

(b) obtaining SNP rs11171739 sequence from said genomic DNA;
wherein the presence of risk allele (C) at rs11171739 predicts that said patient would benefit from treatment with a MAdCAM antagonist antibody.

E106. A method of treating a patient susceptible to or diagnosed with a condition associated with an increase in MAdCAM expression comprising administering to the patient an initial dose of between about 5 mg and about 150 mg of MAdCAM antagonist antibody, wherein said patient comprises risk allele (C) at rs11171739.

E107. A method of treating a patient susceptible to or diagnosed with a condition associated with an increase in MAdCAM expression comprising administering to the patient an initial dose of between about 5 mg and about 150 mg of MAdCAM antagonist antibody, wherein said is identified by any one of the method of embodiments E86-E105.

E108. A kit comprising:

- (a) a detection agent for detecting the presence of a biomarker, or for measuring the level of a biomarker in a biological sample, wherein said biomarker is: (i) any one of the biomarkers listed in Tables 12, 13, 15; (ii) circulating $\alpha 4\beta 7^+$ cells; (iii) rs11171739 risk allele; or (iv) any combination of the foregoing; and
- (b) instructions to use said detection agent.

The present invention also provides use of a MAdCAM antagonist antibody in the manufacture of a medicament for the treatment of a patient susceptible to or diagnosed with a condition associated with an increase in MAdCAM expression, wherein the medicament is to be administered to the patient an initial dose of between 5 mg and 150 mg.

The invention provides as a further embodiment that may be used independent or in combination with any of the previous embodiments, a method for the treatment of a patient susceptible to or diagnosed with a condition associated with an increase in MAdCAM expression comprising administering to the patient an initial dose of between about 5 mg and about 150 mg of MAdCAM antagonist antibody following one or more doses of tofacitinib.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1: Clinical remission rate based on total mayo score at week 12 (treatment failure approach).

Figure 2: Clinical remission rate based on naïve and experience population at week 12 (treatment failure approach).

Figure 3: Clinical response and mucosal healing rates at week 12 (treatment failure approach).

Figure 4: Analysis results of placebo corrected clinical remission rate, clinical response rate and mucosal healing rate based on total mayo score at week 12 (cmh method, central read, mitt population).

5 Figure 5: Analysis results of placebo corrected clinical remission rate, clinical response rate and mucosal healing rate based on total mayo score at week 12 (cmh method, local read, mitt population).

CLAIMS

1. Use of a MAdCAM antagonist antibody in the manufacture of a medicament for the treatment of a patient susceptible to or diagnosed with a condition associated with an increase in MAdCAM expression, wherein the medicament is to be administered to the patient an initial dose of between 5
5 mg and 150 mg.
2. The use of claim 1, wherein a subsequent dose is to be administered in an amount that is about the same or less than the initial dose, said subsequent dose being provided between about 1 week and about 12 weeks after the initial dose.
3. The use of claim 1 or 2, wherein either or both of the initial dose or subsequent dose of the
10 MAdCAM antagonist antibody is dosed at a range whose lower limit is selected from the group consisting of 5 mg, 6 mg, 7 mg, 7.5 mg, 8 mg, 9 mg, 10 mg, 12 mg, 15 mg, 20 mg, 22.5 mg, 25 mg, 30 mg, 35 mg, 45 mg, 50 mg, 55 mg, 65 mg, 65 mg, 70 mg, 75 mg, 80 mg, 85 mg, 90 mg, 95 mg, 100 mg, and whose upper limit is selected from the group consisting of 22.5 mg, 25 mg, 30 mg, 35 mg, 40 mg, 45 mg, 50 mg, 55 mg, 60 mg, 65 mg, 70 mg, less than 75 mg, 75 mg, 80 mg, 85 mg, 90
15 mg, 95 mg, 100 mg, 105 mg, 110 mg, 115 mg, 120 mg, 125 mg, 130 mg, 135 mg, 140 mg, 145 mg, less than 150 mg, and 150 mg.
4. The use of claim 1 or 2, wherein an initial dose and one or more subsequent doses of between 22.5 mg and 75 mg of MAdCAM antagonist antibody is to be administered to the patient.
5. The use of any one of claims 2-4, wherein the subsequent dose is to be administered about
20 4 weeks after the initial dose.
6. The use of any one of claims 2-4, wherein the subsequent dose is to be administered about 8 weeks after the initial dose.
7. The use of any one of claims 1-6, wherein the observed clinical remission rate at about 12 weeks after initial dose, as determined using the MAYO score, is at least about 3%.
8. The use of any one of claims 1-7, wherein the clinical response rate at about 12 week after
25 the initial dose is at least about 28%.
9. The use of any one of claims 1-8, wherein the mucosal healing rate at about 12 week after the initial dose is at least about 10%.
10. The use of any one of claims 1-9, wherein the patient is not taking a TNF antagonist or TNF
30 inhibitor.
11. The use of any one of claims 1-10, wherein an initial dose of about 50 mg of MAdCAM antagonist antibody, followed by one or more subsequent doses of the MAdCAM antagonist antibody in an amount that is about the same as the initial dose is to be administered to the patient, and wherein the one or more subsequent doses are doses about every 4 weeks.

