

CLAIMS

1 . Use of mosunetuzumab in the manufacture of a medicament for treating a subject aged about 65 years or older having a relapsed or refractory (R/R) non-Hodgkin's lymphoma (NHL), wherein mosunetuzumab is formulated for intravenous administration to the subject according to a dosing regimen comprising at least a first dosing cycle, a second dosing cycle, and a third dosing cycle, wherein:

(a) the first three-dose dosing cycle comprises a first dose (C1D1), a second dose (C1D2), and a third dose (C1D3) of mosunetuzumab, wherein the C1D1 is about 1 mg, the C1D2 is about 2 mg, and the C1D3 is about 60 mg;

(b) the second dosing cycle comprises a single dose (C2D1) of mosunetuzumab, wherein the C2D1 is about 60 mg; and

(c) the third dosing cycle comprises a single dose (C3D1) of mosunetuzumab, wherein the C3D1 is about 30 mg.

2. The use of claim 1, wherein:

(a) the first, second, and third dosing cycles are 21-day dosing cycles;

(b) the C1D1, the C1D2, and the C1D3 are to be administered on Days 1, 8, and 15, respectively, of the first dosing cycle;

(c) the C2D1 is to be administered on Day 1 of the second dosing cycle; and/or

(d) the C3D1 is to be administered on Day 1 of the third dosing cycle.

3. The use of claim 1 or 2, wherein the dosing regimen further comprises one or more additional dosing cycles.

4. The use of claim 3, wherein the dosing regimen comprises:

(a) five to 14 additional dosing cycles;

(b) five additional dosing cycles; or

(c) 14 additional dosing cycles.

5. The use of claim 3 or 4, wherein:

(a) the one or more additional dosing cycles are each 21-day dosing cycles; and/or

(b) each of the one or more additional dosing cycles comprises an additional single dose of mosunetuzumab.

6. The use of claim 5, wherein the additional single dose of mosunetuzumab is:

(a) to be administered to the subject on Day 1 of each respective additional dosing cycle; and/or

(b) about 30 mg.

7. Use of mosunetuzumab in the manufacture of a medicament for treating a population of subjects aged about 65 years or older having an R/R NHL, wherein mosunetuzumab is formulated for intravenous administration to each subject in the population according to a dosing regimen comprising at least a first 21-day dosing cycle, a second 21-day dosing cycle, and a third 21-day dosing cycle, wherein:

(a) the first three-dose dosing cycle comprises a first dose (C1D1), a second dose (C1D2), and a third dose (C1D3) of mosunetuzumab to be administered on Days 1, 8, and 15, respectively, of the first dosing cycle, wherein the C1D1 is about 1 mg, the C1D2 is about 2 mg, and the C1D3 is about 60 mg;

(b) the second dosing cycle comprises a single dose (C2D1) of mosunetuzumab to be administered on Day 1 of the second dosing cycle, wherein the C2D1 is about 60 mg; and

(c) the third dosing cycle comprises a single dose (C3D1) of mosunetuzumab to be administered on Day 1 of the third dosing cycle, wherein the C3D1 is about 30 mg.

8. Use of mosunetuzumab in the manufacture of a medicament for treating a population of subjects aged about 65 years or older having an R/R NHL, wherein mosunetuzumab is formulated for intravenous administration to each subject in the population according to a dosing regimen comprising eight 21-day dosing cycles, wherein:

(a) the first three-dose dosing cycle comprises a first dose (C1D1), a second dose (C1D2), and a third dose (C1D3) of mosunetuzumab to be administered on Days 1, 8, and 15, respectively, of the first dosing cycle, wherein the C1D1 is about 1 mg, the C1D2 is about 2 mg, and the C1D3 is about 60 mg;

(b) the second dosing cycle comprises a single dose (C2D1) of mosunetuzumab to be administered on Day 1 of the second dosing cycle, wherein the C2D1 is about 60 mg; and

(c) the third to eighth dosing cycles each comprises a single dose (C3D1-C8D1) of mosunetuzumab to be administered on Day 1 of each respective dosing cycle, wherein each of the C3D1-C8D1 is about 30 mg.

