At present, there are few treatment options available to sensitized patients with antibody mediated rejection. The treatments available include, for example, rituximab, and plasmapheresis with, or without, intravenous immunoglobulin (IVIg).

Although the treatments available show varying effectiveness for treating AMR initially, their effects become diminished and are not sustained in nearly half of patients. Thus, the long term effect of currently available treatments is poor and an enormous unmet need exists in the field for efficacious treatments of AMR and treatments and compositions that improve overall transplant survival for patients receiving cross-match positive organ transplants.

Summary

The present disclosure meets the needs in the field by providing methods and compositions for advantageously administering a C1-esterase inhibitor (C1-INH) protein to organ transplant patients who experience or are at risk of experiencing antibody-mediated rejection (AMR) of the transplanted organ.

In one aspect of the present disclosure, there is provided a use of a composition comprising a C1 esterase inhibitor (C1-INH) protein in the manufacture of a medicament for treating antibody-mediated rejection (AMR) of an organ allograft in a patient in need thereof, characterized in that the medicament is to be intravenously administered at a dose of 5,000 units to 25,000 units of C1-INH given in divided doses over a duration of 10-20 days.

In another aspect of the present disclosure, there is provided a use of a composition comprising a C1 esterase inhibitor (C1-INH) protein in the manufacture of a medicament for treating antibody-mediated rejection (AMR) of a kidney allograft in a patient in need thereof, characterized in that the medicament is to be intravenously administered at a dose of 5,000 units to 25,000 units of C1-INH given in divided doses over a duration of 10-20 days.

In one example, the present disclosure provides a method of treating AMR of an organ allograft in a patient in need thereof. A therapeutically effective amount of a C1-INH is used. The method includes early and/or short term duration administration of a therapeutically effective amount of a C1-INH. The method includes use of a therapeutically effective amount of the C1-INH that is

Claims

1. Use of a composition comprising a C1 esterase inhibitor (C1-INH) protein in the manufacture of a medicament for treating antibody-mediated rejection (AMR) of an organ allograft in a patient in need thereof, characterized in that the medicament is to be intravenously administered at a dose of 5,000 units to 25,000 units of C1-INH given in divided doses over a duration of 10-20 days.
2. The use according to claim 1, characterized in that administration of the medicament is to be initiated within 1 to 90 days of organ transplantation, treatment with plasmapheresis, treatment with intravenous immunoglobulin (IVIg), or diagnosis of AMR of the patient.
3. The use according to claim 1 or 2 wherein C1-INH is plasma derived or recombinantly produced.
4. The use according to any one of claims 1-3, wherein the patient has been subjected to plasmapheresis or is currently subject to plasmapheresis.
5. The use according to any one of claims 1-4, characterized in that the medicament is to be administered in combination with: (i) plasmapheresis;
   (ii) fresh frozen plasma; (iii) intravenous immunoglobulin; and/or (iv) rituximab, bortezomib, eculizumab, or a combination thereof.
6. The use according to any one of claims 1-4, characterized in that the medicament is to be administered in combination with plasmapheresis.
7. The use according to any one of claims 1-4 and 6, characterized in that the medicament is to be administered in combination with intravenous immunoglobulin.
8. The use according to any one of claims 1-7, wherein the organ is a solid organ.
9. The use according to claim 8, wherein the solid organ is selected from the group consisting of kidney, pancreas, intestine, heart, lung, liver, and a combination thereof.
10. The use according to claim 9, wherein the solid organ is a kidney.
11. The use according to any one of claims 1-10, characterized in that the total dose of the medicament is to be administered in divided doses over a duration of 13 days.

12. The use according to any one of claims 1-10, characterized in that the medicament is to be administered in a total dose of 20,000 units of C1-INH.
13. The use according to any one of claims 1-11, characterized in that administration of the medicament results in a therapeutic effect lasting for at least 3 months after cessation of therapy.
14. The use according to claim 13, wherein the therapeutic effect comprises a reduced incidence of chronic glomerulopathy, transplant glomerulopathy, or prevention of AMR.
15. The use according to claim 14, wherein the therapeutic effect comprises the prevention of AMR.
16. The use according to any one of claims 1-15, characterized in that the medicament is to be administered in a total dose of 20,000 units of C1-INH divided over 13 days, wherein the initial dose is 5,000 units of C1-INH, and six additional doses of 2,500 units of C1-INH are administered every other day after the initial dose.
17. The use according to claim 16, characterized in that administration of the medicament is to be initiated within 5 to 10 days of organ transplantation, treatment with plasmapheresis, treatment with IVIg, or diagnosis of AMR.
18. Use of a composition comprising a C1 esterase inhibitor (C1-INH) protein in the manufacture of a medicament for treating antibody-mediated rejection (AMR) of a kidney allograft in a patient in need thereof, characterized in that the medicament is to be intravenously administered at a dose of 5,000 units to 25,000 units of C1-INH given in divided doses over a duration of 10-20 days.
19. The use according to claim 18, characterized in that administration of the medicament is initiated within 1 to 90 days of organ transplantation, treatment with plasmapheresis, treatment with intravenous immunoglobulin (IVIg), or diagnosis of AMR of the patient.
20. The use according to claim 18 or 19, wherein C1-INH is plasma derived or recombinantly produced.
21. The use according to any one of claims 18-20, characterized in that the medicament is to be administered in combination with:
    (i) plasmapheresis;

(ii) fresh frozen plasma;

(iii) intravenous immunoglobulin; and/or

(iv) rituximab, bortezomib, eculizumab, or a combination thereof.

22. The use according to any one of claims 18-20, characterized in that the medicament is to be administered in combination with plasmapheresis.
23. The use according to any one of claims 18-20 and 22, characterized in that the medicament is to be administered in combination with intravenous immunoglobulin.
24. The use according to any one of claims 18-23, characterized in that the medicament is to be administered in a total dose of 20,000 units of C1-INH.
25. The use according to any one of claims 18-24, characterized in that administration of the medicament results in a therapeutic effect lasting for at least 3 months after cessation of therapy.
26. The use according to claim 25, wherein the therapeutic effect comprises improvement in renal function.
27. The use according to claim 25, wherein the therapeutic effect comprises the prevention of AMR.
28. The use according to claim 25, wherein the therapeutic effect comprises the treatment or prevention of chronic or transplant glomerulopathy.
29. The use according to claim 19, characterized in that administration of the medicament is initiated within 5 to 10 days of one of organ transplantation, treatment with plasmapheresis, treatment with IVIg, or diagnosis of AMR.
30. The use according to any one of claims 18-29, characterized in that the total dose pof the medicament is to be administered in divided doses over a duration of 13 days.