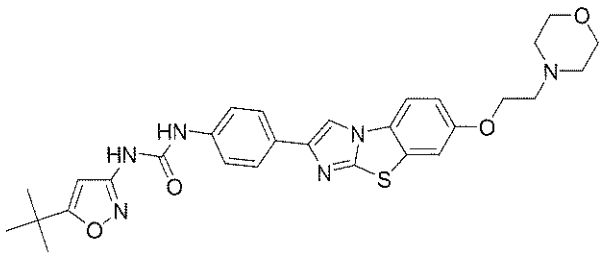
What is claimed is:

1. Use of a compound of formula A



A

or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of a proliferative disease in a mammal, wherein said medicament is to be administered to the mammal having or suspected to have the proliferative disease to deliver the compound of formula A or a pharmaceutically acceptable salt thereof in a dose of about 27 to 1000 mg per day, in combination with a second agent selected from azacitidine, cytarabine, etoposide, daunorubicin, cladribine, wherein azacitidine is to be administered in a dose of 50-100 mg/m^2/day, cytarabine is to be administered intravenously or subcutaneously in a dose of 5 mg/m^2/day-3 g/m^2/day, etoposide is to be administered in a dose of 10-150 mg/m^2/day, and daunorubicin is to be administered in a dose of 10-60 mg/m^2/day.

2. The use of claim 1, wherein the compound of formula A or a pharmaceutically acceptable salt thereof is to be administered in a dose of about 40 to 450 mg per day.

3. The use of claim 1, wherein the compound of formula A or a pharmaceutically acceptable salt thereof is to be administered in a dose of about 27, about 30, about 40, about 60, about 90, about 135, about 200, or about 450 mg per day.

4. The use of claim 1, wherein the compound of formula A, or a pharmaceutically acceptable salt thereof, is to be administered once per day for one week, two weeks, or three weeks.

5. The use of claim 4, wherein the compound of formula A, or a pharmaceutically acceptable salt thereof is to be administered once per day for fourteen days.

6. The use of claim 1, wherein cytarabine is to be administered in a dose of about 100 mg/m^2/day, 200 mg/m^2/day, 750 mg/m^2/day, 1 g/m^2/day or 3 g/m^2/day.

7. The use of claim 20, wherein daunorubicin is to be administered in a dose of about 25, 30, 45, or 60 mg/m^2/day.

8. The use of claim 1, wherein the dose of etoposide is about 35, 50, 100 or 150 mg/m^2/day.

9. The use of claim 1, wherein the compound of formula A, or a pharmaceutically acceptable salt thereof is to be administered once a day for one week, two weeks, three weeks, four weeks or five weeks and etoposide is to be administered once a day for 5 days.

10. The use of claim 1, wherein the compound of formula A, or a pharmaceutically acceptable salt thereof is to be administered once a day for one week, two weeks, three weeks, four weeks or five weeks and etoposide is to be administered once a day on days 1, 3, and 5.

11. The use of claim 1, wherein the compound of formula A, or a pharmaceutically acceptable salt thereof is to be administered once a day for one week, two weeks, three weeks, four weeks or five weeks and cytarabine is to be administered once a day for 7 days.

12. The use of claim 1, wherein the compound of formula A, or a pharmaceutically acceptable salt thereof is to be administered once a day for one week, two weeks, three weeks, four weeks or five weeks and cytarabine is to be administered once a day on days 1, 3 and 5.

13. The use of claim 1, wherein the compound of formula A, or a pharmaceutically acceptable salt thereof is to be administered once a day for one week, two weeks, three weeks, four weeks or five weeks and daunorubicin is to be administered once a day on days 1, 2 and 3.

14. The use of claim 1, wherein the compound of formula A, or a pharmaceutically acceptable salt thereof is to be administered once a day for one week, two weeks, three weeks, four weeks or five weeks, cytarabine is to be administered once a day for 7 days and daunorubicin is to be administered once a day on days 1, 2 and 3.

15. The use of claim 1, wherein the compound of formula A, or a pharmaceutically acceptable salt thereof is to be administered once a day for one week, two weeks, three weeks, four weeks or five weeks and cytarabine is to be administered once a day for 5 days.

