

CLAIMS

1. Use of a therapeutically effective amount of an anti-OX40L antibody, or antigen-binding fragment thereof, in the manufacture of a medicament for treating Atopic Dermatitis in a human subject, wherein the antibody or fragment thereof is to be administered via injection.
2. The use according to claim 1, wherein:
 - (a) the antibody or fragment thereof is to be administered via subcutaneous injection;
 - (b) the antibody or fragment thereof is to be administered via injection, wherein at least one injection is to be administered at a dose of at least about 20 mg of the antibody or fragment thereof;
 - (c) the antibody or fragment thereof is a disease modifying drug;
 - (d) the antibody or fragment thereof is a disease modifying drug and wherein after administering the disease modifying drug, the subject achieves an IGA-AD score of 0 or 1 for at least six months; and/or
 - (e) the antibody or fragment thereof is to be administered at least twice with at least one interval of 2 to 6 months, optionally at least twice with at least one interval of around 3 months.
3. Use of a therapeutically effective amount of an anti-OX40L antibody, or antigen-binding fragment thereof, in the manufacture of a medicament for treating an inflammatory disease, an inflammatory disorder, an immune-mediated disease, an immune-mediated disorder, an inflammatory skin disease or an inflammatory skin disorder in a human subject, wherein the antibody or fragment thereof is to be administered via subcutaneous injection, optionally wherein
 - (a) the inflammatory disease, an inflammatory disorder, an immune-mediated disease, an immune-mediated disorder, an inflammatory skin disease or an inflammatory skin disorder is atopic dermatitis;
 - (b) the antibody or fragment thereof is to be administered once every 4 weeks during induction phase and once every 12 weeks during maintenance phase;
 - (c) the antibody or fragment thereof is to be administered once every 4 weeks during induction phase and once every 12 weeks during maintenance phase, via subcutaneous injection;
 - (d) the antibody or fragment thereof is a disease modifying drug; and/or
 - (e) the antibody or fragment thereof is to be administered once every 4 weeks or once every 12 weeks or once every 6 months.
4. The use according to any preceding claim wherein
 - (a) each dose of the antibody or antigen-binding fragment thereof is of from 20 mg to 1000 mg;
 - (b) each dose is 62.5 mg, 125 mg, 150 mg, 250 mg or 500 mg;
 - (c) the dose of the antibody or antigen-binding fragment thereof is 125 mg;
 - (d) the dose of the antibody or antigen-binding fragment thereof is 150 mg;
 - (e) the dose of the antibody or antigen-binding fragment thereof is 62.5 mg;
 - (f) the dose of the antibody or antigen-binding fragment thereof is 250 mg;
 - (g) the dose of the antibody or antigen-binding fragment thereof is from 0.7 mg/kg to 6 mg/kg; and/or
 - (h) the dose of the antibody or antigen-binding fragment thereof is from 1.4 mg/kg to 3 mg/kg.

