Unfortunately, this therapy is insufficient to keep patients in remission, and flaring of the disease is frequent. Flares can be controlled with high dose glucocorticoid via intravenous pulses at 30 mg methylprednisolone/kg/day for 3 consecutive days. However, steroid treatment at high dosage can present severe side effects for patients.

[7] These standard treatments are generally nonspecific, are frequently associated with serious side-effects and do not significantly affect the progression of the disease or transition to life threatening kidney complications (lupus nephritis or LN). Consequently, there is a long-felt need in the art to develop new methods for treating SLE.

SUMMARY OF THE INVENTION

[8a] In one aspect of the present invention, there is provided the use of a fusion molecule in the manufacture of a medicament for the treatment of SLE in a patient with mild-to-moderate SLE wherein said fusion molecule comprises :

(i) a TACI extracellular domain or fragment thereof which binds BlyS: and

(ii) a human immunoglobulin-constant domain;

wherein said fusion molecule is for administration in a dosage from about 1 to about 10 mg/kg and said fusion molecule is for administration in a dosing interval consisting of administration every week for multiple weeks after the initial dose.

[8] In various ~~embodiments~~examples, the present ~~invention~~disclosure is directed to methods of treating autoimmune diseases. Illustratively, the methods of the ~~invention~~disclosure include administering to a patient a composition comprising a human immunoglobulin-constant domain and TACI extracellular domain or a fragment thereof which binds BlyS and/or APRIL.

[9] In another ~~embodiment~~example, the ~~invention~~present disclosure comprises methods of treating autoimmune diseases, including SLE using a molecule that comprises a fusion of the TACI extracellular domain or any fragment thereof that retains the ability to bind BlyS and/or APRIL, such as atacicept.

[10] In another ~~embodiment~~example, the ~~invention~~present disclosure comprises methods of treating SLE comprising administering to a patient in need thereof, an effective amount of a fusion molecule comprising a human immunoglobulin-constant chain and TACI extracellular domain or a fragment of TACI extracellular domain that binds BlyS and/or APRIL. In one ~~embodiment~~example, the fragment of the extracellular domain of TACI comprises one or two cysteine repeat motifs. In another ~~embodiment~~example, the fragment is a fragment comprising amino acids 30-110 of the extracellular domain of TACI. In yet another ~~embodiment~~example, the fragment is a fragment comprising amino acids 1-154 of the extracellular domain of TACI (SEQ ID NO: 1).

[11] In another ~~embodiment~~example, the ~~invention~~present disclosure comprises methods of treating SLE by administering to a patient a composition comprising a fusion polypeptide, TACI-Fc5, comprising a human immunoglobulin-constant domain, Fc5, having the sequence set out as SEQ ID NO: 2 and a TACI extracellular domain having the sequence set out as SEQ ID NO: 1.

[12] In still another ~~embodiment~~example, the ~~invention~~present disclosure comprises methods of treating SLE by administering to a patient a composition comprising a fusion polypeptide comprising a human immunoglobulin-constant domain with the sequence set out as SEQ ID NO: 2 and a polypeptide which binds BlyS and/or APRIL and which is at least about 50%, at least about 60%, at least about

65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95% or at least about 99% identical to SEQ ID NO: 1.

[13] Other autoimmune diseases can be treated by the methods of the ~~invention~~present disclosure by administering to a patient a fusion polypeptide comprising a human immunoglobulin-constant chain and TACI extracellular domain or a fragment of TACI extracellular domain that binds BlyS and/or APRIL. Such autoimmune diseases include, but are not limited to rheumatoid arthritis (RA), Graves disease, type I and type II diabetes, multiple sclerosis, Sjogren syndrome, scleroderma, glomerulonephritis, transplant rejection, e.g., organ and tissue allograft and xenograft rejection and graft versus host disease.

[14] In one ~~embodiment~~example, the methods of the instant ~~invention~~disclosure comprise administering to a SLE patient atacicept fusion molecule in amounts from about 0.01 mg/kg of patient's body weight to about 25 mg/kg of patient's body weight. The atacicept molecule can be administered repeatedly at predetermined intervals. Illustratively, the molecule can be administered multiple times during predetermined dosing intervals. For example, dosing can be of a relatively lower dose of drug at weekly or every three week intervals. An initial treatment with a Atacicept fusion polypeptide can be followed by administering the polypeptide on a bi-weekly (every other week) or tri-weekly (every third week) basis for at least 2 or 3 more additional weeks, respectively. For example, the polypeptide can be administered on a bi-weekly basis for an additional 2 to 30 weeks. Alternately, the polypeptide may be administered on a weekly or daily basis.

[15] According to the methods of the instant ~~invention~~disclosure, atacicept polypeptide can be administered to a SLE patient subcutaneously, orally, or intravenously and in combination with other medicaments. Such medicaments include, but are not limited to: NSAIDS (nonsteroidal anti-inflammatory drugs) both over the counter and those requiring a prescription such as diclofenac sodium, indomethacin diflunisal and nabumetone; anti-malarials such as hydroxychloroquine sulfate and chloroquine; corticosteroids such as prednisone, hydrocortisone, and methylprednisolone; and immunosuppressives such as azathioprine, cyclophosphamide, methotrexate, cyclosporine, and mycophenolate mofetil, and IVIg, DHEA, and thalidomide.

