

cells within tumours, alone or in combination with other antibodies or other anti-cancer compounds. As discussed above the infiltration of Treg cells in tumors, and in particular a low ratio of Teff cells to Treg cells, can lead to poor clinical outcome. CD25 has been identified as a Treg marker and could thus be an interesting target for therapeutic antibodies aiming at depleting Treg. Importantly, CD25 is the alpha subunit of the receptor for IL-2 and IL-2 is a key cytokine for Teff responses. Anti-CD25 antibodies that have undergone clinical testing so far, whilst depleting Treg cells also block IL-2 signalling via CD25. The present inventors have now found that such a blockade of IL-2 signalling limits Teff responses and that an anti-CD25 antibody that does not block the IL2 signalling can effectively deplete Treg cells, whilst still allowing IL-2 to stimulate Teff cells, providing antibodies that exhibit a strong anti-cancer effect. Thus, there is a need in the art for a method of treating cancer involving depletion of Tregs, particularly while still allowing IL-2 to stimulate Teff cells, in particular by using appropriate anti-CD25 antibodies.

SUMMARY OF THE DISCLOSURE

- [08] The present disclosure provides anti-CD25 antibodies and uses of anti-CD25 antibodies that are characterized by structural elements that allow both binding CD25 without substantially blocking the binding of Interleukin 2 (IL-2) to CD25 or signalling of IL-2 via CD25, and depleting efficiently Tregs, in particular within tumours. The structural and functional features of 7D4-IgM (as described with respect to mouse CD25) have been modified in order to provide antibodies that present surprisingly improved features in terms of use for depleting Tregs and efficacy against tumours, alone or in combination with other anti-cancer agents. Structural and functional features of further anti-CD25 antibodies which do not block the binding of interleukin 2 to CD25 (and do not block the signalling of IL2 via CD25) and efficiently deplete Tregs have also been characterised. These findings can be used for defining and generating further anti-human CD25 antibodies that provide comparable effects against tumours in human subjects. References herein to “anti-CD25 antibodies” and the like include antigen-binding fragments thereof, as well as variants (including affinity matured variants), unless the context implies otherwise.
- [08a] In one aspect, the present disclosure provides a use of an anti-CD25 antibody, wherein said antibody does not inhibit the binding of Interleukin-2 (IL-2) to CD25 in the manufacture of a medicament for treating a human subject who has cancer , wherein said subject has a solid tumour, and wherein the medicament is to be administered to the subject.
- [08b] In another aspect, the present disclosure provides an anti-CD25 antibody as described herein.
- [08c] In another aspect, the present disclosure provides an anti-CD25 antibody as described herein for use in medicine.

- [08d] In another aspect, the present disclosure provides an anti-CD25 antibody as described herein for use in the treatment of cancer in a human subject, wherein the subject has a solid tumour.
- [08e] In another aspect, the present disclosure provides a combination of an anti-CD25 antibody, as as described herein, and a further therapeutic agent for use in the treatment of cancer in a human subject, wherein said subject has a solid tumour and the anti-CD25 antibody and the further therapeutic agent are administered simultaneously, separately or sequentially.
- [08f] In another aspect, the present disclosure provides a kit for use in the treatment of cancer comprising an anti-CD25 antibody as described herein, and a further therapeutic agent.
- [08g] In another aspect, the present disclosure provides a pharmaceutical composition comprising an anti-CD25 antibody as described herein in a pharmaceutically acceptable medium.
- [08h] In another aspect, the present disclosure provides a bispecific antibody comprising: (a) a first antigen binding moiety that binds to CD25; and (b) a second antigen binding moiety that binds to an immune checkpoint protein; wherein the CD25 binding moiety does not inhibit the binding of Interleukin-2 (IL-2) to CD25, and preferably the bispecific antibody is an IgG1 antibody that binds to at least one activating Fcγ Receptor, selected from FcγRI, FcγRIIa, FcγRIII with a high affinity and depletes tumour-infiltrating regulatory T cells.
- [08i] In another aspect, the present disclosure provides a use of a bispecific antibody as described herein in the manufacture of a medicament for treating cancer in a subject.
- [08j] In another aspect, the present disclosure provides a bispecific antibody as described herein, for use in the treatment of cancer in a subject.
- [08k] In another aspect, the present disclosure provides a use of an anti-CD25 antibody, wherein the antibody is as described herein in the manufacture of a medicament for depleting regulatory T cells in a subject.
- [09] In a main example, the present disclosure provides a method of treating a human subject who has cancer comprising the step of administering an anti-CD25 antibody to a subject, wherein said subject has a tumour (preferably a solid tumour), wherein said antibody does not inhibit the binding of Interleukin-2 (IL-2) to CD25.
- [10] References to “does not block”, “non-blocking”, “non-IL-2 blocking”, “without blocking” and similar terminology herein (with respect to the non-blocking of IL-2 binding to CD25 in the presence of the anti-CD25 antibody) include examples wherein the anti-CD25 antibody does not block the signalling of IL-2 via CD25. That is, the anti-CD25 antibody of the disclosure inhibits less than 50% of IL-2

