of cell types including but not limited to fibroblasts, epithelial cells, and monocytes (NPL 13). Interleukin-17A, IL-17F, IL-17A/F, IL-17C, and IL-25 stimulate cellular responses by binding to IL-17RA. Interleukin-17A, IL-17F, and IL-17A/F signal via a heteromeric IL-17RA/IL-17RC complex, IL-17C signals via a heteromeric IL 17RA/IL-17RE complex, and IL-25 signals via a heteromeric IL-17RA/IL-17RB complex (NPLs 12, 14-17). Interleukin-17RA blockade represents a novel mechanism to inhibit the inflammation and clinical symptoms associated with autoimmune and inflammatory diseases including but not limited to psoriasis, psoriatic arthritis, and asthma.

[0006] AM-14 is a human CHO cell-derived IgG2 monoclonal antibody that binds to human IL-17RA and blocks the biological activities of IL-17A, IL-17F, IL-17A/F heterodimer, and IL-25 involved in the various autoimmune disorder and inflammatory disorder (NPLs 18-20).

Citation List

Non Patent Literature

[0007] NPL 1: Nat Rev Immunol. 2010;10:479-490
[0008] NPL 2: Cell. 2010;140:845-858
[0009] NPL 3; Nature Rev Immunol.2009;9(8):556-567
[0010] NPL 4:Immunity. 2008;28(4):454-67
[0011] NPL 5: J Exp Med. 2005;201(2):233-240
[0012] NPL 6: Nat Immunol. 2005;6(11):1133-1141
[0013] NPL 7: Immunity.2004;21:467-476
[0014] NPL 8: J Immunol. 1999;162(1):577-584
[0015] NPL 9: Immunological Rev. 2008;226:172-190
[0016] NPL 10: J Exp Med. 2007;204(8):1837-1847
[0017] NPL 11: Immunity. 2001;15:985-995
[0018] NPL 12: Nat Immunol.2011;12(12):1159-1166
[0019] NPL 13: Cytokine. 1997;9(11):794-800
[0020] NPL 14: Nat Immunol. 2011;12(12):1151-1158
[0021] NPL 15: J Immunol. 2008;181(6):4299-4310
[0022] NPL 16: J Immunol. 2008;181(4):2799-2805
[0023] NPL 17: J Immunol. 2006;177(1):36-39
[0024] NPL 18: Immunity. 2008;28(4):454-67
[0025] NPL 19: J. Allergy. Clin. Immunol. 2007;120(6):1324-31
[0026] NPL 20: J Immunol. 2005;175(1):404-12

Summary of Disclosure

Technical Problem

[0027] In one embodiment, the present disclosure provides a therapeutic agent for pustular psoriasis or psoriatic erythroderma that is administered to a psoriasis patient that has been administered with an anti-TNF-alpha antibody, comprising an IL-17RA antagonist as an active ingredient. In one aspect, there is provided a therapeutic agent for psoriasis that is administered to a psoriasis patient that cannot be treated with an anti-TNF-alpha antibody, comprising an IL-17RA antagonist as an active ingredient. In another embodiment, the present disclosure also intended to provide a method for the treatment of pustular psoriasis or psoriatic erythroderma, comprising administering an IL-17RA antagonist to a psoriasis patient that has been administered with an anti-TNF-alpha antibody. In another aspect, there is provided a method for the treatment of psoriasis, comprising administering an IL-17RA antagonist to a psoriasis patient that cannot be treated with an anti-TNF-alpha antibody. In another aspect, there is provided the use of an IL-17RA antagonist for the manufacture of a medicament, wherein the medicament is to be administered to a psoriasis patient that cannot be treated with an anti-TNF-alpha antibody.

Solution to Problem

[0028] The present invention relates to the following (1) to (34).

(1) A therapeutic agent for pustular psoriasis or psoriatic erythroderma that is administered to a psoriasis patient that has been administered with an anti-TNF-alpha antibody, comprising an IL-17RA antagonist as an active ingredient.

(2) The therapeutic agent described in (1), wherein the anti-TNF-alpha antibody is at least one antibody selected from adalimumab, infliximab, certolizumab pegol, certolizumab, and golimumab.

(3) The therapeutic agent described in (1) or (2), wherein the IL-17RA antagonist is an anti-IL-17RA antibody or an antibody fragment thereof.

(4) The therapeutic agent described in (3), wherein the anti-IL-17RA antibody is selected from the following a) and b):

a) a monoclonal antibody in which a complementarity determining region (hereinafter, referred to as CDR)1, CDR2, and CDR3 of a heavy chain variable region (hereinafter, referred to as VH) of the antibody comprise the amino acid sequences shown in SEQ ID NOs:1, 2, and 3, respectively, and CDR1, CDR2, and CDR3 of a light chain variable region (hereinafter, referred to as VL) of the antibody comprise the amino acid sequences shown in SEQ ID NOs:4, 5, and 6, respectively; and

b) a monoclonal antibody in which VH of the antibody comprises the amino acid sequence shown in SEQ ID NO:7, and VL of the antibody comprises the amino acid sequence shown in SEQ ID NO:8.

