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[PTL8] WO 2002/30985

[PTL9] WO 2004/007553

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[PTL11] WO 2009/125825

[PTL12] WO 2011/122011

[PTL13] WO 2011/111007

[Non-Patent Literature]

[0019]

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[NPL2] Dmytrijuk et al., The Oncologist 13(9):993-1000 (2008)

[NPL3] Yeung et al., J Immunol. 182(12): 7663-7671 (2009)

[NPL4] Datta-Mannan et al., J Biol. Chem. 282(3):1709-1717 (2007)

[NPL5] Dall'Acqua et al., J. Immunol. 169(9):5171-5180 (2002)

[Summary]

[0019a]

In one aspect, the present invention refers to use of an anti-C5 antibody in the manufacture of a first and a second pharmaceutical compositions for treating or preventing a C5-related disease, wherein the first pharmaceutical composition is formulated for intravenous injection, comprises the anti-C5 antibody, and is to be administered intravenously, wherein the second pharmaceutical composition is formulated for subcutaneous injection, comprises the anti-C5 antibody, and is to be administered subcutaneously, and wherein administration of the first and the second

pharmaceutical compositions is to be carried out in the order of one or more intravenous doses of the first pharmaceutical composition and one or more subcutaneous doses of the second pharmaceutical composition; wherein the C5-related disease is any one selected from the group consisting of rheumatoid arthritis (RA); lupus nephritis; ischemia-reperfusion injury; paroxysmal nocturnal hemoglobinuria (PNH); atypical hemolytic uremic syndrome (aHUS); dense deposit disease (DDD); macular degeneration; hemolysis, elevated liver enzymes, and low platelets (HELLP) syndrome; thrombotic thrombocytopenic purpura (TTP); spontaneous fetal loss; Pauci-immune vasculitis; epidermolysis bullosa; recurrent fetal loss; multiple sclerosis (MS); traumatic brain injury; and injury resulting from myocardial infarction, cardiopulmonary bypass or hemodialysis; refractory generalized myasthenia gravis (gMG); neuromyelitis optica (NMO).

[0019b]

In another aspect, the present invention refers to use of an anti-C5 antibody in the manufacture of a pharmaceutical composition for treating or preventing a C5-related disease, wherein the composition is formulated for subcutaneous injection, comprises the anti-C5 antibody, and is to be administered subcutaneously, wherein an initial dose of the composition is to be administered after a dose of another pharmaceutical composition is administered intravenously, and wherein the other pharmaceutical composition is formulated for intravenous injection and comprises the anti-C5 antibody; wherein the C5-related disease is any one selected from the group consisting of rheumatoid arthritis (RA); lupus nephritis; ischemia-reperfusion injury; paroxysmal nocturnal hemoglobinuria (PNH); atypical hemolytic uremic syndrome (aHUS); dense deposit disease (DDD); macular degeneration; hemolysis, elevated liver enzymes, and

low platelets (HELLP) syndrome; thrombotic thrombocytopenic purpura (TTP); spontaneous fetal loss; Pauci-immune vasculitis; epidermolysis bullosa; recurrent fetal loss; multiple sclerosis (MS); traumatic brain injury; and injury resulting from myocardial infarction, cardiopulmonary bypass or hemodialysis; refractory generalized myasthenia gravis (gMG); neuromyelitis optica (NMO).

[0019c]

In still another aspect, the present invention refers to use of an anti-C5 antibody in the manufacture of a pharmaceutical composition for treating or preventing a C5-related disease, wherein the composition is formulated for intravenous injection, comprises the anti-C5 antibody, and is to be administered intravenously, wherein a dose of the composition is to be administered before an initial dose of another pharmaceutical composition is administered subcutaneously, wherein the other pharmaceutical composition is formulated for subcutaneous injection and comprises the anti-C5 antibody; wherein the C5-related disease is any one selected from the group consisting of rheumatoid arthritis (RA); lupus nephritis; ischemia-reperfusion injury; paroxysmal nocturnal hemoglobinuria (PNH); atypical hemolytic uremic syndrome (aHUS); dense deposit disease (DDD); macular degeneration; hemolysis, elevated liver enzymes, and low platelets (HELLP) syndrome; thrombotic thrombocytopenic purpura (TTP); spontaneous fetal loss; Pauci-immune vasculitis; epidermolysis bullosa; recurrent fetal loss; multiple sclerosis (MS); traumatic brain injury; and injury resulting from myocardial infarction, cardiopulmonary bypass or hemodialysis; refractory generalized myasthenia gravis (gMG); neuromyelitis optica (NMO).[0020]

The disclosure provides pharmaceutical compositions for use in the treatment or prevention of a C5-related disease and methods for treating or preventing a C5-related

disease. The disclosure also provides dosages and administrations of anti-C5 antibody or pharmaceutical compositions containing the anti-C5 antibody.

