companies. The first such biologic to demonstrate clinical benefit in autoimmune disease was ustekinumab, which is a Food and Drug Administration–approved monoclonal antibody for the treatment of psoriasis, psoriatic arthritis and CD. Ustekinumab binds the common p40 subunit of IL-12 and IL-23; therefore, it targets both cytokines, rather than IL-23 specifically. Blockade of the IL-12 pathway may prevent Th1 cell–induced interferon blockade of Th17 cell development, thus potentially limiting the clinical activity of p40 targeting antibodies. Agents specifically targeting the IL-23 p19 subunit have demonstrated clinical activity in psoriasis and CD (Kopp T *et al.*, Nature, Volume 521, No. 7551, pages 222-226, 2015; Sands BE *et al*., Journal of Crohn's and Colitis, Volume 9, Issue Supplement 1, ppS15-S16, 2015).

The IL-23/Th17 pathway is believed to have a role in UC (El-Bassat H *et al*, Journal of Molecular Biomarkers & Diagnosis, Vol. 5, No. 5, 100191, 2014). Nevertheless, clinical evaluation of an IL-23 targeted therapy in UC has yet to occur and there remains a need for treatment options for ulcerative colitis that lead to favourable outcomes for patients, for example, in terms of efficacy, safety and/or tolerability of the treatment. In particular, there remains a need for treatment options in the form of dosage regimen that provide optimal efficacy.

Summary

In one aspect of the present disclosure, there is provided a use of mirikizumab in the manufacture of a medicament for treating ulcerative colitis (UC) in a patient, wherein:

a) three induction doses of mirikizumab are to be administered to the patient by intravenous infusion at 4 week intervals, wherein each induction dose comprises 300 mg of mirikizumab, and wherein each induction dose is to be administered by intravenous infusion; and

b) multiple maintenance doses of mirikizumab are to be administered to the patient by subcutaneous injection at 4 week or 12 week intervals, wherein the first maintenance dose is to be administered 2-8 weeks after the last induction dose is administered and wherein each maintenance dose comprises 200 mg of mirikizumab.

In another aspect of the present disclosure, there is provided a use of mirikizumab in the manufacture of a medicament for treating UC in a patient, wherein:

a) three induction doses of mirikizumab are to be administered to the patient by intravenous infusion at 4 week intervals, wherein, if the patient has not achieved clinical response 4 weeks after the last induction dose is administered, three extended induction doses of mirikizumab are to be administered to the patient, and, wherein each induction dose and each extended induction dose comprises 300 mg of mirikizumab, and wherein each induction dose is to be administered by intravenous infusion; and

b) multiple maintenance doses of mirikizumab are to be administered to the patient by subcutaneous injection at 4 week or 12 week intervals, wherein the first maintenance dose is to be administered 2-8 weeks after the last induction dose is administered and wherein each maintenance dose comprises 200 mg of mirikizumab.

In a further aspect of the present disclosure, there is provided a use of mirikizumab in the manufacture of a medicament for treating UC in a patient, wherein:

a) three induction doses of mirikizumab are to be administered to the patient by intravenous infusion at 4 week intervals, wherein each induction dose comprises 300 mg of mirikizumab, and wherein each induction dose is to be administered by intravenous infusion; and

b) multiple maintenance doses of mirikizumab are to be administered to the patient by subcutaneous injection at 4 week or 12 week intervals, wherein the first maintenance dose is to be administered 2-8 weeks after the last induction dose is administered,

wherein if the patient develops a loss of response during the maintenance period, three rescue doses of mirikizumab are to be administered to the patient at 4 week intervals, wherein each rescue dose comprises 300 mg of mirikizumab,

wherein further maintenance doses of mirikizumab are to be administered to the patient if the patient achieves clinical response 4 weeks after the last rescue dose is administered, wherein the first

further maintenance dose is to be administered 2-8 weeks after the last rescue dose is administered,

wherein loss of response is defined as: (a) ≥2-point increase from baseline in the combined stool frequency (SF) and rectal bleeding (RB) scores (b) combined SF and RB score of ≥4, on 2 consecutive visits ≥ 7 days apart with confirmation of negative *Clostridium. difficile* testing and (c) endoscopic subscore (ES) of 2 or 3,

wherein clinical response is defined as achieving a decrease in the 9 point Modified Mayo Score (MMS) subscore of ≥2 points and ≥ 30-35% from baseline, with either a decrease of rectal bleeding (RB) subscore of ≥1 or a RB subscore of 0 or 1; and

wherein each maintenance dose and each further maintenance dose comprises 200 mg of mirikizumab.

