacture of a medicament for inhibiting antibody responses to a protein therapeutic in a subject in need of treatment with the therapeutic, wherein the methotrexate is administered in a single cycle thereby inhibiting antibody responses to the therapeutic in the subject, wherein the single cycle of methotrexate consists of 1 day of methotrexate administration or 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 consecutive days of methotrexate administration.

3. Use of an effective amount of methotrexate for the manufacture of a medicament for alleviating an infusion reaction to a therapeutic in a subject in need of treatment with the therapeutic, wherein the methotrexate is administered in a single cycle thereby alleviating an infusion reaction to the protein therapeutic in the subject, wherein the single cycle of methotrexate consists of 1 day of methotrexate administration or 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 consecutive days of methotrexate administration.

4. Use of an effective amount of methotrexate for the manufacture of a medicament for reducing secondary autoimmunity in an autoimmune subject in need of treatment with a therapeutic, wherein the methotrexate is administered in a single cycle thereby reducing secondary autoimmunity in the subject, wherein the single cycle of methotrexate consists of 1 day of methotrexate administration or 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 consecutive days of methotrexate administration.

5. Use of an effective amount of methotrexate for the manufacture of a medicament for increasing the efficacy of a therapeutic in a subject in need of treatment with the therapeutic, wherein the methotrexate is administered in a single cycle thereby increasing the efficacy of the protein

therapeutic in the subject, wherein the single cycle of methotrexate consists of 1 day of methotrexate administration or 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 consecutive days of methotrexate administration.

6. Use of an effective amount of methotrexate for the manufacture of a medicament for increasing the percentage of T regulatory cells in the T cell population in a subject in need of treatment with a therapeutic, wherein the methotrexate is administered in a single cycle thereby increasing said percentage in said subject, wherein the single cycle of methotrexate consists of 1 day of methotrexate administration or 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 consecutive days of methotrexate administration.

7. The use of any one of claims 1-6, wherein the therapeutic is a protein therapeutic.

8. The use of any one of claims 1-6, wherein the subject is suffering from a disease selected from from multiple sclerosis, Fabry disease, Gaucher disease, Mucopolysaccharidosis I, Pompe disease, host-vs-graft disease, graft-vs-host disease, rheumatoid arthritis, psoriasis, diabetes, lupus, sclerodoma, chronic B-cell lymphocytic leukaemia, vasculitis, thyroid autoimmunity, thrombocytopenic purpura, immune thrombocytopenia, Goodpasture's disease, autoimmune neutropenia, autoimmune hemolytic anemia, and autoimmune lymphopenia.

9. The use of any one of claims 1-6, wherein the subject is in need of tissue transplantation.

10. Use of an effective amount of methotrexate for the manufacture of a medicament for increasing the percentage of B regulatory cells in the B cell population in a subject in need of treatment with an antibody therapeutic, wherein the methotrexate is administered in a single cycle thereby increasing said percentage in said subject, wherein the single cycle of methotrexate consists of 1 day of methotrexate administration or 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 consecutive days of methotrexate administration.

11. The use of claim 10, wherein the subject is suffering from a disease selected from from multiple sclerosis, Fabry disease, Gaucher disease, Mucopolysaccharidosis I, Pompe disease, host-vs-graft

disease, graft-vs-host disease, rheumatoid arthritis, psoriasis, diabetes, lupus, sclerodoma, chronic B-cell lymphocytic leukaemia, vasculitis, thyroid autoimmunity, thrombocytopenic purpura, immune thrombocytopenia, Goodpasture's disease, autoimmune neutropenia, autoimmune hemolytic anemia, and autoimmne lymphopenia.

12. The use of claim 10, wherein the subject is in need of tissue transplantation.

13. Use of an effective amount of methotrexate for the manufacture of a medicament for prolonging the pharmacokinetics of a therapeutic agent in a subject, wherein the methotrexate is administered to the subject before or during or after administration of the therapeutic agent, wherein the single cycle of methotrexate consists of 1 day of methotrexate administration or 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 consecutive days of methotrexate administration.