[0021]

The inventors of the disclosure investigated effective dosages and administrations of anti-C5 antibody for use in the treatment and/or prevention of C5-related diseases. As a

result, the inventors found that a plasma concentration of anti-C5 antibody rapidly increases to more than a therapeutically efficacious level by intravenously administering the antibody and the concentration is kept at the level by subcutaneously administrating the antibody after the intravenous administration.

[0022]

The inventors also discovered suitable conditions for dosing, including a dose of the antibody, frequency and intervals of the intravenous administrations or subcutaneous administrations, an interval between the intravenous administration and the subcutaneous administration, and switching from other drugs.

[0023]

Specifically, the present disclosure relates to:

[1] A pharmaceutical composition for use in the treatment or prevention of a C5-related disease, wherein the composition is formulated for subcutaneous injection, comprises an anti-C5 antibody, and is administered subcutaneously, wherein the initial dose of the composition is administered after a dose of another pharmaceutical composition is administered intravenously, wherein the other pharmaceutical composition is formulated for intravenous injection and comprises the anti-C5 antibody.

[2] A pharmaceutical composition for use in the treatment or prevention of a C5-related disease, wherein the composition is formulated for intravenous injection, comprises an anti-C5 antibody, and is administered intravenously, wherein a dose of the composition is administered before the initial dose of another pharmaceutical composition is administered subcutaneously, wherein the other pharmaceutical composition is formulated for subcutaneous injection and comprises the anti-C5 antibody.

CLAIMS

[Claim 1]

Use of an anti-C5 antibody in the manufacture of a first and a second pharmaceutical compositions for treating or preventing a C5-related disease, wherein the first pharmaceutical composition is formulated for intravenous injection, comprises the anti-C5 antibody, and is to be administered intravenously, wherein the second pharmaceutical composition is formulated for subcutaneous injection, comprises the anti-C5 antibody, and is to be administered subcutaneously, and wherein administration of the first and the second pharmaceutical compositions is to be carried out in the order of one or more intravenous doses of the first pharmaceutical composition and one or more subcutaneous doses of the second pharmaceutical composition; wherein the C5-related disease is any one selected from the group consisting of rheumatoid arthritis (RA); lupus nephritis; ischemia-reperfusion injury; paroxysmal nocturnal hemoglobinuria (PNH); atypical hemolytic uremic syndrome (aHUS); dense deposit disease (DDD); macular degeneration; hemolysis, elevated liver enzymes, and low platelets (HELLP) syndrome; thrombotic thrombocytopenic purpura (TTP); spontaneous fetal loss; Pauci-immune vasculitis; epidermolysis bullosa; recurrent fetal loss; multiple sclerosis (MS); traumatic brain injury; and injury resulting from myocardial infarction, cardiopulmonary bypass or hemodialysis; refractory generalized myasthenia gravis (gMG); neuromyelitis optica (NMO).

[Claim 2]

Use of an anti-C5 antibody in the manufacture of a pharmaceutical composition for treating or preventing a C5-related disease, wherein the composition is formulated for subcutaneous injection, comprises the anti-C5 antibody, and is to be administered subcutaneously, wherein an initial dose of the composition is to be administered after a dose of another pharmaceutical composition is administered intravenously, and wherein the other pharmaceutical composition is formulated for intravenous injection and comprises the anti-C5 antibody; wherein the C5-related disease is any one selected from the group consisting of rheumatoid arthritis (RA); lupus nephritis; ischemia-reperfusion injury; paroxysmal nocturnal hemoglobinuria (PNH); atypical hemolytic uremic syndrome (aHUS); dense deposit disease (DDD); macular degeneration; hemolysis, elevated liver enzymes, and low platelets (HELLP) syndrome; thrombotic thrombocytopenic purpura (TTP); spontaneous fetal loss; Pauci-immune vasculitis; epidermolysis bullosa; recurrent fetal loss; multiple sclerosis (MS); traumatic brain injury; and injury resulting from myocardial infarction, cardiopulmonary bypass or hemodialysis; refractory generalized myasthenia gravis (gMG); neuromyelitis optica

(NMO).