In another aspect of the present disclosure, there is provided a use of mirikizumab in the manufacture of a medicament for treating UC in a patient, wherein:

a) three induction doses of mirikizumab are to be administered to the patient by intravenous infusion at 4 week intervals, wherein, if the patient has not achieved clinical response 4 weeks after the last induction dose is administered, three extended induction doses of mirikizumab are to be administered to the patient, and, wherein each induction dose and each extended induction dose comprises 300 mg of mirikizumab, and wherein each induction dose is to be administered by intravenous infusion; and

b) multiple maintenance doses of mirikizumab are to be administered to the patient by subcutaneous injection at 4 week or 12 week intervals, wherein the first maintenance dose is to be administered 2-8 weeks after the last induction dose is administered,

wherein if the patient develops a loss of response during the maintenance period, three rescue doses of mirikizumab are to be administered to the patient at 4 week intervals, wherein each rescue dose comprises 300 mg of mirikizumab,

wherein further maintenance doses of mirikizumab are to be administered to the patient if the patient achieves clinical response 4 weeks after the last rescue dose is administered, wherein the first further maintenance dose is to be administered 2-8 weeks after the last rescue dose is administered,

wherein loss of response is defined as: (a) ≥2-point increase from baseline in the combined stool frequency (SF) and rectal bleeding (RB) scores (b) combined SF and RB score of ≥4, on 2 consecutive visits ≥ 7 days apart with confirmation of negative Clostridium. difficile testing and (c) endoscopic subscore (ES) of 2 or 3,

wherein clinical response is defined as achieving a decrease in the 9 point Modified Mayo Score (MMS) subscore of ≥2 points and ≥ 30-35% from baseline, with either a decrease of rectal bleeding (RB) subscore of ≥1 or a RB subscore of 0 or 1,

and wherein each maintenance dose and each further maintenance dose comprises 200 mg of mirikizumab.

Description

The present disclosure provides a method of treating ulcerative colitis (UC) comprising administering to a patient in need thereof an effective amount of an anti-IL-23p19 antibody, said method comprising:

a) administering at least one induction dose of the anti-IL-23p19 antibody to the patient, wherein the induction dose comprises 50 mg to 1200 mg of the antibody; and

b) administering at least one maintenance dose(s) of the anti-IL-23p19 antibody to the patient after the last induction dose is administered, wherein the maintenance dose comprises 150 to 400 mg of the anti-IL-23p19 antibody.

The method of the present invention comprises administration of at least one induction dose of an anti-IL-23p19 antibody to a patient in need thereof in an induction period to induce a desired therapeutic effect, the desired therapeutic effect being clinical remission, clinical response, endoscopic remission, endoscopic healing and/or symptomatic remission. If the patient achieves a desired therapeutic effect at the end of

CLAIMS

1. Use of mirikizumab in the manufacture of a medicament for treating ulcerative colitis (UC) in a patient, wherein:
   a) three induction doses of mirikizumab are to be administered to the patient by intravenous infusion at 4 week intervals, wherein each induction dose comprises 300 mg of mirikizumab, and wherein each induction dose is to be administered by intravenous infusion; and
   b) multiple maintenance doses of mirikizumab are to be administered to the patient by subcutaneous injection at 4 week or 12 week intervals, wherein the first maintenance dose is to be administered 2-8 weeks after the last induction dose is administered and wherein each maintenance dose comprises 200 mg of mirikizumab.

2. The use according to claim 1, wherein the first maintenance dose is to be administered 4-6 weeks after the last induction dose is administered.

3. The use according to claim 1 or claim 2, wherein subsequent maintenance dose(s) of mirikizumab are to be administered at 4 week intervals after administration of the first maintenance dose.

4. The use according to claim 1 or claim 2, wherein subsequent maintenance dose(s) of mirikizumab are to be administered at 12 week intervals after administration of the first maintenance dose.

5. The use according to claim 1, wherein the patient achieves a therapeutic effect comprising one or more of clinical remission, clinical response, endoscopic remission, endoscopic healing, symptomatic remission, or histologic remission.

6. The use according to claim 1, wherein the patient achieves corticosteroid free remission.

7. The use according to claim 5, wherein the patient achieves the therapeutic effect in the induction period.

8. The use according to claim 5, wherein the patient achieves the therapeutic effect in the maintenance period.

9. The use according to claim 7 or claim 8, wherein the patient maintains the therapeutic effect in the maintenance period.

