METHODS OF TREATING VIRALLY ASSOCIATED CANCERS WITH HISTONE DEACETYLASE INHIBITORS

CROSS-REFERENCE

[0001] This application claims the benefit of U.S. Provisional Application Ser. No. 62/855,454 filed on May 31, 2019, which is incorporated by reference herein in its entirety.

SUMMARY

[0001a] In one aspect, provided herein is the use of nanatinostat in the manufacture of a first medicament and use of an effective amount of an antiviral agent in the manufacture of a second medicament, wherein the first and second medicaments are to be used in combination therapy to treat an Epstein-Barr virus associated lymphoproliferative disorder in an individual, wherein the nanatinostat is to be administered at a total daily dose from 10 milligrams to 20 milligrams per day, wherein the individual is to be treated according to a treatment schedule having a duration of one week, and wherein the individual is to be administered nanatinostat for 4 days of the treatment schedule.

[0001b] In another aspect, provided herein is the use of nanatinostat in the manufacture of a first medicament and use of valganciclovir in the manufacture of a second medicament, wherein the first and second medicaments are to be used in combination therapy to treat an Epstein-Barr virus associated lymphoproliferative disorder in an individual, wherein the nanatinostat is to be administered at a total daily dose of 20 mg, wherein the valganciclovir is to be administered at a total daily dose of 900 mg, wherein the individual is to be treated according to a weekly treatment schedule, and wherein the individual is to be administered nanatinostat for 4 consecutive days of the treatment schedule, and valganciclovir is to be administered every day of the treatment schedule.

[0002] Described herein are certain dosing schedules and amounts that effectively provide efficacy and prevent and manage side effects associated with treatment of histone deacetylase inhibitor (HDACi) treatment. Optionally, these schedules and dosing regimens include treatment with an antiviral agent.

[0003] Described herein, in one example, is a method of treating a cancer in an individual, the method comprising administering to the individual: (a) an effective amount of a histone deacetylase inhibitor (HDACi) as a viral inducing agent, wherein the HDACi is characterized by an elimination half-life of less than 30 hours; and (b) an effective amount of an antiviral drug; wherein the individual is treated according to a treatment schedule, wherein the individual is administered a lower dosage of the HDACi for at least one dose of the treatment schedule. In

certain examples, the individual is not administered the HDACi for at least one day of the treatment schedule. In certain examples, the HDACi is administered orally. In certain examples, the HDACi is selected from the list consisting of: vorinostat, romidepsin, mocetinostat, belinostat, pracinostat, givinostat, panobinostat, CUDC-101, CDX101, chidamide, domatinostat, and nanatinostat. In certain examples, the HDACi inhibits activity of a class I histone deacetylase. In certain examples, the HDACi is characterized by an elimination half-life of less than 24 hours. In certain examples, the HDACi is characterized by an elimination half-life of less than 12 hours. In certain examples, the HDACi is characterized by an elimination half-life of less than 4 hours. In certain examples, the HDACi is nanatinostat. In certain examples, the HDACi is administered at a total daily dose from about 10 milligrams to about 40 milligrams. In certain examples, the HDACi is administered at a total daily dose of about 10 milligrams. In certain examples, the HDACi is administered at a total daily dose of about 15 milligrams. In certain examples, the HDACi is administered at a total daily dose of about 20 milligrams. In certain examples, the HDACi is administered at a total daily dose of about 25 milligrams. In certain examples, the HDACi is administered at a total daily dose of

CLAIMS

What is claimed is:

1. Use of nanatinostat in the manufacture of a first medicament and use of an effective amount of an antiviral agent in the manufacture of a second medicament, wherein the first and second medicaments are to be used in combination therapy to treat an Epstein-Barr virus associated lymphoproliferative disorder in an individual,
wherein the nanatinostat is to be administered at a total daily dose from 10 milligrams to 20 milligrams per day,
wherein the individual is to be treated according to a treatment schedule having a duration of one week, and
wherein the individual is to be administered nanatinostat for 4 days of the treatment schedule.

2. The use of claim 1, wherein the nanatinostat is to be administered at a total daily dose of 10 milligrams.

3. The use of claim 1, wherein the nanatinostat is to be administered at a total daily dose of 20 milligrams.

4. The use of claim 1, wherein the nanatinostat is to be administered once per day.

5. The use of claim 1, wherein the nanatinostat is to be administered twice per day.

6. The use of claim 1, wherein the antiviral agent is valganciclovir.

7. The use of claim 6, wherein the valganciclovir is to be administered at a total daily dose of 1,800 milligrams.

8. The use of claim 6, wherein the valganciclovir is to be administered at a total daily dose of 900 milligrams.

9. The use of claim 6, wherein the valganciclovir is to be administered at a total daily dose of 450 milligrams.

10. The use of claim 1, wherein the antiviral agent is to be administered every day of the treatment schedule.

11. The use of claim 1, wherein the antiviral agent is not to be administered on one or more days of the treatment schedule.

12. The use of claim 1, wherein the antiviral agent is to be administered once a day.

13. The use of claim 1, wherein the antiviral agent is to be administered twice a day.

14. The use of claim 1, wherein the antiviral agent is to be administered orally.

15. The use of claim 1, wherein the nanatinostat is to be administered orally.

16. The use of claim 1, wherein the treatment schedule is to be repeated.

17. The use of claim 1, wherein the Epstein-Barr virus associated lymphoproliferative disorder is an Epstein-Barr virus associated leukemia or a lymphoma.

18. The use of claim 17, wherein the leukemia or lymphoma is a B cell or a T cell leukemia or lymphoma.

19. The use of claim 1, wherein the individual is afflicted with thrombocytopenia.

20. The use of claim 1, wherein the individual has a platelet count of less than 150,000 platelets per microliter.

21. Use of nanatinostat in the manufacture of a first medicament and use of valganciclovir in the manufacture of a second medicament, wherein the first and second medicaments are to be used in combination therapy to treat an Epstein-Barr virus associated lymphoproliferative disorder in an individual,
wherein the nanatinostat is to be administered at a total daily dose of 20 mg,
wherein the valganciclovir is to be administered at a total daily dose of 900 mg,
wherein the individual is to be treated according to a weekly treatment schedule, and
wherein the individual is to be administered nanatinostat for 4 consecutive days of the treatment schedule, and valganciclovir is to be administered every day of the treatment schedule.

22. The use of claim 21, wherein nanatinostat and valganciclovir are to be administered orally.

23. The use of claim 21, wherein nanatinostat and valganciclovir are each to be administered once a day.

24. The use of claim 21, wherein nanatinostat and valganciclovir are each to be administered twice a day.

25. The use of claim 21, wherein the treatment schedule is to be repeated.