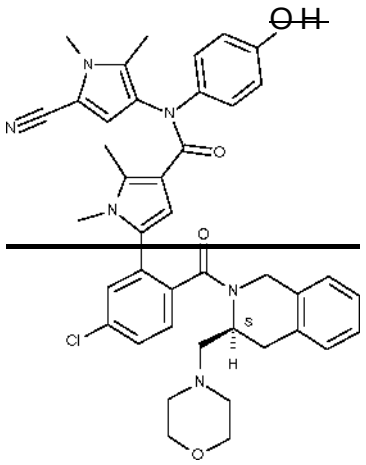
CLAIMS

1. A combination comprising:

(a) a Bcl-2 inhibitor which is 5-(5-chloro-2-{[(3S)-3-(morpholin-4-ylmethyl)-3,4-dihydroisoquinolin-2(1H)-yl]carbonyl}phenyl)-N-(5-cyano-1,2-dimethyl-1H-pyrrol-3-yl)-N-(4-hydroxyphenyl)-1,2-dimethyl-1H-pyrrole-3-carboxamide (Compound A'):



and

(b) a hypomethylating agent selected from decitabine, azacitidine and guadecitabine,

for simultaneous, sequential or separate use.

2. The combination according to claim 1 wherein the hypomethylating agent is azacitidine.

3. The combination according to claim 1 or 2, wherein Compound A is in the form of a hydrogen sulfate salt.

4. The combination according to any one of claims 1 to 3, for use in the treatment of cancer.

5. The combination for use according to claim 4 wherein the cancer is a haematological malignancy.

6. The combination for use according to claim 5 wherein the haematological malignancy is acute myeloid leukemia (AML).

7. The combination for use according to claim 5 wherein the haematological malignancy is myelodysplastic syndromes.

8. The combination for use according to claim 5 wherein the haematological malignancy is lymphoma.

9. The combination for use according to claim 5 wherein the haematological malignancy is chronic lymphocytic leukemia.

10. The combination for use according to claim 5 wherein the haematological malignancy is multiple myeloma.

11. The combination for use according to any one of claims 4 to 10, wherein Compound A and the hypomethylating agent are provided in amounts which are jointly therapeutically effective for the treatment of cancer.

12. The combination for use according to any one of claims 4 to 10, wherein Compound A and the hypomethylating agent are provided in amounts which are synergistically effective for the treatment of cancer.

13. The combination for use according to claim 12, wherein the Compound A and the hypomethylating agent are provided in synergistically effective amounts which enable a reduction of the dose required for each compound in the treatment of cancer, whilst providing an efficacious cancer treatment, with eventually a reduction in side effects.

14. The combination for use according to any one of claims 4 to 13, wherein Compound A is administered parentally, more particularly intravenously.

15. The combination for use according to claim 14, wherein the dose of Compound A per administration is from 25 mg to 1000 mg.

~~16. The combination for use according to claim 15, wherein Compound A is administered once a week.~~

~~17. The combination for use according to claim 16 wherein Compound A and azacitidine are administered during a 28-day cycle as follows:~~

~~(i) Compound A is administered on day 1 (D1), day 8 (D8), day 15 (D15) and day 22 (D22) and,~~

~~(ii) azacitidine is administered according to a 5-2-2 schedule:~~

~~- 5 consecutive days (D1-D5) followed by a 2-day break (D6-D7) and then for 2 days (D8-D9),~~

~~- followed by a rest period of 19 days.~~

~~18. The combination according to any one of claims 1 to 3, further comprising one or more excipients.~~

~~19. The use of a combination according to any one of claims 1 to 3, in the manufacture of a medicament for the treatment of cancer.~~

~~**20.** The use according to claim 19 wherein the cancer is a haematological malignancy.~~

~~21. The use according to claim 20 wherein the haematological malignancy is acute myeloid leukemia (AML).~~

~~22. The use according to claim 20 wherein the haematological malignancy is myelodysplastic syndromes.~~

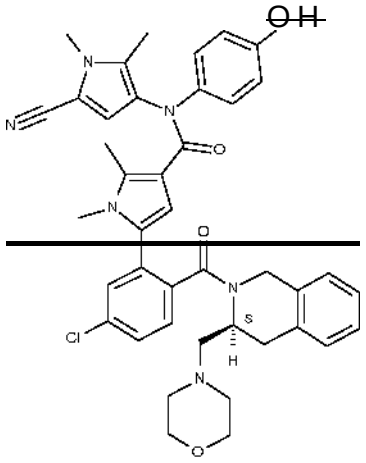
~~23. The use according to claim 20 wherein the haematological malignancy is lymphoma.~~

~~24. The use according to claim 20 wherein the haematological malignancy is chronic lymphocytic leukemia.~~

