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BRIEF SUMMARY ~~OF THE INVENTION~~

[0022] The present disclosure ~~invention~~ provides methods of treating progressive multiple sclerosis in a patient comprising administering to the patient an effective amount of an anti-CD20 antibody, wherein treatment is based upon the patient having one or more characteristics selected from the group consisting of (a) an age less than about 55 years, (b) one or more gadolinium staining lesions, (c) at least about a one point increase in Expanded Disability Status Scale (EDSS) over two years prior to starting treatment, and (d) a Multiple Sclerosis Severity Score (MSSS) greater than about 5 points.

[0022a] In one aspect, there is provided the use of a composition comprising an anti-CD20 antibody for the manufacture of a medicament for treating progressive multiple sclerosis in a patient, wherein treatment is based upon the patient having an age less than about 55 years and one or more characteristics selected from the group consisting of: (a) one or more gadolinium staining lesions and (b) an EDSS when starting treatment is between about 3.0 and about 6.5.

[0023] In some embodiments, the progressive multiple sclerosis is primary progressive multiple sclerosis. In some embodiments, the progressive multiple sclerosis is secondary progressive multiple sclerosis. In some embodiments, the progressive multiple sclerosis is progressive relapsing multiple sclerosis. In some embodiments, the patient is not diagnosed with relapsing remitting multiple sclerosis when starting treatment.

[0024] In some embodiments, the patient further has evidence of inflammation in a sample. In some embodiments, the sample is a cerebrospinal fluid sample. In some embodiments, the evidence of inflammation is indicated by an elevated IgG index. In some embodiments, the evidence of inflammation is indicated by IgG oligoclonal bands detected by isoelectric focusing.

[0025] In some embodiments, the patient has had an EDSS of greater than about 5.0 for less than about 15 years. In some embodiments, the patient has had an EDSS less than or equal to about 5.0 for less than about 10 years. In some embodiments, the increase in EDSS over two years prior to starting treatment is not attributable to relapse. In some embodiments, the increase in EDSS is at least about a 1.5 point increase in EDSS over two years prior to starting treatment. In some embodiments, the at least about a 1.5 point increase in EDSS over two years prior to

starting treatment is not attributable to relapse. In some embodiments, the patient further had two or more relapses within two years prior to starting treatment. In some embodiments, the EDSS when starting treatment is between about 3.0 and about 6.5.

[0026] In some embodiments, the age of the patient is less than about 51.

[0027] In some embodiments, the treatment reduces the time to confirmed disease progression. In some embodiments, the confirmed disease progression is an increase in EDSS that is sustained for twelve weeks. In some embodiments, the confirmed disease progression is an increase in EDSS that is sustained for twenty-four weeks.

[0028] In some embodiments, the effective amount of the anti-CD20 antibody is administered to the patient to provide an initial anti-CD20 antibody exposure of between about 0.3 to about 4.0 grams followed by a second anti-CD20 antibody exposure of between about 0.3 to about 4.0 grams. In some embodiments, the initial anti-CD20 antibody exposure and/or the second anti-CD20 antibody exposure is between about 0.3 to about 1.5 grams. In some embodiments, the second exposure not being provided until from about 16 to 60 weeks from the initial exposure. In some embodiments, each of the anti-CD20 antibody exposures is provided to the patient as one or two doses of anti-CD20 antibody.

[0029] In some embodiments, the anti-CD20 antibody comprises: a) a heavy chain variable region comprising SEQ ID NO:10, SEQ ID NO:11, and SEQ ID NO:12, and b) a light chain variable region comprising SEQ ID NO:4, SEQ ID NO:5, and SEQ ID NO:6. In some embodiments, the anti-CD20 antibody is ocrelizumab. In some embodiments, the anti-CD20 antibody is rituximab. In some embodiments, the anti-CD20 antibody is ofatumumab. In some embodiments, the anti-CD20 antibody is TRU-015 or SBI-087. In some embodiments, the anti-CD20 antibody is GA101. In some embodiments, the anti-CD20 antibody is hA20.

[0030] The present disclosure ~~invention~~ provides methods of treating progressive multiple sclerosis in a patient provided that the patient has been found to have one or more characteristics selected from the group consisting of (a) an age less than about 55 years, (b) one or more gadolinium staining lesions, (c) at least about a one point increase in Expanded Disability Status Scale (EDSS) over two years prior to starting treatment, and (d) a Multiple Sclerosis Severity Score (MSSS) greater than about 5 points, the treatment comprising administering to the patient an effective amount of an anti-CD20 antibody.

[0031] In some embodiments, the progressive multiple sclerosis is primary progressive multiple sclerosis. In some embodiments, the progressive multiple sclerosis is secondary progressive multiple sclerosis. In some embodiments, the progressive multiple sclerosis is

embodiments, the anti-CD20 antibody is TRU-015 or SBI-087. In some embodiments, the anti-CD20 antibody is GA101. In some embodiments, the anti-CD20 antibody is hA20.