signalling via CD25 compared to IL-2 signalling in the absence of the antibodies. Preferably the anti-CD25 antibody inhibits less than about 40%, 35%, 30%, preferably less than about 25% of IL-2 signalling compared to IL-2 signalling in the absence of the antibodies.

- [11] In one example, the anti-CD25 antibody competes with the antibody 7G7B6 for binding to human CD25; and/or competes with the antibody MA251 for binding to human CD25.
- [12] In one example, the anti-CD25 antibody binds to the same epitope recognised by antibody 7G7B6 and/or binds to the same epitope recognised by antibody MA251.
- [13] In one example the anti-CD25 antibody specifically binds to an epitope of human CD25 wherein the epitope comprises one or more amino acid residues comprised in one or more of the amino acid stretches selected from amino acids 150-163 of SEQ ID NO:1 (YQCVQGYRALHRGP), amino acids 166-186 of SEQ ID NO:1 (SVCKMTHGKTRWTQPQLICTG), amino acids 42-56 of SEQ ID NO:1 (KEGTM LNCECKRGFR) and amino acids 70-88 of SEQ ID NO:1 (NSSHSSWDNQCQCTSSATR). Preferably the epitope comprises at least two, at least three, at least four, at least five, at least six, at least seven, at least eight, at least nine, at least ten, at least eleven, at least twelve, at least thirteen, at least fourteen, at least fifteen, at least sixteen, at least seventeen, at least eighteen or more amino acid residues comprised in one of more the amino acid stretches selected from amino acids 150-163 of SEQ ID NO:1 (YQCVQGYRALHRGP), amino acids 166-186 of SEQ ID NO:1 (SVCKMTHGKTRWTQPQLICTG), amino acids 42-56 of SEQ ID NO:1 (KEGTM LNCECKRGFR) and/or amino acids 70-88 of SEQ ID NO:1 (NSSHSSWDNQCQCTSSATR).
- [14] In one example, the anti-CD25 antibody specifically binds to an epitope of human CD25 wherein the epitope comprises at least one sequence selected from: amino acids 150-158 of SEQ ID NO:1 (YQCVQGYRA), amino acids 176-180 of SEQ ID NO:1 (RWTQP), amino acids 42-56 of SEQ ID NO:1 (KEGTM LNCECKRGFR) and amino acids 74-84 of SEQ ID NO:1 (SSWDNQCQCTS).
- [15] In one example, the anti-CD25 antibody specifically binds to an epitope of human CD25 wherein the epitope comprises at least one sequence selected from amino acids wherein the epitope comprises at least one sequence selected from: amino acids 150-158 of SEQ ID NO:1 (YQCVQGYRA), amino acids 166-180 of SEQ ID NO:1 (SVCKMTHGKTRWTQP), amino acids 176-186 of SEQ ID NO:1 (RWTQPQLICTG), amino acids 42-56 of SEQ ID NO:1 (KEGTM LNCECKRGFR) and amino acids 74-84 of SEQ ID NO:1 (SSWDNQCQCTS).
- [16] In one example, the anti-CD25 antibody specifically binds to an epitope of human CD25 wherein the epitope comprises at least one sequence selected from: amino acids 42-56 of SEQ ID NO:1 (KEGTM LNCECKRGFR), amino acids 70 to 84 of SEQ ID NO: 1 (NSSHSSWDNQCQCTS) and amino acids 150 to 158 of SEQ ID NO: 1 (YQCVQGYRA)

