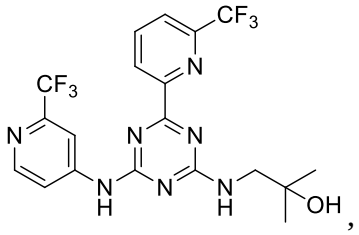
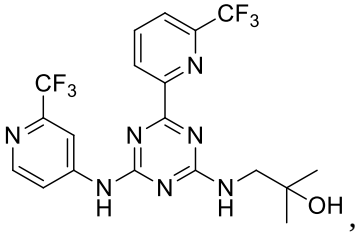
Claims

1. Use of a therapeutically effective amount of a mutant isocitrate dehydrogenase 2 (IDH2) inhibitor in the manufacture of a medicament for treating acute myelogenous leukemia (AML) in the subject, wherein the mutant IDH2 inhibitor is to be administered to the subject with a combination of Cytarabine and Daunorubicin as an induction therapy, and further with Cytarabine as a consolidation therapy, wherein the mutant IDH2 inhibitor is 2-methyl-1-[(4-[6-(trifluoromethyl)pyridin-2-yl]-6-{[2-(trifluoromethyl)pyridin-4-yl]amino}-1,3,5-triazin-2-yl)amino]propan-2-ol, having the following formula:



or a pharmaceutically acceptable salt, solvate, tautomer, stereoisomer, isotopologue, prodrug, metabolite, or a polymorph thereof (COMPOUND 1), and wherein the AML is characterized by the presence of a mutant allele of IDH2.

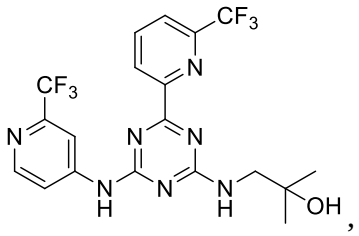
2. Use of a therapeutically effective amount of a mutant IDH2 inhibitor in the manufacture of a medicament for treating AML, comprising administering to a subject, wherein the mutant IDH2 inhibitor is to be administered to the subject with a combination of Cytarabine and Idarubicin as an induction therapy and further with Cytarabine as a consolidation therapy, wherein the mutant IDH2 inhibitor is 2-methyl-1-[(4-[6-(trifluoromethyl)pyridin-2-yl]-6-{[2-(trifluoromethyl)pyridin-4-yl]amino}-1,3,5-triazin-2-yl)amino]propan-2-ol having the following formula:



or a pharmaceutically acceptable salt, solvate, tautomer, stereoisomer, isotopologue, prodrug, metabolite, or a polymorph thereof (COMPOUND 1), and wherein the AML is characterized by the presence of a mutant allele of IDH2.

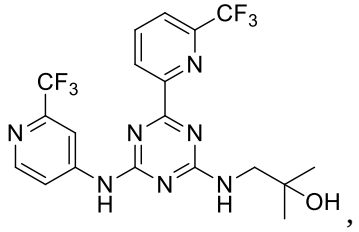
3. Use of a therapeutically effective amount of a mutant IDH2 inhibitor in the manufacture of a medicament for treating AML in a subject, wherein the mutant IDH2 inhibitor is to be administered to the subject with a combination of Cytarabine and Daunorubicin as an

induction therapy, and further with a combination of Mitoxantrone and Etoposide as a consolidation therapy, wherein the mutant IDH2 inhibitor is 2-methyl-1-[(4-[6-(trifluoromethyl)pyridin-2-yl]-6-{[2-(trifluoromethyl)pyridin-4-yl]amino}-1,3,5-triazin-2-yl)amino]propan-2-ol having the following formula:



or a pharmaceutically acceptable salt, solvate, tautomer, stereoisomer, isotopologue, prodrug, metabolite, or a polymorph thereof (COMPOUND 1), and wherein the AML is characterized by the presence of a mutant allele of IDH2.

4. Use of a therapeutically effective amount of a mutant IDH2 inhibitor in the manufacture of a medicament for treating AML in a subject, wherein the mutant IDH2 inhibitor is to be administered to the subject with a combination of Cytarabine and Idarubicin as an induction therapy, and further with a combination of Mitoxantrone and Etoposide as a consolidation therapy, wherein the mutant IDH2 inhibitor is 2-methyl-1-[(4-[6-(trifluoromethyl)pyridin-2-yl]-6-{[2-(trifluoromethyl)pyridin-4-yl]amino}-1,3,5-triazin-2-yl)amino]propan-2-ol having the following formula:



or a pharmaceutically acceptable salt, solvate, tautomer, stereoisomer, isotopologue, prodrug, metabolite, or a polymorph thereof (COMPOUND 1), and wherein the AML is characterized by the presence of a mutant allele of IDH2.