[0038] The present disclosure ~~invention~~ provides methods of treating progressive multiple sclerosis, comprising: (a) selecting a patient having progressive multiple sclerosis, wherein said patient has one or more characteristics selected from the group consisting of (i) an age less than about 55 years, (ii) one or more gadolinium staining lesions, (iii) at least about a one point increase in Expanded Disability Status Scale (EDSS) over two years prior to starting treatment, and (iv) a Multiple Sclerosis Severity Score (MSSS) greater than about 5 points; and (b) administering to the patient thus selected an effective amount of an anti-CD20 antibody.

[0039] In some embodiments, the progressive multiple sclerosis is primary progressive multiple sclerosis. In some embodiments, the progressive multiple sclerosis is secondary progressive multiple sclerosis. In some embodiments, the progressive multiple sclerosis is progressive relapsing multiple sclerosis. In some embodiments, the patient is not diagnosed with relapsing remitting multiple sclerosis when starting treatment.

[0040] In some embodiments, the patient further has evidence of inflammation in a sample. In some embodiments, the sample is a cerebrospinal fluid sample. In some embodiments, the evidence of inflammation is indicated by an elevated IgG index. In some embodiments, the evidence of inflammation is indicated by IgG oligoclonal bands detected by isoelectric focusing.

[0041] In some embodiments, the patient has had an EDSS of greater than about 5.0 for less than about 15 years. In some embodiments, the patient has had an EDSS less than or equal to about 5.0 for less than about 10 years. In some embodiments, the increase in EDSS over two years prior to starting treatment is not attributable to relapse. In some embodiments, the increase in EDSS is at least about a 1.5 point increase in EDSS over two years prior to starting treatment. In some embodiments, the at least about a 1.5 point increase in EDSS over two years prior to starting treatment is not attributable to relapse. In some embodiments, the patient further had two or more relapses within two years prior to starting treatment. In some embodiments, the EDSS when starting treatment is between about 3.0 and about 6.5.

[0042] In some embodiments, the age of the patient is less than about 51.

[0043] In some embodiments, the treatment reduces the time to confirmed disease progression. In some embodiments, the confirmed disease progression is an increase in EDSS that is sustained for twelve weeks. In some embodiments, the confirmed disease progression is an increase in EDSS that is sustained for twenty-four weeks.

[0044] In some embodiments, the effective amount of the anti-CD20 antibody is administered to the patient to provide an initial anti-CD20 antibody exposure of between about 0.3 to about 4.0 grams followed by a second anti-CD20 antibody exposure of between about 0.3 to about 4.0 grams. In some embodiments, the initial anti-CD20 antibody exposure and/or the second anti-CD20 antibody exposure is between about 0.3 to about 1.5 grams. In some embodiments, the second exposure not being provided until from about 16 to 60 weeks from the initial exposure. In some embodiments, each of the anti-CD20 antibody exposures is provided to the patient as one or two doses of anti-CD20 antibody.

[0045] In some embodiments, the anti-CD20 antibody comprises: a) a heavy chain variable region comprising SEQ ID NO:10, SEQ ID NO:11, and SEQ ID NO:12, and b) a light chain variable region comprising SEQ ID NO:4, SEQ ID NO:5, and SEQ ID NO:6. In some embodiments, the anti-CD20 antibody is ocrelizumab. In some embodiments, the anti-CD20 antibody is rituximab. In some embodiments, the anti-CD20 antibody is ofatumumab. In some embodiments, the anti-CD20 antibody is TRU-015 or SBI-087. In some embodiments, the anti-CD20 antibody is GA101. In some embodiments, the anti-CD20 antibody is hA20.

[0045a] In one aspect, there is provided the use of one or more characteristics selected from the group consisting of (a) an age less than about 55 years; (b) one or more gadolinium staining lesions; and (c) an EDSS when starting treatment is between about 3.0 and about 6.5 for assessing whether a patient with progressive multiple sclerosis will respond to treatment with an anti-CD20 antibody wherein one or more of the characteristics in the patient indicates the patient will be responsive to the treatment.

[0046] The present disclosure ~~invention~~ also provides methods of assessing whether a patient with progressive multiple sclerosis will respond to treatment with an anti-CD20 antibody comprising assessing one or more characteristics selected from the group consisting of (a) an age less than about 55 years, (b) one or more gadolinium staining lesions, (c) at least about a one point increase in Expanded Disability Status Scale (EDSS) over two years prior to starting treatment, and (d) a Multiple Sclerosis Severity Score (MSSS) greater than about 5 points, wherein one or more of the characteristics in the patient indicates the patient will be responsive to the treatment.

[0047] In some embodiments, the progressive multiple sclerosis is primary progressive multiple sclerosis. In some embodiments, the progressive multiple sclerosis is secondary progressive multiple sclerosis. In some embodiments, the progressive multiple sclerosis is progressive relapsing multiple sclerosis. In some embodiments, the patient is not diagnosed with relapsing remitting multiple sclerosis when starting treatment.

[0048] In some embodiments, the patient further has evidence of inflammation in a sample. In some embodiments, the sample is a cerebrospinal fluid sample. In some embodiments, the evidence of inflammation is indicated by an elevated IgG index. In some embodiments, the evidence of inflammation is indicated by IgG oligoclonal bands detected by isoelectric focusing.

