splenic response was obscured in this study in subjects in either arm. In addition, patients enrolled in this study were not selected based on splenic progression on RUX.

[0016] We have re-analyzed the data from the SIMPLIFY-1 and SIMPLIFY-2 trials and discovered that momelotinib is effective in reducing spleen size (SSR), improving total symptom scores (TSS), and improving transfusion independence rates in patients whose platelet counts are 150 x 10^9 per liter (/L) or below, without momelotinib administration causing thrombocytopenia, and without therefore requiring dose reduction or interruption for thrombocytopenia. Our reanalyses indicate that MMB is effective in JAKi-naïve patients and in patients as a second line therapy to RUX, providing benefits of reducing enlarged spleens and improving myelofibrosis-related symptoms and improving transfusion independence rates in a patient population with or at risk for thrombocytopenia from the underlying disease and from current standard of care.

[0017] Accordingly, this disclosure describes methods of treating myeloproliferative neoplasms (MPN) such as myelofibrosis. In some examples, the method includes administering a therapeutically effective amount of momelotinib or a pharmaceutically acceptable salt thereof to a subject identified as having (i) myelofibrosis and (ii) a platelet count of less than 150 x 10^9/L. Also provided are methods of treating myeloproliferative neoplasms (MPN) such as myelofibrosis that include administering to a subject a therapeutically effective stable dose of momelotinib or a pharmaceutically acceptable salt thereof, for a period of a plurality of weeks, where the subject is assessed as maintaining a platelet count above a predetermined threshold platelet count during the treatment period.

[0017a] In one aspect, the present disclosure refers to use of a therapeutically effective amount of momelotinib or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating myelofibrosis in a subject identified as having (i) myelofibrosis and (ii) a platelet count of less than 150 x 10^9/L.

[0017b] In another aspect, the present disclosure refers to use of a therapeutically effective stable dose of momelotinib or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating myelofibrosis in a subject, for a treatment period of a plurality of weeks, wherein the subject is assessed as maintaining a platelet count above a predetermined threshold platelet count during the treatment period.

BRIEF DESCRIPTION OF THE DRAWINGS

[0018] These and other features, aspects, and advantages of the present disclosure will become better understood with regard to the following description, and accompanying drawings.

[0019] FIG. 1 shows a schematic related to characteristics of myelofibrosis, a chronic myeloproliferative neoplasm (MPN).

[0020] FIG. 2 shows a schematic illustrating three characteristics of disease for myelofibrosis and the proportion of patients who exhibit these manifestations one year after initial diagnosis. See Tefferi A *et al.* Mayo Clin. Proc. 2012; 87:25-33.

[0021] FIG. 3 shows a graph of survival rate over time for myelofibrosis subjects having mild, moderate or severe anemia versus no anemia, indicating anemia is an important prognostic factor. Baseline Anemia: Mild = Hgb ≥ 10 g/dl but below lower limit of normal.

What is claimed is:

1. Use of a therapeutically effective amount of momelotinib or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating myelofibrosis in a subject identified as having (i) myelofibrosis and (ii) a platelet count of less than 150 x 10^9/L.

2. The use of claim 1, wherein the subject is identified as having a platelet count of less than 100 x 10^9/L.

3. The use of claim 2, wherein the subject is identified as having a platelet count of less than 50 x 10^9/L.

4. The use of any one of claims 1 to 3, wherein the platelet count is a baseline platelet count determined within one week prior to initiation of momelotinib therapy, wherein the subject had not been treated with previous JAK inhibitor therapy for at least 2 weeks prior to momelotinib therapy.

5. The use of any one of claims 1 to 4, further comprising the earlier step of determining the level of platelets in a sample of a subject having myelofibrosis.

6. The use of any one of claims 1 to 5, wherein the subject has previously been treated with a JAK inhibitor.

7. The use of claim 6, wherein the subject has previously been treated with ruxolitinib.

8. The use of claim 7, wherein the subject is an adult human who has had an inadequate response to or is intolerant of ruxolitinib.