5. The use of any one of claim 1 to 4, wherein the dose of Cytarabine used as an induction therapy is between 100 mg/m^2 and 500 mg/m^2.

6. The use of claim 5, wherein the dose of Cytarabine is between 150 mg/m^2 and 300 mg/m^2.

7. The use of claim 6, wherein the dose of Cytarabine is about 200 mg/m^2.

8. The use of claim 1 or 2, therein the dose of Cytarabine used as a consolidation therapy is between 1 g/m^2 and 10 g/m^2.

9. The use of claim 8, wherein the dose of Cytarabine is between 1 g/m^2 and 5 g/m^2.

10. The use of claim 9, wherein the dose of Cytarabine is 1 g/m^2, or 1,5 g/m^2, or 2 g/m^2, or 3 g/m^2.

11. The use of claim 1 or 3, wherein the dose of Daunorubicin is between 10 mg/m^2 and 300 mg/m^2.

12. The use of claim 11, wherein the dose of Daunorubicin is between 30 mg/m^2 and 150 mg/m^2.

13. The use of claim 12, wherein the dose of Daunorubicin is 60 mg/m^2.

14. The use of claim 2 or 4, wherein the dose of Idarubicin is between 1 mg/m^2 and 25 mg/m^2.

15. The use of claim 14, wherein the dose of Idarubicin is between 3 mg/m^2 and 15 mg/m^2.

16. The use of claim 15, wherein the dose of Idarubicin is about 12 mg/m^2.

17. The use of claim 3 or 4, wherein the dose of Mitoxantrone is between 1 mg/m^2 and 25 mg/m^2.

18. The use of claim 17, wherein the dose of Mitoxantrone is between 5 mg/m^2 and 20 mg/m^2.

19. The use of claim 18, wherein the dose of Mitoxantrone is about 10 mg/m^2.

20. The use of claim 3 or 4, wherein the dose of Etoposide is between 50 mg/m^2 and 500 mg/m^2.

21. The use of claim 20, wherein the dose of Etoposide is between 75 mg/m^2 and 250 mg/m^2.

22. The use of claim 21, wherein the dose of Etoposide is about 100 mg/m^2.

23. Use of a therapeutically effective amount of 2-methyl-1-[(4-[6-(trifluoromethyl)pyridin-2-yl]-6-{[2-(trifluoromethyl)pyridin-4-yl]amino}-1,3,5-triazin-2-yl)amino]propan-2-ol (COMPOUND 1) in the manufacture of a medicament for treating AML characterized by the presence of a mutant allele of IDH2 in a subject, wherein the medicament is to be administered with a combination of Cytarabine and Daunorubicin, wherein Cytarabine is to be administered for 7 days and Daunorubicin is to be administered for 3 days.

24. Use of a therapeutically effective amount of 2-methyl-1-[(4-[6-(trifluoromethyl)pyridin-2-yl]-6-{[2-(trifluoromethyl)pyridin-4-yl]amino}-1,3,5-triazin-2-yl)amino]propan-2-ol (COMPOUND 1) in the manufacture of a medicament for treating AML characterized by the presence of a mutant allele of IDH2 in a subject, wherein the medicament

is to be administered with a combination of Cytarabine and Idarubicin, wherein Cytarabine is to be administered for 7 days and Idarubicin is to be administered for 3 days.

25. The use of any one of claims 1-24, wherein the dose of COMPOUND 1 is between 50 mg/m^2 and 1000 mg/m^2.

26. The use of claim 25, wherein the dose of COMPOUND 1 is between 150 mg/m^2 and 300 mg/m^2.

27. The use of claim 26, wherein the dose of COMPOUND 1 is about 200 mg/m^2.

28. The use of any one of claims 1 to 22, wherein AML is selected from newly diagnosed AML, untreated AML, AML arising from myelodysplastic syndrome, AML arising from antecedent hematologic disorder and AML arising after exposure to genotoxic injury.