[0049] In some embodiments, the patient has had an EDSS of greater than about 5.0 for less than about 15 years. In some embodiments, the patient has had an EDSS less than or equal to

about 5.0 for less than about 10 years. In some embodiments, the increase in EDSS over two years prior to starting treatment is not attributable to relapse. In some embodiments, the increase in EDSS is at least about a 1.5 point increase in EDSS over two years prior to starting treatment. In some embodiments, the at least about a 1.5 point increase in EDSS over two years prior to starting treatment is not attributable to relapse. In some embodiments, the patient further had two or more relapses within two years prior to starting treatment. In some embodiments, the EDSS when starting treatment is between about 3.0 and about 6.5.

[0050] In some embodiments, the age of the patient is less than about 51.

[0051] In some embodiments, the method further comprises advising a patient.

[0052] In some embodiments, the anti-CD20 antibody comprises: a) a heavy chain variable region comprising SEQ ID NO:10, SEQ ID NO:11, and SEQ ID NO:12, and b) a light chain variable region comprising SEQ ID NO:4, SEQ ID NO:5, and SEQ ID NO:6. In some embodiments, the anti-CD20 antibody is ocrelizumab. In some embodiments, the anti-CD20 antibody is rituximab. In some embodiments, the anti-CD20 antibody is ofatumumab. In some embodiments, the anti-CD20 antibody is TRU-015 or SBI-087. In some embodiments, the anti-CD20 antibody is GA101. In some embodiments, the anti-CD20 antibody is hA20.

[0052a] In one aspect, there is provided the use of one or more characteristics selected from the group consisting of (a) an age less than about 55 years; (b) one or more gadolinium staining lesions; and (c) an EDSS when starting treatment is between about 3.0 and about 6.5 for identifying a patient with progressive multiple sclerosis likely to respond to anti-CD20 antibody treatment, wherein one or more of the characteristics in the patient indicates the patient will be responsive to the treatment.

[0053] The present disclosure ~~invention~~ also provides methods of identifying a patient with progressive multiple sclerosis likely to respond to anti-CD20 antibody treatment comprising: (a) assessing one or more characteristics selected from the group consisting of (i) an age less than about 55 years, (ii) one or more gadolinium staining lesions, (iii) at least about a one point increase in Expanded Disability Status Scale (EDSS) over two years prior to starting treatment, and (iv) a Multiple Sclerosis Severity Score (MSSS) greater than about 5 points; and (b) identifying the patient having one or more characteristics selected from the group consisting of (i) an age less than about 55 years, (i) one or more gadolinium staining lesions, (iii) at least about a one point increase in Expanded Disability Status Scale (EDSS) over two years prior to starting the anti-CD20 treatment, and (iv) a Multiple Sclerosis Severity Score (MSSS) greater than about 5 points.

[0054] In some embodiments, the progressive multiple sclerosis is primary progressive multiple sclerosis. In some embodiments, the progressive multiple sclerosis is secondary progressive multiple sclerosis. In some embodiments, the progressive multiple sclerosis is progressive relapsing multiple sclerosis. In some embodiments, the patient is not diagnosed with relapsing remitting multiple sclerosis when starting treatment.

[0055] In some embodiments, the patient further has evidence of inflammation in a sample. In some embodiments, the sample is a cerebrospinal fluid sample. In some embodiments, the

evidence of inflammation is indicated by an elevated IgG index. In some embodiments, the evidence of inflammation is indicated by IgG oligoclonal bands detected by isoelectric focusing.

[0056] In some embodiments, the patient has had an EDSS of greater than about 5.0 for less than about 15 years. In some embodiments, the patient has had an EDSS less than or equal to about 5.0 for less than about 10 years. In some embodiments, the increase in EDSS over two years prior to starting treatment is not attributable to relapse. In some embodiments, the increase in EDSS is at least about a 1.5 point increase in EDSS over two years prior to starting treatment. In some embodiments, the at least about a 1.5 point increase in EDSS over two years prior to starting treatment is not attributable to relapse. In some embodiments, the patient further had two or more relapses within two years prior to starting treatment. In some embodiments, the EDSS when starting treatment is between about 3.0 and about 6.5.

[0057] In some embodiments, the age of the patient is less than about 51.

[0058] In some embodiments, the method further comprises advising a patient.

[0059] In some embodiments, the anti-CD20 antibody comprises: a) a heavy chain variable region comprising SEQ ID NO:10, SEQ ID NO:11, and SEQ ID NO:12, and b) a light chain variable region comprising SEQ ID NO:4, SEQ ID NO:5, and SEQ ID NO:6. In some embodiments, the anti-CD20 antibody is ocrelizumab. In some embodiments, the anti-CD20 antibody is rituximab. In some embodiments, the anti-CD20 antibody is ofatumumab. In some embodiments, the anti-CD20 antibody is TRU-015 or SBI-087. In some embodiments, the anti-CD20 antibody is GA101. In some embodiments, the anti-CD20 antibody is hA20.

