SUMMARY

[0008] Provided according to examples of the disclosure are methods of treating a disorder in a subject in need thereof that include administering to the subject an effective amount of cedazuridine, an effective amount of decitabine, and an effective amount of venetoclax, thereby treating the disorder in the subject. In some examples of the disclosure, the disorder is a hyperproliferative disorder such as a cancer. In some examples, the disorder is a hematological cancer such as myelodysplastic syndromes (MDS), myeloproliferative neoplasms (MPN), leukemia (e.g., acute myeloid leukemia), or lymphoma. In some examples, the subject is aged 75 years or older and/or has one or more comorbidities that preclude the use of standard induction chemotherapy.

[0008a] In an aspect, there is provided the use of an effective amount of cedazuridine, an effective amount of decitabine, and an effective amount of venetoclax in the manufacture of a medicament for treating a disorder in a subject.

[0008b] In another aspect, there is provided an oral dosage form comprising cedazuridine, decitabine, and venetoclax, and at least one pharmaceutically acceptable excipient.

[0008c] In another aspect, there is provided a medicament comprising an effective amount of venetoclax for use in the treatment of a disorder in a subject, which is to be used in combination with an effective amount of cedazuridine and an effective amount of decitabine simultaneously, separately, or sequentially.

[0008d] In another aspect, there is provided the use of an effective amount of venetoclax in the manufacture of a medicament for the treatment of a disorder in a subject, which is to be used in combination with an effective amount of cedazuridine and an effective amount of decitabine simultaneously, separately, or sequentially.

[0008e] In another aspect, there is provided an effective amount of venetoclax for use of treating a disorder in a subject, characterized in that the venetoclax is to be administered in combination with an effective amount of cedazuridine and an effective amount of decitabine wherein these three medicaments are administered simultaneously, separately, or sequentially.

[0008f] In another aspect, there is provided the use of an effective amount of venetoclax in the manufacture of a medicament for treating a disorder in a subject, characterized in that the venetoclax is to be administered in combination with an effective amount of cedazuridine and an effective amount of decitabine wherein the venetoclax, cedazuridine and decitabine are to be administered simultaneously, separately, or sequentially.

[0008g] In another aspect, there is provided a combination of an effective amount of venetoclax, an effective amount of cedazuridine and an effective amount of decitabine for use in treating a disorder in a subject, wherein these three medicaments are to be administered simultaneously, separately, or sequentially.

[0008h] In another aspect, there is provided the use of a combination of an effective amount of venetoclax, an effective amount of cedazuridine and an effective amount of decitabine in the manufacture of a medicament for treating a disorder in a subject, wherein the venetoclax, cedazuridine and decitabine are to be administered simultaneously, separately, or sequentially.

[0008i] In another aspect, there is provided a pharmaceutical composition comprising an effective amount of venetoclax which is to be used in combination with an effective amount of cedazuridine and an effective amount of decitabine, wherein these three medicaments are to be administered simultaneously, separately, or sequentially, for treating a disorder in a subject.

[0008j] In another aspect, there is provided the use of pharmaceutical composition comprising an effective amount of venetoclax which is to be used in combination with an effective amount of cedazuridine and an effective amount of decitabine in the manufacture of a medicament for treating a disorder in a subject, wherein the venetoclax, cedazuridine and decitabine are to be administered simultaneously, separately, or sequentially.

[0009] In some examples of the disclosure, the effective amount of cedazuridine, the effective amount of decitabine, and the effective amount of venetoclax are administered as a solid oral dosage form. In some examples, the effective amount of cedazuridine and the effective amount of decitabine are administered together in a combination solid oral dosage form. In some examples, the effective amount of cedazuridine and

the effective amount of decitabine are administered on days 1-5 of a 28-day cycle, and the effective amount of venetoclax is administered each day of the 28-day cycle.

[0010] Also provided according to examples of the disclosure is a solid oral dosage form that includes cedazuridine, decitabine, and venetoclax, and at least one pharmaceutically acceptable excipient.

DETAILED DESCRIPTION OF THE INVENTION

[0011] The present invention is explained in greater detail below. This description is not intended to be a detailed catalog of all the different ways in which the invention may be implemented, or all the features that may be added to the instant invention. For example, features illustrated with respect to one embodiment may be incorporated into other embodiments, and features illustrated with respect to a particular embodiment may be deleted from that embodiment. In addition, numerous variations and additions to the various embodiments suggested herein will be apparent to those skilled in the art in light of the instant disclosure which do not depart from the instant invention. Hence, the following specification is intended to illustrate some particular

What is claimed is:

1. Use of an effective amount of cedazuridine, an effective amount of decitabine, and an effective amount of venetoclax in the manufacture of a medicament for treating a disorder in a subject.

2. The use of claim 1, wherein the disorder is a hyperproliferative disorder.

3. The use of claim 2, wherein the disorder is a cancer.

4. The use of claim 3, wherein the cancer is selected from hematological cancers and solid cancers.

5. The use of claim 4, wherein the hematological cancer is selected from at least one of myelodysplastic syndromes (MDS), myeloproliferative neoplasms (MPN), leukemia, and lymphoma.

