SUMMARY

[0036] The present disclosure relates to methods of preventing or reducing adverse effects in a patient, including by administering acadesine or a prodrug, analog, or salt thereof; or acadesine or a prodrug, analog, or salt thereof and a blood clotting inhibitor. In addition, the disclosure includes pharmaceutical formulations, compositions, cardioplegic solutions, and kits related to preventing or reducing adverse effects in a patient. The disclosure may benefit several types of patients, including a patient with decreased left ventricular function, a patient with a prior myocardial infarction, a patient undergoing non-vascular surgery, or a fetus during labor and delivery.

[0036a] In one aspect, the present disclosure relates to the use of 5-amino-1-β-D-(5-benzylamino-5-deoxy-1-β-D- ribofuranosyl)imidazole-4-carboxamide, 5-amino-1-(5-amino-5-deoxy-β-D- ribofuranosyl)imidazole-4-N-[(4-chlorophenyl)methyl]carboxamide, or a salt thereof, in the manufacture of a medicament for treating a patient with decreased left ventricular function having an ejection fraction that is less than 30%.

INCORPORATION BY REFERENCE

[0037] All publications and patent applications mentioned in this specification are herein incorporated by reference to the same extent as if each individual publication or patent application was specifically and individually indicated to be incorporated by reference.

BRIEF DESCRIPTION OF THE DRAWINGS

[0038] FIG. 1. Metabolic pathways of adenosine.

[0039] FIG. 2. In vitro effect of 48-hour preincubation with AICA riboside on adenosine excretion by human lymphoblasts during ATP breakdown.

[0040] FIG. 3. The effect of AICA riboside treatment on coronary venous adenosine concentrations. Coronary venous blood was collected into chilled 2N perchloric acid at various times before and after coronary artery occlusion. Supernatants from these extracts were neutralized with alamine and freon and evaluated by high performance liquid chromotography. The mean adenosine concentrations +/- standard deviations for the five saline treated ( ) and six AICA riboside treated (.quadrature.) dogs are graph.

[0041] FIG. 4. In vivo effect of AICA riboside on regional myocardial blood flow during coronary artery occlusion in dogs. Regional myocardial blood flow was measured using radiolabelled microspheres infused into the left atrium at 5 minutes (open) and 60 minutes (hatched) of occlusion. The means plus the standard deviations are graphed. The asterisks (*) identify differences from saline-treated dogs that are significant at $p<0.01$.

[0042] FIG. 5. Comparison of the effects of AICA riboside treatment ( ) and control treatment containing only saline (.quadrature.) on inosine levels in dogs.

[0043] FIG. 6. Effects of AICA ribotide and ribavirin ribotide on inhibition of the enzyme AMP deaminase.

[0044] FIG. 7. Effects of 18-hour preincubation with AICA-riboside on adenosine excretion by human lymphoblasts during ATP breakdown.

[0045] FIG. 8. Effect of three-hour preincubation and four-hour incubation with AICA riboside on in vitro adenosine excretion by human lymphoblasts during ATP breakdown.

[0046] FIG. 9. Increased in vitro adenosine release from human lymphoblasts on treatment with ribavirin.

CLAIMS

1. Use of 5-amino-1- β-D-(5-benzylamino-5-deoxy-1-β-D-ribofuranosyl)imidazole-4-carboxamide, 5-amino-1-(5-amino-5-deoxy-β-D-ribofuranosyl)imidazole-4-N-[(4-chlorophenyl)methyl]carboxamide, or a salt thereof, in the manufacture of a medicament for treating a patient with decreased left ventricular function having an ejection fraction that is less than 30%.

2. The use according to claim 1 wherein administration of the medicament provides a blood plasma concentration between 1µg/mL and 20µg/mL.

3. The use according to claim 1 wherein 5-amino-l-β-D-(5- benzylamino-5-deoxy-l-β-D-ribofuranosyl)imidazole-4-carboxamide is used for the manufacture of the medicament.

4. The use according to claim 1 wherein 5-amino-1-(5-amino-5- deoxy- β-D-ribofluranosyl)imidazole-4-N-[(4-chlorophenyl)methyl]carboxamide is used for the manufacture of the medicament.

5. The use according to claim 1 wherein the medicament is to be administered at 0.1mg/kg/minute.