12. The use of any one of claims 1-11, wherein an initial dose of about 100 mg of MAdCAM antagonist antibody, followed by one or more subsequent doses of the MAdCAM antagonist antibody in an amount that is about the same as the initial dose is to be administered to the patient, and wherein the one or more subsequent doses are doses about every 8 weeks.
- 5 13. The use of any one of claims 1-12, wherein the MAdCAM antagonist antibody comprises a light chain whose CDRs are according to the CDRs of SEQ ID NO:3, and a heavy chain whose CDRs are according to the CDRs of SEQ ID NO:4.
- 10 14. The use of any one of claims 1-13, wherein the a condition associated with an increase in MAdCAM expression is selected from the group consisting of ulcerative colitis (UC), Crohn's disease (CD), Irritable bowel syndrome (IBS), irritable bowel disease (IBD), rheumatoid arthritis, reactive arthritis, osteoarthritis, infectious arthritis, psoriatic arthritis, polyarthritis, juvenile arthritis, juvenile rheumatoid arthritis, juvenile reactive arthritis, juvenile psoriatic arthritis, pain, fibrosis, fibromyalgia syndrome, ankylosing spondylitis, undifferentiated spondyloarthropathy, juvenile onset spondylarthritis, psoriasis, gout, Castleman's disease, sepsis, type I diabetes, type II diabetes,
- 15 multiple myeloma, and renal cell carcinoma.
15. The use as claimed in any one of claims 1-14, further comprising
- (a) measuring the level of a biomarker in a biological sample from said patient, wherein said biomarker is: (i) any one or combination of the biomarkers selected from the group consisting of: Fecal calprotectin, sMAdCAM, hsCRP, AR, CHI3L1, CXCL1, CXCL11, CXCL13, CXCL9,
- 20 Dkk-1, EGF, EN-RAGE, EPO, FGF-21, GH, IL-17C, IL-6, IL-7, IL-8, MIP-1 alpha, MMP-1, MMP-10, MMP-12, MMP-3, NT-pro-BNP, OSM, PTPN22, PTX3, REG-4, RETN, TNFRSF4, TRANCE, and VEGF-A; (ii) CCR9; (iii) circulating $\alpha 4\beta 7^+$ cells; or (iv) any combination of the foregoing; and
- (b) comparing said level with a control;
- 25 such that a change in the level of the biomarker, as compared to the control, is predictive of a beneficial therapeutic response in the condition.
16. A MAdCAM antagonist antibody for use in a method of any one of claims 1-15.
17. A pharmaceutical composition comprising the MAdCAM antibody of claim 16.
18. Use of a MAdCAM antagonist antibody of claim 16 in the preparation of a medicament for
- 30 the treatment of ulcerative colitis.
19. A method for assessing the presence or absence of a beneficial response in an ulcerative colitis (UC) patient after administering a MAdCAM antagonist antibody, comprising:
- (a) measuring the level of a biomarker in a biological sample from said patient, wherein said biomarker is: (i) any one or combination of the biomarkers selected from the group