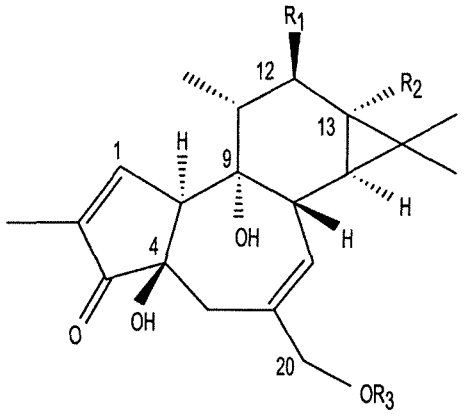
We claim:

1. Use of a phorbol ester of Formula I, or a pharmaceutically-acceptable salt, isomer, enantiomer, solvate, hydrate, or polymorph thereof



FORMULA I

wherein R_1 and R_2 are selected from the group consisting of hydrogen, hydroxyl, —O—C(=O)-alkyl, —O—C(=O)-lower alkenyl, —O—C(=O)-phenyl, and —O—C(=O)-benzyl, R_3 is selected from hydrogen and —C(=O)-lower alkyl; and at least one secondary or adjunctive therapeutic agent that is effective in a combinatorial formulation or coordinate treatment regimen with said phorbol ester of Formula I in the manufacture of a medicament for treating or preventing neoplasms in a mammalian subject who does not have leukemia or lymphoma;

wherein the medicament comprises between about 10 μg to about 1500 μg of said phorbol ester of Formula I, and wherein when administered, the medicament is administered every other day and for at least a total of 5 times.

2. The use of claim 1, wherein R_1 or R_2 is $-O-\overset{O}{\overset{\|}{C}}-C_1-$ C_{15} alkyl the remaining R_1 or R_2 is $-O-\overset{O}{\overset{\|}{C}}$-lower alkyl and R_3 is hydrogen.

3. The use of claim 1, wherein the phorbol ester is phorbol 13-butyrate, phorbol 12-decanoate, phorbol 13-decanoate, phorbol 12,13-diacetate, phorbol 13,20-diacetate, phorbol 12,13-dibenzoal:e, phorbol 12,13-dibutyrate, phorbol 12,13- didecanoate, phorbol 12,13-dihexanoate, phorbol 12,13-dipropionate, phorbol 12-myristate, phorbol 13-myristate, phorbol 12,13,20-triacetate, 12-deoxyphorbol 13-angelate, 12-deoxyphorbol 13-angelate 20-acetate, 12-deoxyphorbol 13-isobutyrate, 12-deoxyphorbol 13-isobutyrate-20-acetate, 12-deoxyphorbol 13-phenylacetate, 12-deoxyphorbol 13-phenylacetate 20-acetate, 12-deoxyphorbol 13-tetradecanoate, phorbol 12-tigliate 13-decanoate, 12-deoxyphorbol 13-acetate, phorbol 12-acetate, or phorbol 13-acetate.

4. The use of claim 1, wherein the phorbol ester is 12-O-tetradecanoylphorbol-13-acetate.

5. The use of claim 1, wherein the at least one secondary or adjunctive therapeutic agent is selected from the group consisting of: doxorubicin, vitamin D3, cytarabine, cytosine arabinoside, daunorubicin, cyclophosphamide, gemtuzumab ozogamicin, idarubicin, mercaptopurine, mitoxantrone, thioguanine, aldesleukin, asparaginase, carboplatin, etoposide phosphate, fludarabine, methotrexate, etoposide, dexamethasone, and choline magnesium trisalicylate.

6. The use of claim 1, wherein two secondary or adjunctive therapeutic agents are used in the manufacture of the medicament.

7. The use of claim 6, wherein the two secondary or adjunctive therapeutic agents are dexamethasone and choline magnesium trisalicylate.