9. The use of claim 7, wherein the subject failed to respond or ceased to respond to previous ruxolitinib therapy.

10. The use of claim 6, wherein the subject has previously been treated with fedratinib.

11. The use of claim 10, wherein the subject is an adult human who has had an inadequate response to or is intolerant of fedratinib.

12. The use of claim 10, wherein the subject failed to respond or ceased to respond to previous fedratinib therapy.

13. The use of any one of claims 1 to 5, wherein the subject is naïve to JAK inhibitor therapy.

14. The use of any one of claims 1 to 13, wherein the myelofibrosis is intermediate or high-risk myelofibrosis.

15. The use of claim 14, wherein the myelofibrosis is intermediate-2 or high-risk myelofibrosis.

16. The use of any one of claims 1 to 15, wherein the myelofibrosis is primary myelofibrosis (PMF).

17. The use of any one of claims 1 to 15, wherein the myelofibrosis is post-polycythemia vera or post-essential thrombocythemia myelofibrosis (Post-PV/ET MF).

18. The use of any one of claims 1 to 17, wherein the momelotinib or a pharmaceutically acceptable salt thereof is momelotinib dihydrochloride salt.

19. The use of claim 18, wherein the momelotinib or a pharmaceutically acceptable salt thereof is momelotinib dihydrochloride monohydrate.

20. The use of claim 19, wherein the momelotinib or a pharmaceutically acceptable salt thereof is momelotinib dihydrochloride monohydrate Form II.

21. The use of claim 20, wherein the momelotinib dihydrochloride monohydrate Form II is a crystalline form comprising crystals having unit cell parameters at T=100° K of: a=10.2837(6) Å, b=10.4981(6) Å, c=11.5143(7) Å, α=83.297(2)°, β=87.649(2)°, y=67.445(2)°, and a triclinic P-1 space group.

22. The use of claim 20, wherein the momelotinib dihydrochloride monohydrate Form II is characterized by an X-ray powder diffraction (XRPD) pattern substantially as set forth in FIG. 19.

23. The use of claim 20, wherein the momelotinib dihydrochloride monohydrate Form II is characterized by an x-ray powder diffraction (XRPD) pattern as having peaks at about 7.7°, 19.3°, 24.0°, 25.7°, and 29.6° 2-θ ± 0.2° 2-θ.

24. The use of claim 20, wherein the momelotinib dihydrochloride monohydrate Form II is characterized by differential scanning calorimetry (DSC) pattern substantially as set forth in FIG. 22.

25. The use of claim 20, wherein the momelotinib dihydrochloride monohydrate Form II is characterized by a dynamic vapor sorption (DVS) pattern substantially as set forth in FIG. 28.

26. The use of any one of claims 1 to 25, wherein the momelotinib or a pharmaceutically acceptable salt thereof is to be administered orally.

27. The use of any one of claims 1 to 26, wherein the momelotinib or a pharmaceutically acceptable salt thereof is to be administered daily.

28. The use of claim 27, wherein the momelotinib or a pharmaceutically acceptable salt thereof is to be administered once daily.

29. The use of any one of claims 1 to 28, wherein the therapeutically effective amount is between 50 mg/day and 200 mg/day.

30. The use of claim 29, wherein the therapeutically effective amount is 200 mg/day.

31. The use of claim 29, wherein the therapeutically effective amount is 150 mg/day.

32. The use of claim 29, wherein the therapeutically effective amount is 100 mg/day.

33. The use of claim 29, wherein the therapeutically effective amount is 50 mg/day.

34. Use of a therapeutically effective stable dose of momelotinib or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating myelofibrosis in a subject, for a treatment period of a plurality of weeks, wherein the subject is assessed as maintaining a platelet count above a predetermined threshold platelet count during the treatment period.

35. The use of claim 34, wherein the stable dose is 200 mg/day.

36. The use of claim 35, wherein the momelotinib or a pharmaceutically acceptable salt thereof is to be administered orally.

37. The use of claim 35 or 36, wherein the momelotinib or a pharmaceutically acceptable salt thereof is to be administered once daily.