(5) The therapeutic agent described in any one of (1) to (4), wherein the clinical global impression (hereinafter, also referred to as CGI) of a patient after administration of the therapeutic agent becomes 2 or 1.

(6) The therapeutic agent described in any one of (1) to (5), wherein psoriasis area and severity index (hereinafter, referred to as PASI) score of a patient after admin-

Claims

[Claim 1] A therapeutic agent for psoriasis that is administered to a psoriasis patient that cannot be treated with an anti-TNF-alpha antibody, comprising an IL-17RA antagonist as an active ingredient.

[Claim 2] The therapeutic agent according to claim 1, wherein the patient that cannot be treated with the anti-TNF-alpha antibody is a patient that does not respond to the anti-TNF-alpha antibody or that is of in-

sufficient tolerability to the anti-TNF-alpha antibody.

[Claim 3] The therapeutic agent according to claim 1 or 2, the anti-TNF-alpha antibody is at least one selected from adalimumab, infliximab, certolizumab pegol, certolizumab, and golimumab.

[Claim 4] The therapeutic agent according to any one of claims 1 to 3, wherein the IL-17RA antagonist is an anti-IL-17RA antibody or an antibody fragment thereof.

[Claim 5] The therapeutic agent according to claim 4, wherein the anti-IL-17RA antibody is selected from the following a) and b):
a) a monoclonal antibody in which CDR1, CDR2, and CDR3 of VH of the antibody comprise the amino acid sequences shown in SEQ ID NOs:1, 2, and 3, respectively, and CDR1, CDR2, and CDR3 of VL of the antibody comprise the amino acid sequences shown in SEQ ID NOs:4, 5, and 6, respectively; and
b) a monoclonal antibody in which VH of the antibody comprises the amino acid sequence shown in SEQ ID NO:7, and VL of the antibody comprises the amino acid sequence shown in SEQ ID NO:8.

[Claim 6] The therapeutic agent according to any one of claims 1 to 5, wherein the psoriasis is at least one selected from psoriasis vulgaris, psoriasis arthropica, pustular psoriasis, psoriatic erythroderma, and psoriasis guttata.

[Claim 7] The therapeutic agent according to any one of claims 1 to 6, wherein the CGI of a patient after administration of the therapeutic agent becomes 2 or 1.

[Claim 8] The therapeutic agent according to any one of claims 1 to 7, wherein the PASI score of a patient after administration of the therapeutic agent is lower than that before administration of the therapeutic agent.

[Claim 9] Use of an IL-17RA antagonist for the manufacture of a medicament, wherein the medicament is to be administered to a psoriasis patient that cannot be treated with an anti-TNF-alpha antibody.

[Claim 10] The use according to claim 9, wherein the patient that cannot be treated with the anti-TNF-alpha antibody is a patient that is ineffective to the anti-TNF-alpha antibody or that is of insufficient tolerability to the anti-TNF-alpha antibody.

[Claim 11] The use according to claim 9 or 10, wherein the anti-TNF-alpha antibody is at least one selected from adalimumab, infliximab, certolizumab pegol, certolizumab, and golimumab.

[Claim 12] The use according to any one of claims 9 to 11, wherein the IL-17RA antagonist is an anti-IL-17RA antibody or an antibody fragment thereof.

[Claim 13] The use according to claim 12, wherein the anti-IL-17RA antibody is selected from the following a) and b):
a) a monoclonal antibody in which CDR1, CDR2, and CDR3 of VH of

the antibody comprise the amino acid sequences shown in SEQ ID NOs:1, 2, and 3, respectively, and CDR1, CDR2, and CDR3 of VL of the antibody comprise the amino acid sequences shown in SEQ ID NOs:4, 5, and 6, respectively; and
b) a monoclonal antibody in which VH of the antibody comprises the amino acid sequence shown in SEQ ID NO:7, and VL of the antibody comprises the amino acid sequence shown in SEQ ID NO:8.

[Claim 14] The use according to any one of claims 9 to 13, wherein the psoriasis is at least one selected from psoriasis vulgaris, psoriasis arthropica, pustular psoriasis, psoriatic erythroderma, and psoriasis guttata.

[Claim 15] The use according to any one of claims 9 to 14, wherein the CGI of a patient after the administration of the IL-17RA antagonist becomes 2 or 1.

[Claim 16] The use according to any one of claims 9 to 15, wherein the PASI score of a patient after the administration of the IL-17RA antagonist is lower than that before the administration of the antagonist.

[Claim 17] The use according to any one of claims 9 to 16, wherein the IL-17RA antagonist is to be administered in a dose of 140 mg or more.

[Claim 18] The use according to any one of claims 9 to 17, wherein the IL-17RA antagonist is to be administered in a dose of 140 mg or 210 mg.

[Claim 19] The use according to any one of claims 9 to 18, wherein the IL-17RA antagonist is to be administered in a dose of 140 mg or 210 mg on the 1st day, the 1st week and the 2nd week, and thereafter once every two weeks.