

CLAIMS

1. Use of an isolated antibody or antigen-binding fragment thereof, specifically binding to CCR8 for use in the manufacture of a medicament for treatment of a tumor or a disease characterized by CCR8 positive cells, wherein a therapeutically effective amount of an anti-CCR8 antibody is to be administered to a human patient having the tumor, wherein the human patient has been diagnosed as having the tumor based on the level of a biomarker in the tumor or a tumor sample comprising regulatory T cells being higher than or equal to a reference sample or value, wherein the biomarker is selected from
 - i) an immune checkpoint protein PD-1, PD-L1 or CTLA4,
 - 10 ii) an interferon or interferon-inducible protein selected from IFN gamma, IL10, IL12p70, IL1beta, IL2 and TNF alpha, and/or
 - iii) a molecule derived from a gene according to Table 12.7.2.1, 12.7.2.2 or 12.7.2.3, CD8, PD-L1, PD-1, CTLA4, CCR4, CCR8, FOXP3, NCR1, MS4A7, FCGR2, IFNg, ACOD1, MRC1, NCR1, CD3, CD19, CD22, LTA, LTB, CXCR5 and/or
15 CXCL13.
2. A method for diagnosing a subject as having a tumor that is sensitive for treatment with an anti-CCR8 antibody, comprising
 - a. determining the level of the biomarker in a tumor sample comprising regulatory T cells,
20 wherein the tumor sample has been obtained from the subject,
 - b. comparing the level of the biomarker with a reference sample or value, and
 - c. diagnosing the subject as having a tumor that is sensitive for treatment with an anti-CCR8 antibody, if the level of the biomarker is higher than or equal to a reference sample or value, wherein the biomarker is selected from
 - 25 i) an immune checkpoint protein selected from PD-1, PD-L1 or CTLA4,
 - ii) an interferon or interferon-inducible protein selected from IFN gamma, IL10, IL12p70, IL1beta, IL2 and TNF alpha, and/or
 - iii) a molecule derived from a gene according to Table 12.7.2.1, 12.7.2.2 or 12.7.2.3, CD8, PD-L1, PD-1, CTLA4, CCR4, CCR8, FOXP3, NCR1, MS4A7, FCGR2,
30 IFNg, ACOD1, MRC1, NCR1, CD3, CD19, CD22, LTA, LTB, CXCR5 and/or CXCL13 .
3. A method to predict or monitor the therapeutic success of a therapy, wherein the therapy comprised the administration of an anti-CCR8 antibody, the method comprising
 - a. determining the level of a biomarker in a tumor sample, and
 - 35 b. comparing the level of the biomarker with a reference sample or value, wherein the biomarker is selected from
 - i) an immune checkpoint protein, selected from PD-1, PD-L1 or CTLA4,

- ii) an interferon or interferon-inducible protein selected from IFN gamma, IL10, IL12p70, IL1beta, IL2 and TNF alpha, and/or
 - iii) a molecule derived from a gene according to Table 12.7.2.1, 12.7.2.2 or 12.7.2.3, CD8, PD-L1, PD-1, CTLA4, CCR4, CCR8, FOXP3, NCR1, MS4A7, FCGR2, IFNg, ACOD1, MRC1, NCR1, CD3, CD19, CD22, LTA, LTB, CXCR5 and/or CXCL13.
- 4. The method according to claim 2 or 3, wherein the biomarker is an immune checkpoint protein selected from PD-1, PD-L1 or CTLA4.
- 5. The method according to claim 2 or 3, wherein the biomarker is PD-1, PD-L1, and/or an interferon or interferon-inducible protein.
- 6. Use of a molecule binding a biomarker for the manufacture of a diagnostic agent for use in a method of diagnosing a subject as having a tumor that is sensitive for treatment with an anti-CCR8 antibody, the method comprising:
 - a) determining the level of the biomarker in a tumor or tumor sample comprising regulatory T cells using the molecule binding the biomarker,
 - b) comparing the level of the biomarker with a reference sample or value, and
 - c) diagnosing a subject as having a tumor that is sensitive for treatment with an anti-CCR8 antibody, if the level of the biomarker is higher than or equal to a reference sample or value, wherein the biomarker is selected from
 - i) an immune checkpoint protein selected from PD-1, PD-L1 or CTLA4,
 - ii) an interferon or interferon-inducible protein selected from IFN gamma, IL10, IL12p70, IL1beta, IL2 and TNF alpha,
 - and/or
 - iii) a molecule derived from a gene according to Table 12.7.2.1, 12.7.2.2 or 12.7.2.3, CD8, PD-L1, PD-1, CTLA4, CCR4, CCR8, FOXP3, NCR1, MS4A7, FCGR2, IFNg, ACOD1, MRC1, NCR1, CD3, CD19, CD22, LTA, LTB, CXCR5 and/or CXCL13,
- and wherein the molecule binding the biomarker is preferably an antibody or antigen-binding fragment, or a conjugate thereof.
- 7. Use of a molecule binding a biomarker for the manufacture of a diagnostic agent for use in a method to predict or monitor the therapeutic success of a therapy, wherein the therapy comprised the administration of an anti-CCR8 antibody, the method comprising:
 - a) determining the level of the biomarker in a tumor or tumor sample using the molecule binding the biomarker, and