8. The use of claim 1, wherein the medicament comprises between about 150 to 500 μg of said phorbol ester of Formula I.

9. The use of claim 1 wherein the neoplasm is caused by a haematological malignancy/bone marrow disorder.

10. The use of claim 9, wherein the hematological malignancy/bone marrow disorder is leukemia.

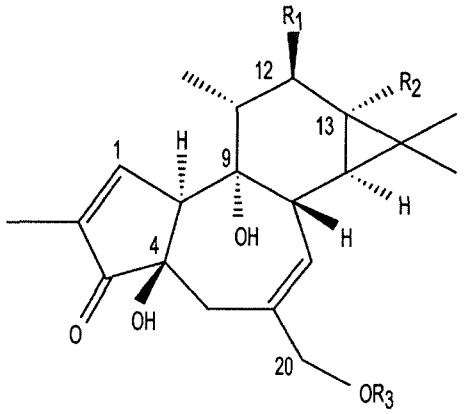
11. The use of claim 10, wherein the leukemia is acute myeloid leukemia.

12. The use of claim 1, wherein the neoplasm is a solid tumor.

13. The use of claim 1, wherein the neoplasm is a relapsing neoplasm.

14. The use of claim 1, wherein the neoplasm is refractory.

15. Use of a phorbol ester of Formula I, or a pharmaceutically-acceptable salt, isomer, enantiomer, solvate, hydrate, or polymorph thereof



FORMULA I

wherein R_1 and R_2 are selected from the group consisting of hydrogen, hydroxyl, —O—C(=O)-alkyl, —O—C(=O)-lower alkenyl, —O—C(=O)-phenyl, and —O—C(=O)-benzyl, R_3 is hydrogen and —C(=O)-lower alkyl; and at least one secondary or adjunctive therapeutic agent that is effective in a combinatorial formulation or coordinate treatment regimen with said phorbol ester of Formula I in the manufacture of a medicament for treating or preventing one or more symptoms or conditions of neoplastic disease in a mammalian subject who does not have leukemia or lymphoma;

wherein the medicament comprises between about 10 μg to about 1500 μg of said phorbol ester of Formula I, and wherein when administered, the medicament is administered every other day for at least a total of 5 times.

16. The use of claim 15, wherein R_1 or R_2 is —O—C(=O)—C_1— C_{15} alkyl the remaining R_1 or R_2 is —O—C(=O)-lower alkyl and R_3 is hydrogen.

17. The use of claim 15, wherein the phorbol ester is phorbol 13-butyrate, phorbol 12-decanoate, phorbol 13-decanoate, phorbol 12,13-diacetate, phorbol 13,20-diacetate, phorbol 12,13-dibenzoate, phorbol 12,13-dibutyrate, phorbol 12,13-didecanoate,

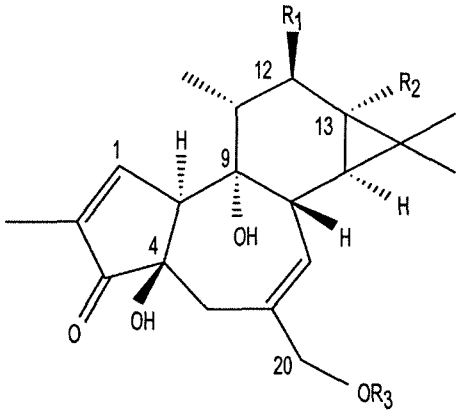
phorbol 12,13-dihexanoate, phorbol 12,13-dipropionatc, phorbol 12-myristate, phorbol 13-myristate, phorbol 12,13,20-triacetate, 12-deoxyphorbol 13-angelate, 12-deoxyphorbol 13-angelate 20-acetate, 12-deoxyphorbol 13-isobutyrate, 12-deoxyphorbol 13-isobutyrate-20-acetate, 12-deoxyphorbol 13-phenylacetate, 12-deoxyphorbol 13-phenylacetate 20-acetate, 12-deoxyphorbol 13-tetradecanoate, phorbol 12-tigliate 13-decanoate, 12-deoxyphorbol 13-acetate, phorbol 12-acetate, or phorbol 13-acetate.