14. The use of any one of claims 1-13, wherein the subject is a human.

15. The use of any one of claims 1-13, wherein the therapeutic is an antibody therapeutic.

16. The use of claim 15, wherein the antibody therapeutic is a monoclonal antibody therapeutic.

17. The use of any one of claims 15 or 16, wherein the antibody therapeutic is a lymphocyte-depleting agent.

18. The use of claim 17, wherein the antibody therapeutic is alemtuzumab.

19. The use of claim 18, wherein the subject is a multiple sclerosis patient.

20. The use of claim 15, wherein the antibody therapeutic is a polyclonal antibody therapeutic.

21. The use of claim 20, wherein the antibody therapeutic is polyclonal rabbit anti-thymocyte globulin antibody.

22. The use of claim 21, wherein the subject is a human patient who is in need of organ transplantation, has aplastic anemia, and/or has or is at risk of having graft-versus-host disease.

23. The use of any one of claims 1-14, wherein the therapeutic is an enzyme.

24. The use of claim 23, wherein the enzyme is human alpha-galactosidase A.

25. The use of claim 23, wherein the enzyme is human acid alpha-glucosidase.

26. The use of any one of claims 1-25, wherein the effective amount is 0.1 mg/kg to 5 mg/kg.

27. The use of any one of claims 1-25, wherein the single cycle of methotrexate is administered between 48 hours prior to and 48 hours after the onset of the therapeutic treatment.

28. Use of an effective amount of methotrexate for the manufacture of a medicament for depleting lymphocytes in a human patient in need thereof, wherein the methotrexate is administered to the patient in a single cycle, before or during or after the treatment with the lymphocyte-depleting agent to induce immune tolerance in the patient toward the lymphocyte-depleting agent, wherein the single cycle of methotrexate consists of 1 day of methotrexate administration or 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 consecutive days of methotrexate administration.

29. The use of claim 28, wherein the lymphocyte-depleting agent is a monoclonal antibody therapeutic.

30. The use of claim 28, wherein the lympocyte-depleting agent is a polyclonal antibody therapeutic.

31. The use of claim 29, wherein the monoclonal antibody therapeutic is alemtuzumab.

32. The use of claim 29, wherein the monoclonal antibody therapeutic is rituximab.

33. The use of any one of claims 28-32, wherein the patient is a multiple sclerosis patient.

34. The use of claim 33, wherein the patient has remitting-relapsing multiple sclerosis.

35. The use of claim 30, wherein the polyclonal antibody therapeutic is anti-thymocyte globulin polyclonal antibody.

36. Use an effective amount of methotrexate for the manufacture of a medicament for inducing immune tolerance in a subject in need of tissue transplantation, wherein the methotrexate is administered in a single cycle thereby inducing immune tolerance toward the transplanted tissue in the subject, wherein the single cycle of methotrexate consists of 1 day of methotrexate administration or 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 consecutive days of methotrexate administration.

37. The use of claim 36, wherein the transplanted tissue is renal tissue or cardiac tissue.

38. The use of claim 37, wherein the subject also receives another agent for immune modulation.

39. The use of claim 38, wherein the agent for immune modulation is an immunosuppressant.

40. The use of claim 38, wherein the agent for immune modulation is polyclonal anti-thymocyte globulin antibody.

41. Use of an effective amount of methotrexate for the manufacture of a medicament for inhibiting T cell responses in a subject in need of a therapeutic or tissue transplantation, wherein the methotrexate is administered in a single cycle prior to, concurrently with, or after, treating the subject with the therapeutic or tissue transplantation thereby inhibiting T cell responses in the subject, wherein the single cycle of methotrexate consists of 1 day of methotrexate administration or 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 consecutive days of methotrexate administration.