[Claim 3]

Use of an anti-C5 antibody in the manufacture of a pharmaceutical composition for treating or preventing a C5-related disease, wherein the composition is formulated for intravenous injection, comprises the anti-C5 antibody, and is to be administered intravenously, wherein a dose of the composition is to be administered before an initial dose of another pharmaceutical composition is administered subcutaneously, wherein the other pharmaceutical composition is formulated for subcutaneous injection and comprises the anti-C5 antibody; wherein the C5-related disease is any one selected from the group consisting of rheumatoid arthritis (RA); lupus nephritis; ischemia-reperfusion injury; paroxysmal nocturnal hemoglobinuria (PNH); atypical hemolytic uremic syndrome (aHUS); dense deposit disease (DDD); macular degeneration; hemolysis, elevated liver enzymes, and low platelets (HELLP) syndrome; thrombotic thrombocytopenic purpura (TTP); spontaneous fetal loss; Pauci-immune vasculitis; epidermolysis bullosa; recurrent fetal loss; multiple sclerosis (MS); traumatic brain injury; and injury resulting from myocardial infarction, cardiopulmonary bypass or hemodialysis; refractory generalized myasthenia gravis (gMG); neuromyelitis optica (NMO).

[Claim 4]

The use of any one of claims 1 to 3, wherein an initial dose of the composition for subcutaneous injection is to be administered on the same day as or 1 day to 28 days after the dose of the composition for intravenous injection.

[Claim 5]

The use of any one of claims 1 to 4, wherein the composition for subcutaneous injection is to be given once every 3 to 42 days.

[Claim 6]

The use of any one of claims 1 to 5, wherein the composition for the intravenous injection is to be administered twice or more times and is to be given once an hour to once every 14 days.

[Claim 7]

The use of any one of claims 1 to 6, wherein the composition for subcutaneous injection is to be given at a dose of 17 to 6,000 mg of the antibody.

[Claim 8]

The use of any one of claims 1 to 7, wherein the composition for intravenous injection is to be given at a dose of 50 to 5,000 mg of the antibody.

[Claim 9]

The use of any one of claims 1 to 8, wherein the composition for intravenous injection and the composition for subcutaneous injection are for treating or preventing the C5-related disease in a subject who has been treated with at least one pharmacological product for use in treatment or prevention of the disease, wherein the initial dose of the composition for intravenous injection is to be administered after the final dose of the pharmacological product.

[Claim 10]

The use of claim 9, wherein the initial dose of the composition for intravenous injection is to be administered on the third day or after 3 days after the final dose of the pharmacological product.

[Claim 11]

The use of claim 9 or 10, wherein the pharmacological product comprises an siRNA targeting C5 mRNA, or an anti-C5 antibody which is different from the anti-C5 antibody comprised in the composition.

[Claim 12]

The use of any one of claims 9 to 11, wherein the pharmacological product comprises eculizumab or its derivative.

[Claim 13]

The use of any one of claims 1 to 12, wherein the anti-C5 antibody comprised in the composition for subcutaneous injection and in the composition for intravenous injection comprises a heavy chain variable domain (VH) comprising HVR-H1 comprising the amino acid sequence of SEQ ID NO: 3, HVR-H2 comprising the amino acid sequence of SEQ ID NO: 4, and HVR-H3 comprising the amino acid sequence of SEQ ID NO: 5 and a light chain variable domain (VL) comprising HVR-L1 comprising the amino acid sequence of SEQ ID NO: 7, HVR-L2 comprising the amino acid sequence of SEQ ID NO: 8, and HVR-L3 comprising the amino acid sequence of SEQ ID NO: 9.

[Claim 14]

The use of any one of claims 1 to 13, wherein the anti-C5 antibody comprised in the composition for subcutaneous injection and in the composition for intravenous injection comprises the heavy chain variable domain (VH) consisting of the amino acid sequence of SEQ ID NO: 2 and the light chain variable domain (VL) consisting of the amino acid sequence of SEQ ID NO: 6.