- b) comparing the level of the biomarker with a reference sample or value, wherein the biomarker is selected from
- i) an immune checkpoint protein selected from PD-1, PD-L1 or CTLA4,
 - ii) an interferon or interferon-inducible protein selected from IFN gamma, IL10, IL12p70, IL1beta, IL2 and TNF alpha, and/or
 - iii) a molecule derived from a gene according to Table 12.7.2.1, 12.7.2.2 or 12.7.2.3, CD8, PD-L1, PD-1, CTLA4, CCR4, CCR8, FOXP3, NCR1, MS4A7, FCGR2, IFNg, ACOD1, MRC1, NCR1, CD3, CD19, CD22, LTA, LTB, CXCR5 and/or CXCL13,
- and wherein the molecule binding the biomarker is preferably an antibody or antigen-binding fragment, or a conjugate thereof.
8. The use according to claim 6 or 7, wherein the molecule binding the biomarker is an anti-PD-1, anti-PD-L1 or anti-CTLA4 antibody such as Nivolumab, Pembrolizumab, Atezolizumab, Avelumab, Durvalumab, Cemiplimab, Dostarlimab or Ipilimumab.
9. The use according to claim 6 or 7, wherein the molecule binding the biomarker is an antibody binding an interferon or interferon-inducible protein selected from INF gamma, IL10, IL12p70, IL1beta, IL2 and TNF alpha.
10. Use of an anti-CCR8 antibody inducing ADCC and ADCP in the manufacture of a medicament for the treatment of a tumor, wherein the medicament is to be administered in combination with a further therapeutically active compound or therapy, wherein a dose of the further therapeutically active compound or therapy is to be administered after a first dose of the medicament, wherein the further therapeutically active compound or therapy is selected from
- i) paclitaxel, doxorubicin oxaliplatin, or gemcitabine,
 - ii) radiation therapy, and/or
 - iii) depletion of intra-tumoral B cells, preferably CD19+ B cells.
11. Use of an anti-CCR8 antibody inducing ADCC and ADCP in the manufacture of a medicament for the treatment of a tumor, wherein the medicament is to be administered in combination with a further therapeutically active compound or therapy which does not target a checkpoint protein and is selected from
- i) paclitaxel, doxorubicin, oxaliplatin, or gemcitabine,
 - ii) radiation therapy, and/or
 - iii) depletion of intra-tumoral B cells, preferably CD19+ B cells.
12. The use according to claims 10 or 11, wherein the medicament is to be administered in combination with a checkpoint inhibitor such as an anti-PD-1 antibody, an anti-PD-L1 antibody or a CTLA4 antibody.

13. Use of an anti-CCR8 antibody inducing ADCC and ADCP in the manufacture of a medicament for the treatment of a tumor, wherein only a single dose of the anti-CCR8 antibody is to be administered to a subject, such that no further dose of the same or a different anti-CCR8 antibody is to be administered to the subject.