

Mild to moderate asthma is treated with anti-inflammatories like inhaled steroids, long and short acting beta-agonists, montelukast and theophylline. In the more severe populations oral steroids are added, but do not suffice to control all asthma phenotypes. There is therefore a medical need for the treatment of more severe forms of asthma, for example for phenotypes which display a high number of certain cell subpopulations and/or are steroid resistant.

Summary

The present disclosure addresses the above needs and provides methods for treating asthma, in particular severe persistent asthma, comprising administering an anti-IL-23A antibody to a patient.

There is provided a method of the present disclosure for treating neutrophilic asthma. There is provided a method of the present disclosure for treating eosinophilic asthma. There is provided a method of the present disclosure for treating mixed neutrophilic and eosinophilic asthma. There is provided a method of the present disclosure for treating paucigranulocytic asthma. In the present disclosure, asthma is categorized by induced sputum.

In one aspect, there is provided use of an anti-IL-23A antibody in the manufacture of a medicament for the treatment of severe persistent asthma in a patient.

In the present disclosure, a patient as provided above is not responsive to corticosteroids.

In the present disclosure, as provided above, the treatment is assessed by the reduction of the annual rate of exacerbations in patients, for example patients with severe persistent asthma, for example with a hazard ratio (HR) of 0.75. In the present disclosure, as provided above, the treatment is assessed by the relative improvement in proportion of patients having symptomatic improvements, for example an Asthma Control Questionnaire (ACQ) reduction of 0.5 units: 20 %. In the present disclosure, as provided above, the treatment is assessed by improvement in trough Forced Expiratory Volume in 1 second (FEV_1), e.g. > 125ml, reduction of current controller therapies,

improvement in health related QoL (e.g. Asthma Quality of Life Questionnaire (AQLQ)), or improvement in symptoms score / rescue medication use.

In the present disclosure, as provided above, asthma is mediated by Th17 cells or cells responsive to IL-23. In the present disclosure, as provided above, asthma is mediated by Th2 cells. In the present disclosure, as provided above, asthma is mediated by Th2/Th17 dual-positive cells or cells responsive to Th2 responsive cytokines and IL-23.

There is also provided a method for the treatment or prophylaxis of asthma exacerbations comprising administering an anti-IL-23A antibody to a patient with asthma, in particular severe asthma, for example severe persistent asthma.

In the present disclosure a patient is a patient who experiences frequent exacerbations and in a further embodiment, the present disclosure provides a method for improving exacerbations in patients who experience frequent exacerbations comprising administering an anti-IL-23A antibody to the patient with asthma, in particular severe asthma, for example severe persistent asthma.

There is also provided a method for the treatment or control of symptoms of severe asthma comprising administering an anti-IL-23A antibody to a patient with severe persistent asthma.

There is also provided a method for the treatment or prophylaxis of asthma exacerbations and for the treatment or control of symptoms of severe asthma comprising administering an anti-IL-23A antibody to a patient with severe persistent asthma.

There is also provided a method to reduce the rate of asthma exacerbations comprising administering an anti-IL-23A antibody to a patient with severe persistent asthma.

In the present disclosure, as provided above, asthma is neutrophilic asthma. In the present disclosure, as provided above, asthma is eosinophilic asthma. In the present disclosure, as provided above, asthma is mixed neutrophilic and eosinophilic asthma. In the present disclosure, as provided above, asthma is paucigranulocytic asthma. In the present disclosure, the type of asthma is categorized or phenotyped by induced sputum, by blood cell counts or by blood biomarkers which could be eosinophiles and/ or various cytokines or other proteins.

In the present disclosure, as provided above, the patient is not adequately controlled on inhaled corticosteroids. In the present disclosure, as provided above, the patient is not adequately controlled on inhaled corticosteroids and a second controller medication. In the present disclosure, as provided above, the patient is 12 years of age and older. In the present disclosure, as provided above, the patient is 12 years of age and older not adequately controlled on inhaled corticosteroids and a second controller medication.

