Myelodysplastic syndrome

[0010] A myelodysplastic syndrome (MDS) is a group of symptoms that includes cancer of the blood and bone marrow. Myelodysplastic syndromes (MDS) includes diseases such as, refractory anemia, refractory anemia with excess blasts, refractory cytopenia with multilineage dysplasia, refractory cytopenia with unilineage dysplasia, and chronic myelomonocytic leukemia. The immature blood stem cells (blasts) do not become healthy red blood cells, white blood cells or platelets. The blast die in the bone marrow or soon after they travel to the blood. This leaves less room for healthy white cells, red cells and/or platelets to form in the bone marrow.

[0011] The myelodysplastic syndromes (MDS) are a collection of hematological medical conditions that involve ineffective production of the myeloid class of blood cells. Patients with MDS often develop severe anemia and require frequent blood transfusions. Bleeding and risk of infections also occur due to low or dysfunctional platelets and neutrophils, respectively. In some cases the disease worsens and the patient develops cytopenias (low blood counts) caused by progressive bone marrow failure. In some cases the disease transforms into acute myelogenous leukemia (AML). If the overall percentage of bone marrow myeloblasts rises over a particular cutoff (20% for WHO and 30% for FAB), then transformation to acute myelogenous leukemia (AML) is said to have occurred.

[0012] What is needed, therefore, are new treatments for myelodysplastic proliferative disorders or neoplasm such as ET, PV, MF, CML and AML, and for myelodysplastic syndrome which target the neoplastic progenitor cells responsible for the disease's malignant phenotype, particularly in individuals who are resistant to or experience adverse events as a result of taking commonly prescribed front-line therapies for this disorder.

[0013] Throughout this specification, various patents, patent applications and other types of publications (*e.g.*, journal articles) are referenced. The disclosure of all patents, patent applications, and publications cited herein are hereby incorporated by reference in their entirety for all purposes.

SUMMARY

[0013a] The present disclosure refers to use of a telomerase inhibitor in the manufacture of a medicament for treating myelodysplastic syndrome in an individual, wherein the telomerase inhibitor is imetelstat or a pharmaceutically acceptable salt thereof.

[0014] The disclosure provided herein discloses, *inter alia*, methods for using telomerase inhibitor compounds to treat and alleviate symptoms associated with myeloproliferative

Claims

What is claimed is:

1. Use of a telomerase inhibitor in the manufacture of a medicament for treating myelodysplastic syndrome in an individual, wherein the telomerase inhibitor is imetelstat or a pharmaceutically acceptable salt thereof.

2. The use of claim 1, wherein the myelodysplastic syndrome is selected from the group consisting of refractory anemia, refractory anemia with excess blasts, refractory cytopenia with multilineage dysplasia, refractory cytopenia with unilineage dysplasia, and chronic myelomonocytic leukemia (CMML).

3. The use of claim 2, wherein the myelodysplastic syndrome (MDS) is chronic myelomonocytic leukemia (CMML).

4. The use of claim 1, wherein neoplastic progenitor cell proliferation is reduced by the inhibitor in an individual diagnosed with or suspected of having myelodysplastic syndrome.

5. The use of claim 1, wherein the individual has anemia and requires blood transfusions.

6. The use of any one of claims 1 to 5, wherein the individual carries a V617F gain of function mutation in the Janus kinase 2 (JAK2) gene and the percentage of JAK2 V617F allelic burden is decreased by the telomerase inhibitor in the individual.

7. The use of any one of claims 1 to 6, wherein the individual is resistant or intolerant to a prior non-telomerase inhibitor-based therapy.

8. The use of any one of claims 1 to 7, wherein the medicament is to be used with a pharmaceutically acceptable excipient.

9. The use of any one of claims 1 to 7, wherein the medicament is formulated for oral, intravenous, subcutaneous, intramuscular, topical, intraperitoneal, intranasal, inhalation, or intraocular administration.

10. The use of any one of claims 1 to 7, wherein the effective amount of the telomerase inhibitor is 3.5 mg/kg to 11.7 mg/kg.

11. The use of any one of claims 1 to 7, wherein the effective amount of the telomerase inhibitor is 5 mg/kg to 11.7 mg/kg.

12. The use of any one of claims 1 to 7, wherein the effective amount of the telomerase inhibitor is 6.5 mg/kg to 11.7 mg/kg.

13. The use of any one of claims 1 to 7, wherein the effective amount of the telomerase inhibitor is 7.5 mg/kg to 9.4 mg/kg.

14. The use of any one of claims 1 to 7, wherein the effective amount of the telomerase inhibitor is 9.5 mg/kg to 11.7 mg/kg.

15. The use of any one of claims 1 to 7, wherein the telomerase inhibitor does not inhibit cytokine-dependent megakaryocyte growth.

16. The use of any one of claims 1 to 7, wherein the telomerase inhibitor inhibits cytokine-independent megakaryocyte growth.

17. The use of any one of claims 1 to 7, wherein the telomerase inhibitor inhibits colony-forming unit megakaryocytes (CFU-Mega).

18. The use of claim 17, wherein inhibition of CFU-Mega is independent of reduction in JAK2 allelic burden.

19. The use of any one of claims 1 to 7, wherein the telomerase inhibitor is imetelstat sodium.

20. The use of claim 19, wherein the effective amount of the telomerase inhibitor is 3.5 mg/kg to 11.7 mg/kg.

21. The use of claim 19, wherein the effective amount of the telomerase inhibitor is 5 mg/kg to 11.7 mg/kg.

22. The use of claim 19, wherein the effective amount of the telomerase inhibitor is 6.5 mg/kg to 11.7 mg/kg.

23. The use of claim 19, wherein the effective amount of the telomerase inhibitor is 7.5 mg/kg to 9.4 mg/kg.

24. The use of claim 19, wherein the effective amount of the telomerase inhibitor is 9.5 mg/kg to 11.7 mg/kg.