

CLAIMS

We claim:

1. A method of treating pemphigus, comprising
 - (i) selecting a subject that has
 - (a) newly diagnosed pemphigus,
 - (b) relapsing pemphigus, or
 - (c) refractory pemphigus, and
 - (ii) administering to a subject in need thereof an effective amount of a human neonatal Fc receptor (FcRn) antagonist, wherein the FcRn antagonist consists of a variant Fc region, wherein said variant Fc region consists of two Fc domains which form a homodimer, and wherein the amino acid sequence of each of the Fc domains is selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2, and SEQ ID NO: 3, thereby treating pemphigus in the subject.
2. The method of claim 1, whereby disease control or complete remission is achieved.
3. The method of any one of the preceding claims, whereby complete remission is achieved.
4. The method of any one of the preceding claims, wherein disease control or complete remission is achieved and/or maintained at a corticosteroid dose of ≤ 0.5 mg prednisone/kg/day or equivalent.
5. The method of any one of the preceding claims, wherein disease control or complete remission is achieved at a corticosteroid dose of about 0.20 to about 0.50 mg prednisone/kg/day or equivalent.
6. The method of any one of the preceding claims, wherein disease control or complete remission is achieved at a corticosteroid dose of ≤ 20 mg prednisone/day or equivalent.
7. The method of any one of the preceding claims, wherein disease control or complete remission is achieved at a corticosteroid dose of ≤ 10 mg prednisone/day or equivalent.

8. The method of any one of the preceding claims, wherein disease control or complete remission is achieved without co-administration of a corticosteroid.
9. The method of any one of claims 1 to 8, wherein disease control is obtained in 1 to 24 weeks, in 1 to 20 weeks, 1 to 15 weeks, in 1 to 13 weeks, in 1 to 12 weeks, in 1 to 10 weeks, in 1 to 6 weeks, in 1 to 4 weeks, in 1 week to 16 days, or in 1 to 2 weeks of administration of the initial dose of FcRn antagonist.
10. The method of any one of claims 1 to 8, wherein complete remission is obtained in 2 to 41 weeks, 2 to 24 weeks, in 2 to 20 weeks, in 2 to 15 weeks, in 2 to 13 weeks, in 2 to 12 weeks, in 2 to 10 weeks, or in 2 to 6 weeks of administration of the initial dose of FcRn antagonist.
11. The method of any one of the preceding claims, wherein a Pemphigus Disease Area Index (PDAI) activity score improvement of at least about 50%, at least about 60%, at least about 70%, at least about 80%, or at least about 90% is achieved.
12. The method of any one of the preceding claims, wherein an absolute PDAI activity score of 6, an absolute PDAI activity score of 5, an absolute PDAI activity score of 4, an absolute PDAI activity score of 3, an absolute PDAI activity score of 2, an absolute PDAI activity score of 1, or an absolute PDAI activity score of 0 is achieved.
13. The method of any one of the preceding claims, wherein the pemphigus comprises pemphigus vulgaris (PV), pemphigus foliaceus (PF), or both PV and PF.
14. The method of any one of the preceding claims, wherein the subject has mild, moderate, or severe pemphigus as classified by the Pemphigus Disease Area Index (PDAI).
15. The method of any one of the preceding claims, wherein the FcRn antagonist is administered once weekly or biweekly until disease control or complete remission is achieved.