18. The use of claim 15, wherein the phorbol ester is 12-O-tetradecanoylphobol-13-acetate.

19. The use of claim 15, wherein the at least one secondary or adjunctive therapeutic agent is selected from the group consisting of: doxorubicin, vitamin D3, cytarabine, cytosine arabinoside, daunorubicin, cyclophosphamide, gemtuzumab ozogamicin, idarubicin, mercaptopurine, mitoxantrone, thioguanine, aldesleukin, asparaginase, carboplatin, etoposide phosphate, fludarabine, methotrexate, etoposide, dexamethasone, and choline magnesium trisalicylate.

20. The use of claim 18, wherein the one or more symptoms or conditions of neoplastic disease are anemia, chronic fatigue, excessive or easy bleeding, easy bruising, shortness of breath, petechiae, recurrent fever, swollen gums, slow healing of cuts, bone and joint discomfort, recurrent infections, weight loss, itching, night sweats, lymph node swelling, fever, abdominal pain and discomfort, disturbances in vision, coughing, loss of appetite, pain in the chest, difficulty swallowing, swelling, a need to urinate frequently, difficulty starting urination, difficulty holding back urine, weak or interrupted flow of urine, painful or burning urination, difficulty in having an erection, painful ejaculation, blood in urine or semen, frequent pain or stiffness, or weakness.

21. Use of a phorbol ester of Formula I, or a pharmaceutically-acceptable salt, isomer, enantiomer, solvate, hydrate, or polymorph thereof,



FORMULA I

wherein R_1 and R_2 are selected from the group consisting of hydrogen, hydroxyl, —O—C(=O)-alkyl, —O—C(=O)-lower alkenyl, —O—C(=O)-phenyl, and —O—C(=O)-benzyl; R_3 is hydrogen and —C(=O)-lower alkyl; in the manufacture of a medicament for inducing remission in a mammalian subject suffering from neoplastic disease;

wherein the medicament comprises between about 10 μg to about 1500 μg of said phorbol ester of Formula I, and wherein when administered, the medicament is administered for at least a total of 15 times.

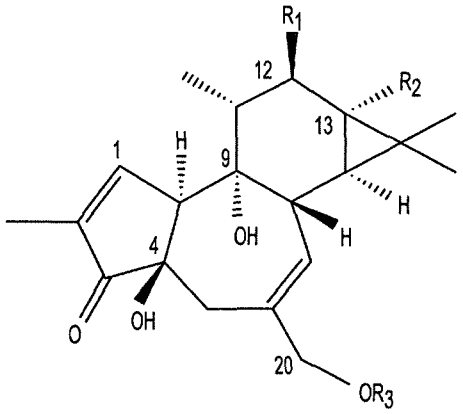
22. The use of claim 21, wherein R_1 or R_2 is —O—C(=O)—C_1— C_{15} alkyl the remaining R_1 or R_2 is —O—C(=O)-lower alkyl and R_3 is hydrogen and at least one secondary or adjunctive therapeutic agent that is effective in a combinatorial formulation or coordinate treatment regimen with said phorbol ester of Formula I to induce remission in said subject.

23. The use of claim 21, wherein the phorbol ester is phorbol 13-butyrate, phorbol 12-decanoate, phorbol 13-decanoate, phorbol 12,13-diacetate., phorbol 13,20-diacetate, phorbol 12,13-dibenzoate, phorbol 12,13-dibutyrate, phorbol 12,13-didecanoate, phorbol 12,13-dihexanoate, phorbol 12,13-dipropionate, phorbol 12-myristate, phorbol 13-myristate, phorbol 12,13,20-triacetate, 12-deoxyphorbol 13-angelate, 12-deoxyphorbol 13-angelate 20-acetate, 12-deoxyphorbol 13-isobutyrate, 12-deoxyphorbol 13-isobutyrate-20-acetate, 12-deoxyphorbol 13-phenylacetate, 12-deoxyphorbol 13-phenylacetate 20-acetate, 12-deoxyphorbol 13-tetradecanoate, phorbol 12-tigliate 13-decanoate, 12-deoxyphorbol 13-acetate, phorbol 12-acetate, or phorbol 13-acetate.