[0060] The present disclosure ~~invention~~ further provides methods for marketing an anti-CD20 antibody or a pharmaceutically acceptable composition thereof for use in a progressive multiple sclerosis patient subpopulation, the methods comprising informing a target audience about the use of the anti-CD20 antibody for treating the patient subpopulation characterized by the patients of such subpopulation having one or more characteristics selected from the group consisting of (a) an age less than about 55 years, (b) one or more gadolinium staining lesions, (c) at least about a one point increase in Expanded Disability Status Scale (EDSS) over two years prior to starting treatment, and (d) a Multiple Sclerosis Severity Score (MSSS) greater than about 5 points.

[0061] In some embodiments, the progressive multiple sclerosis is primary progressive multiple sclerosis. In some embodiments, the progressive multiple sclerosis is secondary progressive multiple sclerosis. In some embodiments, the progressive multiple sclerosis is progressive relapsing multiple sclerosis. In some embodiments, the patient subpopulation is not diagnosed with relapsing remitting multiple sclerosis when starting treatment.

[0062] In some embodiments, the patient subpopulation further has evidence of inflammation in a sample. In some embodiments, the sample is a cerebrospinal fluid sample. In some embodiments, the evidence of inflammation is indicated by an elevated IgG index. In some embodiments, the evidence of inflammation is indicated by IgG oligoclonal bands detected by isoelectric focusing.

[0063] In some embodiments, the patient subpopulation had an EDSS of greater than about 5.0 for less than about 15 years. In some embodiments, the patient subpopulation had an EDSS less than or equal to about 5.0 for less than about 10 years. In some embodiments, the increase in EDSS over two years prior to starting treatment is not attributable to relapse. In some embodiments, the increase in EDSS is at least about a 1.5 point increase in EDSS over two years prior to starting treatment. In some embodiments, the at least about a 1.5 point increase in EDSS over two years prior to starting treatment is not attributable to relapse. In some embodiments, the patient subpopulation further had two or more relapses within two years prior to starting treatment. In some embodiments, the EDSS when starting treatment is between about 3.0 and about 6.5.

[0064] In some embodiments, the age of the patient subpopulation is less than about 51.

[0065] In some embodiments, the anti-CD20 antibody comprises: a) a heavy chain variable region comprising SEQ ID NO:10, SEQ ID NO:11, and SEQ ID NO:12, and b) a light chain variable region comprising SEQ ID NO:4, SEQ ID NO:5, and SEQ ID NO:6. In some embodiments, the anti-CD20 antibody is ocrelizumab. In some embodiments, the anti-CD20 antibody is rituximab. In some embodiments, the anti-CD20 antibody is ofatumumab. In some embodiments, the anti-CD20 antibody is TRU-015 or SBI-087. In some embodiments, the anti-CD20 antibody is GA101. In some embodiments, the anti-CD20 antibody is hA20.

[0066] The present disclosure ~~invention~~ provides articles of manufacture comprising, packaged together a pharmaceutical composition comprising an anti-CD20 antibody and a pharmaceutically acceptable carrier and a label denoting (*i.e.*, indicating) that the anti-CD20 antibody or pharmaceutical composition is indicated for treating patients with multiple sclerosis having one or more characteristics selected from the group consisting of (a) an age less than about 55 years, (b) one or more gadolinium staining lesions, (c) at least about a one point increase in Expanded Disability Status Scale (EDSS) over two years prior to starting the treatment, and (d) a Multiple Sclerosis Severity Score (MSSS) greater than about 5 points.

[0067] In some embodiments, the progressive multiple sclerosis is primary progressive multiple sclerosis. In some embodiments, the progressive multiple sclerosis is secondary

variable region comprising SEQ ID NO:4, SEQ ID NO:5, and SEQ ID NO:6. In some embodiments, the anti-CD20 antibody is ocrelizumab. In some embodiments, the anti-CD20 antibody is rituximab. In some embodiments, the anti-CD20 antibody is ofatumumab. In some embodiments, the anti-CD20 antibody is TRU-015 or SBI-087. In some embodiments, the anti-CD20 antibody is GA101. In some embodiments, the anti-CD20 antibody is hA20.

[0074] The present disclosure ~~invention~~ also provides methods for predicting whether a subject with progressive multiple sclerosis will respond to a treatment with a drug used to treat multiple sclerosis, the methods comprising assessing one or more characteristics selected from the group consisting of (a) an age less than about 55 years, (b) one or more gadolinium staining lesions, (c) at least about a one point increase in Expanded Disability Status Scale (EDSS) over two years prior to starting treatment, and (d) a Multiple Sclerosis Severity Score (MSSS) greater than about 5 points, whereby the age, the gadolinium staining lesions, the increase in EDDS over two years prior to starting the treatment, the MSSS, or a combination thereof indicates that the subject will respond to the treatment.

[0075] In some embodiments, the progressive multiple sclerosis is primary progressive multiple sclerosis. In some embodiments, the progressive multiple sclerosis is secondary progressive multiple sclerosis. In some embodiments, the progressive multiple sclerosis is progressive relapsing multiple sclerosis. In some embodiments, the subject is not diagnosed with relapsing remitting multiple sclerosis when starting treatment.