9. Use of mosunetuzumab in the manufacture of a medicament for treating a population of subjects aged about 65 years or older having an R/R NHL, wherein mosunetuzumab is formulated for intravenous administration to each subject in the population according to a dosing regimen comprising 17 21-day dosing cycles, wherein:

(a) the first three-dose dosing cycle comprises a first dose (C1D1), a second dose (C1D2), and a third dose (C1D3) of mosunetuzumab to be administered on Days 1, 8, and 15, respectively, of the first dosing cycle, wherein the C1D1 is about 1 mg, the C1D2 is about 2 mg, and the C1D3 is about 60 mg;

(b) the second dosing cycle comprises a single dose (C2D1) of mosunetuzumab to be administered on Day 1 of the second dosing cycle, wherein the C2D1 is about 60 mg; and

(c) the third to 17th dosing cycles each comprises a single dose (C3D1-C17D1) of mosunetuzumab to be administered on Day 1 of each respective dosing cycle, wherein each of the C3D1-C17D1 is about 30 mg.

10. The use of any one of claims 7-9, wherein:
- (a) the objective response rate in the population of subjects is $\geq 65\%$, $\geq 75\%$, or $\geq 85\%$;
 - (b) the complete response rate in the population of subjects is $\geq 50\%$, $\geq 60\%$, or $\geq 70\%$;
 - (c) $\geq 40\%$ or $\geq 50\%$ of subjects having an objective response maintained remission for 18 months;
 - (d) $\geq 50\%$ or $\geq 60\%$ of subjects having a complete response maintained complete remission for 18 months;
 - (e) the median duration of response in the population of subjects is ≥ 9 months or ≥ 15 months;
 - (f) the median duration of complete response in the population of subjects is ≥ 12 months or ≥ 16 months;
 - (g) $\geq 35\%$ or $\geq 45\%$ of subjects have a progression-free survival of 18 months; and/or
 - (h) the median progression-free survival in the population of subjects is ≥ 12 months or ≥ 17 months.
11. The use of any one of claims 7-10, wherein:
- (a) the rate of serious adverse events, excluding Grade 5 malignant neoplasm progression, in the population of subjects is $\leq 45\%$ or $\leq 40\%$;
 - (b) the rate of serious adverse events related to mosunetuzumab in the population of subjects is $\leq 40\%$ or $\leq 30\%$;
 - (c) the rate of cytokine release syndrome having a grade of 3 or higher (as defined by the American Society for Transplantation and Cellular Therapy, 2018; ASTCT) in the population of subjects is $\leq 5\%$ or $\leq 3\%$; and/or
 - (d) the rate of cytokine release syndrome of any grade (as defined by the ASTCT) in the population of subjects is $\leq 40\%$ or $\leq 30\%$.
12. Use of mosunetuzumab in the manufacture of a medicament for achieving an objective response, a complete response, or progression-free survival in a subject aged about 65 years or older having an R/R NHL, wherein mosunetuzumab is formulated for intravenous administration to the subject according to a dosing regimen comprising at least a first 21-day dosing cycle, a second 21-day dosing cycle, and a third 21-day dosing cycle, wherein:
- (a) the first three-dose dosing cycle comprises a first dose (C1D1), a second dose (C1D2), and a third dose (C1D3) of mosunetuzumab to be administered on Days 1, 8, and 15, respectively, of the first dosing cycle, wherein the C1D1 is about 1 mg, the C1D2 is about 2 mg, and the C1D3 is about 60 mg;
 - (b) the second dosing cycle comprises a single dose (C2D1) of mosunetuzumab to be administered on Day 1 of the second dosing cycle, wherein the C2D1 is about 60 mg; and

(c) the third dosing cycle comprises a single dose (C3D1) of mosunetuzumab to be administered on Day 1 of the third dosing cycle, wherein the C3D1 is about 30 mg.