- [17] In one example, the anti-CD25 antibody binds to an epitope comprising the sequence of amino acids 42-56 of SEQ ID NO:1 (KEGTM LNCECKRGFR). In one example the anti-CD25 antibody binds to an epitope comprising the sequence of amino acids 42-56 of SEQ ID NO:1 (KEGTM LNCECKRGFR) and amino acids 150-160 of SEQ ID NO:1 (YQCVQGYRALH). In another example, the anti-CD25 antibody binds to an epitope comprising the sequence of amino acids 42-56 of SEQ ID NO:1 (KEGTM LNCECKRGFR) and amino acids 74-88 of SEQ ID NO:1 (SSWDNQCQCTSSATR). In another example the anti-CD25 antibody binds to an epitope comprising the sequence of amino acids 150-163 of SEQ ID NO:1 (YQCVQGYRALHRGP), amino acids 166-180 of SEQ ID NO:1 (SVCKMTHGKTRWTQP), amino acids 42-56 of SEQ ID NO:1 (KEGTM LNCECKRGFR) and amino acids 74-88 of SEQ ID NO:1 (SSWDNQCQCTSSATR).
- [18] In one example, the anti-CD25 antibody binds to an epitope comprising the sequence of amino acids 176-180 of SEQ ID NO:1 (RWTQP). In one example, the anti-CD-25 antibody binds to an epitope comprising the sequence of amino acids 166-180 of SEQ ID NO:1 (SVCKMTHGKTRWTQP). In one example, the anti-CD-25 antibody binds to an epitope comprising the sequence of amino acids 176-186 of SEQ ID NO:1 (RWTQPQLICTG).
- [19] In one example, the anti-CD25 antibody specifically binds to an epitope comprising the sequence of amino acids 150-158 of SEQ ID NO:1 (YQCVQGYRA) and amino acid 176-180 of SEQ ID NO:1 (RWTQP). In one example, the anti-CD25 antibody specifically binds to an epitope comprising the sequence of amino acids 150-158 of SEQ ID NO:1 (YQCVQGYRA) and amino acids 176-186 of SEQ ID NO:1 (RWTQPQLICTG). In one example the anti-CD25 antibody specifically binds to an epitope comprising the sequence of amino acids 150-163 of SEQ ID NO:1 (YQCVQGYRALHRGP) and amino acids 166-180 of SEQ ID NO:1 (SVCKMTHGKTRWTQP).
- [20] In one example, the anti-CD25 antibody binds to an epitope comprising the sequence of amino acids 74-84 of SEQ ID NO:1 (SSWDNQCQCTSSATR). In one example, the anti-CD25 antibody binds to an epitope comprising the sequence of amino acids 70-84 of SEQ ID NO:1 (NSSHSSWDNQCQCTS).
- [21] The present inventors having surprisingly found that antibodies that bind to particular epitopes of CD25, including those that compete with 7G7B6 and/or MA251 for binding to CD25, are useful in the treatment of cancer, in particular solid tumours. Such antibodies still permit signalling of IL-2 via the CD25 bound by the antibody, and the inventors have discovered for the first time that in addition to depleting Treg cells, the antibodies used in the present disclosure allow Teff cells to optimally exert their anti-cancer effects, at least in part by allowing the binding of IL-2 to, and signalling through, CD25 expressed on the Teff cells.
- [22] Such antibodies preferably have a dissociation constant (K_d) for CD25 of less than 10^{-7} M and/or a dissociation constant for at least one activating Fc γ receptor of less than about 10^{-6} M. Preferably the

antibody has a dissociation constant (K_d) for CD25 in the 10^{-8} or 10^{-9} or 10^{-10} or 10^{-11} or 10^{-12} or 10^{-13} range or below. Most preferably, it is a human IgG1 antibody that binds to at least one activating Fcγ receptor with high affinity and depletes tumour-infiltrating regulatory T cells. Most preferably, the anti-CD25 is characterized by other features related to Fcγ receptors, in particular:

- (a) binds to Fcγ receptors with an activatory to inhibitory ratio (A/I) superior to 1; and/or
- (b) binds to FcγRIIIa with higher affinity than it binds to FcγRIIIb.

