

[Non-patent Document 4] Biochim.Biophys.Acta 871, 268-278 (1986)

[Non-patent Document 5] Nature Medicine 18, 1570-1574(2012)

[Non-patent Document 6] PLOS ONE 8, 1-13(2013)

[Non-patent Document 7] J Thromb Haemost. 12, 206-213(2014)

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Summary

[Problems to be solved by the Disclosure]

10 An objective of the present disclosure is to provide a more effective pharmaceutical composition or a dosage regimen for preventing and/or treating a disease that develops and/or progresses due to a decrease or deficiency in the activity of blood coagulation factor VIII and/or activated blood coagulation factor VIII.

[Means for Solving the Problems]

15 As a result of dedicated research, the present inventors succeeded in discovering a more effective dosage regimen for a pharmaceutical composition containing a bispecific antigen-binding molecule that recognizes blood coagulation factor IX and/or activated blood coagulation factor IX and blood coagulation factor X and/or activated blood coagulation factor X for preventing and/or treating a disease that develops and/or progresses due to a decrease or deficiency in the activity of blood coagulation factor VIII and/or activated blood coagulation factor VIII.

20 In one aspect, the present disclosure refers to the use of a bispecific antigen-binding molecule that recognizes blood coagulation factor IX and/or activated blood coagulation factor IX and blood coagulation factor X and/or activated blood coagulation factor X in the manufacture of a medicament for preventing and/or treating hemophilia A, in a subject in need thereof, wherein in said preventing and/or treating the bispecific antigen-binding molecule is to be administered subcutaneously at an initial dose of 3 mg/kg and is to be continually administered subcutaneously several times at continued doses, each of which is the same as the initial dose, wherein the interval between individual subcutaneous administrations is one week, and wherein the bispecific antigen-binding molecule is the bispecific antibody described below, wherein the first polypeptide and the third polypeptide are associated and the second polypeptide and the fourth polypeptide are associated:

25 a bispecific antibody comprising a first polypeptide which is an H chain comprising the amino acid sequence of SEQ ID NO: 20; a second polypeptide which is an H chain comprising the amino acid sequence of SEQ ID NO: 25; a third polypeptide and a fourth polypeptide which are a commonly shared L chain comprising the amino acid sequence of SEQ ID NO: 32.

35 Specifically, the present disclosure relates to the use of a composition

comprising a bispecific antigen-binding molecule that recognizes blood coagulation factor IX and/or activated blood coagulation factor IX and blood coagulation factor X and/or activated blood coagulation factor X in the manufacture of a medicament for preventing and/or treating a disease that develops and/or progresses due to a decrease or deficiency in the activity of blood coagulation factor VIII and/or activated blood coagulation factor VIII, wherein the antigen-binding molecule is to be administered at an initial dose of approximately 0.001 to 100 mg/kg and is to be continually administered several times at continued doses that are nearly the same as or less than the initial dose, wherein the interval between individual administrations is at least one day or longer. In another example, the present disclosure refers to a product comprising (i) a container; (ii) a pharmaceutical composition in the container, wherein the composition comprises a bispecific antigen-binding molecule that recognizes blood coagulation factor IX and/or activated blood coagulation factor IX and blood coagulation factor X and/or activated blood coagulation factor X; and (iii) a document instructing administration of the antigen-binding molecule at an initial dose of approximately 0.001 to 100 mg/kg and several continued administrations of continued doses that are nearly the same as or less than the initial dose, wherein the interval between individual administrations is at least one day or longer. Also described herein is a pharmaceutical composition or a dosage regimen used for preventing and/or treating a disease that develops and/or progresses due to a decrease or deficiency in the activity of blood coagulation factor VIII and/or activated blood coagulation factor VIII, and specifically relates to the following:

[1] a pharmaceutical composition for use in preventing and/or treating a disease that develops and/or progresses due to a decrease or deficiency in the activity of blood coagulation factor VIII and/or activated blood coagulation factor VIII, wherein the composition comprises a bispecific antigen-binding molecule that recognizes blood coagulation factor IX and/or activated blood coagulation factor IX and blood coagulation factor X and/or activated blood coagulation factor X, wherein the antigen-binding molecule is administered at an initial dose of approximately 0.001 to 100 mg/kg and is continually administered several times at continued doses that are nearly the same as or less than the initial dose, wherein the interval between individual administrations is at least one day or longer;

[2] the pharmaceutical composition of [1], wherein the continued dose is a dose selected from the group consisting of the same dose as the initial dose, and approximately one-half, approximately one-third, approximately 0.3-times, approximately one-fourth, approximately

CLAIMS

1. Use of a bispecific antigen-binding molecule that recognizes blood coagulation factor IX and/or activated blood coagulation factor IX and blood coagulation factor X and/or activated blood coagulation factor X in the manufacture of a medicament for preventing and/or treating hemophilia A, in a subject in need thereof, wherein in said preventing and/or treating the bispecific antigen-binding molecule is to be administered subcutaneously at an initial dose of 3 mg/kg and is to be continually administered subcutaneously several times at continued doses, each of which is the same as the initial dose, wherein the interval between individual subcutaneous administrations is one week, and wherein the bispecific antigen-binding molecule is the bispecific antibody described below, wherein the first polypeptide and the third polypeptide are associated and the second polypeptide and the fourth polypeptide are associated:

a bispecific antibody comprising a first polypeptide which is an H chain comprising the amino acid sequence of SEQ ID NO: 20; a second polypeptide which is an H chain comprising the amino acid sequence of SEQ ID NO: 25; a third polypeptide and a fourth polypeptide which are a commonly shared L chain comprising the amino acid sequence of SEQ ID NO: 32.

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