24. The use of claim 21, wherein the phorbol ester is 12-O-tetradecanoylphorbol-13-acetate.

25. The use of claim 21, wherein the at least one secondary or adjunctive therapeutic agent is selected from the group consisting of: doxorubicin, vitamin D3, cytarabine, cytosine arabinoside, daunorubicin, cyclophosphamide, gemtuzumab ozogamicin, idarubicin, mercaptopurine, mitoxantrone, thioguanine, aldesleukin, asparaginase, carboplatin, etoposide phosphate, fludarabine, methotrexate, etoposide, dexamethasone, and choline magnesium trisalicylate.

26. Use a phorbol ester of Formula I, or a pharmaceutically-acceptable salt, isomer, enantiomer, solvate, hydrate, or polymorph thereof,



FORMULA I

wherein R_1 and R_2 are selected from the group consisting of hydrogen, hydroxyl, —O—C(=O)-alkyl, —O—C(=O)-lower alkenyl, —O—C(=O)-phenyl, and —O—C(=O)-benzyl, R_3 is hydrogen and —C(=O)-lower alkyl; and at least one secondary or adjunctive therapeutic agent that is effective in a combinatorial formulation or coordinate treatment regimen with said phorbol ester of Formula I in the manufacture of a medicament for inducing apoptosis in a neoplasm in a mammalian subject suffering from neoplastic disease that is not leukemia or lymphoma;

wherein the medicament comprises between about 10 μg to about 1500 μg of said phorbol ester of Formula I, and wherein when administered, the medicament is administered every other day for at least a total of 5 times.

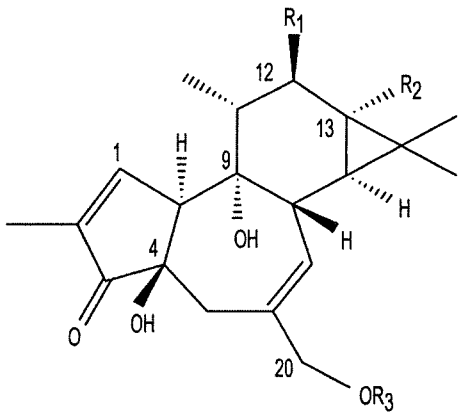
27. The use of claim 26, wherein R_1 or R_2 is —O—C(=O)—C_1— C_{15} alkyl the remaining R_1 or R_2 is —O—C(=O)-lower alkyl and R_3 is hydrogen and at least one secondary or adjunctive therapeutic agent that is effective in a combinatorial formulation or coordinate treatment regimen with said phorbol ester of Formula I to treat or prevent malignancy in said subject.

28. The use of claim 26, wherein the phorbol ester is phorbol 13-butyrate, phorbol 12-decanoate, phorbol 13-decanoate, phorbol 12,13-diacetate, phorbol 13,20-diacetate, phorbol 12,13-dibenzoate, phorbol 12,13-dibutyrate, phorbol 12,13-didecanoate, phorbol 12,13-dihexanoate, phorbol 12,13-dipropionate, phorbol 12-myristate, phorbol 13-rnyristate, phorbol 12,13,20-triacetate, 12-deoxyphorbol 13-angelate, 12-deoxyphorbol 13-angelate 20-acetate, 12-deoxyphorbol 13-isobutyrate, 12-deoxyphorbol 13-isobutyrate-20-acetate, 12-deoxyphorbol 13-phenylacetate, 12-deoxyphorbol 13-phenylacetate 20-acetate, 12-deoxyphorbol 13-tetradecanoate, phorbol 12-tigliate 13-decanoate, 12-deoxyphorbol 13-acetate, phorbol 12-acetate, or phorbol 13-acetate.