In the present disclosure, as provided above, the treatment, prophylaxis, control or reduction is assessed by the reduction of annual rate of exacerbations in a patient, for example a patient with severe persistent asthma, for example with a hazard ratio (HR) of 0.75. In the present disclosure, as provided above, the treatment, prophylaxis, control or reduction is assessed by the relative improvement in proportion of patients having symptomatic improvements, for example an Asthma Control Questionnaire (ACQ) reduction of 0.5 units: 20 %. In the present disclosure, as provided above, the treatment, prophylaxis, control or reduction is assessed by improvement in trough FEV_1 (e.g. > 125ml), reduction of current controller therapies, improvement in health related QoL (e.g. Asthma Quality of Life Questionnaire (AQLQ)), or improvement in symptoms score / rescue medication use.

In the present disclosure, as provided above, the anti-IL-23A antibody is Antibody A, Antibody B, Antibody C or Antibody D.

In the present disclosure, as provided above, the anti-IL-23A antibody is administered to said patient by subcutaneous administration.

The present disclosure provides an anti-IL-23A antibody for use in a method described herein, for example in the treatment of asthma, in particular severe persistent asthma, for example as described herein.

The present disclosure provides for the use of an anti-IL-23A antibody for the preparation of a medicament for the treatment of asthma, in particular severe persistent asthma, for example as described herein.

In the present disclosure, in any one of the methods or uses above, the anti-IL-23A antibody is disclosed below.

- 5 In one embodiment, the anti-IL-23A antibody comprises a light chain variable region comprising the amino acid sequence of SEQ ID NO:1 (*CDR1-L*); the amino acid sequence of SEQ ID NO:2 (*CDR2-L*); and the amino acid sequence of SEQ ID NO:3 (*CDR3-L*); and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 4, 7, 8 or 9 (*CDR1-H*); the amino acid sequence of SEQ ID NO:5 (*CDR2-H*); and the amino acid sequence of SEQ ID NO:6 (*CDR3-H*).
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- In one embodiment, the anti-IL-23A antibody comprises a light chain variable region comprising the amino acid sequence of SEQ ID NO:1 (*CDR1-L*); the amino acid sequence of SEQ ID NO:2 (*CDR2-L*); and the amino acid sequence of SEQ ID NO:3 (*CDR3-L*); and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:4 (*CDR1-H*); the amino acid sequence of SEQ ID NO:5 (*CDR2-H*); and the amino acid sequence of SEQ ID NO:6 (*CDR3-H*).
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- In one embodiment, the anti-IL-23A antibody comprises a light chain variable region comprising the amino acid sequence of SEQ ID NO:1 (*CDR1-L*); the amino acid sequence of SEQ ID NO:2 (*CDR2-L*); and the amino acid sequence of SEQ ID NO:3
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Claims

1. Use of an anti-IL-23A antibody in the manufacture of a medicament for the treatment of severe persistent asthma in a patient.
2. The use according to claim 1, wherein said patient is not responsive to corticosteroids.
3. The use according to any one of claims 1 or 2, wherein said anti-IL-23A antibody is Antibody A, Antibody B, Antibody C or Antibody D.

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4. The use according to any one of claims 1 to 3, wherein said anti-IL-23A antibody is to be administered to said patient by subcutaneous administration.
5. The use according to any one of claims 1 to 4, wherein said asthma is neutrophilic asthma, eosinophilic asthma, mixed neutrophilic and eosinophilic asthma or paucigranulocytic asthma.
6. The use according to any one of claims 1 to 5, wherein the anti-IL-23A antibody comprises a light chain comprising the amino acid sequence of SEQ ID NO:18 and a heavy chain comprising the amino acid sequence of SEQ ID NO:19.
7. The use according to any one of claims 1 to 5, wherein the anti-IL-23A antibody comprises a light chain comprising the amino acid sequence of SEQ ID NO:18 and a heavy chain comprising the amino acid sequence of SEQ ID NO:20.
8. The use according to any one of claims 1 to 5, wherein the anti-IL-23A antibody comprises a light chain comprising the amino acid sequence of SEQ ID NO:21 and a heavy chain comprising the amino acid sequence of SEQ ID NO:19.

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9. The use according to any one of claims 1 to 5, wherein the anti-IL-23A antibody comprises a light chain comprising the amino acid sequence of SEQ ID NO: 21 and a heavy chain comprising the amino acid sequence of SEQ ID NO: 20.