[0076] In some embodiments, the subject further has had evidence of inflammation in a sample. In some embodiments, the sample is a cerebrospinal fluid sample. In some embodiments, the evidence of inflammation is indicated by an elevated IgG index. In some embodiments, the evidence of inflammation is indicated by IgG oligoclonal bands detected by isoelectric focusing.

[0077] In some embodiments, the subject has had an EDSS of greater than about 5.0 for less than about 15 years. In some embodiments, the subject had an EDSS less than or equal to about 5.0 for less than about 10 years. In some embodiments, the increase in EDSS over two years prior to starting treatment is not attributable to relapse. In some embodiments, the increase in EDSS is at least about a 1.5 point increase in EDSS over two years prior to starting treatment. In some embodiments, the at least about a 1.5 point increase in EDSS over two years prior to starting treatment is not attributable to relapse. In some embodiments, the subject further had two or more relapses within two years prior to starting treatment. In some embodiments, the EDSS when starting treatment is between about 3.0 and about 6.5.

[0078] In some embodiments, the age of the subject is less than about 51.

[0079] In some embodiments of any of the methods or articles of manufacture described herein, the patients have one or more characteristics selected from the group consisting of (a) an age less than about 55 years, (b) one or more gadolinium staining lesions, and (c) at least about a one point increase in Expanded Disability Status Scale (EDSS) over two years prior to starting treatment.

[0080] The ~~invention~~ disclosure further provides methods of treating multiple sclerosis in a patient comprising administering an effective amount of ocrelizumab to the patient to provide an initial ocrelizumab exposure of between about 0.3 to about 0.6 grams followed by a second ocrelizumab exposure of between about 0.3 to about 0.6 grams, the second exposure not being provided until from about 16 to 60 weeks from the initial exposure, and each of the ocrelizumab exposures is provided to the patient as one or two doses of ocrelizumab.

[0080a] In one aspect, there is provided the use of a composition comprising ocrelizumab for the manufacture of a medicament for treating multiple sclerosis in a patient, wherein an effective amount of ocrelizumab is to be administered to the patient to provide an initial ocrelizumab exposure of between about 0.3 to about 0.6 grams followed by a second ocrelizumab exposure of between about 0.3 to about 0.6 grams, the second exposure not being provided until from about 16 to 60 weeks from the initial exposure, and each of the ocrelizumab exposures is to be provided to the patient as one or two doses of ocrelizumab.

[0081] In some embodiments, the initial ocrelizumab exposure is about 0.6 grams. In some embodiments, the second ocrelizumab exposure is about 0.6 grams. In some embodiments, the second exposure is administered from about 24 weeks from the initial exposure. In some embodiments, one or more of the ocrelizumab exposures are provided to the patient as one dose of ocrelizumab. In some embodiments, one or more of the ocrelizumab exposures are provided to the patient as two doses of ocrelizumab. In some embodiments, the initial ocrelizumab exposure comprises a first dose and a second dose of ocrelizumab, wherein the first dose and second dose of ocrelizumab is about 0.3 grams. In some embodiments, the second ocrelizumab exposure comprises a single dose of ocrelizumab, wherein the single dose of ocrelizumab is 0.6 grams. In some embodiments, the methods further comprising providing a third ocrelizumab exposure. In some embodiments, the methods further comprising providing a fourth ocrelizumab exposure. In some embodiments, the methods further comprising providing a fifth ocrelizumab exposure. In some embodiments of any of the methods, the methods further comprising providing between about one to about three subsequent ocrelizumab exposures.

[0082] ~~The invention also provides articles of manufacture comprising~~In one aspect, there is provided an article of manufacture comprising: (a) a container comprising ocrelizumab; and (b) a package insert with instructions for treating multiple sclerosis in a patient, wherein the instructions ~~denote~~ indicate that an amount of ocrelizumab is to be administered to the patient that is effective to provide an initial ocrelizumab exposure of between about 0.3 to about 0.6 grams followed by a second ocrelizumab exposure of between about 0.3 to about 0.6 grams, the second exposure not being administered until from about 16 to 60 weeks from the initial exposure, and each of the ocrelizumab exposures is provided to the patient as one or two doses of ocrelizumab.

CLAIMS

1. Use of a composition comprising an anti-CD20 antibody for the manufacture of a medicament for treating progressive multiple sclerosis in a patient, wherein treatment is based upon the patient having an age less than about 55 years and one or more characteristics selected from the group consisting of: (a) one or more gadolinium staining lesions and (b) an EDSS when starting treatment is between about 3.0 and about 6.5.

2. The use of claim 1, wherein the treatment is further based on the patient having evidence of inflammation in a sample.

3. The use of claim 2, wherein the sample is a cerebrospinal fluid sample.

4. The use of claim 3, wherein evidence of inflammation is indicated by an elevated IgG index.

5. The use of claim 3, wherein evidence of inflammation is indicated by IgG oligoclonal bands detected by isoelectric focusing.

6. The use of any one of claims 1-5, wherein treatment is further based upon the patient having an EDSS of greater than or equal to 5.0 for less than about 15 years or an EDSS of less than or equal to 5.0 for less than about 10 years.