16. The use of claim 1, wherein the proliferative disease is cancer.

17. The use of claim 16, wherein the cancer is a leukemia.

18. The use of claim 17, wherein the leukemia is an acute leukemia.

19. The use of claim 17, wherein the leukemia is acute myeloid leukemia.

20. The use of claim 17, wherein the leukemia is promyelocytic leukemia.

21. The use of claim 17, wherein the leukemia is acute lymphoblastic leukemia.

22. The use of claim 17, wherein the leukemia is positive for the FLT3-ITD mutation.

23. The use of claim 17, wherein the leukemia is relapsed or refractory.

24. The use of claim 17, wherein the leukemia is a drug-resistant leukemia.

25. The use of claim 24, wherein the drug-resistant leukemia is resistant to a FLT3 kinase inhibitor.

26. The use of claim 16, wherein the cancer is a solid tumor.

27. The use of claim 26, wherein the cancer is a bladder cancer, breast cancer, cervical cancer, CNS cancer, colon cancer, esophageal cancer, head and neck cancer, liver cancer, lung cancer, nasopharyngeal cancer, neuroendocrine cancer, ovarian cancer, pancreatic cancer, prostate cancer, renal cancer, salivary gland cancer, small cell lung cancer, skin cancer, stomach cancer, testicular cancer, thyroid cancer, uterine cancer, or hematologic malignancy.

28. The use of claim 1, wherein the compound of formula A, or a pharmaceutically acceptable salt thereof is to be administered orally.

29. The use of claim 1, wherein the compound of formula A, or a pharmaceutically acceptable salt thereof is to be administered parenterally.

30. The use of claim 1, wherein the compound of formula A, or a pharmaceutically acceptable salt thereof is to be administered intravenously.

31. The use of claim 1, wherein the dose of the compound is to be administered orally for 14 to 32 days, in combination with cytarabine, wherein cytarabine is to be administered intravenously in a dose of 3 g/m^2/day over three hours for every 12 hours on days 1, 3 and 5.

32. A use of claim 1, wherein the dose of the compound is to be administered orally for 14 to 32 days in a dose of 12 mg/day, 20 mg/day, 25 mg/day, 50 mg/day, 60 mg/day, 75 mg/day, 90 mg/day, 100 mg/day, 125 mg/day, 135 mg/day, 200 mg/day, 225 mg/day, 250 mg/day, or 300 mg/day, in combination with cytarabine which is to be administered intravenously or subcutaneously as follows:

5 mg/m^2/day of cytarabine for 7-25 days,
5 mg/m^2/day of cytarabine for 10-14 days,
10 mg/m^2/day of cytarabine for 7-14 days,
10 mg/m^2/day of cytarabine for 7 days,
10 mg/m^2/day of cytarabine for 10 days,
20 mg/m^2/day of cytarabine for 7 -25 days,
20 mg/m^2/day of cytarabine for 10 -14 days,
20 mg/m^2/day of cytarabine for 10 days,
20 mg/m^2/day of cytarabine for 14 days,
20 mg/m^2/day of cytarabine for 21 days,
5 – 30 mg/m^2/day of cytarabine for 1-4 weeks,
100 mg/m^2/day of cytarabine for 7 days,
150 mg/m^2/day of cytarabine for 7 days,
200 mg/m^2/day of cytarabine for 7 days,
100-200 mg/m^2/day of cytarabine for 7 days,
1 g/m^2/day of cytarabine for 7 days,
1 g/m^2/day of cytarabine for 5 days,
1 g/m^2/day of cytarabine for 4 days,
1 g/m^2/day of cytarabine for 3 days,

1 g/m^2/day of cytarabine for 7 days,

1.5 g/m^2/day of cytarabine for 4 days,

1.5 g/m^2/day of cytarabine for 3 days,

2 g/m^2/day of cytarabine for 3 days,

2 g/m^2/day of cytarabine for 4 days,

2 g/m^2/day of cytarabine for 5 days,

2 g/m^2/day of cytarabine for 6 days,

2 g/m^2/day of cytarabine for 12 doses every 12 hours,

3 g/m^2/day of cytarabine for 3 days,

3 g/m^2/day of cytarabine for 4 days,

3 g/m^2/day of cytarabine for 5 days,

3 g/m^2/day of cytarabine for 6 days,

3 g/m^2 of cytarabine for 12 doses every 12 hours,

3 g/m^2 of cytarabine for 8 doses every 12 hours,

3 g/m^2/day of cytarabine for 6 doses every 12 hours,

3 g/m^2 of cytarabine every 12 hours for days 1, 3 and 5,

3 g/m^2/day of cytarabine for 12 doses every 12 hours,

1 g/m^2 of cytarabine every 12 hours for days 1, 3 and 5,

20 mg/day of cytarabine for 10 days, or

40 mg/day of cytarabine for 10 days.

