based on the Mayo four stage prognostic staging system discussed in Kumar et al., 2012 (Kumar et al., Revised Prognostic Staging System for Light Chain Amyloidosis Incorporating Cardiac Biomarkers and Serum Free Light Chain Measurements, J Clin Oncol 30:989-995 2012), with the outcome for Stage IV patients being quite dire.

Current treatment of patients with AL amyloidosis is aimed at reducing or eliminating the bone marrow disorder, *i.e*. the plasma cells that are responsible for producing the light chains, thereby limiting or halting the production of amyloid. The most aggressive treatment options include stem cell transplant and high-dose chemotherapy for those patients who can tolerate it. Other treatment regimens include combinations of drugs often used to treat hematological malignancies, such as melphalan, prednisone, dexamethasone and proteosome inhibitors such as bortezomib, in an attempt to reduce light chain production. There are no currently approved treatments for AL amyloidosis, and none that directly target potentially toxic forms of the amyloidogenic proteins. While some treatment options may ameliorate some of the morbidity associated with AL amyloidosis, few if any have been demonstrated to improve the prognosis in patients. Furthermore, Mayo Stage IV patients with AL amyloidosis represent a patient subset with a very high burden of morbidity and mortality, with no currently approved treatments, and population estimates of approximately 2,760 patients in the U.S., and from 6,900 to 10,350 patients in the U.S. and the European Union combined.

Thus, there is an unmet need for therapies that improve health status, including reducing the risk of mortality or enhancing the quality of life in patients with AL amyloidosis.

SUMMARY

The present disclosure relates to methods of treating certain AL amyloidosis patients.

In one aspect, provided herein is a use of an antibody comprising a heavy chain variable region comprising heavy chain CDRs of SEQ ID NOs: 6, 7, and 8 and a light chain variable region comprising light chain CDRs of SEQ ID NOs: 3, 4, and 5, in the manufacture of a medicament for treating a patient having AL amyloidosis, wherein the patient has been previously selected as having (a) Mayo Stage

IV AL amyloidosis, (b) a 6 minute walk distance (6MWD) ≥ 150 meters and EF > 50% at baseline, (c) Mayo Stage IV AL amyloidosis and an EF > 50% at baseline, or (d) Mayo Stage IV AL amyloidosis, a 6MWD ≥ 150 meters, and EF > 50% at baseline.

In one aspect, provided herein is a use of an antibody comprising a heavy chain variable region comprising heavy chain CDRs of SEQ ID NOs: 6, 7, and 8 and a light chain variable region comprising light chain CDRs of SEQ ID NOs: 3, 4, and 5, in the manufacture of a medicament for reducing the risk of mortality in a patient with AL amyloidosis by at least 45%, wherein the patient has been previously selected as having: (a) Mayo Stage IV AL amyloidosis, (b) a 6 minute walk distance (6MWD) of greater than or equal to 150 meters and an ejection fraction (EF) of more than 50% at baseline, or (c) Mayo Stage IV AL amyloidosis and an EF of > 50% at baseline.

In one aspect, provided herein is a use of an antibody comprising a heavy chain variable region comprising heavy chain CDRs of SEQ ID NOs: 6, 7, and 8 and a light chain variable region comprising light chain CDRs of SEQ ID NOs: 3, 4, and 5 in the manufacture of a medicament for improving a 6 minute walk distance (6MWD) in a patient having AL amyloidosis, wherein the patient has been previously selected as having a 6MWD of greater than or equal to 150 meters, and EF > 50% at baseline.

Provided herein are methods of treating a patient having AL amyloidosis, comprising determining the Mayo Stage of the patient's AL amyloidosis, and/or the 6 minute walk distance (6MWD) and ejection fraction (EF) of the patient, or determining the Mayo Stage

and EF of the patient, selecting the patient for treatment with an antibody which competes for binding to human amyloid A peptide or human kappa or lambda light chain immunoglobulin with 2A4 (ATCC Accession Number PTA-9662) or 7D8 (ATCC Accession Number PTA-9468), or competes for binding to human kappa (κ) or lambda light chain immunoglobulin with 11-1F4 (ATCC Accession Number PTA-105) if the patient has Mayo Stage IV AL amyloidosis, has a 6MWD ≥ 150 meters and an EF > 50% at baseline, has Mayo Stage IV and EF > 50% at baseline, or has Mayo Stage IV, a 6MWD ≥ 150 meters and an EF > 50% at

CLAIMS

What is claimed is:

1. Use of an antibody comprising a heavy chain variable region comprising heavy chain CDRs of SEQ ID NOs: 6, 7, and 8 and a light chain variable region comprising light chain CDRs of SEQ ID NOs: 3, 4, and 5, in the manufacture of a medicament for treating a patient having AL amyloidosis, wherein the patient has been previously selected as having (a) Mayo Stage IV AL amyloidosis, (b) a 6 minute walk distance (6MWD) ≥ 150 meters and EF > 50% at baseline, (c) Mayo Stage IV AL amyloidosis and an EF > 50% at baseline, or (d) Mayo Stage IV AL amyloidosis, a 6MWD ≥ 150 meters, and EF > 50% at baseline.

2. The use of claim 1, wherein the patient has been previously selected as having Mayo Stage IV AL amyloidosis.

3. The use of claim 1, wherein the patient has been previously selected as having a 6MWD ≥ 150 meters and an EF > 50% at baseline.