16. The method of any one of the preceding claims, wherein the FcRn antagonist is administered intravenously at a dose of 10 mg/kg to 30 mg/kg once weekly or every two weeks.
- 5 17. The method of claim 16, wherein the FcRn antagonist is administered intravenously at a dose of 10 mg/kg once weekly or every two weeks.
18. The method of claim 16, wherein the FcRn antagonist is administered intravenously at a dose of 25 mg/kg once weekly or every two weeks.
- 10 19. The method of any one of claims 1 to 15, wherein the FcRn antagonist is administered subcutaneously at a fixed dose of 750 mg to 3000 mg once weekly or every two weeks.
20. The method of claim 19, wherein the FcRn antagonist is administered subcutaneously at a fixed dose of 1000 mg or 2000 mg once weekly or every two weeks.
- 15 21. The method of claim 19, wherein the FcRn antagonist is first administered subcutaneously at a fixed dose of about 1000 mg twice on the same day.
- 20 22. The method of any one of claims 19-21, wherein the FcRn antagonist is co-formulated with hyaluronidase and administered subcutaneously.
23. The method of any one of the preceding claims, further comprising administering a tapering dose of corticosteroid after disease control or complete remission has been achieved.
- 25 24. The method of any one of the preceding claims, wherein the tapering dose of corticosteroid begins at ≤ 0.5 mg prednisone/kg/day or equivalent.
25. The method of any one of the preceding claims, wherein the tapering dose of corticosteroid begins at a dose of 10 mg prednisone/day or equivalent.
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26. The method of any one of the preceding claims, wherein corticosteroid tapering is initiated within about 1 month, within about 3 weeks, within about 2 weeks or within about 1 week of administration of the initial dose of FcRn antagonist.
- 5 27. The method of any one of the preceding claims, wherein a reduction of the initial or subsequent tapering dose can occur every month, every 3 weeks, every 2 weeks, or every week.
28. The method of claim 27, wherein the reduction of the initial or subsequent tapering
10 dose can occur every 2 weeks.
29. The method of any one of the preceding claims, wherein the tapering of corticosteroids can comprise a reduction of about 0.5 mg prednisone/kg/day or equivalent, about 0.25 mg prednisone/kg/day or equivalent, or about 0.1 mg prednisone/kg/day or
15 equivalent.
30. The method of any one of the preceding claims, wherein the corticosteroid is a systemic corticosteroid.
- 20 31. The method of any one of the preceding claims, further comprising the administration of a topical corticosteroid.
32. The method of any one of the preceding claims, wherein the FcRn antagonist is administered in an induction phase and a consolidation phase, wherein
25 (i) during the induction phase the FcRn antagonist is administered once weekly or biweekly and a corticosteroid is administered at a dose of ≤ 0.5 mg prednisone/kg/day or equivalent until disease control, and
(ii) during the consolidation phase the FcRn antagonist dose is reduced or the FcRn antagonist dosing interval is lengthened, and/or the corticosteroid dose is decreased or the
30 corticosteroid dosing interval is lengthened, to an end-of-consolidation dose or dosing interval effective to prevent new lesions from appearing.
33. The method of claim 32, further comprising a maintenance phase, wherein

(iii) during the maintenance phase the end-of-consolidation dose or dosing interval for the FcRn antagonist and/or the prednisone or equivalent is continued until complete clearance of lesions.

5 34. The method of claim 32 or claim 33, wherein during the induction phase the FcRn antagonist is administered intravenously at a dose of 10 mg/kg to 30 mg/kg.

35. The method of claim 32 or claim 33, wherein during the induction phase the FcRn antagonist is administered intravenously at a dose of 10 mg/kg.

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36. The method of claim 32 or claim 33, wherein during the induction phase the FcRn antagonist is administered intravenously at a dose of 25 mg/kg.

15 37. The method of claim 32 or claim 33, wherein during the induction phase the FcRn antagonist is administered subcutaneously at a fixed dose of 750 mg to 3000 mg.

38. The method of claim 32 or claim 33, wherein during the induction phase the FcRn antagonist is first administered subcutaneously at a fixed dose of about 1000 mg twice on the same day.

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39. The method of any one of the previous claims, wherein the subject has refractory pemphigus.

25 40. The method of any one of the previous claims, wherein the subject has newly diagnosed pemphigus vulgaris, with a Pemphigus Disease Area Index (PDAI) score of ≥ 15 .

41. The method of any one of the previous claims, wherein the subject has relapsing pemphigus vulgaris.

30 42. The method of any one of the previous claims, wherein the subject has newly diagnosed pemphigus foliaceus, with a Pemphigus Disease Area Index (PDAI) score of ≥ 15 .

43. The method of any one of the previous claims, wherein the subject has relapsing pemphigus foliaceus.

44. The method of any one of the previous claims, wherein the subject is rituximab-refractory.
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45. The method of any one of the previous claims, wherein the subject is corticosteroid-intolerant.
46. The method of any one of the previous claims, further comprising administering a B-cell depleting agent to the subject.
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47. The method of any one of the previous claims, wherein the B-cell depleting agent is rituximab.
48. A human neonatal Fc receptor (FcRn) antagonist for use in a method of treating pemphigus, wherein the FcRn antagonist consists of a variant Fc region, wherein said variant Fc region consists of two Fc domains which form a homodimer, and wherein the amino acid sequence of each of the Fc domains is selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2, and SEQ ID NO: 3, and wherein the method of treating pemphigus is as
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- 20 defined in any one of the previous claims.