33. A use of claim 1, wherein the dose of the compound is to be administered orally in combination with cytarabine,

wherein compound of formula A or a pharmaceutically acceptable salt thereof is to be administered as follows:

60 mg/day of a compound of formula (I) or A for 14 days,

60 mg/day of a compound of formula (I) or A for 28 days,

60 mg/day of a compound of formula (I) or A for 14-32 days,

90 mg/day of a compound of formula (I) or A for 14 days,

90 mg/day of a compound of formula (I) or A for 28 days,

90 mg/day of a compound of formula (I) or A for 14-32 days,

135 mg/day of a compound of formula (I) or A for 14 days,

135 mg/day of a compound of formula (I) or A for 28 days,

135 mg/day of a compound of formula (I) or Afor 14-32 days,

200 mg/day of a compound of formula (I) or A for 14 days,

200 mg/day of a compound of formula (I) or A for 28 days,

200 mg/day of a compound of formula (I) or A for 14-32 days,

300 mg/day of a compound of formula (I) or A for 14 days,

300 mg/day of a compound of formula (I) or A for 28 days,

300 mg/day of a compound of formula (I) or A for 14-32 days,

450 mg/day of a compound of formula (I) or A for 14 days,

450 mg/day of a compound of formula (I) or A for 28 days; and

450 mg/day of a compound of formula (I) or A for 14-32 days, and

cytarabine is to be administered intravenously or subcutaneously as follows:

5 mg/m^2/day of cytarabine for 7-25 days,

5 mg/m^2/day of cytarabine for 10-14 days,

10 mg/m^2/day of cytarabine for 7-14 days,

10 mg/m^2/day of cytarabine for 7 days,

10 mg/m^2/day of cytarabine for 10 days,

20 mg/m^2/day of cytarabine for 7 -25 days,

20 mg/m^2/day of cytarabine for 10 -14 days,

20 mg/m^2/day of cytarabine for 10 days,

20 mg/m^2/day of cytarabine for 14 days,

20 mg/m^2/day of cytarabine for 21 days,

5 – 30 mg/m^2/day of cytarabine for 1-4 weeks,

100 mg/m^2/day of cytarabine for 7 days,

150 mg/m^2/day of cytarabine for 7 days,

200 mg/m^2/day of cytarabine for 7 days,

100-200 mg/m^2/day of cytarabine for 7 days,

1 g/m^2/day of cytarabine for 7 days,

1 g/m^2/day of cytarabine for 5 days,

1 g/m^2/day of cytarabine for 4 days,

1 g/m^2/day of cytarabine for 3 days,

1 g/m^2/day of cytarabine for 7 days,

1.5 g/m^2/day of cytarabine for 4 days,

1.5 g/m^2/day of cytarabine for 3 days,

2 g/m^2/day of cytarabine for 3 days,

2 g/m^2/day of cytarabine for 4 days,

2 g/m^2/day of cytarabine for 5 days,
2 g/m^2/day of cytarabine for 6 days,
2 g/m^2/day of cytarabine for 12 doses every 12 hours,
3 g/m^2/day of cytarabine for 3 days,
3 g/m^2/day of cytarabine for 4 days,
3 g/m^2/day of cytarabine for 5 days,
3 g/m^2/day of cytarabine for 6 days,
3 g/m^2 of cytarabine for 12 doses every 12 hours,
3 g/m^2 of cytarabine for 8 doses every 12 hours,
3 g/m^2/day of cytarabine for 6 doses every 12 hours,
3 g/m^2 of cytarabine every 12 hours for days 1, 3 and 5,
3 g/m^2/day of cytarabine for 12 doses every 12 hours,
1 g/m^2 of cytarabine every 12 hours for days 1, 3 and 5,
20 mg/day of cytarabine for 10 days, or
40 mg/day of cytarabine for 10 days.

34. The use of claim 1, wherein the compound is to be administered orally to the mammal for 28 days in a treatment cycle, wherein compound is to be administered in a dose of 60 mg/day, 90 mg/day or 135 mg/day in combination with azacytidine, wherein azacytidine is to be administered in a dose of 75 mg/m^2/day for the first 7 days in the same treatment cycle.