10. The use according to claim 1, wherein the patient is biologic-naïve, biologic-experienced, or is conventional failed.

11. pUse of mirikizumab in the manufacture of a medicament for treating UC in a patient, wherein:

a) three induction doses of mirikizumab are to be administered to the patient by intravenous infusion at 4 week intervals, wherein, if the patient has not achieved clinical response 4 weeks after the last induction dose is administered, three extended induction doses of mirikizumab are to be administered to the patient, and, wherein each induction dose and each extended induction dose comprises 300 mg of mirikizumab, and wherein each induction dose is to be administered by intravenous infusion; and

b) multiple maintenance doses of mirikizumab are to be administered to the patient by subcutaneous injection at 4 week or 12 week intervals, wherein the first maintenance dose is to be administered 2-8 weeks after the last induction dose is administered and wherein each maintenance dose comprises 200 mg of mirikizumab.

12. The use according to claim 11, wherein the first maintenance dose is to be administered 4-6 weeks after the last induction dose or last extended induction dose is administered.

13. The use according to claim 11 or claim 12, wherein subsequent maintenance dose(s) of mirikizumab are to be administered at 4 week intervals after administration of the first maintenance dose.

14. The use according to claim 11 or claim 12, wherein subsequent maintenance dose(s) of mirikizumab are to be administered at 12 week intervals after administration of the first maintenance dose.

15. The use according to claim 11, wherein the patient achieves a therapeutic effect comprising one or more of clinical remission, clinical response, endoscopic remission, endoscopic healing, symptomatic remission, or histologic remission.

16. The use according to claim 11, wherein the patient achieves corticosteroid free remission.

17. The use according to claim 15, wherein the patient achieves the therapeutic effect in the induction period.

18. The use according to claim 15, wherein the patient achieves the therapeutic effect in the extended induction period.

19. The use according to claim 15, wherein the patient achieves the therapeutic effect in the maintenance period.

20. The use according to any one of claims 17 to 19, wherein the patient maintains the therapeutic effect in the maintenance period.

21. The use according to claim 11, wherein the patient is biologic-naïve, biologic-experienced, or is conventional failed.

22. Use of mirikizumab in the manufacture of a medicament for treating UC in a patient, wherein:

a) three induction doses of mirikizumab are to be administered to the patient by intravenous infusion at 4 week intervals, wherein each induction dose comprises 300 mg of mirikizumab, and wherein each induction dose is to be administered by intravenous infusion; and

b) multiple maintenance doses of mirikizumab are to be administered to the patient by subcutaneous injection at 4 week or 12 week intervals, wherein the first maintenance dose is to be administered 2-8 weeks after the last induction dose is administered,

wherein if the patient develops a loss of response during the maintenance period, three rescue doses of mirikizumab are to be administered to the patient at 4 week intervals, wherein each rescue dose comprises 300 mg of mirikizumab,

wherein further maintenance doses of mirikizumab are to be administered to the patient if the patient achieves clinical response 4 weeks after the last rescue dose is administered, wherein the first further maintenance dose is to be administered 2-8 weeks after the last rescue dose is administered,

wherein loss of response is defined as: (a) ≥2-point increase from baseline in the combined stool frequency (SF) and rectal bleeding (RB) scores (b) combined SF and RB score of ≥4, on 2 consecutive visits ≥ 7 days apart with confirmation of negative *Clostridium. Difficile* testing and (c) endoscopic subscore (ES) of 2 or 3,

wherein clinical response is defined as achieving a decrease in the 9 point Modified Mayo Score (MMS) subscore of ≥2 points and ≥ 30-35% from baseline, with either a decrease of rectal bleeding (RB) subscore of ≥1 or a RB subscore of 0 or 1; and

wherein each maintenance dose and each further maintenance dose comprises 200 mg of mirikizumab.

23. The use according to claim 22, wherein the first maintenance dose is to be administered 4-6 weeks after the last induction dose is administered and the first further maintenance dose is to be administered 4-6 weeks after the last rescue dose is administered.

24. The use according to claim 22 or claim 23, wherein subsequent maintenance dose(s) of mirikizumab are to be administered at 4 week intervals after administration of the first maintenance dose and subsequent further maintenance dose(s) of mirikizumab are to be administered at 4 week intervals after administration of the first further maintenance dose.

