

further lines of therapy remains high. Therefore, the development of novel agents to treat chronic GVHD and these related conditions remains an unmet medical need

SUMMARY

Inhibitors of CSF-1R activity are active in the treatment of sclerotic conditions and chronic host versus graft disease. Axatilimab, is an anti-CSF-1R antibody or antigen binding fragment thereof, comprises a heavy chain, wherein the variable domain of the heavy chain comprises at least one of a CDR having the sequence given in SEQ ID NO:4 for CDR-H1, a CDR having the sequence given in SEQ ID NO:5 for CDR-H2 and a CDR having the sequence given in SEQ ID NO:6 for CDR-H3; and/or a light chain, wherein the variable domain of the light chain comprises at least one of a CDR having the sequence given in SEQ ID NO: 1 for CDR-L1, a CDR having the sequence given in SEQ ID NO:2 for CDR-L2 and a CDR having the sequence given in SEQ ID NO: 3 for CDR-L3.

In one aspect, the present disclosure refers to use of an anti-CSF-1R antibody or anti-CSF-1 antibody or antigen binding fragment thereof in the manufacture of a medicament for the treatment of chronic graft versus host disease (cGVHD) in a patient in need thereof.

In some embodimentexamples, the anti-CSF-1R antibody or antigen binding fragment thereof comprises a heavy chain and a light chain, wherein the variable domain of the heavy chain comprises three CDRs and the sequence of CDR-H1 has at least 60% identity or similarity to the sequence given in SEQ ID NO:4, the sequence of CDR-H2 has at least 60% identity or similarity to the sequence given in SEQ ID NO:5 and the sequence of CDR-H3 has at least 60% identity or similarity to the sequence given in SEQ ID NO:6; and wherein the variable domain of the light chain comprises three CDRs and the sequence of CDR-L1 has at least 60% identity or similarity to the sequence given in SEQ ID NO: 1, the sequence of CDR-L2 has at least 60% identity or similarity to the sequence given in SEQ ID NO:2 and the sequence of CDR-L3 has at least 60% identity or similarity to the sequence given in SEQ ID NO:3.

In some embodimentexamples, the anti-CSF-1R antibody or antigen binding fragment thereof comprises a heavy chain, wherein the heavy chain comprises the sequence given in SEQ ID NO:23; and a light chain, wherein the light chain comprises the sequence given in SEQ ID NO:15.

In some embodimentexamples, the anti-CSF-1R antibody or anti-CSF-1 antibody or antigen binding fragment thereof is selected from the group consisting of a complete antibody molecule having full length heavy and light chains, a Fab, modified Fab', Fab', F(ab')₂, Fv, VH, VL and scFv fragment thereof.

In some embodimentexamples, the anti-CSF-1R antibody or antigen binding fragment thereof

comprises a heavy chain comprising the sequence given in SEQ ID NO:27 and a light chain comprising the sequence given in SEQ ID NO:19.

In some embodimentexamples, the anti-CSF-1R antibody or antigen binding fragment thereof cross-blocks the binding of an antibody comprising the 6 CDRs given in sequence SEQ ID NO:1 for CDR-L1, SEQ ID NO:2 for CDR-L2, SEQ ID NO:3 for CDR-L3, SEQ ID NO:4 for CDR-H1, SEQ ID NO:5 for CDR-H2 and SEQ ID NO:6 for CDR-H3.

In some embodimentexamples, the anti-CSF-1R as defined herein is axatilimab.

In some embodimentexamples, the dosing of axatilimab is 0.3 mg/kg Q2W, 1 mg/kg Q2W, or 3 mg/kg Q4W. In some embodimentexamples, the administration of axatilimab is for the prevention or treatment of a sclerotic skin condition. In some embodimentexamples, the administration of axatilimab is for the prevention or treatment of chronic graft versus host disease.

The details of the disclosure are set forth in the accompanying description below. Although methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present application, illustrative methods and materials are now described. In the case of conflict, the present specification, including definitions, will control. In addition, the materials, methods, and examples are illustrative only and are not intended to be limiting. Other features, objects, and advantages of the disclosure will be apparent from the description and from the claims. In the specification and the appended claims, the singular forms also include the plural unless the context clearly dictates otherwise. Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this disclosure belongs.

The contents of all references (including literature references, issued patents, published patent applications, and co-pending patent applications) cited throughout this application are hereby expressly incorporated herein in their entireties by reference. The references cited herein are not admitted to be prior art to the application.

BRIEF DESCRIPTION OF THE DRAWINGS

The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.