- [23] Given the use of the anti-CD25 antibody in therapeutic methods, it can present further preferred features. The anti-CD25 antibody is preferably a monoclonal antibody, in particular a human, chimeric, or humanized antibody. The antibody may be an affinity matured variant thereof, optionally a humanised or affinity matured variant of 7G7B6 or MA251. Moreover, in view of its interactions with immune cells and/or other components of the immune system for exerting its activities, the anti-CD25 antibody may further elicit an enhanced CDC, ADCC and/or ADCP response, preferably an increased ADCC and/or ADCP response, more preferably an increased ADCC response, as compared to existing anti-human CD25 clinical antibodies, Daclizumab and Basiliximab. In some examples the anti-CD25 antibody may elicit a decreased CDC response, as compared to existing anti-human CD25 clinical antibodies, Daclizumab and Basiliximab, more preferably the anti-CD25 antibody does not elicit a CDC response.
- [24] The anti-CD25 antibody of the present disclosure (as generally defined above and in further details in the Detailed Description) can be used in methods of treating a human subject wherein said anti-CD25 antibody is administered to a subject. In one example the subject has cancer. Preferably the subject has an established, solid tumour (preferably in a method further comprising the step of identifying a subject who has a solid tumour). Such methods may further comprise administering a further therapeutic agent to said subject. In one example the further agent may be an immune checkpoint inhibitor to said subject, for example in the form of an antibody binding and inhibiting an immune checkpoint protein. A preferred immune checkpoint inhibitor is a PD-1 antagonist, which can be an anti-PD-1 antibody or an anti-PD-L1 antibody. More in general, an anti-CD25 antibody can be used in methods of depleting regulatory T cells in a solid tumour in a subject comprising the step of administering said anti-CD25 antibody to said subject.
- [25] In a further example, the anti-CD25 antibody of the disclosure can be used for the manufacture of a medicament for the treatment of cancer in a human subject, preferably wherein said subject has a tumour, preferably a solid tumour. Said antibody may be administered in combination with a further therapeutic agent, preferably a further cancer therapeutic agent for example with an immune checkpoint inhibitor, preferably a PD-1/PD-L1 pathway antagonist, a cancer vaccine, and/or used in combination with standard of care therapies such as chemotherapy or radiotherapy.
- [26] In a further example, the present disclosure provides a combination of an anti-CD25 antibody as defined above with another anti-cancer compound (preferably an immune checkpoint inhibitor or other

compounds as indicated in the Detailed Description) for use in the treatment of cancer in a human subject, preferably wherein said subject has a solid tumour and the anti-cancer compound (for example, an immune checkpoint inhibitor such a PD-1 antagonist or a cytokine such as Interleukin 2) can be administered simultaneously, separately or sequentially. At this scope the present disclosure also provides a kit for use in the treatment of cancer comprising an anti- CD25 antibody, as defined above, and an anti-cancer compound (for example, an immune checkpoint inhibitor such a PD-1 antagonist).

[27] In a further example, the present disclosure also provides a pharmaceutical composition comprising an anti-CD25 antibody as defined above in a pharmaceutically acceptable medium. Such composition may also comprise an anti-cancer compound (for example, an immune checkpoint inhibitor such a PD-1 antagonist).

[28] In a still further example, the present disclosure also provides a bispecific antibody comprising:

- (a) a first antigen binding moiety that binds to CD25; and
- (b) a second antigen binding moiety that binds to another antigen;

wherein the anti-CD25 antibody does not inhibit the binding of Interleukin-2 (IL-2) to CD25, and preferably the bispecific antibody is an IgG1 antibody that binds to at least one activatory Fcγ receptor with high affinity and depletes tumour-infiltrating regulatory T cells. Preferably, such second antigen binding moiety binds to an antigen selected from an immune checkpoint protein, or a tumour-associated antigen, or may be, or be based on, an anti-human activatory Fc Receptor antibody (anti-FcγRI, anti-FcγRIIa, anti-FcγRIII), or an antagonistic anti-human FcγRIIb antibody. As such, the second antigen binding moiety may bind to FcγRIIb. It may alternatively bind to FcγRI, FcγRIIa, and/or FcγRIII with antagonistic activity.

[29] Preferably, such bispecific antibody comprises a second antigen binding moiety that binds an immune checkpoint protein that is selected from the group consisting of PD-1, CTLA-4, BTLA, KIR, LAG3, VISTA, TIGIT, TIM3, PD-L1, B7H3, B7H4, PD-L2, CD80, CD86, HVEM, LLT1, GAL9, GITR, OX40, CD137, and ICOS. Such immune checkpoint protein is preferably expressed on a tumour cell. Preferably the immune checkpoint protein is selected from PD-1, PD-L1, and CTLA-4. The second antigen binding moiety that binds to an immune checkpoint protein can be comprised in a commercially available antibody that acts as an immune checkpoint inhibitor, for example:

- (a) in the case of PD-1, the anti-PD-1 antibody can be Nivolumab or Pembrolizumab.
- (b) In the case of PD-L1, the anti-PD-L1 is Atezolizumab;
- (c) In case of CTLA-4, the anti-CTLA-4 is Ipilimumab.