29. The use of claim 26, wherein the phorbol ester is 12-O-tetradecanoylphorbol-13-acetate.

30. The use of claim 26, wherein the at least one secondary or adjunctive therapeutic agent is selected from the group consisting of: doxorubicin, vitamin D3, cytarabine, cytosine arabinoside, daunorubicin, cyclophosphamide, gemtuzumab ozogamicin, idarubicin, mercaptopurine, mitoxantrone, thioguanine, aldesleukin, asparaginase, carboplatin, etoposide phosphate, fludarabine, methotrexate, etoposide, dexamethasone, and choline magnesium trisalicylate.

31. Use of a phorbol ester of Formula I, or a pharmaceutically-acceptable salt, isomer, enantiomer, solvate, hydrate, or polymorph thereof



FORMULA I

wherein R_1 and R_2 are selected from the group consisting of hydrogen, hydroxyl, —O—C(=O)-alkyl, —O—C(=O)-lower alkenyl, —O—C(=O)-phenyl, and —O—C(=O)-benzyl, R_3 is hydrogen and —C(=O)-lower alkyl; and at least one secondary or adjunctive therapeutic agent that is effective in a combinatorial formulation with said phorbol ester of Formula I in the manufacture of a medicament for treating or preventing neoplastic disease in a mammalian subject who does not have leukemia or lymphoma;

wherein the medicament comprises between about 10 μg to about 1500 μg of said phorbol ester of Formula I, and when administered, the medicament is administered every other day for at least a total of 5 times.

32. The use of claim 31, wherein R_1 or R_2 is —O—C(=O)—C_1— C_{15} alkyl the remaining R_1 or R_2 is —O—C(=O)-lower alkyl and R_3 is hydrogen.

33. The use of claim 31, wherein the phorbol ester is phorbol 13-butyrate, phorbol 12-decanoate, phorbol 13-decanoate, phorbol 12,13-diacetate, phorbol 13,20-diacetate, phorbol 12,13-dibenzoate, phorbol 12,13-dibutyrate, phorbol 12,13-didecanoate,

phorbol 12,13-dihexanoate, phorbol 12,13-dipropionate, phorbol 12-myristate, phorbol 13-myristate, phorbol 12,13,20-triacetate, 12-deoxyphorbol 13-angelate, 12-deoxyphorbol 13-angelate 20-acetate, 12-deoxyphorbol 13-isobutyrate, 12-deoxyphorbol 13-isobutyrate-20-acetate, 12-deoxyphorbol 13-phenylacetate, 12-deoxyphorbol 13-phenylacetate 20-acetate, 12-deoxyphorbol 13-tetradecanoate, phorbol 12-tigliate 13-decanoate, 12-deoxyphorbol 13-acetate, phorbol 12-acetate, or phorbol 13-acetate.

34. The use of claim 31, wherein the phorbol ester is 12-O-tetradecanoylphorbol-13-acetate.

35. The use of claim 31, wherein the at least one secondary or adjunctive therapeutic agent is selected from the group consisting of: doxorubicin, vitamin D3, cytarabine, cytosine arabinoside, daunorubicin, cyclophosphamide, gemtuzumab ozogamicin, idarubicin, mercaptopurine, mitoxantrone, thioguanine, aldesleukin, asparaginase, carboplatin, etoposide phosphate, fludarabine, methotrexate, etoposide, dexamethasone, and choline magnesium trisalicylate.

36. The use of claim 31, wherein the medicament contains at least two secondary or adjunctive therapeutic agents.

37. The use of claim 36, wherein the at least two secondary or adjunctive therapeutic agents are dexamethasone and choline magnesium trisalicylate.