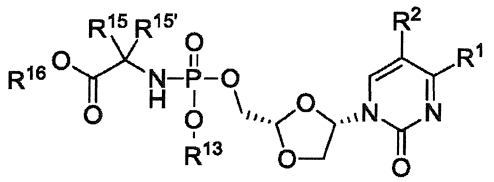
Claims

1. A compound represented by formula I:



(I)

wherein:

R^1 is OR^{11}, or $NR^5R^{5'}$;

R^2 is H or F;

R^5 is H, C_1-C_6alkyl, OH, $C(=O)R^6$, $OC(=O)R^6$ or $OC(=O)OR^6$;

$R^{5'}$ is H or C_1-C_6alkyl;

R^6 is C_1-C_{22}alkyl or C_3-C_7cycloalkyl;

R^{11} is H or C_1-C_6alkyl;

R^{13} is H, phenyl, pyridyl, benzyl, indolyl or naphthyl wherein the phenyl, pyridyl, benzyl, indolyl and naphthyl is optionally substituted with 1, 2 or 3 R^{22};

R^{15} is H, C_1-C_6alkyl, C_3-C_7cycloalkyl, C_3-C_7cycloalkylC_1-C_3alkyl, phenyl, benzyl or indolyl;

$R^{15'}$ is H or C_1-C_6alkyl; or

R^{15} and $R^{15'}$ together with the carbon atom to which they are attached from a C_3-C_7cycloalkylene group, wherein each C_1-C_6alkyl is optionally substituted with a group selected from halo, OR^{18} and SR^{18}, and each C_3-C_7cycloalkyl, C_3-C_7cycloalkylene, phenyl and benzyl is optionally substituted with one or two groups independently selected from C_1-C_3alkyl, halo and OR^{18};

R^{16} is H, C_1-C_{10}alkyl, C_2-C_{10}alkenyl, C_3-C_7cycloalkyl, C_3-C_7cycloalkylC_1-C_3alkyl, benzyl, or phenyl, any of which is optionally substituted with 1, 2 or 3 groups, each independently selected from halo, OR^{18} and $N(R^{18})_2$;

each R^{18} is independently H, C_1-C_6alkyl, C_1-C_6haloalkyl or C_3-C_7cycloalkyl;

each R^{22} is independently selected from halo, C_1-C_6alkyl, C_2-C_6alkenyl, C_1-C_6haloalkyl, C_1-C_6alkoxy, C_1-C_6haloalkoxy, phenyl, hydroxyC_1-C_6alkyl, C_3-C_6cycloalkyl, C_1-C_6alkylcarbonyl, C_3-C_6cycloalkylcarbonyl, carboxyC_1-C_6alkyl, hydroxy, amino CN, and NO_2, or any two R^{22} groups attached to adjacent ring carbon atoms can combine to form $-O-(CR^{23}R^{23'})_{1-6}-O-$;

R^{23} and $R^{23'}$ are independently H or C_1-C_3alkyl;

or a pharmaceutically acceptable salt and/or solvate thereof.

2. The compound according to claim 1, wherein R^1 is NH_2 or $NHC(=O)C_1$-C_6alkyl.

3. A compound according to claim 1, wherein R^1 is NH_2 and R^2 is H.

4. A compound according to any one of claims 1 to 3, wherein $R^{15'}$ is H and R^{15} is C_1-C_3alkyl

5. A compound according to claim 4, wherein R^{15} is methyl.

6. A compound according to any one of claims 1 to 5, wherein R^{16} is C_3-C_{10}alkyl.

7. A compound according to any one of claims 1 to 6, wherein R^{16} is 2-propylpentyl or 2-ethylbutyl.

8. A compound according to any one of claims 1 to 5, wherein R^{16} is benzyl.

9. A compound according to any one of claims 1 to 5, wherein R^{16} is C_3-C_7cycloalky.

10. A compound according to any one of claims 1-9 wherein R^{13} is phenyl or naphthyl, any of which is optionally substituted with one or two R^{22}.

11. A compound according to any one of claims 1-10 wherein R^{13} is phenyl;

12. A compound according to any one of claims 1 to 11, for use as a medicament.

13. A compound according to any one of claims 1 to 11, for use in the treatment of cancer.

14. A compound according to any one of claims 1 to 11, for use in the treatment of liver cancer.

15. A pharmaceutical composition comprising a therapeutically effective amount of a compound according to any one of claims 1 to 11 in association with a pharmaceutically acceptable adjuvant, diluent or carrier.

16. A pharmaceutical composition according to claim 15, for use in the treatment of cancer.

17. The use according to claim 15, wherein the cancer is liver cancer.

18. The use according to claim 15, wherein the cancer is hepatocellular cancer.

19. A pharmaceutical combination comprising a therapeutically effective amount of compound according to any one of claims 1 to 11, further comprising one or more additional therapeutic

agent(s) selected from the group consisting of chemotherapeutical agent, multi-drug resistance reversing agent and biological response modifier.

