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Summary of the Invention

[Problems to be Solved by the Invention]

Even with SA237 (an antibody having the heavy chain sequence of SEQ ID NO: 3 and the light chain sequence of SEQ ID NO: 4), which is produced by applying technologies for reducing immunogenicity, in a Phase I study (SA-001JP) of subcutaneously administering a single dose of 120 mg of SA237 to healthy adult male subjects, anti-SA237 antibodies were generated in 54.2% of the cases (39 out of 72 cases) and an immunogenic problem occurred. An objective of the present invention is to suppress anti-antibody generation and provide more effective pharmaceutical compositions or dosage regimen to be used in the treatment of IL-6-related diseases.

[Means for Solving the Problems]

To solve the above-mentioned problems, the present inventors focused on immunological tolerance, and discovered that anti-antibody generation can be suppressed by administering a pharmaceutical composition with a predetermined administration method and dose.

More specifically, the present inventors discovered that anti-antibody generation can be suppressed by using a pharmaceutical composition administered at a predetermined dose and administration method to treat IL-6-related diseases, and thereby completed the present invention. Thus, in one aspect, the present invention refers to the use of an IL-6 receptor antibody comprising a heavy chain having the sequence of SEQ ID NO: 3 and a light chain having the sequence of SEQ ID NO: 4 for the manufacture of a medicament for treating or preventing an IL-6-related disease, wherein the medicament is a formulation for subcutaneous administration and is to be administered three times at the same dose as the routine dose with two-week intervals from the initial administration in a short interval dosing period, and then to be administered routinely with four-week intervals starting from the final administration in the short-interval dosing period, wherein the routine dose is 120 mg per administration. In another aspect, the present invention refers to the use of an IL-6 receptor antibody comprising a heavy chain having the sequence of SEQ ID NO: 3 and a light chain having the sequence of SEQ ID NO: 4 for the manufacture of a medicament for suppressing the generation of an antibody against the IL-6 receptor antibody, wherein the medicament is a formulation for subcutaneous administration and is to be administered three times at the same dose as the routine dose with two-week intervals from the initial administration in a short interval dosing period, and then to be administered routinely with four-week intervals starting from the final administration in the

short-interval dosing period, wherein the routine dose is 120 mg per administration.

Also described herein is the following:

[1] A pharmaceutical composition for use in treating an IL-6-related disease comprising an IL-6 inhibitor as an active ingredient, wherein the pharmaceutical composition is routinely administered after a short-interval dosing period where the same dose as the routine dose is administered multiple times at a shorter interval than the routine dosing interval.

[2] The pharmaceutical composition of [1], wherein the routine dosing interval is three to five weeks.

[3] The pharmaceutical composition of [1], wherein the routine dosing interval is four weeks.

[4] The pharmaceutical composition of any one of [1] to [3], wherein the dosing interval during the short-interval dosing period where the dose is administered multiple times at a shorter interval than the routine dosing interval is one to two weeks.

[5] The pharmaceutical composition of any one of [1] to [3], wherein the dosing interval during the short-interval dosing period where the dose is administered multiple times at a shorter interval than the routine dosing interval is two weeks.

CLAIMS

1. Use of an IL-6 receptor antibody comprising a heavy chain having the sequence of SEQ ID NO: 3 and a light chain having the sequence of SEQ ID NO: 4 for the manufacture of a medicament for treating or preventing an IL-6-related disease, wherein the medicament is a formulation for subcutaneous administration and is to be administered three times at the same dose as the routine dose with two-week intervals from the initial administration in a short interval dosing period, and then to be administered routinely with four-week intervals starting from the final administration in the short-interval dosing period, wherein the routine dose is 120 mg per administration.

2. The use of claim 1, wherein the IL-6 receptor antibody is SA237.

3. The use of claim 1 or 2, wherein the IL-6-related disease is rheumatoid arthritis, juvenile idiopathic arthritis, systemic-onset juvenile idiopathic arthritis, Castleman's disease, systemic lupus erythematosus (SLE), lupus nephritis, Crohn's disease, lymphoma, ulcerative colitis, anemia , vasculitis, Kawasaki disease, Still's disease, amyloidosis, multiple sclerosis, transplantation, age-related macular degeneration, ankylosing spondylitis, psoriasis, psoriatic arthritis, chronic obstructive pulmonary disease (COPD), IgA nephropathy, osteoarthritis, asthma, diabetic nephropathy, GVHD, endometriosis, hepatitis (NASH), myocardial infarction, arteriosclerosis, sepsis, osteoporosis, diabetes, multiple myeloma, prostate cancer, kidney cancer, B-cell non-Hodgkin's lymphoma, pancreatic cancer, lung cancer, esophageal cancer, colon cancer, cancer cachexia, cancer nerve invasion, myocardial infarction, myopic choroidal neovascularization, idiopathic choroidal neovascularization, uveitis, chronic thyroiditis, delayed hypersensitivity, contact dermatitis, atopic dermatitis, mesothelioma, polymyositis, dermatomyositis, panuveitis, anterior uveitis, intermediate uveitis, scleritis, keratitis, orbital inflammation, optic neuritis , diabetic retinopathy, proliferative vitreoretinopathy, dry eye, post-operative inflammation, neuromyelitis optica, myasthenia gravis, or pulmonary hypertension.

4. The use of any one of claims 1 to 3, wherein the medicament is to be administered to a human.

5. Use of an IL-6 receptor antibody comprising a heavy chain having the sequence of SEQ ID NO: 3 and a light chain having the sequence of SEQ ID NO: 4 for the manufacture of a medicament for suppressing the generation of an antibody against the IL-6 receptor antibody,

wherein the medicament is a formulation for subcutaneous administration and is to be administered three times at the same dose as the routine dose with two-week intervals from the initial administration in a short interval dosing period, and then to be administered routinely with four-week intervals starting from the final administration in the short-interval dosing period, wherein the routine dose is 120 mg per administration.