38. The use of any one of claims 34 to 37, wherein the subject was previously treated with a JAK inhibitor.

39. The use of claim 38, wherein the subject has previously been treated with ruxolitinib.

40. The use of claim 39, wherein the subject is an adult human who has had an inadequate response to or is intolerant of ruxolitinib.

41. The use of claim 39, wherein the subject failed to respond or ceased to respond to previous ruxolitinib therapy.

42. The use of claim 38, wherein the subject has previously been treated with fedratinib.

43. The use of claim 42, wherein the subject is an adult human who has had an inadequate response to or is intolerant of fedratinib.

44. The use of claim 42, wherein the subject failed to respond or ceased to respond to previous fedratinib therapy.

45. The use of any one of claims 34 to 37, wherein the subject is naïve to JAK inhibitor therapy.

46. The use of any one of claims 34 to 45, wherein the myelofibrosis is intermediate or high-risk myelofibrosis.

47. The use of claim 46, wherein the myelofibrosis is intermediate-2 or high-risk myelofibrosis.

48. The use of any one of claims 34 to 47, wherein the myelofibrosis is primary myelofibrosis (PMF).

49. The use of any one of claims 34 to 47, wherein the myelofibrosis is post-polycythemia vera or post-essential thrombocythemia myelofibrosis.

50. The use of any one of claims 34 to 49, wherein the momelotinib or a pharmaceutically acceptable salt thereof is momelotinib dihydrochloride salt.

51. The use of claim 50, wherein the momelotinib or a pharmaceutically acceptable salt thereof is momelotinib dihydrochloride monohydrate.

52. The use of claim 51, wherein the momelotinib or a pharmaceutically acceptable salt thereof is momelotinib dihydrochloride monohydrate Form II.

53. The use of claim 52, wherein the momelotinib dihydrochloride monohydrate Form II is a crystalline form comprising crystals having unit cell parameters at T=100° K of: a =10.2837(6) Å, b=10.4981(6) Å, c=11.5143(7) Å, α=83.297(2)°, β=87.649(2)°, y=67.445(2)°, and a triclinic P-1 space group.

54. The use of claim 52, wherein the momelotinib dihydrochloride monohydrate Form II is characterized by an X-ray powder diffraction (XRPD) pattern substantially as set forth in FIG. 19.

55. The use of claim 52, wherein the momelotinib dihydrochloride monohydrate Form II is characterized by an x-ray powder diffraction (XRPD) pattern as having peaks at about 7.7°, 19.3°, 24.0°, 25.7°, and 29.6° 2-θ±0.2° 2-θ.

56. The use of claim 52, wherein the momelotinib dihydrochloride monohydrate Form II is characterized by differential scanning calorimetry (DSC) pattern substantially as set forth in FIG. 22.

57. The use of claim 52, wherein the momelotinib dihydrochloride monohydrate Form II is characterized by a dynamic vapor sorption (DVS) pattern substantially as set forth in FIG. 28.

58. The use of any one of claims 34 to 57, wherein the subject maintains a platelet count above a threshold platelet count of 50 x 10^9/L or more during the treatment period.

59. The use of any one of claims 34 to 57, wherein the subject maintains a platelet count above a threshold platelet count of 100 x 10^9/L or more during the treatment period.

60. The use of any one of claims 34 to 59, wherein the subject maintains a platelet count during the treatment period that is less than 150 x 10^9/L.

61. The use of any one of claims 34 to 59, wherein the subject maintains a platelet count above a threshold platelet count of 150 x 10^9/L or more during the treatment period.

62. The use of claim 61, wherein the subject maintains a platelet count above a threshold platelet count of 200 x 10^9/L or more during the treatment period.

63. The use of claim 61, wherein the subject maintains a platelet count above a threshold platelet count of 250 x 10^9/L or more during the treatment period.

64. The use of any one of claims 34 to 63, wherein the treatment period of a plurality of weeks is 12 weeks or more.

65. The use of claim 64, wherein the treatment period of a plurality of weeks is 24 weeks or more.

66. The use of claim 64, wherein the treatment period of a plurality of weeks is 36 weeks or more.