

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 in the manufacture of a medicament for the treatment of chronic graft versus host disease (cGVHD) in a human patient in need thereof, wherein the anti-CSF-1R antibody comprises: a heavy chain, wherein the variable domain of the heavy chain comprises a complementarity determining region (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 a light chain, wherein the variable domain of the light chain comprises 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; and wherein the anti-CSF-1R antibody is to be administered intravenously at a dosage of about 0.3 mg/kg every two weeks or about 1.0 mg/kg every two weeks. In some examples, 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 examples, 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 examples, 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 examples, the anti-CSF-1R antibody or antigen binding fragment thereof

CLAIMS

1. Use of an anti-CSF-1R antibody in the manufacture of a medicament for the treatment of chronic graft versus host disease (cGVHD) in a human patient in need thereof, wherein the anti-CSF-1R antibody comprises:
 - a heavy chain, wherein the variable domain of the heavy chain comprises a complementarity determining region (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
 - a light chain, wherein the variable domain of the light chain comprises 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;
 - and wherein the anti-CSF-1R antibody is to be administered intravenously at a dosage of about 0.3 mg/kg every two weeks or about 1.0 mg/kg every two weeks.
2. The use of claim 1, wherein:
 - the heavy chain comprises the sequence given in SEQ ID NO:23; and
 - the light chain comprises the sequence given in SEQ ID NO:15.
3. The use of claim 1, wherein:
 - the heavy chain comprises the sequence given in SEQ ID NO:27; and
 - the light chain comprises the sequence given in SEQ ID NO:19.
4. The use of any one of claims 1-3, wherein the anti-CSF-1R antibody is to be administered at a dosage of about 1.0 mg/kg every two weeks.
5. The use of any one of claims 1-3, wherein the anti-CSF-1R antibody to be administered at a dosage of about 0.3 mg/kg every two weeks.
6. The use of any one of claims 1-5, 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.

7. The use of any one of claims 1-6, wherein the chronic graft versus host disease is mouth chronic graft versus host disease.

8. The use of any one of claims 1-7, wherein the human patient has progressed on one or more prior therapies.

9. The use of any one of claims 1-8, wherein the human patient progressed from a previous ibrutinib treatment.

10. The use of any one of claims 1-8, wherein one of the one or more prior therapies was ibrutinib.

11. The use of any one claims 1-10, wherein the use decreases a level of non-classical, intermediate, and/or classical monocytes, and wherein the level of non-classical, intermediate, and/or classical monocytes is not fully depleted between doses of the anti-CSF-1R antibody.

12. The use of any one of claims 1-11, wherein the anti-CSF-1R antibody is axatilimab.

13. The use of any one of claims 1-12, wherein the cGVHD is sclerodermatous.

14. The use of any one of claims 1-13, wherein the cGVHD is sclerodermatous with ulceration.

15. The use of any one of claims 1-14, wherein the heavy chain C-terminal lysine is absent.

16. The use of any one of claims 1-15, wherein the anti-CSF-1R antibody is to be administered in combination with a second therapeutic agent, wherein the second therapeutic agent is a corticosteroid.

17. The use of claim 16, wherein the second therapeutic agent is prednisone.
18. The use of any one of claims 1-17, wherein the anti-CSF-1R antibody is to be further used at a dosage of 0.6 mg/kg every four weeks once the patient has a partial response, a complete response, or the cGVHD has not progressed.
19. The use of any one claims 1-18, wherein the anti-CSF-1R antibody is to be further administered at a dosage of 0.6 mg/kg every four weeks once the patient has a partial response after at least twenty weeks.
20. The use of any one claims 1-18, wherein the anti-CSF-1R antibody is to be further administered at a dosage of 0.6 mg/kg every four weeks once the patient has a complete response after at least twenty weeks.
21. The use of any one claims 1-18, wherein the anti-CSF-1R antibody is to be further administered at a dosage of 0.6 mg/kg every four weeks once the cGVHD has not progressed after at least twenty weeks.
22. The use of any one of claims 1-17, wherein the anti-CSF-1R antibody is to be further used at a dosage of 2.0 mg/kg every four weeks once the patient has a partial response, a complete response, or the cGVHD has not progressed.
23. The use of any one claims 1-17 or 22, wherein the anti-CSF-1R antibody is to be further administered at a dosage of 2.0 mg/kg every four weeks once the patient has a partial response after at least twenty weeks.
24. The use of any one claims 1-17 or 22, wherein the anti-CSF-1R antibody is to be further administered at a dosage of 2.0 mg/kg every four weeks once the patient has a complete response after at least twenty weeks.

25. The use of any one claims 1-17 or 22, wherein the anti-CSF-1R antibody is to be further administered at a dosage of 2.0 mg/kg every four weeks once the cGVHD has not progressed after at least twenty weeks.