42. The use of claim 41, wherein the therapeutic is a protein therapeutic.

43. The use of claim 42, wherein the protein therapeutic is an antibody therapeutic.

44. The use of claim 43, wherein the antibody therapeutic is a monoclonal antibody therapeutic.

45. The use of any one of claims 43 or 44, wherein the antibody therapeutic is a lymphocyte-depleting agent.

46. The use of claim 45, wherein the antibody therapeutic is alemtuzumab.

47. The use of claim 46, wherein the subject is a multiple sclerosis patient.

48. The use of claim 43, wherein the antibody therapeutic is a polyclonal antibody therapeutic.

49. The use of claim 48, wherein the polyclonal antibody therapeutic is polyclonal rabbit anti-thymocyte globulin antibody.

50. The use of claim 42, wherein the transplanted tissue is renal tissue or cardiac tissue.

51. The use of claim 50, wherein the subject also receives another agent for immune modulation.

52. The use of claim 51, wherein the agent for immune modulation is an immunosuppressant.

CLAIMS

1. Use of an effective amount of methotrexate for the manufacture of a medicament for the treatment of a disease selected from multiple sclerosis, Fabry disease, Gauche disease, Mucopolysaccharidosis I, Pompe disease, host-vs-graft disease, graft-vs-host disease, rheumatoid arthritis, psoriasis, diabetes, lupus, sclerodoma, chronic B-cell lymphocytic leukemia, vasculitis, thyroid autoimmunity, thrombocytopenic purpura, immune thrombocytopenia, Goodpasture's disease, autoimmune neutropenia, autoimmune hemolytic anemia, and autoimmune lymphopenia or a subject is in need of tissue transplantation, wherein the methotrexate increases the efficacy of a therapeutic in a subject having said disease or in need of said tissue transplantation who is in need of treatment with the therapeutic, wherein methotrexate is administered in a single cycle consisting of 1 day of methotrexate administration or 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 consecutive days of methotrexate administration, wherein the effective amount of methotrexate is less than 5 mg/kg.

2. The use of claim 1, wherein the efficacy of the therapeutic comprises

a. inducing immune tolerance toward the therapeutic treatment;

b. inhibiting antibody responses to the therapeutic in the subject;

c. alleviating an infusion reaction to the therapeutic in the subject;

d. reducing secondary autoimmunity in the subject;

e. increasing the percentage of T regulatory cells in the T cell population in the subject;

f. increasing the percentage of B regulatory cells in the B cell population in the subject;

g. inhibiting T cell responses in the subject;

h. prolonging the pharmacokinetics of a therapeutic agent in the subject; or

i. depleting lymphocytes in the subject; or

j. inducing immune tolerance toward the transplanted tissue in the subject.

3. The use of claim 1-2, wherein the therapeutic is a protein therapeutic.

4. The use of claim 1-2, wherein the subject is a human.

5. The use of claim 1-2, wherein the therapeutic is an antibody therapeutic.

6. The use of claim 5, wherein the antibody therapeutic is a monoclonal antibody therapeutic.

7. The use of any one of claims 5 or 6, wherein the antibody therapeutic is a lymphocyte-depleting agent.

8. The use of claim 7, wherein the antibody therapeutic is alemtuzumab.

9. The use of claim 8, wherein the subject is a multiple sclerosis patient.

10. The use of claim 9, wherein the antibody therapeutic is a polyclonal antibody therapeutic.

11. The use of claim 10, wherein the antibody therapeutic is polyclonal rabbit anti-thymocyte globulin antibody.

12. The use of claim 11, wherein the subject is a human patient who is in need of organ transplantation, has aplastic anemia, and/or has or is at risk of having graft-versus-host disease.

13. The use of any one of claims 1-2, wherein the therapeutic is an enzyme.

14. The use of claim 13, wherein the enzyme is human alpha-galactosidase A.

15. The use of claim 14, wherein the enzyme is human acid alpha-glucosidase.

16. The use of any one of claims 1-15, wherein the effective amount is 0.1mg/kg to 5mg/kg.

17. The use of any one of claims 1-15, wherein the single cycle of methotrexate is administered between 48 hours prior to and 48 hours after the onset of the therapeutic treatment.