5. The use of any preceding claim wherein

(a) the minimum blood serum concentration reached by the antibody or fragment thereof between any two injections (C_{min}) is at least 2.5 µg/ml, 2.6 µg/ml, at least 2.7 µg/ml, at least 2.8 µg/ml, at least 2.9 µg/ml, at least 3 µg/ml, at least 3.1 µg/ml, at least 3.2 µg/ml, at least 3.3 µg/ml, at least 3.4 µg/ml, at least 3.5 µg/ml, at least 3.6 µg/ml, at least 3.7 µg/ml, at least 3.8 µg/ml, at least 3.9 µg/ml, at least 4 µg/ml, at least 4.1 µg/ml, at least 4.2 µg/ml, at least 4.3 µg/ml, at least 4.4 µg/ml, at least 4.5 µg/ml, at least 4.6 µg/ml, at least 4.7 µg/ml, at least 4.8 µg/ml, at least 4.9 µg/ml, at least 5 µg/ml, at least 5.1 µg/ml, at least 5.2 µg/ml, at least 5.3 µg/ml, at least 5.4 µg/ml, at least 5.5 µg/ml, at least 5.6 µg/ml, at least 5.7 µg/ml, at least 5.8 µg/ml, at least 5.9 µg/ml, at least 6 µg/ml, at least 6.5 µg/ml, at least 7 µg/ml, at least 7.5 µg/ml, at least 8 µg/ml, at least 8.5 µg/ml, at least 9 µg/ml, at least 9.5 µg/ml, at least 10 µg/ml, at least 11 µg/ml, at least 12 µg/ml, at least 13 µg/ml, at least 14 µg/ml, at least 15 µg/ml, at least 16 µg/ml, at least 17 µg/ml, at least 18 µg/ml, at least 19 µg/ml, at least 20 µg/ml, at least 25 µg/ml, at least 30 µg/ml, at least 35 µg/ml, at least 40 µg/ml, at least 50 µg/ml, at least 60 µg/ml, at least 70 µg/ml, at least 80 µg/ml, at least 90 µg/ml, or at least 100 µg/ml;

(b) the maximum blood serum concentration reached by the antibody or fragment thereof after administration of an injection and prior to administration of a subsequent injection (C_{max}) is at least about 1.5 µg / ml, at least about 2 µg / ml, at least about 5 µg / ml, at least about 10 µg / ml, at least about 20 µg / ml, at least about 30 µg / ml, at least about 40 µg / ml, at least about 50 µg / ml, at least about 60 µg / ml, at least about 70 µg / ml, at least about 80 µg / ml, at least about 90 µg / ml, at least about 100 µg / ml, at least about 150 µg / ml, at least about 200 µg / ml, at least about 300 µg / ml or at least about 550 µg / ml;

(c) blood serum concentrations of the antibody or fragment thereof during treatment range between about 4 µg/mL to about 15 µg/mL;

(d) blood serum concentrations of the antibody or fragment thereof during treatment range between about 20 µg/mL to about 45 µg/mL;

(e) blood serum concentrations of the antibody or fragment thereof during treatment range between about 5 µg/mL to about 23 µg/mL;

(f) blood serum concentrations of the antibody or fragment thereof during treatment are around or below 10 µg/mL; and/or

(g) the area under the serum concentration-time curve (AUC) following the first (AUC extrapolated to infinity [AUC_{0-inf}]) injection may be from around 100,000 ng/ml*day to around 4,500,000 ng/ml*day or around 1,000,000 ng/ml*day to around 3,800,000 ng/ml*day.

6. The use of any preceding claim, comprising an induction phase and a maintenance phase.

7. The use of claim 6 wherein

(a) the induction dose is about 500 mg, 250 mg, about 125 mg or about 62.5 mg;

(b) the maintenance dose is about 500 mg, 250 mg, about 125 mg or about 62.5 mg; and/or

(c) the interval between two or more induction phase injections is about 4 weeks and the interval between two or more maintenance phase injections is about 12 weeks.

8. The use of claim 6 or 7 wherein

(a) the induction phase comprises administering at least five induction phase injections, wherein the first induction phase injection is a loading dose of 500 mg of the antibody or fragment thereof, followed by at least four subsequent induction phase injections, wherein each subsequent induction phase injection is a dose of 250 mg of the antibody or fragment thereof and wherein each subsequent induction phase injection is to be administered 4 weeks after the preceding induction phase injection;

(b) the maintenance phase comprises administering at least 3 maintenance phase injections, wherein each maintenance phase injection is a dose of 250 mg of the antibody or fragment thereof, wherein a first maintenance phase injection is to be administered at least 4 weeks after the final induction phase injection and wherein a second maintenance phase injection and each subsequent maintenance phase injection is to be administered at least 4 weeks after the preceding maintenance phase injection;

(c) the induction phase comprises administering at least five induction phase injections, wherein each induction phase injection is a dose of 250 mg of the antibody or fragment thereof and wherein a second induction phase injection and each subsequent induction phase injection is to be administered 4 weeks after the preceding induction phase injection;