[30] Such bispecific antibody can be provided in any commercially available format, including Duobody, BiTE DART, CrossMab, Knobs-in-holes, Triomab, or other appropriate molecular format of bispecific antibody and fragments thereof.

- [31] Alternatively, such bispecific antibody comprises a second antigen binding moiety that binds to tumour-associated antigen. In this alternative example, such antigens and corresponding antibodies include, without limitation CD22 (Blinatumomab), CD20 (Rituximab, Tositumomab), CD56 (Lorvotuzumab), CD66e/CEA (Labetuzumab), CD152/CTLA-4 (Ipilimumab), CD221/IGF1R (MK-0646), CD326/Epcam (Edrecolomab), CD340/HER2 (Trastuzumab, Pertuzumab), and EGFR (Cetuximab, Panitumumab).
- [32] The combination of anti-CD25 antibody of the disclosure with another anti-cancer compound, as well as the bispecific antibodies as defined above, can be used in a method of treating cancer, comprising the step of administering said combination or said bispecific antibody to a subject, in particular when the subject has a solid tumour, and for use in the treatment of cancer in a subject.
- [33] Further objects of the disclosure, including further definitions of the anti-human CD25 antibodies of the disclosure and of their uses in methods for treating cancer, in pharmaceutical compositions, in combinations with other anti-cancer compounds, in bispecific antibodies, are provided in the Detailed Description and in the Examples.

Claims

1. Use of an anti-CD25 antibody, wherein said antibody does not inhibit the binding of Interleukin-2 (IL-2) to CD25 in the manufacture of a medicament for treating a human subject who has cancer, wherein said subject has a solid tumour, and wherein the medicament is to be administered to the subject.
2. The use according to claim 1 wherein the anti-CD25 antibody competes with the antibody 7G7B6 for binding to human CD25; and/or competes with the antibody MA251 for binding to human CD25.
3. The use according to claim 1 or claim 2 wherein the anti-CD25 antibody binds to the same epitope recognised by antibody 7G7B6 and/or the epitope recognised by antibody MA251.
4. The use according to any one of claims 1 to 3 wherein the anti-CD25 antibody specifically binds to an epitope of human CD25 wherein the epitope comprises one or more amino acid residues comprised in one or more of the amino acid stretches selected from amino acids 150-163 of SEQ ID NO:1 (YQCVQGYRALHRGP), amino acids 166-186 of SEQ ID NO:1 (SVCKMTHGKTRWTQPQLICTG), amino acids 42-56 of SEQ ID NO:1 (KEGTM LNCECKRGFR) and amino acids 70-88 of SEQ ID NO:1 (NSSHSSWDNQCQCTSSATR).
5. The use according to claim 4 wherein the anti-CD25 antibody specifically binds to an epitope of human CD25 wherein the epitope comprises at least one sequence selected from: amino acids 150-158 of SEQ ID NO:1 (YQCVQGYRA), amino acids 176-180 of SEQ ID NO:1 (RWTQP), amino acids 42-56 of SEQ ID NO:1 (KEGTM LNCECKRGFR) and amino acids 74-84 of SEQ ID NO:1 (SSWDNQCQCTS).
6. The use according to claim 4 wherein the anti-CD25 antibody specifically binds to an epitope of human CD25 wherein the epitope comprises at least one sequence selected from: amino acids 150-158 of SEQ ID NO:1 (YQCVQGYRA), amino acids 166-180 of SEQ ID NO:1 (SVCKMTHGKTRWTQP), amino acids 176-186 of SEQ ID NO:1 (RWTQPQLICTG), amino acids 42-56 of SEQ ID NO:1 (KEGTM LNCECKRGFR) and amino acids 74-84 of SEQ ID NO:1 (SSWDNQCQCTS).
7. The use according to claim 4 wherein the anti-CD25 antibody specifically binds to an epitope of human CD25 wherein the epitope comprises at least one sequence selected from: amino acids 42-56 of SEQ ID NO:1 (KEGTM LNCECKRGFR), amino acids 70 to 84 of SEQ ID NO: 1 (NSSHSSWDNQCQCTS) and amino acids 150 to 158 of SEQ ID NO: 1 (YQCVQGYRA).

