IL-13 INHIBITORS FOR THE TREATMENT OF PRURIGO NODULARIS

SEQUENCE LISTING

[0001] The present application is being filed along with a Sequence Listing in ST.26 XML format. The Sequence Listing is provided as a file titled "X23072_SequenceListing" created September 13, 2022 and is 15 kilobytes in size. The Sequence Listing information in the ST.26 XML format is incorporated herein by reference in its entirety.

FIELD

[0002] The present invention relates to methods and uses of interleukin (IL)-13 inhibitors for treating prurigo nodularis or reducing pruritis associated with prurigo nodularis.

BACKGROUND

[0003] Prurigo nodularis (PN) is a chronic inflammatory skin disorder characterized by intensely pruritic, hyperkeratotic nodules (Huang et al., *J Am Acad Dermatol*. 2020;83(6):1559-1565). PN lesions can cause intense itching, bleeding, burning, and stinging sensations. The physical discomfort combined with the potential psychological effects of the disease interfere with everyday activities and significantly impact an individual's quality of life. To date, no treatment for PN has been approved and patients are often refractory to off-label treatments and experience a significant burden on their quality of life (Huang et al., *J Am Acad Dermatol*. 2020;83(6):1559-1565).

[0004] Interleukin (IL)-13 is a key mediator of T-helper type 2 (Th2) inflammation and signals through a heterodimeric receptor IL-4Rα/IL-13Rα1. Some evidence suggest that Th2 cytokines might play a role in the pathogenesis of PN.

[0005] There remains a substantial unmet medical need for effective therapies for treating PN.

SUMMARY

[0005a] In an aspect of the present disclosure, there is provided a use of an IL-13 inhibitor or a pharmaceutical composition comprising an IL-13 inhibitor in the manufacture of a medicament for the treatment of prurigo nodularis (PN) or reducing pruritus associated with PN in a patient in need thereof.

[0006] Provided herein are methods and uses of an IL-13 inhibitor (e.g., an anti-IL-13 antibody), or pharmaceutical compositions comprising an IL-13 inhibitor (e.g., an anti-IL-13 antibody), for treating prurigo nodularis or reducing pruritis associated with prurigo nodularis.

[0007] In one example, provided herein are methods of treating prurigo nodularis or reducing pruritus associated with prurigo nodularis in a patient in need thereof, and such methods

comprise administering to the patient a therapeutically effective amount of an IL-13 inhibitor. In some examples, the IL-13 inhibitor is an anti-IL-13 antibody. In some examples, the anti-IL-13 antibody comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises a HCDR1 comprising SEQ ID NO: 1, a HCDR2 comprising SEQ ID NO: 2, and a HCDR3 comprising SEQ ID NO: 3, and the VL comprises a LCDR1 comprising SEQ ID NO: 4, a LCDR2 comprising SEQ ID NO: 5, and a LCDR3 comprising SEQ ID NO: 6. In some examples, the anti-IL-13 antibody comprises a VH comprising SEQ ID NO: 7, and a VL comprising SEQ ID NO: 8. In some examples, the anti-IL-13 antibody comprises a heavy chain comprising SEQ ID NO: 9, and a light chain comprising SEQ ID NO: 10. In some examples, the anti-IL-13 antibody is lebrikizumab.

[0008] In some examples, the anti-IL-13 antibody is administered subcutaneously to the patient. In some examples, the anti-IL-13 antibody is administered at a dose of 250 mg to 500 mg. In some examples, the anti-IL-13 antibody is administered subcutaneously to the patient at a dose of 250 mg once every two weeks. In some examples, the anti-IL-13 antibody is administered subcutaneously to the patient at a dose of 250 mg once every four weeks. In some examples, the patient is further treated with a loading dose of 500 mg of the anti-IL-13 antibody. In some examples, the loading dose is administered once or twice to the patient. In some examples, the loading dose is administered to the patient twice at week 0 (baseline) and week 2. In some examples, the patient is treated with the anti-IL-13 antibody for a period of about 16 weeks or more (e.g., about 16 to about 24 weeks).

[0009] In some examples, the patient has moderate to severe prurigo nodularis. In some examples, the patient has (1) a clinical diagnosis of PN for at least 6 months; (2) PN lesions on upper limbs, trunk, and/or lower limbs, at least 20 nodules on the entire body with a bilateral distribution; (3) a IGA PN-S score ≥3 at baseline; and/or (4) an Itch NRS score ≥7 at baseline. In some examples, the patient has inadequate response to topical corticosteroids (TCS) or topical calcineurin inhibitors (TCI), or TCS or TCI are medically inadvisable for the patient. In some examples, the patient is aged 18 years or older.

[0010] In some examples, the methods further comprise determining the Itch Numerical Rating Scale (NRS) score of the patient before and after the treatment. In some examples, the methods further comprise determining one or more of the following characteristics of the patient: IGA PN-S (Investigator's Global Assessment: Prurigo Nodularis-Stage), IGA PN-A

(Investigator's Global Assessment: Prurigo Nodularis-Activity), Skin Pain NRS, nighttime awakenings DSS (Dermatology Sleep Scale), PGI-S-PN (Patient Global Impression of Severity-Prurigo Nodularis), DLQI (Dermatology Life Quality Index), PAS (Prurigo Activity Score), PROMIS (Patient-Reported Outcomes Measurement Information System) Anxiety and Depressive Symptoms, and EuroQol-5D (European Quality of Life-5 Dimensions-5 Levels or EQ-5D-5L) before and after the treatment.