7. The use of claim 6, wherein the patient has had an EDSS of greater than or equal to 5.0 for less than about 15 years.

8. The use of claim 6, wherein the patient has had an EDSS of less than or equal to 5.0 for less than about 10 years.

9. The use of any one of claims 1-8, wherein treatment is further based upon the patient having a Functional Systems Score of 2.0 or more for the pyramidal system or gait that is due to lower extremity findings.

10. The use of any one of claims 1-9, wherein the progressive multiple sclerosis is primary progressive multiple sclerosis.

11. The use of any one of claims 1-9, wherein the progressive multiple sclerosis is secondary progressive multiple sclerosis.

12. The use of any one of claims 1-9, wherein the progressive multiple sclerosis is progressive relapsing multiple sclerosis.

13. The use of any one of claims 1-9, wherein the patient is not diagnosed with relapsing remitting multiple sclerosis when starting treatment.

14. The use of any one of claims 1-9, wherein the increase in EDSS over two years prior to starting treatment is not attributable to relapse.

15. The use of any one of claims 1-9, wherein the increase in EDSS is at least about a 1.5 point increase in EDSS over two years prior to starting treatment.

16. The use of claim 15, wherein the increase in EDSS over two years prior to starting treatment is not attributable to relapse.

17. The use of any one of claims 1-9, wherein the age of the patient is less than about 51.

18. The use of any one of claims 1-9, wherein the patient further had two or more relapses within two years prior to starting treatment.

19. The use of any one of claims 1-9, wherein the treatment reduces the time to confirmed disease progression.

20. The use of claim 19, wherein confirmed disease progression is an increase in EDSS that is sustained for twelve weeks.

21. The use of claim 19, wherein confirmed disease progression is an increase in EDSS that is sustained for twenty-four weeks.

22. The use of any one of claims 1-21, wherein the anti-CD20 antibody comprises: a) a heavy chain variable region comprising three CDR regions comprising SEQ ID NO: 10, SEQ ID NO: 11, and SEQ ID NO: 12, and b) a light chain variable region comprising three CDR regions comprising SEQ ID NO:4, SEQ ID NO:5, and SEQ ID NO:6.

23. The use of any one of claims 1-21, wherein the anti-CD20 antibody is ocrelizumab.

24. The use of any one of claim 1-21, wherein the effective amount of the anti-CD20 antibody is to be administered to the patient to provide an initial anti-CD20 antibody exposure of between about 0.3 to about 4.0 grams followed by a second anti-CD20 antibody exposure of between about 0.3 to about 4.0 grams.

25. The use of claim 24, wherein the initial anti-CD20 antibody exposure and/or the second anti-CD20 antibody exposure is between about 0.3 to about 1.5 grams.

26. The use of claim 25, wherein the second exposure not being provided until from about 16 to 60 weeks from the initial exposure.

27. The use of claim 26, wherein each of the anti-CD20 antibody exposures is to be provided to the patient as one or two doses of anti-CD20 antibody.

28. Use of one or more characteristics selected from the group consisting of (a) an age less than about 55 years; (b) one or more gadolinium staining lesions; and (c) an EDSS when starting treatment is between about 3.0 and about 6.5 for assessing whether a patient with progressive multiple sclerosis will respond to treatment with an anti-CD20 antibody wherein one or more of the characteristics in the patient indicates the patient will be responsive to the treatment.

29. Use of one or more characteristics selected from the group consisting of (a) an age less than about 55 years; (b) one or more gadolinium staining lesions; and (c) an EDSS when starting treatment is between about 3.0 and about 6.5 for identifying a patient with progressive multiple sclerosis likely to respond to anti-CD20 antibody treatment, wherein one or more of the characteristics in the patient indicates the patient will be responsive to the treatment.

30. Use of a composition comprising ocrelizumab for the manufacture of a medicament for treating multiple sclerosis in a patient, wherein an effective amount of ocrelizumab is to be administered to the patient to provide an initial ocrelizumab exposure of between about 0.3 to about 0.6 grams followed by a second ocrelizumab exposure of between about 0.3 to about 0.6 grams, the second exposure not being provided until from about 16 to 60 weeks from the initial exposure, and each of the ocrelizumab exposures is to be provided to the patient as one or two doses of ocrelizumab.

31. The use of claim 30, wherein the initial ocrelizumab exposure comprises a first dose and a second dose of ocrelizumab, wherein the first dose and second dose of ocrelizumab is about 0.3 grams.

32. The use of claim 31, wherein the second ocrelizumab exposure comprises a single dose of ocrelizumab, wherein the single dose of ocrelizumab is 0.6 grams.

33. The use of claim 32, wherein the second ocrelizumab exposure is to be provided approximately 24 weeks after the initial ocrelizumab exposure.

34. The use of claim 33, wherein a third ocrelizumab exposure is to be further provided.

35. The use of claim 34, wherein a fourth ocrelizumab exposure is to be further provided.

36. The use of claim 35, wherein a fifth ocrelizumab exposure is to be further provided.

37. The use of claim 33, wherein between about one to about three subsequent ocrelizumab exposures are to be further provided.