(d) the induction phase comprises administering at least five induction phase injections, wherein each induction phase injection is a dose of 125 mg of the antibody or fragment thereof and wherein a second induction phase injection and each subsequent induction phase injection is to be administered 4 weeks after the preceding induction phase injection;

(e) the maintenance phase comprises administering at least 3 maintenance phase injections, wherein each maintenance phase injection is a dose of 125 mg of the antibody or fragment thereof, wherein a first maintenance phase injection is to be administered at least 4 weeks after the final induction phase injection and wherein a second maintenance phase injection and each subsequent maintenance phase injection is to be administered at least 4 weeks after the preceding maintenance phase injection;

(f) the induction phase comprises administering at least five induction phase injections, wherein each induction phase injection is a dose of 62.5 mg of the antibody or fragment thereof and wherein a second induction phase injection and each subsequent induction phase injection is to be administered 4 weeks after the preceding induction phase injection;

(g) the maintenance phase comprises administering at least 3 maintenance phase injections, wherein each maintenance phase injection is a dose of 62.5 mg of the antibody or fragment thereof, wherein a first maintenance phase injection is to be administered at least 4 weeks after the final induction phase injection and wherein a second maintenance phase injection and each subsequent maintenance phase injection is to be administered at least 4 weeks after the preceding maintenance phase injection;

(h) the first maintenance phase injection is to be administered 12 weeks after the final induction phase injection; and/or

(i) the second maintenance phase injection and each subsequent maintenance phase injection is to be administered 12 weeks after the preceding maintenance phase injection.

9. The use of any preceding claim wherein

(a) the antibody or fragment thereof is capable of exhibiting one or more pharmacokinetic properties selected from the group consisting of:

- (i) a rate of clearance (CL) of about 0.05 to about 0.18 L/day;
- (ii) an absorption constant (k_a) of about 0.11 to about 0.33 L/day;
- (iii) a volume of central compartment volume (V_c) of about 1.6 to about 5.0 L;
- (iv) a second (peripheral compartment) volume (V_{p1}) of about 1.2 to about 3.6 L;
- (v) a rate of clearance from the central compartment to the second compartment (Q) of about 0.31 to about 0.93 L/day; and
- (vi) a bioavailability (F_{abs1}) of about about 0.6 to about 1.0;

(b). the subject is at least 18 years of age and/or less than 75 years of age;

(c) the atopic dermatitis is moderate-to-severe Atopic Dermatitis;

(d) the subject is a patient candidate for systemic therapy;

(e) the subject is a patient whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable; and/or

(f) in the atopic dermatitis is resistant, non responsive or inadequately responsive to treatment by either topical corticosteroids and/or systemic therapies or when those therapies are not advisable or wherein the subject has had an inadequate response to, was intolerant to, or is refractory to one or more topical corticosteroids.

10. The use according to any preceding claim, wherein a therapeutically effective amount of one or more topical corticosteroid is to be further administered, optionally wherein the topical corticosteroid is selected from the group consisting of betamethasone dipropionate, clobetasol propionate, dexamethasone, methylprednisolone, methylprednisolone aceponate, mometasone furoate, diflorasone diacetate, halobetasol propionate, amcinonide, augmented betamethasone dipropionate, fluocinonide, halcinonide, triamcinolone acetonide, betamethasone valerate, clocortolone pivalate, desoximetasone, fluocinolone acetonide, flurandrenolide, fluticasone propionate, hydrocortisone butyrate, hydrocortisone probutate, hydrocortisone valerate, prednicarbate, alclometasone dipropionate, desonide, hydrocortisone and hydrocortisone acetate, further optionally wherein the topical corticosteroid is selected from the group consisting of betamethasone dipropionate, betamethasone dipropionate;gentamicin sulphate, clobetasol propionate, dexamethasone, methylprednisolone, methylprednisolone aceponate and mometasone furoate.