BRIEF DESCRIPTION OF THE FIGURES

[16] FIGURE 1 graphically represents the free atacicept concentration plotted versus time in days for subcutaneous administration, a key pharmakinetic measurement. Each line of the graph is a dosage, as shown in the key.

What is claimed is:

1. The use of a composition comprising a fusion molecule comprising:
(i) a TACI extracellular domain or a fragment thereof which binds BlyS; and
(ii) a human immunoglobulin-constant domain
in the manufacture of a medicament for treatment of SLE in a patient, wherein said patient is to be administered with said medicament and wherein said dosage is from about 1 to about 10 mg/kg and said fusion molecule is to be administered in a dosing interval consisting of administration every week for multiple weeks after the initial dose.

2. The use of claim 1, wherein said TACI extracellular domain has a sequence comprising amino acids 30-110 of SEQ ID NO:1.

3. The use of claim 1, wherein said TACI extracellular domain has a sequence comprising SEQ ID NO: 1.

4. The use of claim 1, wherein said TACI extracellular domain is at least 50% identical to SEQ ID NO: 1.

5. The use of claim 1, wherein said human immunoglobulin-constant domain has a sequence comprising SEQ ID NO: 2.

6. The use of claim 1, wherein said fusion molecule is atacicept.

7. The use of claim 1, wherein said composition is to be administered in amount of about 1 to about 9 mg/kg.

8. The use of claim 7, wherein said treatment lasts between about 2 to about 52 weeks.

9. The use of claim 1, wherein a second medicament is further to be co-administered to the patient.

10. The use of claim 9, wherein said second medicament is selected from the group consisting of: NSAIDS, anti-malarials, corticosteroids, immunosuppressives, IVIg, DHEA, and thalidomide.

11. The use of claim 8, wherein said fusion molecule is atacicept.

12. The use of claim 1, wherein said composition is to be administered subcutaneously, orally or intravenously.

13. The use of claim 1 in which the patient is a human.

14. The use of a pharmaceutical composition comprising atacicept in the manufacture of a medicament for treatment of SLE in a patient, wherein said patient is to be administered with said medicament and wherein said dosage is from about 1 to about 10 mg/kg and said administration occurs at weekly intervals after the initial dose wherein said administration is subcutaneous.

15. The use of claim 14 wherein said dosage is 1 mg/kg.

16. The use of claim 14 wherein said dosage is 3 mg/kg.

17. Use of a pharmaceutical composition comprising atacicept in the manufacture of a medicament for treatment of SLE in a patient, wherein said patient is to be administered with said pharmaceutical composition and wherein said dosage is from about 1 to about 10 mg/kg and said medicament is to be administered in a dosing interval consisting of administration every week for multiple weeks after the initial dose.

CLAIMS:

1. Use of a fusion molecule in the manufacture of a medicament for the treatment of SLE in a patient with mild-to-moderate SLE wherein said fusion molecule comprises :

(i) a TACI extracellular domain or fragment thereof which binds B1yS; and

(ii) a human immunoglobulin-constant domain;

wherein said fusion molecule is for administration in a dosage from about 1 to about 10 mg/kg and said fusion molecule is for administration in a dosing interval consisting of administration every week for multiple weeks after the initial dose.

2. The use according to claim 1, wherein said TACI extracellular domain has a sequence comprising SEQ ID NO: 1.

3. The use according to claim 1, wherein said TACI extracellular domain is at least 50% identical to SEQ ID NO: 1.

4. The use according to claim 1, whrein said TACI extracellular domain has a sequence comprising amino acids 30-110 of SEQ ID NO: 1.

5. The use according to claim 1, wherein said human immunoglobulin-constant domain has a sequence comprising SEQ ID NO: 2.

6. The use according to claim 1, wherein said fusion molecule is atacicept.

7. The use according to claim 1, wherein said medicament is suitable to be administered in amount of about 1 to about 9 mg/kg.

8. The use according to claim 7, wherein said treatment lasts between about 2 to about 52 weeks.

9. The use according to claim 1, wherein said medicament is to be co-administered with a second medicament.

10. The use according to claim 9, wherein said second medicament is selected from the group consisting of: NSAIDS, anti-malarials, corticosteroids, immunosuppressives, IVIg, DHEA, and thalidomide.

11. The use according to claim 10, wherein said fusion molecule is atacicept.

12. The use according to claim 1, wherein the medicament is suitable to be administered subcutaneously, orally or intravenously.

13. The use according to any one of claims 1 to 12, wherein the patient is a human.

SEQUENCE LISTING

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<120> DOSING METHODS FOR TREATING AUTOIMMUNE DISEASES USING A TACI-IG FUSION MOLECULE SUCH AS ATACICEPT

<130> 07-15PC

<150> 60/943,618
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<151> 2008-01-28

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