25. The use according to claim 20 wherein the haematological malignancy is multiple myeloma.

26. A medicament containing, separately or together,

(a) a B-c1-2 inhibitor which is 5-(5-chloro-2-{ [(3S)-3-(morpholin-4-ylmethyl)-3,4-dihydroisoquinolin-2(1H)-yl]carbonyllpheny1)-N-(5-cyano-1,2-dimethyl-1H-pyrrol-3-y1)-N-(4-hydroxypheny1)-1,2-dimethyl-1H-pyrrole-3-carboxamide (Compound A'):



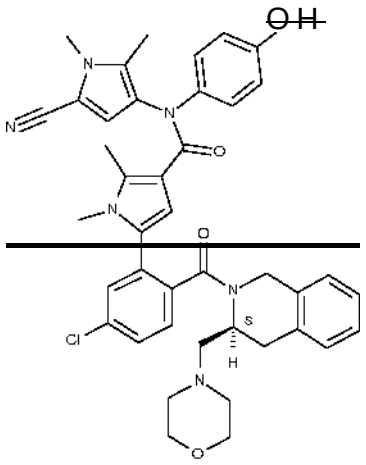
and

(b) a hypomethylating agent, preferably azacitidine,

for simultaneous, sequential or separate administration, and wherein the Compound A and the hypomethylating agent are provided in effective amounts for the treatment of cancer.

27. A method of treating cancer, comprising administering a jointly therapeutically effective amount of:

(a) a B-c1-2 inhibitor which is 5-(5-chloro-2-{ [(3S)-3-(morpholin-4-ylmethyl)-3,4-dihydroisoquinolin-2(1H)-yl]carbonyllpheny1)-N-(5-cyano-1,2-dimethyl-1H-pyrrol-3-y1)-N-(4-hydroxypheny1)-1,2-dimethyl-1H-pyrrole-3-carboxamide (Compound A'):

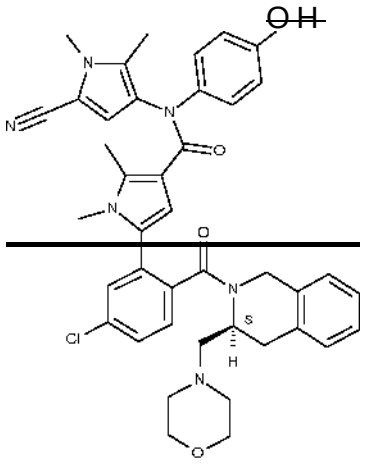


and

(b) a hypomethylating agent,

to a subject in need thereof

28. A method for sensitizing a patient who is (i) refractory to at least one chemotherapy treatment, or (ii) in relapse after treatment with chemotherapy, or both (i) and (ii), wherein the method comprises administering a jointly therapeutically effective amount of 545-chloro-2-{[(3S)-3-(morpholin-4-ylmethyl)-3,4-dihydroisoquinolin-2(1H)-yl]carb onylIpheny1)-N-(5-cyano-1,2-dimethyl-1H-pyrrol-3-yl)-N-(4-hydroxyphenyl)-1,2-(Compound A'):



in combination with a hypomethylating agent, to said patient.

29. The method according to claim 27 or 28 wherein the hypomethylating agent is azacitidine.

~~**30.** The method according to claim 29 wherein Compound A and azacitidine are administered during a 28-day cycle as follows:~~

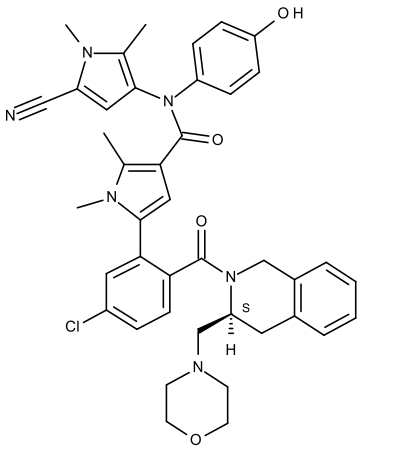
~~(iii) Compound A is administered on day 1 (D1), day 8 (D8), day 15 (D15) and day 22 (D22) and,~~

~~(iv) azacitidine is administered according to a 5-2-2 schedule:~~

- ~~5 consecutive days (D1-135) followed by a 2-day break (D6-D7) and then for 2 days (D8-D9),~~
- ~~followed by a rest period of 19 days.~~

1. A combination comprising:

(a) a Bcl-2 inhibitor which is 5-(5-chloro-2-{[(3*S*)-3-(morpholin-4-ylmethyl)-3,4-dihydroisoquinolin-2(1*H*)-yl]carbonyl}phenyl)-*N*-(5-cyano-1,2-dimethyl-1*H*-pyrrol-3-yl)-*N*-(4-hydroxyphenyl)-1,2-dimethyl-1*H*-pyrrole-3-carboxamide ('Compound A'):



and

(b) a hypomethylating agent selected from decitabine, azacitidine and guadecitabine,

for simultaneous, sequential or separate use.