11. Use of a pharmaceutical composition comprising a therapeutically effective amount of an anti-OX40L antibody, or antigen-binding fragment thereof, in the manufacture of a medicament for treating Atopic Dermatitis in a patient, wherein the administration of the anti-OX40L antibody, or antigen-binding fragment thereof results in at least one improvement selected from the group consisting of:

- a. a decrease from baseline in vIGA score of at least 2 points, or
- b. achieving clear or almost clear skin (vIGA0/1) from baseline.

- c. a decrease from baseline in EASI score of at least 50%, or
- d. a decrease from baseline in EASI score of at least 75%, or
- e. achieving EASI-75, or
- f. achieving EASI-90, or
- g. achieve at least 3 points a pruritus NRS, or
- h. achieve at least 4 points a pruritus NRS, or
- i. a decrease from baseline in SCORAD Index of at least 50%, or
- j. a decrease from baseline in SCORAD Index of at least 55%, or
- k. a decrease from baseline in affected BSA of at least 60%
- l. a decrease from baseline in affected BSA of at least 70%

12. Use of a pharmaceutical composition comprising a therapeutically effective amount of an anti-OX40L antibody, or antigen-binding fragment thereof, in the manufacture of a medicament for treating an inflammatory disease, an inflammatory disorder, an immune-mediated disease, an immune-mediated disorder, an inflammatory skin disease, an inflammatory skin disorder, atopic dermatitis or moderate-to-severe atopic dermatitis in a patient, wherein

(a) the administration of the anti-OX40L antibody, or antigen-binding fragment thereof results in the decrease in serum levels of at least one biomarker selected from the group consisting of: IL-13, IL-22, IL-17A, IL-31 and IgE, optionally wherein the at least one of the decrease in serum levels of at least one biomarker selected from the group consisting of: IL-13, IL-22, IL-17A, IL-31 and IgE is maintained for at least 12 weeks or at least 24 weeks following the final dose and/or wherein at least one of the improvements is maintained for at least 12 weeks or at least 24 weeks following the final dose;

(b) the atopic dermatitis has been assessed by determining a baseline EASI score;

(c) the atopic dermatitis has been assessed by determining a baseline EASI score and wherein the post-administration EASI score is maintained, without additional administration of an anti-OX40L antibody, or antigen-binding fragment thereof, for:

(i) at least 2 months, at least 3 months, at least 4 months, at least 5 months or at least 6 months after administration of the last injection; or

(ii) at least about 4, 8, 15, 22, 25, 29, 36, 43, 50, 57, 64, 71, 85, 113, 169 or 253 days;

(d) the atopic dermatitis has been assessed by determining a baseline EASI score and the post-administration EASI and/or further post-administration EASI is determined at least around 113 days after administering a first injection of the antibody or fragment thereof and wherein the post-administration EASI and/or further post-administration EASI is EASI50, EASI75, EASI90 or EASI100;

(e) the atopic dermatitis has been assessed by determining a baseline EASI score and the post-administration EASI and/or further post-administration EASI is determined at least around 169 days after administering a first injection of the antibody or fragment thereof and wherein the post-administration EASI and/or further post-administration EASI is EASI50, EASI75, EASI90 or EASI100;

(f) the atopic dermatitis has been assessed by determining a baseline EASI score and the post-administration EASI and/or further post-administration EASI is determined at least around 253 days after administering a first injection of the antibody or fragment thereof and wherein the post-

administration EASI and/or further post-administration EASI is EASI50, EASI75, EASI90 or EASI100; and/or

(g) the atopic dermatitis has been assessed by determining a baseline EASI score and the Atopic Dermatitis is treated as evidenced by a reduction in the EASI score by at least 40% after the third injection as a treatment dose and wherein the reduction in EASI score is persistent for at least 2 months, at least 3 months, at least 4 months, at least 5 months or at least 6 months after administration of the last injection as a treatment dose.