Fig. 1 shows the general schematic for treatment of cGVHD with the anti-CSF-1R

CLAIMS

1. Use of an anti-CSF-1R antibody or anti-CSF-1 antibody or antigen binding fragment thereof in the manufacture of a medicament~~A method~~ for the treatment of chronic graft versus host disease (cGVHD), ~~wherein the method comprises comprising administering to a patient an anti-CSF-1R antibody or anti-CSF-1 antibody or antigen binding fragment thereof to~~ in a patient in need thereof.
2. The ~~method~~use of any one of the preceding claims, wherein the anti-CSF-1R antibody or antigen binding fragment thereof comprises:
 - a heavy chain, wherein the heavy chain comprises the sequence given in SEQ ID NO:23;
 - and
 - a light chain, wherein the light chain comprises the sequence given in SEQ ID NO:15.
3. The ~~method~~use of claim 1, wherein the anti-CSF-1R antibody or antigen binding fragment thereof comprises a heavy chain comprising the sequence given in SEQ ID NO:27 and a light chain comprising the sequence given in SEQ ID NO:19.
4. The ~~method~~use of any one of the preceding claims, wherein the anti-CSF-1R antibody or anti-CSF-1 antibody or antigen binding fragment thereof, or the inhibitor of CSF-1R activity is to be administered between once every three weeks and four times every week.
5. The ~~method~~use of any one of the preceding claims, wherein the anti-CSF-1R antibody or anti-CSF-1 antibody or antigen binding fragment thereof, or the inhibitor of CSF-1R activity is to be administered between once every two weeks.
6. The ~~method~~use of any one of the preceding claims, wherein the anti-CSF-1R antibody or anti-CSF-1 antibody or antigen binding fragment thereof, or the inhibitor of CSF-1R activity is to be administered at a dosage of between about 0.3 mg/kg and 3 mg/kg.

7. The ~~method-use~~ of any one of the preceding claims, wherein the anti-CSF-1R antibody or anti-CSF-1 antibody or antigen binding fragment thereof, or the inhibitor of CSF-1R activity is to be administered at a dosage of about 0.3 mg/kg.
8. The ~~method-use~~ of any one of the preceding claims, wherein the anti-CSF-1R antibody or anti-CSF-1 antibody or antigen binding fragment thereof, or the inhibitor of CSF-1R activity is to be administered at a dosage of about 1 mg/kg.
9. The ~~method-use~~ of any one of the preceding claims, wherein the anti-CSF-1R antibody or anti-CSF-1 antibody or antigen binding fragment thereof, or the inhibitor of CSF-1R activity is to be administered at a dosage of about 0.3 mg/kg every two weeks.
10. The ~~method-use~~ of any one of the preceding claims, wherein the anti-CSF-1R antibody or anti-CSF-1 antibody or antigen binding fragment thereof, or the inhibitor of CSF-1R activity is to be administered at a dosage of about 3 mg/kg every four weeks.
11. The ~~method-use~~ of any one of the preceding claims, wherein the chronic graft versus host disease is selected from skin chronic graft versus host disease, eyes chronic graft versus host disease, mouth chronic graft versus host disease, esophagus chronic graft versus host disease, upper GI chronic graft versus host disease, lower GI chronic graft versus host disease, liver chronic graft versus host disease, lungs chronic graft versus host disease, joints and fascia chronic graft versus host disease, or global chronic graft versus host disease.
12. The ~~method-use~~ of any one of the preceding claims, wherein the chronic graft versus host disease is selected from one or more of skin chronic graft versus host disease, eyes chronic graft versus host disease, lungs chronic graft versus host disease, joints and fascia chronic graft versus host disease, mouth chronic graft versus host disease, lower GI chronic graft versus host disease, and esophagus chronic graft versus host disease.
13. The ~~method-use~~ of any one of the preceding claims, wherein the patient has progressed on one or more prior therapies.

14. The ~~method-use~~ of any one of the preceding claims, wherein the patient has progressed on at least two prior therapies.
15. The ~~method-use~~ of any one of the preceding claims, wherein the patient progressed from a previous ibrutinib treatment.
16. The ~~method-use~~ of any one of the preceding claims, wherein the patient has progressed on at least two prior therapies, wherein one of the prior therapies was ibrutinib.
17. The ~~method-use~~ of any one of the preceding claims, wherein the level of monocytes is not fully depleted between doses of the CSF-1R inhibitor.
18. The ~~method-use~~ of any one of the preceding claims, wherein the level of monocytes are fully depleted between doses of the CSF-1R inhibitor.
19. The ~~method-use~~ of claims 17 or 18, wherein the monocytes are non-classical, intermediate and/or classical monocytes.
20. The ~~method-use~~ of any one of the preceding claims, wherein the CSF-1R inhibitor or anti-CSF-1R antibody is axatilimab.
21. The ~~method-use~~ of any preceding claim, wherein the cGVHD is sclerodermatous.
22. The ~~method-use~~ of any preceding claim, wherein the cGVHD is sclerodermatous with ulceration.
23. The ~~method-use~~ of any preceding claim, wherein the terminal C-terminal lysine of the axatilimab antibody heavy chain is absent.
24. The ~~method-use~~ of any preceding claim, wherein ~~the method further comprises administering~~ a second therapeutic agent is to be further administered.

25. The ~~method-use~~ of any preceding claim, wherein ~~the method further comprises administering~~ a second therapeutic agent is to be further administered, wherein the second therapeutic agent is a corticosteroid.

26. The ~~method-use~~ of any preceding claim, wherein ~~the method further comprises administering~~ a second therapeutic agent is to be further administered, wherein the second therapeutic agent is prednisone.