for sickle cell disease is stem cell transplantation; however, this is available to a very limited number of patients due to scarcity of matched donors.

Since the mid 90's, an oral medication called Hydroxyurea has been available for prevention of "painful crises". For those who can take this medication on a regular basis, it has improved their quality life immensely. However, it is a medicine that was originally designed for certain types of cancer and has many side effects, including suppression of white blood cells that fight infection, skin ulcers, stomach problems and anemia.

Now it has been found that the present compounds of formulas I and II due to a unique mechanism of action and well-defined dose-dependent effects, may reduce the production of heme and hemoglobin and the absorption of iron in the developing erythroblasts and reticulocytes. This effect offers the opportunity to induce production of microcytic hypochromic cells in diseases which would benefit from a reduction in the intracellular Hb concentration, and to reduce erythropoietic iron absorption in diseases characterized by oxidant damage and increased erythroid uptake of iron.

In all animal studies it was observed that the cellular Hb value (MCH) was reduced dose-dependently, to a maximum of about 20 % at the highest doses, if treated with a compound of formula I or II. In consequence a regenerative micocroytic erythropoisesis developed into a normochromic or hypochromic stage, leading to reduced systemic Hb level in all species tested (mouse, rat, cynomolgus monkey and human).

Therefore, the present compounds of formulas I and II may be useful in the treatment of hematology disorders, in particular for use in sickle cell disease and thalassemia, or for the treatment of the iron overload syndrome, such as hereditary hemochromatosis.

Summary

The object of the embodiments disclosed herein are therefore compounds of formulas I and II as described herein, for use in the treatment of sickle cell disease.

One further object of the embodiments disclosed herein are compounds of formulas I and II for use in the treatment of thalassemia.

One further object of the embodiments disclosed herein are compounds of formulas I and II for use in the treatment of the iron overload syndrome, such as hereditary hemochromatosis.

In one aspect, the disclosure relates to a Glyt1 inhibitor, selected from

[4-(2-fluoro-4-methanesulfonyl-phenyl)-piperazin-1-yl]-(2-isopropoxy-5-methanesulfonyl-phenyl)-methanone

[5-methanesulfonyl-2-(2,2,2-trifluoro-1-methyl-ethoxy)-phenyl]-[4-(5-trifluoromethyl-pyridin-2-yl)-piperazin-1-yl]-methanone

4-isopropoxy-N-methyl-3-[4-(4-trifluoromethyl-phenyl)-piperazine-1-carbonyl]-benzenesulfonamide

[4-(3-fluoro-5-trifluoromethyl-pyridin-2-yl)-piperazin-1-yl]-[5-methanesulfonyl-2-((S)-2,2,2-trifluoro-1-methyl-ethoxy)-phenyl]-methanone

[5-methanesulfonyl-2-((S)-2,2,2-trifluoro-1-methyl-ethoxy)-phenyl]-(3-trifluoromethyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-methanone

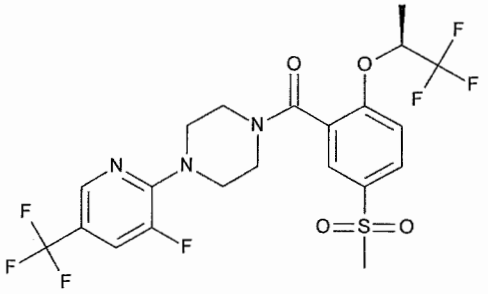
[5-methanesulfonyl-2-((S)-2,2,2-trifluoro-1-methyl-ethoxy)-phenyl]-(6-trifluoromethyl-1,3-dihydro-pyrrolo[3,4-c]pyridin-2-yl)-methanone

or

[5-methanesulfonyl-2-((S)-2,2,2-trifluoro-1-methyl-ethoxy)-phenyl]-(5-methoxy-6-trifluoromethyl-1,3-dihydro-isoindol-2-yl)-methanone

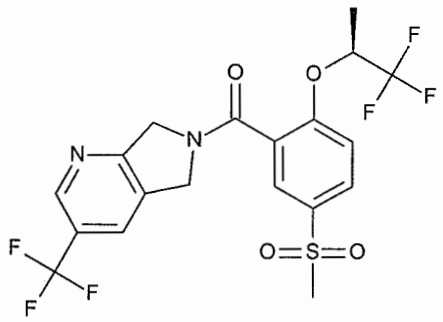
for use in the treatment or prevention of hematological disorders, selected from sickle cell disease, thalassemia and the iron overload syndrome, in particular for the treatment of hereditary hemochromatosis.

One further object of the embodiments disclosed herein is the use of the specific compound of formula I, which compound is



[4-(3-fluoro-5-trifluoromethyl-pyridin-2-yl)-piperazin-1-yl]-[5-methanesulfonyl-2-((S)-2,2,2-trifluoro-1-methyl-ethoxy)-phenyl]-methanone.

One further object of the embodiments disclosed herein is the use of the specific compound of formula II, which compound is



[5-methanesulfonyl-2-((S)-2,2,2-trifluoro-1-methyl-ethoxy)-phenyl]-(3-trifluoromethyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-methanone.

One object of the embodiments disclosed herein relates to a method for the treatment or prevention of hematological disorders, in particular for use in sickle cell disease and thalassemia, or for the treatment of patients with an iron overload syndrome, such as hereditary hemochromatosis, in a subject in need of such treatment, which comprises administering to said subject a therapeutically effective amount of a GlyT1 inhibitor as described herein.

One further object of the embodiments disclosed herein relates to a pharmaceutical composition comprising a GlyT1 inhibitor as described herein in a pharmaceutically acceptable form for the treatment or prevention of hematological disorders, in particular for use in sickle cell disease and thalassemia, or for the treatment of the iron overload syndrome, such as hereditary hemochromatosis.

A further embodiment of the disclosure relates to the use of a GlyT1 inhibitor as described herein for the preparation of medicaments for the treatment or prevention of hematological disorders, in particular for use in sickle cell disease and thalassemia, or for the treatment of patients with an iron overload syndrome, such as hereditary hemochromatosis.