13. The use of any preceding claim, wherein the atopic dermatitis has been assessed by determining a baseline vIGA-AD score and

(a) the post-administration vIGA-AD score is 0 or 1;

(b) the post-administration vIGA-AD score is maintained, without additional administration of an anti-OX40L antibody, or antigen-binding fragment thereof, for:

(i) at least 2 months, at least 3 months, at least 4 months, at least 5 months or at least 6 months after administration of the last injection; or

(ii) at least about 4, 8, 15, 22, 25, 29, 36, 43, 50, 57, 64, 71, 85, 113, 169 or 253 days;

(c) the post-administration vIGA-AD and/or further post-administration vIGA-AD is determined at least around 113 days after administering a first injection of the antibody or fragment thereof and wherein the post-administration vIGA-AD and/or further post-administration vIGA-AD is:

(i) A vIGA-AD score of 0 or 1, and/or

(ii) reduced at least 2 points relative to the baseline vIGA-AD score;

(d) the post-administration vIGA-AD and/or further post-administration vIGA-AD is determined at least around 169 days after administering a first injection of the antibody or fragment thereof and wherein the post-administration vIGA-AD and/or further post-administration vIGA-AD is:

(i) A vIGA-AD score of 0 or 1, and/or

(ii) reduced at least 2 points relative to the baseline vIGA-AD score;

(e) the post-administration vIGA-AD and/or further post-administration vIGA-AD is determined at least around 253 days after administering a first injection of the antibody or fragment thereof and wherein the post-administration vIGA-AD and/or further post-administration vIGA-AD is:

(i) A vIGA-AD score of 0 or 1, and/or

(ii) reduced at least 2 points relative to the baseline vIGA-AD score; and/or

(f) the Atopic Dermatitis is treated as evidenced by a reduction in the vIGA-AD score by at least 2 points after the third injection as a treatment dose and wherein the reduction in vIGA-AD score is persistent for at least 2 months, at least 3 months, at least 4 months, at least 5 months or at least 6 months after administration of the last injection as a treatment dose.

13. A glass vial, drug delivery device, prefilled syringe, microinfusor, pen delivery device, autoinjector or kit comprising an anti-OX40L antibody, or antigen-binding fragment thereof for the use in accordance with any one of claims 1 to 12.

14. A glass vial, drug delivery device, prefilled syringe, microinfusor, pen delivery device, autoinjector, or kit according to claim 13, or use according to any of claims 1 to 12, wherein the antibody or fragment thereof comprises:

- (a) a HCDR1 amino acid sequence of SEQ ID NO: 36 or 42;
- (b) a HCDR2 amino acid sequence of SEQ ID NO: 38 or 44;
- (c) a HCDR3 amino acid sequence of SEQ ID NO: 40 or 46;
- (d) a LCDR1 amino acid sequence of SEQ ID NO: 50 or 56;
- (e) a LCDR2 amino acid sequence of SEQ ID NO: 52 or SEQ ID NO: 58; and
- (f) a LCDR3 amino acid sequence of SEQ ID NO: 54 or 60.

15. A glass vial, drug delivery device, prefilled syringe, microinfusor, pen delivery device, autoinjector, or kit according to any of claims 13 to 14, or use according to any of claims 1 to 12, wherein the antibody or fragment thereof comprises the heavy chain variable (VH) domain of SEQ ID NO: 34 and/or the light chain variable region (VL) of SEQ ID No:48.

16. A glass vial, drug delivery device, prefilled syringe, microinfusor, pen delivery device, autoinjector, or kit according to any of claims 13 to 15, or use according to any of claims 1 to 12, wherein the antibody or fragment thereof comprises a heavy chain having an amino acid sequence according to SEQ ID No:62 and a light chain having an amino acid sequence according to SEQ ID No:64.

17. A glass vial, drug delivery device, prefilled syringe, microinfusor, pen delivery device, autoinjector, or kit according to any of claims 13 to 16, or use according to any of claims 1 to 12, wherein the subject is classified as a Th2 AD patient and/or a non-Th2 AD patient.