13. Use of mosunetuzumab in the manufacture of a medicament for achieving an objective response, a complete response, or progression-free survival in a subject aged about 65 years or older having an R/R NHL, wherein mosunetuzumab is formulated for intravenous administration to the subject according to a dosing regimen comprising eight 21-day dosing cycles, wherein:

(a) the first three-dose dosing cycle comprises a first dose (C1D1), a second dose (C1D2), and a third dose (C1D3) of mosunetuzumab to be administered on Days 1, 8, and 15, respectively, of the first dosing cycle, wherein the C1D1 is about 1 mg, the C1D2 is about 2 mg, and the C1D3 is about 60 mg;

(b) the second dosing cycle comprises a single dose (C2D1) of mosunetuzumab to be administered on Day 1 of the second dosing cycle, wherein the C2D1 is about 60 mg; and

(c) the third to eighth dosing cycles each comprises a single dose (C3D1-C8D1) of mosunetuzumab to be administered on Day 1 of each respective dosing cycle, wherein each of the C3D1-C8D1 is about 30 mg.

14. Use of mosunetuzumab in the manufacture of a medicament for achieving an objective response, a complete response, or progression-free survival in a subject aged about 65 years or older having an R/R NHL, wherein mosunetuzumab is formulated for intravenous administration to the subject according to a dosing regimen comprising 17 21-day dosing cycles, wherein:

(a) the first three-dose dosing cycle comprises a first dose (C1D1), a second dose (C1D2), and a third dose (C1D3) of mosunetuzumab to be administered on Days 1, 8, and 15, respectively, of the first dosing cycle, wherein the C1D1 is about 1 mg, the C1D2 is about 2 mg, and the C1D3 is about 60 mg;

(b) the second dosing cycle comprises a single dose (C2D1) of mosunetuzumab to be administered on Day 1 of the second dosing cycle, wherein the C2D1 is about 60 mg; and

(c) the third to 17th dosing cycles each comprises a single dose (C3D1-C17D1) of mosunetuzumab to be administered on Day 1 of each respective dosing cycle, wherein each of the C3D1-C17D1 is about 30 mg.

15. The use of any one of claims 1-14, wherein the subject or each subject in the population has relapsed after, or is refractory to, two or more prior lines of therapy.

16. The use of claim 15, wherein the two or more prior lines of therapy comprise an anti-CD20 monoclonal antibody, an alkylating agent, or both an anti-CD20 monoclonal antibody and an alkylating agent.

17. The use of any one of claims 1-16, wherein the R/R NHL is R/R FL, R/R trFL, or R/R DLBCL.

18. The use of claim 17, wherein the R/R NHL is R/R FL, and wherein the R/R FL is histologically documented as Grade 1, 2, or 3a, but not 3b according to the World Health Organization classification of lymphoid neoplasms (as referenced in Swerdlow SH, et al. *Blood* 2016; 127:2375-90).

19. The use of any one of claims 1-18, wherein mosunetuzumab is to be administered by intravenous infusion.

20. The use of any one of claims 12-19, wherein:

- (a) the subject achieves an objective response;
- (b) the subject achieves a complete response; and/or
- (c) the progression-free survival is maintained for ≥ 12 months or ≥ 18 months.

21. The use of any one of claims 1-20, wherein the subject or each subject in the population of subjects is to be further administered one or more additional therapeutic agents.

22. The use of claim 21, wherein the one or more additional therapeutic agents comprises tocilizumab.

23. The use of claim 21 or 22, wherein the one or more additional therapeutic agents comprises a corticosteroid, an anti-histamine, an anti-pyretic, or a combination thereof.