2. The combination according to claim 1 wherein the hypomethylating agent is azacitidine.

3. The combination according to claim 1 or 2, wherein Compound A is in the form of a hydrogen sulfate salt.

4. The combination according to any one of claims 1 to 3, for use in the treatment of cancer.

5. The combination for use according to claim 4 wherein the cancer is a haematological malignancy.

6. The combination for use according to claim 5 wherein the haematological malignancy is acute myeloid leukemia (AML).

7. The combination for use according to claim 5 wherein the haematological malignancy is myelodysplastic syndromes.

8. The combination for use according to claim 5 wherein the haematological malignancy is lymphoma.

9. The combination for use according to claim 5 wherein the haematological malignancy is chronic lymphocytic leukemia.

10. The combination for use according to claim 5 wherein the haematological malignancy is multiple myeloma.

11. The combination for use according to any one of claims 4 to 10, wherein Compound A and the hypomethylating agent are provided in amounts which are jointly therapeutically effective for the treatment of cancer.

12. The combination for use according to any one of claims 4 to 10, wherein Compound A and the hypomethylating agent are provided in amounts which are synergistically effective for the treatment of cancer.

13. The combination for use according to claim 12, wherein the Compound A and the hypomethylating agent are provided in synergistically effective amounts which enable a reduction

of the dose required for each compound in the treatment of cancer, whilst providing an efficacious cancer treatment, with eventually a reduction in side effects.

14. The combination for use according to any one of claims 4 to 13, wherein Compound A is administered parentally, more particularly intravenously.

15. The combination for use according to claim 14, wherein the dose of Compound A per administration is from 25 mg to 1000 mg.

16. The combination for use according to claim 15, wherein Compound A is administered once a week.

17. The combination for use according to claim 16 wherein Compound A and azacitidine are administered during a 28-day cycle as follows:

(i) Compound A is administered on day 1 (D1), day 8 (D8), day 15 (D15) and day 22 (D22) and,

(ii) azacitidine is administered according to a 5-2-2 schedule:

- 5-consecutive days (D1-D5) followed by a 2-day break (D6-D7) and then for 2 days (D8-D9),
- followed by a rest period of 19 days.

18. The combination for use according to claim 14 wherein Compound A and azacitidine are administered during a 28-day cycle as follows:

(i) Compound A is administered on day 1 (D1), day 3 (D3), day 5 (D5) and day 8 (D8) in the two first weeks of the cycle, wherein the single doses administered on D1, D3, D5 and D8 are identical to each other;

(ii) azacitidine is administered according to a 5-2-2 schedule:

- 5-consecutive days (D1-D5) followed by a 2-day break (D6-D7) and then for 2 days (D8-D9),
- followed by a rest period of 19 days.

19. The combination for use according to claim 14 wherein Compound A and azacitidine are administered during a 28-day cycle as follows:

(i) Compound A is administered on day 1 (D1), day 2 (D2), day 3 (D3), day 4 (D4), day 5 (D5), day 8 (D8) and day 9 (D9) in the two first weeks of the cycle, wherein the single doses administered on D1, D2, D3, D4, D5, D8 and D9 are identical to each other;

(ii) azacitidine is administered according to a 5-2-2 schedule:

- 5-consecutive days (D1-D5) followed by a 2-day break (D6-D7) and then for 2 days (D8-D9),
- followed by a rest period of 19 days.

20. The combination according to any one of claims 1 to 3, further comprising one or more excipients.

21. The use of a combination according to any one of claims 1 to 3, in the manufacture of a medicament for the treatment of cancer.

22. The use according to claim 21 wherein the cancer is a haematological malignancy.

23. The use according to claim 22 wherein the haematological malignancy is acute myeloid leukemia (AML).

24. The use according to claim 22 wherein the haematological malignancy is myelodysplastic syndromes.

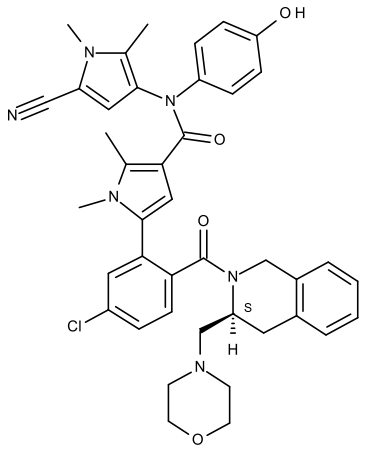
25. The use according to claim 22 wherein the haematological malignancy is lymphoma.