38. An article of manufacture comprising:

(a) a container comprising ocrelizumab; and

(b) a package insert with instructions for treating multiple sclerosis in a patient, wherein the instructions indicate that an amount of ocrelizumab is to be administered to the patient that is effective to provide an initial ocrelizumab exposure of between about 0.3 to about 0.6 grams followed by a second ocrelizumab exposure of between about 0.3 to about 0.6 grams, the second exposure not being administered until from about 16 to 60 weeks from the initial exposure, and each of the ocrelizumab exposures is provided to the patient as one or two doses of ocrelizumab.

What is claimed is:

1. A method of treating progressive multiple sclerosis in a patient comprising administering to the patient an effective amount of an anti-CD20 antibody, wherein treatment is based upon the patient having one or more characteristics selected from the group consisting of (a) an age less than about 55 years, (b) one or more gadolinium staining lesions, (c) at least about a one point increase in Expanded Disability Status Scale (EDSS) over two years prior to starting treatment, and (d) a Multiple Sclerosis Severity Score (MSSS) greater than about 5 points.

2. The method of claim 1, wherein the progressive multiple sclerosis is primary progressive multiple sclerosis.

3. The method of claim 1, wherein the progressive multiple sclerosis is secondary progressive multiple sclerosis.

4. The method of claim 1, wherein the progressive multiple sclerosis is progressive relapsing multiple sclerosis.

5. The method of claim 1, wherein the patient is not diagnosed with relapsing remitting multiple sclerosis when starting treatment.

6. The method of claim 1, wherein the patient further has evidence of inflammation in a sample.

7. The method of claim 6, wherein the sample is a cerebrospinal fluid sample.

8. The method of claim 7, wherein evidence of inflammation is indicated by an elevated IgG index.

9. The method of claim 7, wherein evidence of inflammation is indicated by IgG oligoclonal bands detected by isoelectric focusing.

10. The method of claim 1, wherein the patient has had an EDSS of greater than about 5.0 for less than about 15 years.

11. The method of claim 1, wherein the patient has had an EDSS less than or equal to about 5.0 for less than about 10 years.

12. The method of claim 1, wherein the increase in EDSS over two years prior to starting treatment is not attributable to relapse.

13. The method of claim 1, wherein the increase in EDSS is at least about a 1.5 point increase in EDSS over two years prior to starting treatment.

14. The method of claim 13, wherein the increase in EDSS over two years prior to starting treatment is not attributable to relapse.

15. The method of claim 1, wherein the age of the patient is less than about 51.

16. The method of claim 1, wherein the patient further had two or more relapses within two years prior to starting treatment.

17. The method of claim 1, wherein the EDSS when starting treatment is between about 3.0 and about 6.5.

18. The method of claim 1, wherein the treatment reduces the time to confirmed disease progression.

19. The method of claim 18, wherein confirmed disease progression is an increase in EDSS that is sustained for twelve weeks.

20. The method of claim 18, wherein confirmed disease progression is an increase in EDSS that is sustained for twenty-four weeks.

21. The method of claim 1, wherein the anti-CD20 antibody comprises: a) a heavy chain variable region comprising three CDR regions comprising SEQ ID NO:10, SEQ ID NO:11, and SEQ ID NO:12, and b) a light chain variable region comprising three CDR regions comprising SEQ ID NO:4, SEQ ID NO:5, and SEQ ID NO:6.

22. The method of claim 1, wherein the anti-CD20 antibody is ocrelizumab.

23. The method of claim 1, wherein the anti-CD20 antibody is rituximab.

24. The method of claim 1, wherein the anti-CD20 antibody is ofatumumab.

25. The method of claim 1, wherein the anti-CD20 antibody is TRU-015 or SBI-087.

26. The method of claim 1, wherein the anti-CD20 antibody is GA101.

27. The method of claim 1, wherein the anti-CD20 antibody is hA20.

28. The method of claim 1, wherein the effective amount of the anti-CD20 antibody is administered to the patient to provide an initial anti-CD20 antibody exposure of between about 0.3 to about 4.0 grams followed by a second anti-CD20 antibody exposure of between about 0.3 to about 4.0 grams.

29. The method of claim 28, wherein the initial anti-CD20 antibody exposure and/or the second anti-CD20 antibody exposure is between about 0.3 to about 1.5 grams.

30. The method of claim 29, wherein the second exposure not being provided until from about 16 to 60 weeks from the initial exposure.

31. The method of claim 30, wherein each of the anti-CD20 antibody exposures is provided to the patient as one or two doses of anti-CD20 antibody.

32. A method of treating progressive multiple sclerosis in a patient provided that the patient has been found to have one or more characteristics selected from the group consisting of (a) an age less than about 55 years, (b) one or more gadolinium staining lesions, (c) at least about a one point increase in Expanded Disability Status Scale (EDSS) over two years prior to starting treatment, and (d) a Multiple Sclerosis Severity Score (MSSS) greater than about 5 points, the treatment comprising administering to the patient an effective amount of an anti-CD20 antibody.

33. A method of treating progressive multiple sclerosis, comprising:

(a) selecting a patient having progressive multiple sclerosis, wherein said patient has one or more characteristics selected from the group consisting of (i) an age less than about 55 years, (ii) one or more gadolinium staining lesions, (iii) at least about a one point increase in Expanded Disability Status Scale (EDSS) over two years prior to starting treatment, and (iv) a Multiple Sclerosis Severity Score (MSSS) greater than about 5 points; and

(b) administering to the patient thus selected an effective amount of an anti-CD20 antibody.