24. The use of claim 23, wherein:

(a) the corticosteroid:

- (i) comprises dexamethasone or methylprednisolone;
- (ii) is to be administered to the subject or to each subject in the population of subjects at least one hour prior to the administration of any dose of mosunetuzumab;
- (iii) is only to be administered during dosing cycle 1 or dosing cycle 2; and/or
- (iv) is to be administered intravenously;

(b) the anti-histamine:

- (i) is to be administered to the subject or to each subject in the population of subjects at least 30 minutes prior to the administration of any dose of mosunetuzumab;
- (ii) is only to be administered during dosing cycle 1 or dosing cycle 2; and/or
- (iii) is to be administered orally or intravenously; and/or

(c) the anti-pyretic:

- (i) is to be administered to the subject or to each subject in the population of subjects at least 30 minutes prior to the administration of any dose of mosunetuzumab;

- (ii) is only to be administered during dosing cycle 1 or dosing cycle 2; and/or
- (iii) is to be administered orally.

25. The use of claim 23 or 24, wherein:

- (a) the corticosteroid comprises:
 - (i) dexamethasone and the dexamethasone is to be administered at a dose of about 20 mg; or
 - (ii) methylprednisolone and the methylprednisolone is to be administered at a dose of about 80 mg;
- (b) the anti-histamine comprises diphenhydramine hydrochloride and is to be administered at a dose of about 50-100 mg; and/or
- (c) the anti-pyretic comprises acetaminophen and is to be administered at a dose of about 500-1000 mg.

26. Use of mosunetuzumab in the manufacture of a medicament for treating a subject aged about 65 years or older having an R/R NHL, wherein mosunetuzumab is formulated for intravenous administration to the subject according to a dosing regimen comprising at least a first 21-day dosing cycle, a second 21-day dosing cycle, and a third 21-day dosing cycle, wherein:

- (a) the first three-dose dosing cycle comprises a first dose (C1D1), a second dose (C1D2), and a third dose (C1D3) of mosunetuzumab to be administered on Days 1, 8, and 15, respectively, of the first dosing cycle, wherein the C1D1 is about 1 mg, the C1D2 is about 2 mg, and the C1D3 is about 60 mg;
- (b) the second dosing cycle comprises a single dose (C2D1) of mosunetuzumab to be administered on Day 1 of the second dosing cycle, wherein the C2D1 is about 60 mg; and
- (c) the third dosing cycle comprises a single dose (C3D1) of mosunetuzumab to be administered on Day 1 of the third dosing cycle, wherein the C3D1 is about 30 mg,
wherein the subject has relapsed after, or is refractory to, two or more prior lines of therapy.

27. Use of mosunetuzumab in the manufacture of a medicament for treating a subject aged about 65 years or older having an R/R NHL, wherein mosunetuzumab is formulated for intravenous administration to the subject according to a dosing regimen comprising eight 21-day dosing cycles, wherein:

- (a) the first three-dose dosing cycle comprises a first dose (C1D1), a second dose (C1D2), and a third dose (C1D3) of mosunetuzumab to be administered on Days 1, 8, and 15, respectively, of the first dosing cycle, wherein the C1D1 is about 1 mg, the C1D2 is about 2 mg, and the C1D3 is about 60 mg;
- (b) the second dosing cycle comprises a single dose (C2D1) of mosunetuzumab to be administered on Day 1 of the second dosing cycle, wherein the C2D1 is about 60 mg; and

(c) the third to eighth dosing cycles each comprises a single dose (C3D1-C8D1) of mosunetuzumab to be administered on Day 1 of each respective dosing cycle, wherein each of the C3D1-C8D1 is about 30 mg,

wherein the subject has relapsed after, or is refractory to, two or more prior lines of therapy.

28. Use of mosunetuzumab in the manufacture of a medicament for treating a subject aged about 65 years or older having an R/R NHL, wherein mosunetuzumab is formulated for intravenous administration to the subject according to a dosing regimen comprising 17 21-day dosing cycles, wherein:

(a) the first three-dose dosing cycle comprises a first dose (C1D1), a second dose (C1D2), and a third dose (C1D3) of mosunetuzumab to be administered on Days 1, 8, and 15, respectively, of the first dosing cycle, wherein the C1D1 is about 1 mg, the C1D2 is about 2 mg, and the C1D3 is about 60 mg;

(b) the second dosing cycle comprises a single dose (C2D1) of mosunetuzumab to be administered on Day 1 of the second dosing cycle, wherein the C2D1 is about 60 mg; and

(c) the third to 17th dosing cycles each comprises a single dose (C3D1-C17D1) of mosunetuzumab to be administered on Day 1 of each respective dosing cycle, wherein each of the C3D1-C17D1 is about 30 mg,

wherein the subject has relapsed after, or is refractory to, two or more prior lines of therapy.