8. The use according to claim 4 wherein the anti-CD25 antibody binds to an epitope comprising the sequence of amino acids 42-56 of SEQ ID NO:1 (KEGTMLNCECKRGFR).
9. The use according to claim 4 wherein the anti-CD25 antibody binds to an epitope comprising the sequence of amino acids 42-56 of SEQ ID NO:1 (KEGTMLNCECKRGFR) and amino acids 150-160 of SEQ ID NO:1 (YQCVQGYRALH).
10. The use according to claim 4 wherein the anti-CD25 antibody binds to an epitope comprising the sequence of amino acids 42-56 of SEQ ID NO:1 (KEGTMLNCECKRGFR) and amino acids 74-84 of SEQ ID NO:1 (SSWDNQCQCTSSATR).
11. The use according to claim 4 wherein the anti-CD25 antibody binds to an epitope comprising the sequence of amino acids 150-163 of SEQ ID NO:1 (YQCVQGYRALHRGP), amino acids 166-180 of SEQ ID NO:1 (SVCKMTHGKTRWTQP), amino acids 42-56 of SEQ ID NO:1 (KEGTMLNCECKRGFR) and amino acids 74-84 of SEQ ID NO:1 (SSWDNQCQCTSSATR).
12. The use according to claim 4 wherein the anti-CD25 antibody binds to an epitope comprising the sequence of amino acids 150-158 of SEQ ID NO:1 (YQCVQGYRA) and amino acids 176-180 of SEQ ID NO:1 (RWTQP).
13. The use according to claim 4 wherein the anti-CD25 antibody binds to an epitope comprising the sequence of amino acids 150-158 of SEQ ID NO:1 (YQCVQGYRA) and amino acids 176-186 of SEQ ID NO:1 (RWTQPQLICTG).
14. The use according to claim 4 wherein the anti-CD25 antibody binds to an epitope comprising the sequence of amino acids 150-163 of SEQ ID NO:1 (YQCVQGYRALHRGP) and amino acids 166-180 of SEQ ID NO:1 (SVCKMTHGKTRWTQP)
15. The use according to claim 4 wherein the anti-CD25 antibody binds to an epitope comprising the sequence of amino acids 74-84 of SEQ ID NO:1 (SSWDNQCQCTS).
16. The use according to claim 4 wherein the anti-CD25 antibody binds to an epitope comprising the sequence of amino acids 70-84 of SEQ ID NO:1 (NSSHSSWDNQCQCTS).
17. The use according to claim 4 wherein the anti-CD25 antibody binds to an epitope comprising the sequence of amino acids 176-180 of SEQ ID NO:1 (RWTQP).
18. The use according to claim 4 wherein the anti-CD25 antibody binds to an epitope comprising the sequence of amino acids amino acids 166-180 of SEQ ID NO:1 (SVCKMTHGKTRWTQP).

19. The use according to claim 4 wherein the anti-CD25 antibody binds to an epitope comprising the sequence of amino acids 176-186 of SEQ ID NO:1 (RWTQPQLICTG).
20. The use according to any one of claims 1 to 19 wherein the anti-CD25 antibody is an IgG1 antibody that binds to at least one activating Fcγ receptor selected from FcγRI, FcγRIIc, and/or FcγRIIIa with high affinity, and depletes tumour-infiltrating regulatory T cells.
21. The use according to any one of claims 1 to 19, wherein the anti-CD25 antibody:
- (a) binds to Fcγ receptors with an activatory to inhibitory ratio (A/I) superior to 1; and/or
 - (b) binds to FcγRI, FcγRIIc, and/or FcγRIIIa with higher affinity than it binds to FcγRIIb.
22. The use according to any one of claims 1 to 21 wherein the antibody is selected from the group consisting of:
- (a) an antibody comprising a heavy chain comprising the amino acid sequence of SEQ ID NO: 3 and the light chain comprising the amino acid sequence of SEQ ID NO:4;
 - (b) an antibody comprising a heavy chain comprising the amino acid sequence of SEQ ID NO: 5 and the light chain comprising the amino acid sequence of SEQ ID NO: 6;
 - (c) an antibody comprising a heavy chain comprising the amino acid sequence of SEQ ID NO: 10 and the light chain comprising the amino acid sequence of SEQ ID NO: 14;
 - (d) an antibody comprising a heavy chain comprising the amino acid sequence of SEQ ID NO: 18 and the light chain comprising the amino acid sequence of SEQ ID NO: 22;
 - (d) an antibody comprising a heavy chain comprising the amino acid sequence of SEQ ID NO: 23 and the light chain comprising the amino acid sequence of SEQ ID NO: 25;
 - (e) an antibody comprising a heavy chain comprising the amino acid sequence of SEQ ID NO: 23 and the light chain comprising the amino acid sequence of SEQ ID NO: 26;
 - (f) an antibody comprising a heavy chain comprising the amino acid sequence of SEQ ID NO: 24 and the light chain comprising the amino acid sequence of SEQ ID NO: 25;
 - (g) an antibody comprising a heavy chain comprising the amino acid sequence of SEQ ID NO: 24 and the light chain comprising the amino acid sequence of SEQ ID NO: 26;