25. The use according to claim 22 or claim 23, wherein subsequent maintenance dose(s) of mirikizumab are to be administered at 12 week intervals after administration of the first maintenance dose and subsequent further maintenance doses of mirikizumab are to be administered at 12 week intervals after administration of the first further maintenance dose.

26. The use according to claim 22, wherein the patient achieves a therapeutic effect comprising one or more of clinical remission, clinical response, endoscopic remission, endoscopic healing, symptomatic remission, histologic remission.

27. The use according to claim 22, wherein the patient achieves corticosteroid free remission.

28. The use according to claim 26, wherein the patient achieves the therapeutic effect in the induction period.

29. The use according to claim 26, wherein the patient achieves the therapeutic effect after receiving one or more rescue doses.

30. The use according to claim 26, wherein the patient achieves the therapeutic effect in the maintenance period.

31. The use according to any one of claims 28 to 30, wherein the patient maintains the therapeutic effect in the maintenance period.

32. The use according to claim 22, wherein the patient is biologic-naïve, biologic-experienced, or is conventional failed.

33. Use of mirikizumab in the manufacture of a medicament for treating UC in a patient, wherein:

a) three induction doses of mirikizumab are to be administered to the patient by intravenous infusion at 4 week intervals, wherein, if the patient has not achieved clinical response 4 weeks after the last induction dose is administered, three extended induction doses of mirikizumab are to be administered to the patient, and, wherein each induction dose and each extended induction dose comprises 300 mg of mirikizumab, and wherein each induction dose is to be administered by intravenous infusion; and

b) multiple maintenance doses of mirikizumab are to be administered to the patient by subcutaneous injection at 4 week or 12 week intervals, wherein the first maintenance dose is to be administered 2-8 weeks after the last induction dose is administered,

wherein if the patient develops a loss of response during the maintenance period, three rescue doses of mirikizumab are to be administered to the patient at 4 week intervals, wherein each rescue dose comprises 300 mg of mirikizumab,

wherein further maintenance doses of mirikizumab are to be administered to the patient if the patient achieves clinical response 4 weeks after the last rescue dose is administered, wherein the first further maintenance dose is to be administered 2-8 weeks after the last rescue dose is administered,

wherein loss of response is defined as: (a) ≥2-point increase from baseline in the combined stool frequency (SF) and rectal bleeding (RB) scores (b) combined SF and RB score of ≥4, on 2 consecutive visits ≥ 7 days apart with confirmation of negative Clostridium. difficile testing and (c) endoscopic subscore (ES) of 2 or 3,

wherein clinical response is defined as achieving a decrease in the 9 point Modified Mayo Score (MMS) subscore of ≥2 points and ≥ 30-35% from baseline, with either a decrease of rectal bleeding (RB) subscore of ≥1 or a RB subscore of 0 or 1,

and wherein each maintenance dose and each further maintenance dose comprises 200 mg of mirikizumab.

34. The use according to claim 33, wherein the first maintenance dose is to be administered 4-6 weeks after the last induction dose or last extended induction dose is administered and the first further maintenance is to be administered 4-6 weeks after the last rescue dose is administered.

35. The use according to claim 33 or claim 34, wherein subsequent maintenance doses of mirikizumab are to be administered at 4 week intervals after administration of the first maintenance dose and subsequent further maintenance doses of mirikizumab are to be administered at 4 week intervals after administration of the first further maintenance dose.

36. The use according to claim 33 or claim 34, wherein subsequent maintenance doses of mirikizumab are to be administered at 12 week intervals after administration of the first maintenance dose and subsequent further maintenance doses of mirikizumab are to be administered at 12 week intervals after administration of the first further maintenance dose.

37. The use according to claim 33, wherein the patient achieves a therapeutic effect comprising one or more of clinical remission, clinical response,

endoscopic remission, endoscopic healing, symptomatic remission, histologic remission.

38. The use according to claim 33, wherein the patient achieves corticosteroid free remission.

39. The use according to claim 37, wherein the patient achieves the therapeutic effect in the induction period.

40. The use according to claim 37, wherein the patient achieves the therapeutic effect in the extended induction period.

41. The use according to claim 37, wherein the patient achieves the therapeutic effect after receiving one or more rescue doses.

42. The use according to claim 37, wherein the patient achieves the therapeutic effect in the maintenance period.

43. The use according to any one of claims 39 to 42, wherein the patient maintains the therapeutic effect in the maintenance period.

44. The use according to claim 33, wherein the patient is biologic-naïve, biologic-experienced, or is conventional failed.