29. Use of mosunetuzumab in the manufacture of a medicament for treating a subject aged about 65 years or older having an R/R NHL, wherein mosunetuzumab is formulated for intravenous administration to the subject according to a dosing regimen comprising at least a first 21-day dosing cycle, a second 21-day dosing cycle, and a third 21-day dosing cycle, wherein:

(a) the first three-dose dosing cycle comprises a first dose (C1D1), a second dose (C1D2), and a third dose (C1D3) of mosunetuzumab to be administered on Days 1, 8, and 15, respectively, of the first dosing cycle, wherein the C1D1 is about 1 mg, the C1D2 is about 2 mg, and the C1D3 is about 60 mg;

(b) the second dosing cycle comprises a single dose (C2D1) of mosunetuzumab to be administered on Day 1 of the second dosing cycle, wherein the C2D1 is about 60 mg; and

(c) the third dosing cycle comprises a single dose (C3D1) of mosunetuzumab to be administered on Day 1 of the third dosing cycle, wherein the C3D1 is about 30 mg,

wherein the subject has relapsed after, or is refractory to, two or more prior lines of therapy, and

wherein the dosing regimen further comprises:

(i) a corticosteroid for administration to the subject, wherein a single dose of the corticosteroid is to be administered to the subject at least one hour prior to the administration of each of the C1D1, C1D2, C1D3, and C2D1 of mosunetuzumab;

(ii) an anti-histamine for administration to the subject, wherein a single dose of the anti-histamine is to be administered to the subject at least 30 minutes prior to the administration of each of the C1D1, C1D2, C1D3, and C2D1 of mosunetuzumab; and/or

(iii) an anti-pyretic for administration to the subject, wherein a single dose of the anti-pyretic is to be administered to the subject at least 30 minutes prior to the administration of each of the C1D1, C1D2, C1D3, and C2D1 of mosunetuzumab.

30. Use of mosunetuzumab in the manufacture of a medicament for treating a subject aged about 65 years or older having an R/R NHL, wherein mosunetuzumab is formulated for intravenous administration to the subject according to a dosing regimen comprising eight 21-day dosing cycles, wherein:

(a) the first three-dose dosing cycle comprises a first dose (C1D1), a second dose (C1D2), and a third dose (C1D3) of mosunetuzumab to be administered on Days 1, 8, and 15, respectively, of the first dosing cycle, wherein the C1D1 is about 1 mg, the C1D2 is about 2 mg, and the C1D3 is about 60 mg;

(b) the second dosing cycle comprises a single dose (C2D1) of mosunetuzumab to be administered on Day 1 of the second dosing cycle, wherein the C2D1 is about 60 mg; and

(c) the third to eighth dosing cycles each comprises a single dose (C3D1-C8D1) of mosunetuzumab to be administered on Day 1 of each respective dosing cycle, wherein each of the C3D1-C8D1 is about 30 mg,

wherein the subject has relapsed after, or is refractory to, two or more prior lines of therapy, and wherein the dosing regimen further comprises:

(i) a corticosteroid for administration to the subject, wherein a single dose of the corticosteroid is to be administered to the subject at least one hour prior to the administration of each of the C1D1, C1D2, C1D3, and C2D1 of mosunetuzumab;

(ii) an anti-histamine for administration to the subject, wherein a single dose of the anti-histamine is to be administered to the subject at least 30 minutes prior to the administration of each of the C1D1, C1D2, C1D3, and C2D1 of mosunetuzumab; and/or

(iii) an anti-pyretic for administration to the subject, wherein a single dose of the anti-pyretic is to be administered to the subject at least 30 minutes prior to the administration of each of the C1D1, C1D2, C1D3, and C2D1 of mosunetuzumab.