34. A method of assessing whether a patient with progressive multiple sclerosis will respond to treatment with an anti-CD20 antibody comprising assessing one or more characteristics selected from the group consisting of (a) an age less than about 55 years, (b) one or more gadolinium staining lesions, (c) at least about a one point increase in Expanded Disability Status Scale (EDSS) over two years prior to starting treatment, and (d) a Multiple Sclerosis Severity Score (MSSS) greater than about 5 points, wherein one or more of the characteristics in the patient indicates the patient will be responsive to the treatment.

35. A method of identifying a patient with progressive multiple sclerosis likely to respond to anti-CD20 antibody treatment comprising:

(a) assessing one or more characteristics selected from the group consisting of (i) an age less than about 55 years, (ii) one or more gadolinium staining lesions, (iii) at least about a one point increase in Expanded Disability Status Scale (EDSS) over two years prior to starting treatment, and (iv) a Multiple Sclerosis Severity Score (MSSS) greater than about 5 points; and

(b) identifying the patient having one or more characteristics selected from the group consisting of (i) an age less than about 55 years, (i) one or more gadolinium staining lesions, (iii) at least about a one point increase in Expanded Disability Status Scale (EDSS) over two years prior to starting the anti-CD20 treatment, and (iv) a Multiple Sclerosis Severity Score (MSSS) greater than about 5 points.

36. A method for marketing an anti-CD20 antibody or a pharmaceutically acceptable composition thereof for use in a progressive multiple sclerosis patient subpopulation, the method comprising informing a target audience about the use of the anti-CD20 antibody for treating the patient subpopulation characterized by the patients of such subpopulation having one or more characteristics selected from the group consisting of (a) an age less than about 55 years, (b) one or more gadolinium staining lesions, (c) at least about a one point increase in Expanded Disability Status Scale (EDSS) over two years prior to starting treatment, and (d) a Multiple Sclerosis Severity Score (MSSS) greater than about 5 points.

37. An article of manufacture comprising, packaged together, a pharmaceutical composition comprising an anti-CD20 antibody and a pharmaceutically acceptable carrier and a label denoting that the anti-CD20 antibody or pharmaceutical composition is indicated for treating patients with multiple sclerosis having one or more characteristics selected from the group consisting of (a) an age less than about 55 years, (b) one or more gadolinium staining lesions, (c) at least about a one point increase in Expanded Disability Status Scale (EDSS) over two years prior to starting treatment, and (d) a Multiple Sclerosis Severity Score (MSSS) greater than about 5 points.

38. A method for predicting whether a subject with progressive multiple sclerosis will respond to a treatment with a drug used to treat multiple sclerosis, the method comprising assessing one or more characteristics selected from the group consisting of (a) an age less than about 55 years, (b) one or more gadolinium staining lesions, (c) at least about a one point increase in Expanded Disability Status Scale (EDSS) over two years prior to starting treatment, and (d) a Multiple Sclerosis Severity Score (MSSS) greater than about 5 points, whereby the age, the gadolinium staining lesions, the increase in EDDS over two years prior to starting the treatment, or a combination thereof indicates that the subject will respond to the treatment.

39. A method of treating multiple sclerosis in a patient comprising administering an effective amount of ocrelizumab to the patient to provide an initial ocrelizumab exposure of between about 0.3 to about 0.6 grams followed by a second ocrelizumab exposure of between about 0.3 to about 0.6 grams, the second exposure not being provided until from about 16 to 60 weeks from the

initial exposure, and each of the ocrelizumab exposures is provided to the patient as one or two doses of ocrelizumab.

40. The method of claim 39, wherein the initial ocrelizumab exposure comprises a first dose and a second dose of ocrelizumab, wherein the first dose and second dose of ocrelizumab is about 0.3 grams.

41. The method of claim 40, wherein the second ocrelizumab exposure comprises a single dose of ocrelizumab, wherein the single dose of ocrelizumab is 0.6 grams.

42. The method of claim 41, wherein the second ocrelizumab exposure is provided approximately 24 weeks after the initial ocrelizumab exposure.

43. The method of claim 42, further comprising providing a third ocrelizumab exposure.

44. The method of claim 43, further comprising providing a fourth ocrelizumab exposure.

45. The method of claim 44, further comprising providing a fifth ocrelizumab exposure.

46. The method of claim 42, further comprising providing between about one to about three subsequent ocrelizumab exposures.

47. An article of manufacture comprising:

(a) a container comprising ocrelizumab; and

(b) a package insert with instructions for treating multiple sclerosis in a patient, wherein the instructions indicate that an amount of ocrelizumab is administered to the patient that is effective to provide an initial ocrelizumab exposure of between about 0.3 to about 0.6 grams followed by a second ocrelizumab exposure of between about 0.3 to about 0.6 grams, the second exposure not being administered until from about 16 to 60 weeks from the initial exposure, and each of the ocrelizumab exposures is provided to the patient as one or two doses of ocrelizumab.