6. The use of claim 5, wherein the leukemia is ALL, AML, CML, MPN, or CMML.

7. The use of claim 6, wherein the leukemia is AML.

8. The use of any one of claims 1-7, wherein the subject is aged 75 years or older.

9. The use of any one of claims 1-7, wherein the subject has comorbidities that preclude the use of standard induction chemotherapy (e.g., one or more of (i) severe cardiac disorder, (ii) severe pulmonary disorder, (iii) creatinine clearance greater than or equal to 30 mL/min and less than 45 mL/min, and (iv) moderate hepatic impairment with total bilirubin greater than 1.5 and less than or equal to 3.0 x the upper limit of normal (ULN)).

10. The use of any of claims 1-7, wherein the effective amount of cedazuridine, the effective amount of decitabine, and the effective amount of venetoclax are to be administered simultaneously, sequentially, or separately.

11. The use of any one of claims 1-7, wherein the effective amount of cedazuridine, the effective amount of decitabine, and the effective amount of venetoclax are each to be administered as an oral dosage form.

12. The use of claim 11, wherein each oral dosage form is a solid oral dosage form.

13. The use of claim 12, wherein the effective amount of cedazuridine and the effective amount of decitabine are to be administered together in a combination solid oral dosage form.

14. The use of any one of claims 1-7, wherein the effective amount of cedazuridine and the effective amount of decitabine are to be administered on days 1-5 of a 28-day cycle, and the effective amount of venetoclax is to be administered each day of the 28-day cycle.

15. The use of any of claims 1-7, wherein the effective amount of cedazuridine and the effective amount of the decitabine are present in a first solid oral dosage form that comprises 100 mg cedazuridine, 35 mg decitabine, and at least one pharmaceutically acceptable excipient, and wherein the effective amount of venetoclax is present in at least one second solid oral dosage form that comprises 50 mg or 100 mg of venetoclax and at least one pharmaceutically acceptable excipient.

16. The use of any of claims 1-7, wherein the subject is to be administered an effective amount of cedazuridine, an effective amount of decitabine, and 100 mg of venetoclax on day 1 of a cycle; an effective amount of cedazuridine, an effective amount of decitabine, and 200 mg of venetoclax on day 2 of the cycle; an effective amount of cedazuridine, an effective amount of decitabine, and 400 mg of venetoclax on days 3-5 of the cycle; and 400 mg of venetoclax on days 6-28 of the cycle.

17. The use of any of claims 1-7, wherein the subject is to be administered an effective amount of cedazuridine, an effective amount of decitabine, and 400 mg of venetoclax on days 1-5 of a cycle, and 400 mg of venetoclax on days 6-28 of the cycle.

18. An oral dosage form comprising cedazuridine, decitabine, and venetoclax, and at least one pharmaceutically acceptable excipient.

19. The oral dosage form of claim 18, wherein the oral dosage form is a solid oral dosage form.

20. A medicament comprising an effective amount of venetoclax for use in the treatment of a disorder in a subject, which is to be used in combination with an effective amount of cedazuridine and an effective amount of decitabine simultaneously, separately, or sequentially.

21. Use of an effective amount of venetoclax in the manufacture of a medicament for the treatment of a disorder in a subject, which is to be used in combination with an effective amount of cedazuridine and an effective amount of decitabine simultaneously, separately, or sequentially.

22. An effective amount of venetoclax for use of treating a disorder in a subject, characterized in that the venetoclax is to be administered in combination with an effective amount of cedazuridine and an effective amount of decitabine wherein these three medicaments are administered simultaneously, separately, or sequentially.

23. Use of an effective amount of venetoclax in the manufacture of a medicament for treating a disorder in a subject, characterized in that the venetoclax is to be administered in combination with an effective amount of cedazuridine and an effective amount of decitabine wherein the venetoclax, cedazuridine and decitabine are to be administered simultaneously, separately, or sequentially.

24. A combination of an effective amount of venetoclax, an effective amount of cedazuridine and an effective amount of decitabine for use in treating a disorder in a subject, wherein these three medicaments are to be administered simultaneously, separately, or sequentially.

25. Use of a combination of an effective amount of venetoclax, an effective amount of cedazuridine and an effective amount of decitabine in the manufacture of a medicament for treating a disorder in a subject, wherein the venetoclax, cedazuridine and decitabine are to be administered simultaneously, separately, or sequentially.

26. A pharmaceutical composition comprising an effective amount of venetoclax which is to be used in combination with an effective amount of cedazuridine and an effective amount of decitabine, wherein these three medicaments are to be administered simultaneously, separately, or sequentially, for treating a disorder in a subject.

27. A pharmaceutical composition of claim 26, wherein the pharmaceutical composition comprises an effective amount of venetoclax which is to be used in combination with a solid dosage form comprising an effective amount of cedazuridine and an effective amount of decitabine together, wherein both are to be administered simultaneously, separately, or sequentially, for treating a disorder in a subject.

28. Use of pharmaceutical composition comprising an effective amount of venetoclax which is to be used in combination with an effective amount of cedazuridine and an effective amount of decitabine in the manufacture of a medicament for treating a disorder in a subject, wherein the venetoclax, cedazuridine and decitabine are to be administered simultaneously, separately, or sequentially.

29. The use of claim 28, wherein the pharmaceutical composition comprises an effective amount of venetoclax which is to be used in combination with a solid dosage form comprising an effective amount of cedazuridine and an effective amount of decitabine together, wherein both are to be administered simultaneously, separately, or sequentially, for treating a disorder in a subject.