[0011] In another example, provided herein are an IL-13 inhibitor (e.g., an anti-IL-13 antibody) or pharmaceutical composition comprising an IL-13 inhibitor (e.g., an anti-IL-13 antibody) for use in the treatment of prurigo nodularis or reducing pruritus associated with prurigo nodularis. Also provided herein are uses of an IL-13 inhibitor (e.g., an anti-IL-13 antibody) in the manufacture of a medicament for the treatment of prurigo nodularis or reducing pruritus associated with prurigo nodularis.

BRIEF DESCRIPTION OF THE DRAWINGS

[0012] Figure 1A is a dot plot showing the IL-13 levels in prurigo nodularis patient samples (PN) and healthy control samples (HC). Figure 1B is a dot plot showing periostin levels in PN and HC samples. Figure 1C is a dot plot showing IL-4 levels in PN and HC samples. Figure 1D is a dot plot showing IL-5 levels in PN and HC samples. Figure 1E is a dot plot showing IgE levels in PN and HC samples.

[0013] Figure 2 is a schematic diagram of the Phase 3 study design described in Example 2. Footnotes mean: [a] Participants requiring rescue therapy for PN during the screening period or who are expected to require rescue therapy within 4 weeks following the baseline visit are excluded from the study. [b] Participants who require use of low to mid-potency TCS or TCI may do so only during the first 2 weeks of the treatment period for ≤3 consecutive days and no more than 5 cumulative days. These participants are be considered treatment failures in the efficacy analyses. [c] At Weeks 0 (baseline) and 2, participants in the lebrikizumab treatment arm receive a 500 mg loading dose, and participants in the placebo arm receive a placebo loading dose. [d] After completion of the Week 16 visit, participants are offered the option of continuing treatment in a separate long-term extension study. Participants who discontinue the study early or choose not to enter the long-term extension study must return for a post-treatment safety follow-up visit approximately 12 weeks after the date of the last study drug injection.

CLAIMS

1. Use of an IL-13 inhibitor or a pharmaceutical composition comprising an IL-13 inhibitor in the manufacture of a medicament for the treatment of prurigo nodularis (PN) or reducing pruritus associated with PN in a patient in need thereof.

2. The use of claim 1, wherein the IL-13 inhibitor is an anti-IL-13 antibody.

3. The use of claim 2, wherein the anti-IL-13 antibody comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises a HCDR1 comprising SEQ ID NO: 1, a HCDR2 comprising SEQ ID NO: 2, and a HCDR3 comprising SEQ ID NO: 3, and the VL comprises a LCDR1 comprising SEQ ID NO: 4, a LCDR2 comprising SEQ ID NO: 5, and a LCDR3 comprising SEQ ID NO: 6.

4. The use of claim 2 or 3, wherein the anti-IL-13 antibody comprises a VH comprising SEQ ID NO: 7, and a VL comprising SEQ ID NO: 8.

5. The use of any one of claims 2-4, wherein the anti-IL-13 antibody comprises a heavy chain comprising SEQ ID NO: 9, and a light chain comprising SEQ ID NO: 10.

6. The use of any one of claims 2-5, wherein the anti-IL-13 antibody is lebrikizumab.

7. The use of any one of claims 2-6, wherein the anti-IL-13 antibody is to be administered subcutaneously to the patient.

8. The use of any one of claims 2-7, wherein the anti-IL-13 antibody is to be administered to the patient at a dose of 250 mg to 500 mg.

9. The use of any one of claims 2-8, wherein the anti-IL-13 antibody is to be administered subcutaneously to the patient at a dose of 250 mg once every two weeks.

10. The use of claim 9, wherein the anti-IL-13 antibody is also to be administered to the patient at a loading dose of 500 mg at week 0 (baseline) and week 2.

11. The use of any one of claims 2-10, wherein the anti-IL-13 antibody is to be administered to the patient for a period of about 16 to about 24 weeks.

12. The use of any one of claims 1-11, wherein the Itch Numerical Rating Scale (NRS) score of the patient is to be determined before and after the treatment.

13. The use of any one of claims 1-12, wherein one or more of the following characteristics of the patient is to be determined: IGA PN-S, IGA PN-A, Skin Pain NRS, nighttime awakenings DSS, PGI-S-PN, DLQI, PAS, PROMIS Anxiety and Depressive Symptoms, and EuroQol-5D (EQ-5D-5L), before and after the treatment.

14. The use of any one of claims 2-13, wherein the anti-IL-13 antibody is to be administered to the patient using a subcutaneous administration device.

15. The use of claim 14, wherein the subcutaneous administration device is selected from a prefilled syringe, disposable pen injection device, microneedle device, microinfuser device, needle-free injection device, or autoinjector device.

16. The use of any one of claims 1-15, wherein the patient has moderate to severe prurigo nodularis.

17. The use of claim 16, wherein the patient has (1) a clinical diagnosis of PN for at least 6 months; (2) PN lesions on upper limbs, trunk, and/or lower limbs, at least 20 nodules on the entire body with a bilateral distribution; (3) a IGA PN-S score ≥3 at baseline; and/or (4) an Itch NRS score ≥7 at baseline.

18. The use of any one of claims 1-17, wherein the patient has inadequate response to topical corticosteroids or topical calcineurin inhibitors, or topical corticosteroids or topical calcineurin inhibitors are medically inadvisable for the patient.

19. The use of any one of claims 1-18, wherein the patient is aged 18 years old or older.