4. The use of claim 1, wherein the patient has been previously selected as having Mayo Stage IV AL amyloidosis, a 6MWD ≥ 150 meters and an EF > 50% at baseline.

5. The use of claim 1, wherein the patient has been previously selected as having Mayo Stage IV amyloidosis and an EF > 50% at baseline.

6. The use of any one of claims 1-5, wherein the antibody is a humanized antibody.

7. The use of any one of claims1-6, wherein the light chain variable region comprises the amino acid sequence set forth as SEQ ID NO: 1.

8. The use of any one of claims 1-6, wherein the heavy chain variable region comprises the amino acid sequence set forth as SEQ ID NO: 2.

9. The use of any one of claims 1-6, wherein the light chain variable region comprises the amino acid sequence set forth as SEQ ID NO: 1, and the heavy chain variable region comprises the amino acid sequence set forth as SEQ ID NO: 2.

10. The use of any one of claims 1-6, wherein the antibody is birtamimab.

11. The use of any one of claims 1-10, wherein the patient is newly diagnosed and AL amyloidosis treatment naïve.

12. The use of any one of claims1-10, wherein the patient previously received or concomitantly receives treatment with melphalan, prednisone, dexamethasone, bortezomib, cyclophosphamide, lenalidomide, doxorubicin, doxycycline, daratumumab, autologous transplant, or a combination thereof.

13. The use of any one of claims 1-10, wherein the patient previously received or concomitantly receives treatment with cyclophosphamide, bortezomib, and dexamethasone (CyBorD).

14. Use of an antibody comprising a heavy chain variable region comprising heavy chain CDRs of SEQ ID NOs: 6, 7, and 8 and a light chain variable region comprising light chain CDRs of SEQ ID NOs: 3, 4, and 5, in the manufacture of a medicament for reducing the risk of mortality in a patient with AL amyloidosis by at least 45%, wherein the patient has been previously selected as having: (a) Mayo Stage IV AL amyloidosis, (b) a 6 minute walk distance (6MWD) of greater than or equal to 150 meters and an ejection fraction (EF) of more than 50% at baseline, or (c) Mayo Stage IV AL amyloidosis and an EF of > 50% at baseline.

15. The use of claim 14, wherein the patient has been previously selected as having Mayo Stage IV AL amyloidosis.

16. The use of claim 14, wherein the patient has been previously selected as having a 6MWD of greater than or equal to 150 meters and EF of > 50% at baseline.

17. The use of claim 14, wherein the patient has been previously selected as having Mayo Stage IV AL amyloidosis and an EF of > 50% at baseline.

18. The use of any one of claims 14-17, wherein the risk of mortality is of all-cause mortality.

19. The use of any one of claims 14-17, wherein the risk of mortality is of cardiac mortality.

20. The use of any one of claims 14-19, wherein the antibody is a humanized antibody.

21. The use of any one of claims 14-20, wherein the light chain variable region comprises the amino acid sequence set forth as SEQ ID NO: 1.

22. The use of any one of claims 14-20, wherein the heavy chain variable region comprises the amino acid sequence set forth as SEQ ID NO: 2.

23. The use of any one of claims 14-20, wherein the light chain variable region comprises the amino acid sequence set forth as SEQ ID NO: 1, and the heavy chain variable region comprises the amino acid sequence set forth as SEQ ID NO: 2.

24. The use of any of claims 14-20, wherein the antibody is birtamimab.

25. The use of any one of claims 14-24, wherein the patient exhibits improvement in the 36-Item Short Form Survey Physical Component Score (SF-36 PCS) or SF-36v2 following treatment with the antibody.

26. Use of an antibody comprising a heavy chain variable region comprising heavy chain CDRs of SEQ ID NOs: 6, 7, and 8 and a light chain variable region comprising light chain CDRs of SEQ ID NOs: 3, 4, and 5 in the manufacture of a medicament for improving a 6 minute walk distance (6MWD) in a patient having AL amyloidosis, wherein the patient has been previously selected as having a 6MWD of greater than or equal to 150 meters, and EF > 50% at baseline.

27. The use of claim 26, wherein the antibody is a humanized antibody.

28. The use of claim 26 or 27, wherein the light chain variable region comprises the amino acid sequence set forth as SEQ ID NO: 1.

29. The use of claim 26 or 27, wherein the heavy chain variable region comprises the amino acid sequence set forth as SEQ ID NO: 2.

30. The use of claim 26 or 27, wherein the light chain variable region comprises the amino acid sequence set forth as SEQ ID NO: 1, and the heavy chain variable region comprises the amino acid sequence set forth as SEQ ID NO: 2.

31. The use of claim 26 or 27, wherein the antibody in birtamimab.

32. The use of any one of claims 1-31, wherein an effective dosage of the antibody is to be administered from a pharmaceutical formulation comprising the antibody at a concentration within the range from 1 mg/mL to 100 mg/mL.

33. The use of any one of claims 1-32, wherein a dosage is from 0.5 mg/kg to 30 mg/kg and the antibody is to be administered intravenously or subcutaneously at a frequency of from weekly to quarterly.

34. The use of claim 32 or 33, wherein the antibody is present at a concentration of 50 mg/mL.

35. The use of claim 33 or 34, wherein the dosage is 24 mg/kg and the antibody is to be administered intravenously every 28 days.