31. Use of mosunetuzumab in the manufacture of a medicament for treating a subject aged about 65 years or older having an R/R NHL, wherein mosunetuzumab is formulated for intravenous administration to the subject according to a dosing regimen comprising 17 21-day dosing cycles, wherein:

(a) the first three-dose dosing cycle comprises a first dose (C1D1), a second dose (C1D2), and a third dose (C1D3) of mosunetuzumab to be administered on Days 1, 8, and 15, respectively, of the first dosing cycle, wherein the C1D1 is about 1 mg, the C1D2 is about 2 mg, and the C1D3 is about 60 mg;

(b) the second dosing cycle comprises a single dose (C2D1) of mosunetuzumab to be administered on Day 1 of the second dosing cycle, wherein the C2D1 is about 60 mg; and

(c) the third to 17th dosing cycles each comprises a single dose (C3D1-C17D1) of mosunetuzumab to be administered on Day 1 of each respective dosing cycle, wherein each of the C3D1-C17D1 is about 30 mg,

wherein the subject has relapsed after, or is refractory to, two or more prior lines of therapy, and wherein the dosing regimen further comprises:

(i) a corticosteroid for administration to the subject, wherein a single dose of the corticosteroid is to be administered to the subject at least one hour prior to the administration of each of the C1D1, C1D2, C1D3, and C2D1 of mosunetuzumab;

(ii) an anti-histamine for administration to the subject, wherein a single dose of the anti-histamine is to be administered to the subject at least 30 minutes prior to the administration of each of the C1D1, C1D2, C1D3, and C2D1 of mosunetuzumab; and/or

(iii) an anti-pyretic for administration to the subject, wherein a single dose of the anti-pyretic is to be administered to the subject at least 30 minutes prior to the administration of each of the C1D1, C1D2, C1D3, and C2D1 of mosunetuzumab.

32. The use of any one of claims 26-31, wherein the two or more prior lines of therapy comprise an anti-CD20 monoclonal antibody, an alkylating agent, or both an anti-CD20 monoclonal antibody and an alkylating agent.

33. The use of any one of claims 26-32, wherein the R/R NHL is R/R FL, R/R trFL, or R/R DLBCL.

34. The use of claim 33, wherein the R/R NHL is R/R FL, and wherein the R/R FL is histologically documented as Grade 1, 2, or 3a, but not 3b according to the World Health Organization classification of lymphoid neoplasms (as referenced in Swerdlow SH, et al. *Blood* 2016; 127:2375-90).

35. The use of any one of claims 26-34, wherein mosunetuzumab is to be administered by intravenous infusion.

36. The use of any one of claims 29-31, wherein:

(i) a single dose of the corticosteroid is to be administered prior to the administration of any dose of mosunetuzumab in any of the one or more dosing cycles after the second dosing cycle;

(ii) a single dose of the anti-histamine is to be administered prior to the administration of any dose of mosunetuzumab in any of the one or more dosing cycles after the second dosing cycle; and/or

(iii) a single dose of the anti-pyretic is to be administered prior to the administration of any dose of mosunetuzumab in any of the one or more dosing cycles after the second dosing cycle.

37. The use of any one of claims 29-36, wherein:

- (i) the corticosteroid is to be administered intravenously;
- (ii) the anti-histamine is to be administered orally or intravenously; and/or
- (iii) the anti-pyretic is to be administered orally.

38. The use of any one of claims 29-37, wherein:

(i) the corticosteroid comprises dexamethasone and is to be administered at a dose of about 20 mg or the corticosteroid comprises methylprednisolone and is to be administered at a dose of about 80 mg;

(ii) the anti-histamine comprises diphenhydramine hydrochloride and is to be administered at a dose of about 50-100 mg; and/or

(iii) the anti-pyretic comprises acetaminophen and is to be administered at a dose of about 500-1000 mg.