35. The use of any of claims 31-34, wherein the proliferative disease is leukemia, or

the proliferative disease is acute myeloid leukemia, or
the proliferative disease is positive for the FLT3-ITD mutation.

36. The use of any of claims 31-34, wherein the mammal is a patient of 65 years or younger with newly diagnosed acute myeloid leukemia.

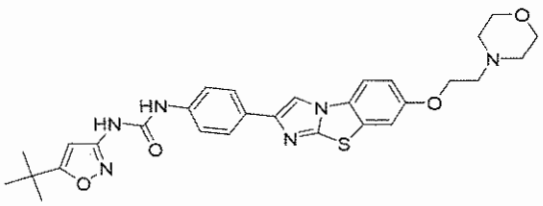
37. The use of any of claims 1 or 31-34, wherein the proliferative disease is hematologic malignancy.

38. The use of claim 38, wherein the hematologic malignancy is myelodysplastic

syndrome.

What is claimed is:

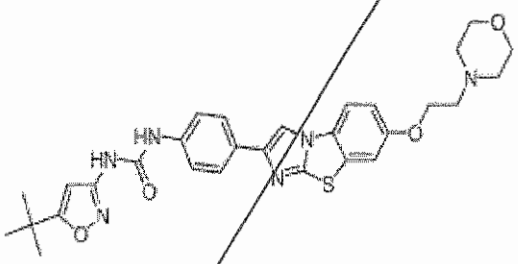
1. Use of a compound of formula A



A

or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for the treatment of a proliferative disease in a mammal, wherein said medicament is to be administered to the mammal having or suspected to have the proliferative disease in combination with a second agent selected from a nucleoside analog, wherein the nucleoside analog is a neoplastic cell antimetabolite; an anthracycline and a topoisomerase inhibitor, or a combination thereof.

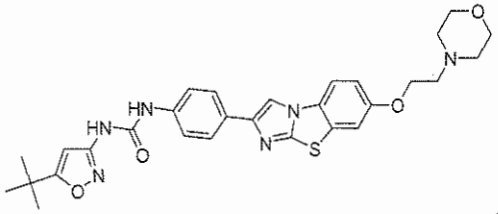
2. Use of a compound of Formula A



A

or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of a proliferative disease in a mammal, wherein said medicament is to be administered the mammal having or suspected to have the proliferative disease in combination with a second agent selected from an anthracycline and a topoisomerase inhibitor.

3. Use of a compound of structural formula A



A

or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of a hematological neoplastic disease, wherein said medicament is to be administered to a patient in need thereof in combination with a nucleoside analog, wherein the nucleoside analog is a neoplastic cell antimetabolite.

4. The use of any of claims 1-3, wherein the compound of formula A or a pharmaceutically acceptable salt thereof is to be administered in a dose of at least 12 mg per day.

5. The use of any of claims1-4, wherein the compound of formula A or a pharmaceutically acceptable salt thereof is to be administered in a dose of about 27 to 1000 mg per day.

6. The use of any of claims1-5, wherein the compound of formula A or a pharmaceutically acceptable salt thereof is administered in a dose of about 40 to 450 mg per day.

7. The use of claim 4, wherein the compound of formula A or a pharmaceutically acceptable salt thereof is to be administered in a dose of about 12, about 18, about 27, about 40, about 60, about 90, about 135, about 200, or about 450 mg per day.

8. The use of claim 4, wherein the compound of formula A, or a pharmaceutically acceptable salt thereof, is to be administered once per day for one week, two weeks, or three weeks.

9. The use of claim 4, wherein the compound of formula A, or a pharmaceutically acceptable salt thereof is to be administered once per day for fourteen days.

10. The use of claim 4, wherein the second agent is a nucleoside analog.

11. The use of claim 10, wherein the nucleoside analog comprises a phosphate moiety.

12. The use of claim11, wherein the nucleoside analog is fludarabine phosphate.

13. The use of claim 10, wherein the nucleoside analog does not comprise a phosphate moiety.

14. The use of claim13, wherein the nucleoside analog is selected from the group consisting of decitabine, azacitidine, clofarabine, cytarabine, cladribine and a combination thereof.

