deficient), could enhance atrial energetics to reduce P-wave duration/dispersion and thereby prevent or treat AF.

An aspect of the invention discloses the use of iron for the reduction of P-wave dispersion/duration for the prevention and treatment of AF where the AF is either paroxysmal, persistent, long-standing, or chronic.

SUMMARY

In one aspect, the present disclosure refers to the use of iron isomaltoside for the manufacture of a medicament for ~~treating iron deficiency in a subject, wherein the treatment of iron deficiency reduces~~reducing the incidence of, or risk for, a cardiovascular adverse event in a~~the~~ subject having iron deficiency, which use comprises that an effective amount of the iron isomaltoside is to be administered, wherein the subject is: (A) a subject being at risk of a cardiovascular adverse event; (B) a subject having a history of congestive heart failure (CHF); or (C) a subject having a history of congestive heart failure (CHF) and being at risk of a cardiovascular adverse event.

~~In another aspect, the present disclosure refers to the use of an iron agent for the manufacture of a medicament for reducing P-wave dispersion/duration for the prevention or treatment of atrial fibrillation (AF) or disorders that predispose to AF in an animal suffering from such a condition which comprises that a therapeutically effective amount of the iron agent is to be administered to such an animal.~~

In one example of this disclosure, iron deficiency is treated in a subject being at risk of a cardiovascular adverse event. Accordingly, subjects are selected for treatment with iron isomaltoside not only based on the criteria commonly used to define eligibility for parenteral iron, i.e. diagnosis of ID or IDA and/or a potential lack of the ability to tolerate or absorb oral iron, but also based on their risk of experiencing a cardiovascular adverse event.

In a second example of this disclosure, the treatment of iron deficiency reduces the incidence of, or risk for, a cardiovascular adverse event in the subject. Accordingly, the subjects that are selected for treatment with iron isomaltoside based on the criteria commonly used to define eligibility for parenteral iron, i.e. diagnosis of ID or IDA and/or a potential lack of the ability to tolerate or absorb oral iron and based on their risk of experiencing a cardiovascular adverse event, benefit from a reduction of the incidence of, or risk for, a cardiovascular adverse event in the subject.

Claims:

1. Use of iron isomaltoside for the manufacture of a medicament for ~~treating iron deficiency in a subject, wherein the treatment of iron deficiency reduces~~reducing the incidence of, or risk for, a cardiovascular adverse event in ~~the~~ a subject having iron deficiency, which use comprises that an effective amount of the iron isomaltoside is to be administered,

wherein the subject is:

(A) a subject being at risk of a cardiovascular adverse event;

(B) a subject having a history of congestive heart failure (CHF); or

(C) a subject having a history of congestive heart failure (CHF) and being at risk of a cardiovascular adverse event.

2. The use of claim 1, wherein the cardiovascular adverse event, the incidence of, or risk for, which reduced is:

(a) selected from the group consisting of congestive heart failure, myocardial infarction, unstable angina, arrhythmia, hypertension, hypotension, stroke, and death;

(b) congestive heart failure;

(c) atrial fibrillation;

(d) hypertension; or

(e) cardiac arrest.

3. The use of claim 1 or claim 2, wherein the subject being at risk of a cardiovascular adverse event is a subject having a history of myocardial infarction (MI), a history of stroke, a history of atrial fibrillation (AF), a history of congestive heart failure (CHF), chronic kidney disease (CKD), a history of hypertension, diabetes, a history of heart valve disorders, a history of obesity, and/or being a smoker, a drinker, and/or an elderly subject.

4~~3~~. The use of any one of claims 1 to 3~~or 2~~, wherein the subject is a subject being at risk of a cardiovascular adverse event, and wherein the cardiovascular adverse event, the incidence of, or risk for, which is reduced, is congestive heart failure.

5~~4~~. The use of any one of claims 1 to 3~~or 2~~, wherein the subject is a subject being at risk of a cardiovascular adverse event, and wherein the cardiovascular adverse event, the incidence of, or risk for, which is reduced, is atrial fibrillation.

65. The use of any one of claims 1 to 3or 2, wherein the subject is a subject being at risk of a cardiovascular adverse event, and wherein the cardiovascular adverse event, the incidence of, or risk for, which is reduced, is cardiac arrest.

76. The use of claim 1 or 2, wherein the subject is a subject having a history of congestive heart failure and the cardiovascular adverse event, the incidence of, or risk for, which is reduced, is cardiac arrest or congestive heart failure or both.

87. The use of claim 1 or 2, wherein the subject is a subject having a history of congestive heart failure (CHF) and the cardiovascular adverse event, the incidence of, or risk for, which is reduced, is atrial fibrillation.

98. The use of claim 1 or 2, wherein the subject is a subject having a history of congestive heart failure (CHF) and the cardiovascular adverse event, the incidence of, or risk for, which is reduced, is cardiac arrest.

109. The use of any one of claims 1 -98, wherein the subject is a subject being at risk of a cardiovascular adverse event and/or having a history of congestive heart failure, wherein the subject has chronic kidney disease (CKD).

110. The use of any one of claims 1 -98, wherein the subject is a subject being at risk of a cardiovascular adverse event and/or having congestive heart failure, wherein the subject does not have chronic kidney disease (CKD).

121. The use of claim 10 or 119 or 10, wherein the chronic kidney disease (CKD) is non-dialysis dependent chronic kidney disease (NDD-CKD).

132. The use of any one of claims 1-3 or 2, or 6-11, wherein the subject having a history of congestive heart failure has HFrEF.

143. The use of any one of claims 1-3 or 2, or 6-12, wherein the subject having a history of congestive heart failure has congestive heart failure in NYHA class II-IV.

154. The use of any one of claims 1-143, wherein the cardiovascular adverse event, the incidence of, or risk for, which is reduced, is cardiovascular death and/or hospitalization due to worsening congestive heart failure.

165. The use of any one of claims 1-154, wherein the iron deficiency is defined as TSAT < 20% and/or ferritin < 100 µg/L.

176. The use of any one of claims 1-165, wherein the iron isomaltoside is ferric derisomaltose.

187. The use of any one of claims 1-176, wherein the subject is also being treated with another agent used to treat or prevent cardiovascular adverse events including but not limited to congestive heart failure (CHF), cardiac arrest, congestive heart failure (CHF), myocardial infarction, unstable angina, arrhythmia, hypertension, hypotension, stroke, and atrial fibrillation.

~~18. Use of an iron agent for the manufacture of a medicament for reducing P-wave dispersion/duration for the prevention or treatment of atrial fibrillation (AF) or disorders that predispose to AF in an animal suffering from such a condition which comprises that a therapeutically effective amount of the iron agent is to be administered to such an animal.~~

~~19. The use of claim 18, wherein said disorders that predispose to AF are selected from heart valve disease, hypertension, heart failure, coronary artery disease, obesity, and diabetes mellitus.~~

~~20. The use of claim 18 or claim 19, wherein said iron agent is an intravenous injection or infusion and said intravenous injection or infusion comprises high molecular weight iron dextran, low molecular weight iron dextran, iron sucrose, ferrous gluconate, ferric carboxymaltose, or iron isomaltoside.~~