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(54) Title: THERAPY FOR LEUKEMIA

(57) Abstract: A pharmaceutically acceptable composition and method for leukemia therapy in a patient in need of such therapy. The composition contains, as the only active agents, the combination of (a) an inhibitor of c-Fos, (b) an inhibitor of Dusp-1, and (c) an inhibitor of BCR-ABL tyrosine kinase. The composition is administered to the patient in a dosing regimen for a period sufficient to provide therapy for leukemia.

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AMENDED CLAIMS
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1. A method of therapy for leukemia in a patient, the method comprising administering to the patient in need thereof a composition containing at least one biocompatible excipient and, as the only active agents, a combination of

(a) an inhibitor of c-Fos,

(b) an inhibitor of Dusp-1 , and

(c) an inhibitor of BCR-ABL tyrosine kinase,

the composition administered to the patient in a dosing regimen for a period sufficient to provide therapy to the patient in need thereof.

2. The method of claim 1 where (a) is an inhibitor of a c-Fos gene, (b) is an inhibitor of a Dusp-1 gene, and (c) is an inhibitor of a BCR-ABL tyrosine kinase gene.

3. The method of claim 1 where (a) is an inhibitor of a c-Fos protein, (b) is an inhibitor of a Dusp-1 protein, and (c) is an inhibitor of a BCR-ABL tyrosine kinase protein.

4. The method of claim 1 where (a) is selected from the group consisting of curcumin, [3-{5-[4-(cyclopentyloxy)-2-hydroxybenzoyl]-2-[(3-hydroxy-1 ,2-benzisoxazol-6-yl) methoxy]phenyl}propionic acid] (T5224), nordihydroguaiaretic acid (NDGA), dihydroguaiaretic acid (DHGA), [(E,E,Z,E)-3-methyl-7-(4-methylphenyl)-9-(2,6,6-trimethyl-1 -cyclohexen-1 -yl)-2,4,6,8-nonatetraenoic acid (SR11302), and combinations thereof; (b) is selected from the group consisting of (EJ-2-benzylidene-3-(cyclohexylamino)-2,3-dihydro-1 H-inden-1 -one (BCI), TPI-2, TPI-3, triptolide, and combinations thereof; and (c) is selected from the group consisting of Imatinib, Nilotinib, Dasatinib, Ponatinib, and combinations thereof.

5. The method of claim 4 where (a) is curcumin, (b) is BCI; and (c) is Imatinib.

6. The method of claim 4 where (a) is NDGA, (b) is BCI; and (c) is Imatinib.

7. The method of claim 4 where (a) is T5224, (b) is BCI; and (c) is Imatinib.

8. The method of claim 1 where (a) is administered at a concentration of 2 grams per day to 8 grams per day, inclusive; (b) is administered at a concentration of 100 mg per day to 600 mg per day, inclusive; and (c) is administered at a concentration of 400 mg per day to 800 mg per day, inclusive.

9. The method of claim 1 where the composition is administered to the patient for 30 days.

10. The method of claim 1 where the composition is administered to the patient intravenously, orally, transdermal^, intramuscularly, and/or intraperitoneally to result in an effective dosing regimen.

11. The method of claim 1 where the composition is administered as a cocktail.

12. The method of claim 1 where the patient has chronic myelogenous leukemia.

13. The method of claim 1 wherein the patient has acute myelogenous leukemia.

14. A pharmaceutically acceptable composition comprising at least one biocompatible excipient and, as the only active agents, Imitinib, (E)-2-benzylidene-3-(cyclohexylamino)-2,3-dihydro-1 H-inden-1 -one (BCI), and curcumin.

15. The composition of claim 14 where the concentration of Imitinib is 400 mg per day to 800 mg per day, inclusive; the concentration of BCI is 100 mg per day to 600 mg per day, inclusive; and the concentration of curcumin is 2 grams per day to 8 grams per day, inclusive.

16. A method of providing therapy to a patient with leukemia comprising administering to the patient with leukemia a composition containing a combination of at least one inhibitor for each of a c-Fos gene and/or protein, a Dusp-1 gene and/or protein, and a BCR-ABL tyrosine kinase gene and/or protein, the composition administered to the patient in a dosing regimen sufficient to eliminate leukemia infiltrating cells from the patient's blood.

17. The method of claim 16 administered to a patient with chronic myelogenous leukemia.

18. The method of claim 16 administered to a patient with acute myelogenous leukemia.

19. A method of treating chronic myelogenous leukemia by preparing a composition for administering to a patient in need thereof, the composition containing as its only active agents at least one of each of at least one inhibitor of a c-Fos gene and/or protein, at least one inhibitor for a Dusp-1 gene and/or protein, and at least one inhibitor for a BCR-ABL tyrosine kinase gene and/or protein; Dusp-1 , c-Fos, and BCR-ABL tyrosine kinase being targets for curative therapy in chronic myelogenous leukemia.

20. The method of claim 19 where the c-Fos inhibitor is selected from the group consisting of curcumin, [3-{5-[4-(cyclopentyloxy)-2-hydroxybenzoyl]-2-[(3-hydroxy-1 ,2-benzisoxazol-6-yl) methoxy]phenyl}propionic acid] (T5224), nordihydroguaiaretic acid (NDGA), dihydroguaiaretic acid (DHGA), [(E,£,Z, E)-3-methyl-7-(4-methylphenyl)-9-(2,6,6-trimethyl-1 -cyclohexen-1 -yl)-2,4,6,8-nonatetraenoic acid (SR1 1302), and combinations thereof; the Dusp-1 inhibitor is selected from the group consisting of ('£j-2-benzylidene-3-(cyclohexylamino)-2,3-dihydro-1 H-inden-1 -one (BCI), TPI-2, TPI-3, triptolide, and combinations thereof; and the BCR-ABL tyrosine kinase inhibitor is selected from the group consisting of Imatinib, Nilotinib, Dasatinib, Ponatinib, and combinations thereof.

21. A pharmaceutically acceptable composition comprising at least one biocompatible excipient and, as the only active agents,

(a) a c-Fos inhibitor selected from the group consisting of curcumin, [3-{5-[4-(cyclopentyloxy)-2-hydroxybenzoyl]-2-[(3-hydroxy-1 ,2-benzisoxazol-6-yl) methoxy]phenyl}propionic acid] (T5224), nordihydroguaiaretic acid (NDGA), dihydroguaiaretic acid (DHGA), and [(E, E,Z, E)-3-methyl-7-(4-methylphenyl)-9-(2,6,6-trimethyl-1 -cyclohexen-1 -yl)-2,4,6,8-nonatetraenoic acid (SR1 1302);

(b) a Dusp-1 inhibitor selected from the group consisting of (E)-2-benzylidene-3-(cyclohexylamino)-2,3-dihydro-1 H-inden-1 -one (BCI - also known as NSC 1501 17), TPI-2, TPI-3, and triptolide; and

(c) a BCR-ABL tyrosine kinase inhibitor selected from the group consisting of Imatinib mesylate (Gleevec™), Nilotinib, Dasatinib and Ponatinib.