- (h) an antibody comprising a heavy chain comprising the amino acid sequence of SEQ ID NO: 27 and the light chain comprising the amino acid sequence of SEQ ID NO: 30;
- (i) an antibody comprising a heavy chain comprising the amino acid sequence of SEQ ID NO: 27 and the light chain comprising the amino acid sequence of SEQ ID NO: 31;
- (j) an antibody comprising a heavy chain comprising the amino acid sequence of SEQ ID NO: 27 and the light chain comprising the amino acid sequence of SEQ ID NO: 32;
- (k) an antibody comprising a heavy chain comprising the amino acid sequence of SEQ ID NO: 27 and the light chain comprising the amino acid sequence of SEQ ID NO: 33;
- (l) an antibody comprising a heavy chain comprising the amino acid sequence of SEQ ID NO: 28 and the light chain comprising the amino acid sequence of SEQ ID NO: 30;
- (m) an antibody comprising a heavy chain comprising the amino acid sequence of SEQ ID NO: 28 and the light chain comprising the amino acid sequence of SEQ ID NO: 31;
- (n) an antibody comprising a heavy chain comprising the amino acid sequence of SEQ ID NO: 28 and the light chain comprising the amino acid sequence of SEQ ID NO: 32;
- (o) an antibody comprising a heavy chain comprising the amino acid sequence of SEQ ID NO: 28 and the light chain comprising the amino acid sequence of SEQ ID NO: 33;
- (p) an antibody comprising a heavy chain comprising the amino acid sequence of SEQ ID NO: 29 and the light chain comprising the amino acid sequence of SEQ ID NO: 30;
- (q) an antibody comprising a heavy chain comprising the amino acid sequence of SEQ ID NO: 29 and the light chain comprising the amino acid sequence of SEQ ID NO: 31;
- (r) an antibody comprising a heavy chain comprising the amino acid sequence of SEQ ID NO: 29 and the light chain comprising the amino acid sequence of SEQ ID NO: 32; and
- (s) an antibody comprising a heavy chain comprising the amino acid sequence of SEQ ID NO: 29 and the light chain comprising the amino acid sequence of SEQ ID NO: 33.

23. The use according to any one of claims 1 to 22 wherein the anti-CD25 antibody is a human IgG2 antibody.
24. The use according to any one of claims 1 to 23, wherein the anti-CD25 antibody has a dissociation constant (K_d) for CD25 of less than 10⁻⁷ M.

25. The use according to any one of claims 1 to 24 wherein the anti-CD25 antibody inhibits IL-2 signalling by less than 50%.
26. The use according to any one of claims 1 to 25, wherein the anti-CD25 antibody is a monoclonal antibody.
27. The use according to any one of claims 1 to 26, wherein the anti-CD25 antibody is a human, chimeric, or humanized antibody.
28. The use according to any one of claims 1 to 27, wherein the antibody is an affinity matured variants thereof.
29. The use according to any one of claims 1 to 28, wherein the antibody the antibody is a humanised and/or affinity matured variant of 7G7B6 or MA251.
30. The use according to any one of claims 1 to 29, wherein the anti-CD25 antibody elicits an enhanced CDC, ADCC and/or ADCP response, preferably an increased ADCC and/or ADCP response, more preferably an increased ADCC response.
31. The use according to any one of claims 1 to 30 wherein the anti-CD25 antibody is administered to a subject who has an established tumour.
32. The use according to any one of claims 1 to 31 further comprising the step of identifying a subject who has a solid tumour.
33. The use according to any one of claims 1 to 32 wherein an immune checkpoint inhibitor is to be further administered to said subject.
34. The use according to claim 33 wherein said immune checkpoint inhibitor is a PD-1 antagonist.
35. The use according to claim 34 wherein said PD-1 antagonist is an anti-PD-1 antibody or an anti-PD-L1 antibody.
36. The use according to any one of claims 1 to 32 wherein a cancer vaccine is to be further administered.
37. The use according to claim 36 wherein the cancer vaccine is a GVAX cancer vaccine.
38. An anti-CD25 antibody as defined in any one of claims 1 to 30.