15. The use of claim 10, wherein the nucleoside analog is a DNA methylation inhibitor.

16. The use of claim15, wherein the nucleoside analog is decitabine, azacitidine, or a combination thereof.

17. The use of claim 1, wherein the second agent is selected from etoposide, cytarabine, clofarabine, idarubicin and daunorubicin, or a combination thereof.

18. The useof claim17, wherein cytarabine is to be administered in a dose of about 100 mg/m^2/day, 200 mg/m^2/day, 750 mg/m^2/day, 1 g/m^2/day or 3 g/m^2/day.

19. The use of claim 18 further comprising co-administration of an anthracycline.

20. The use of claim 1, wherein the anthracycline is selected from the group consisting of doxorubicin, daunorubicin, vulrubicin, idarubicin, epirubicin, and a combination thereof.

21. The use of claim20, wherein daunorubicin is administered in a dose of about 25, 30, 45, or 60 mg/m^2/day.

22. The use of claim17, wherein etoposide is to be administered in a dose from about 10 mg/m^2/day to about 150 mg/m^2/day.

23. The use of claim17, wherein the dose of etoposide is about 35, 50, 100 or 150 mg/m /day.

24. The use of claim 22, wherein the compound of formula A, or a pharmaceutically acceptable salt thereof is to be administered once a day for one week, two weeks, three weeks, four weeks or five weeks and etoposide is to be administered once a day for 5 days.

25. The use of claim 22, wherein the compound of formula A, or a pharmaceutically acceptable salt thereof is to be administered once a day for one week, two weeks, three weeks, four weeks or five weeks and etoposide is to be administered once a day on days 1, 3, and 5.

26. The use of claim 17, wherein the compound of formula A, or a pharmaceutically acceptable salt thereof is to be administered once a day for one week, two weeks, three weeks, four weeks or five weeks and cytarabine is to be administered once a day for 7 days.

27. The use of claim 17, wherein the compound of formula A, or a pharmaceutically acceptable salt thereof is to be administered once a day for one week, two weeks, three weeks, four weeks or five weeks and cytarabine is to be administered once a day on days 1, 3 and 5.

28. The use of claim 4, wherein the compound of formula A, or a pharmaceutically acceptable salt thereof is to be administered once a day for one week, two weeks, three weeks, four weeks or five weeks and daunorubicin is to be administered once a day on days 1, 2 and 3.

29. The use of claim 4, wherein the compound of formula A, or a pharmaceutically salt thereof is to be administered once a day for one week, two weeks, three weeks, four weeks or five weeks, cytarabine is administered once a day for 7 days and daunorubicin is to be administered once a day on days 1 , 2 and 3.

30. The use of any of claims 1, wherein the proliferative disease is cancer.

31. The use of claim 30, wherein the cancer is a leukemia.

32. The use of claim 31, wherein the leukemia is an acute leukemia.

33. The use of claim 31, wherein the leukemia is acute myeloid leukemia.

34. The use of claim 31, wherein the leukemia is promyelocytic leukemia.

35. The use of claim31, wherein the leukemia is acute lymphoblastic leukemia.

36. The use of claim31, wherein the leukemia is positive for the FLT3-ITD mutation.

37. The use of claim 31, wherein the leukemia is relapsed or refractory.

38. The use of claim 31, wherein the leukemia is a drug-resistant leukemia.

39. The use of claim 38, wherein the drug-resistant leukemia is resistant to a FLT3 kinase inhibitor.

40. The use of claim 30 , wherein the cancer is a solid tumor.

41. The use of claim 40, wherein the cancer is a bladder cancer, breast cancer, cervical cancer, CNS cancer, colon cancer, esophageal cancer, head and neck cancer, liver cancer, lung cancer, nasopharyngeal cancer, neuroendocrine cancer, ovarian cancer, pancreatic cancer, prostate cancer, renal cancer, salivary gland cancer, small cell lung cancer, skin cancer, stomach cancer, testicular cancer, thyroid cancer, uterine cancer, or hematologic malignancy.

42. The use of claim 1, wherein the compound of formula A, or a pharmaceutically acceptable salt thereof is to be administered orally.

43. The use of claim 1, wherein the compound of formula A, or a pharmaceutically acceptable salt thereof is to be administered parenterally.

44. The use of claim 1, wherein the compound of formula A, or a pharmaceutically acceptable salt thereof is to be administered intravenously.