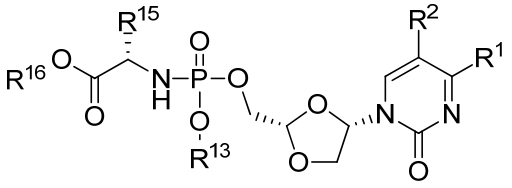
20. The pharmaceutical combination according to claim 19, wherein the further therapeutic agent is a chemotherapeutical agent.

21. A method for the treatment of cancer comprising the administration of a compound according to any one of claims 1 to 11.

22. The use of a compound according to any one of claims 1 to 11 in the manufacture of a medicament for the treatment of cancer.

Claims

1. A compound represented by formula Ia:



(Ia)

wherein:

R^1 is OR^{11}, or $NR^5R^{5'}$;

R^2 is F;

R^5 is H, C_1-C_6alkyl, OH, $C(=O)R^6$, $OC(=O)R^6$ or $OC(=O)OR^6$;

$R^{5'}$ is H or C_1-C_6alkyl;

R^6 is C_1-C_{22}alkyl or C_3-C_7cycloalkyl;

R^{11} is H or C_1-C_6alkyl;

R^{13} is H, phenyl, pyridyl, benzyl, indolyl or naphthyl wherein the phenyl, pyridyl, benzyl, indolyl and naphthyl is optionally substituted with 1, 2 or 3 R^{22};

R^{15} is C_1-C_6alkyl, C_3-C_7cycloalkyl, C_3-C_7cycloalkylC_1-C_3alkyl, phenyl, benzyl or indolyl;

R^{16} is H, C_1-C_{10}alkyl, C_2-C_{10}alkenyl, C_3-C_7cycloalkyl, C_3-C_7cycloalkylC_1-C_3alkyl, benzyl, or phenyl, any of which is optionally substituted with 1, 2 or 3 groups, each independently selected from halo, OR^{18} and $N(R^{18})_2$;

each R^{18} is independently H, C_1-C_6alkyl, C_1-C_6haloalkyl or C_3-C_7cycloalkyl;

each R^{22} is independently selected from halo, C_1-C_6alkyl, C_2-C_6alkenyl, C_1-C_6haloalkyl, C_1-C_6alkoxy, C_1-C_6haloalkoxy, phenyl, hydroxyC_1-C_6alkyl, C_3-C_6cycloalkyl, C_1-C_6alkylcarbonyl, C_3-C_6cycloalkylcarbonyl, carboxyC_1-C_6alkyl, hydroxy, amino, CN, and NO_2, or any two R^{22} groups attached to adjacent ring carbon atoms can combine to form $-O-(CR^{23}R^{23'})_{1-6}-O-$;

R^{23} and $R^{23'}$ are independently H or C_1-C_3alkyl;

or a pharmaceutically acceptable salt and/or solvate thereof.

2. The compound according to claim 1, wherein R^1 is NH_2 or $NHC(=O)C_1$-C_6alkyl.

3. A compound according to claim 1, wherein R^1 is NH_2.

4. A compound according to any one of claims 1 to 3, wherein R^{15} is C_1-C_3alkyl.

5. A compound according to claim 4, wherein R^{15} is methyl.

6. A compound according to any one of claims 1 to 5, wherein R^{16} is C_3-C_{10}alkyl.

7. A compound according to any one of claims 1 to 6, wherein R^{16} is 2-propylpentyl or 2-ethylbutyl.

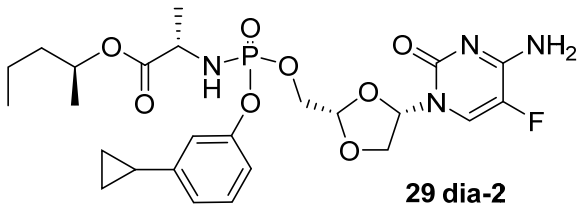
8. A compound according to any one of claims 1 to 5, wherein R^{16} is benzyl.

9. A compound according to any one of claims 1 to 5, wherein R^{16} is C_3-C_7cycloalkyl.

10. A compound according to any one of claims 1-9 wherein R^{13} is phenyl or naphthyl, any of which is optionally substituted with one or two R^{22}.

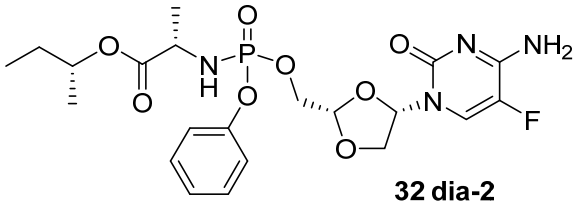
11. A compound according to any one of claims 1-10 wherein R^{13} is phenyl;

12. A compound according to claim 1, which is:



29 dia-2

13. A compound according to claim 1, which is:



32 dia-2

14. A pharmaceutical composition comprising a therapeutically effective amount of a compound according to any one of claims 1 to 13 in association with a pharmaceutically acceptable adjuvant, diluent or carrier.

15. The compound according to any one of claims 1 to 13 for use in the treatment of cancer.