39. The anti-CD25 antibody of claim 38 for use in medicine.
40. An anti-CD25 antibody, as defined in any one of claims 1 to 30, for use in the treatment of cancer in a human subject, wherein the subject has a solid tumour.
41. An anti-CD25 antibody for use according to claim 40 or the use of an anti-CD25 antibody according to any one of claims 1-30 wherein the antibody is for administration in combination with a further therapeutic agent.
42. An anti-CD25 antibody for use according to claim 41 or the use of an anti-CD25 antibody according to claim 41, wherein the further therapeutic agent is an immune checkpoint inhibitor.
43. An anti-CD25 antibody for use according to claim 42 or the use according to claim 42, wherein the immune checkpoint inhibitor is a PD-1 antagonist.
44. An anti-CD25 antibody for use according to claim 43 or the use of an anti-CD25 antibody according to any one of claims 1-30, wherein the further therapeutic agent is a cancer vaccine.
45. A combination of an anti-CD25 antibody, as defined in any one of claims 1 to 30, and a further therapeutic agent for use in the treatment of cancer in a human subject, wherein said subject has a solid tumour and the anti-CD25 antibody and the further therapeutic agent are administered simultaneously, separately or sequentially.
46. A kit for use in the treatment of cancer comprising an anti-CD25 antibody, as defined in any one of claims 1 to 30, and a further therapeutic agent.
47. A pharmaceutical composition comprising an anti-CD25 antibody as defined in any one of claims 1 to 30 in a pharmaceutically acceptable medium.
48. A pharmaceutical composition according to claim 47 further comprising a further therapeutic agent.
49. The combination for use as claimed in claim 45, the kit of claim 46, or the pharmaceutical composition according to claim 48, wherein the further therapeutic agent is an immune checkpoint inhibitor.

50. The combination for use as claimed in claim 45, the kit of claim 46, or the pharmaceutical composition according to claim 48, wherein the immune checkpoint inhibitor is a PD-1 antagonist.
51. The combination for use as claimed in claim 45, the kit of claim 46, or the pharmaceutical composition according to claim 48, wherein the further therapeutic agent is a cancer vaccine.
52. A bispecific antibody comprising:
- (a) a first antigen binding moiety that binds to CD25; and
 - (b) a second antigen binding moiety that binds to an immune checkpoint protein;
- wherein the CD25 binding moiety does not inhibit the binding of Interleukin-2 (IL-2) to CD25, and preferably the bispecific antibody is an IgG1 antibody that binds to at least one activating Fcγ Receptor, selected from FcγRI, FcγRIIa, FcγRIII with a high affinity and depletes tumour-infiltrating regulatory T cells.
53. The bispecific antibody according to claim 52, wherein the immune checkpoint protein is selected from the group consisting of PD-1, CTLA-4, BTLA, KIR, LAG3, VISTA, TIGIT, TIM3, PD-L1, B7H3, B7H4, PD-L2, CD80, CD86, HVEM, LLT1, GAL9, GITR, OX40, CD137, and ICOS.
54. The bispecific antibody according to claim 52 or 53, wherein the immune checkpoint protein is expressed on a tumour cell.
55. The bispecific antibody according to claim 52 or 53, wherein the immune checkpoint protein is PD-L1.
56. The bispecific antibody according to claim 52, wherein the second antigen binding moiety that binds to PD-L1 is comprised in Atezolizumab.
57. Use of a bispecific antibody as defined in any one of claims 52 to 56 in the manufacture of a medicament for treating cancer in a subject.
58. The use according to claim 56, wherein the subject has a solid tumour.
59. A bispecific antibody, as defined in any one of claims 52 to 56, for use in the treatment of cancer in a subject.
60. The bispecific antibody for use according to claim 59, wherein the subject has a solid tumour.

61. Use of an anti-CD25 antibody, wherein the antibody is as defined in any one of claims 1 to 30 in the manufacture of a medicament for depleting regulatory T cells in a subject.
62. The use according to claim 61 wherein the subject has a solid tumour.