26. The use according to claim 22 wherein the haematological malignancy is chronic lymphocytic leukemia.

27. The use according to claim 22 wherein the haematological malignancy is multiple myeloma.

28. A medicament containing, separately or together,

(a) a Bcl-2 inhibitor which is 5-(5-chloro-2-{[(3*S*)-3-(morpholin-4-ylmethyl)-3,4-dihydroisoquinolin-2(1*H*)-yl]carbonyl}phenyl)-*N*-(5-cyano-1,2-dimethyl-1*H*-pyrrol-3-yl)-*N*-(4-hydroxyphenyl)-1,2-dimethyl-1*H*-pyrrole-3-carboxamide ('Compound A'):

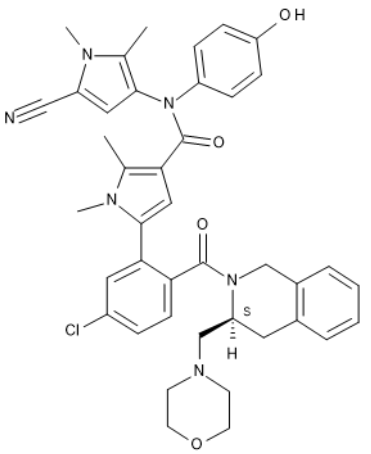


and

(b) a hypomethylating agent, preferably azacitidine,

for simultaneous, sequential or separate administration, and wherein the Compound A and the hypomethylating agent are provided in effective amounts for the treatment of cancer.

29. 5-(5-chloro-2-{[(3*S*)-3-(morpholin-4-ylmethyl)-3,4-dihydroisoquinolin-2(1*H*)-yl]carbonyl}phenyl)-*N*-(5-cyano-1,2-dimethyl-1*H*-pyrrol-3-yl)-*N*-(4-hydroxyphenyl)-1,2-dimethyl-1*H*-pyrrole-3-carboxamide ('Compound A'):



in combination with a hypomethylating agent for use for sensitizing a patient who is (i) refractory to at least one chemotherapy treatment, or (ii) in relapse after treatment with chemotherapy, wherein the compounds of the combination are administered in jointly therapeutically effective amounts.

30. 5-(5-chloro-2-{[(3*S*)-3-(morpholin-4-ylmethyl)-3,4-dihydroisoquinolin-2(1*H*)-yl]carbonyl}phenyl)-*N*-(5-cyano-1,2-dimethyl-1*H*-pyrrol-3-yl)-*N*-(4-hydroxyphenyl)-1,2-dimethyl-1*H*-pyrrole-3-carboxamide ('Compound A') in combination with a hypomethylating agent for use according to claim 29, wherein the hypomethylating agent is azacitidine.

31. 5-(5-chloro-2-{[(3*S*)-3-(morpholin-4-ylmethyl)-3,4-dihydroisoquinolin-2(1*H*)-yl]carbonyl}phenyl)-*N*-(5-cyano-1,2-dimethyl-1*H*-pyrrol-3-yl)-*N*-(4-hydroxyphenyl)-1,2-dimethyl-1*H*-pyrrole-3-carboxamide ('Compound A') in combination with azacitidine for use according to claim 30, wherein Compound A and azacitidine are administered during a 28-day cycle as follows:

(i) Compound A is administered on day 1 (D1), day 8 (D8), day 15 (D15) and day 22 (D22) and,

(ii) azacitidine is administered according to a 5-2-2 schedule:

- 5-consecutive days (D1-D5) followed by a 2-day break (D6-D7) and then for 2 days (D8-D9),
- followed by a rest period of 19 days.

32. 5-(5-chloro-2-{[(3*S*)-3-(morpholin-4-ylmethyl)-3,4-dihydroisoquinolin-2(1*H*)-yl]carbonyl}phenyl)-*N*-(5-cyano-1,2-dimethyl-1*H*-pyrrol-3-yl)-*N*-(4-hydroxyphenyl)-1,2-dimethyl-1*H*-pyrrole-3-carboxamide ('Compound A') in combination with azacitidine for use according to claim 30, wherein Compound A and azacitidine are administered during a 28-day cycle as follows:

(i) Compound A is administered on day 1 (D1), day 3 (D3), day 5 (D5) and day 8 (D8) in the two first weeks of the cycle, wherein the single doses administered on D1, D3, D5 and D8 are identical to each other;

(ii) azacitidine is administered according to a 5-2-2 schedule:

- 5-consecutive days (D1-D5) followed by a 2-day break (D6-D7) and then for 2 days (D8-D9),

- followed by a rest period of 19 days.

33. 5-(5-chloro-2-{[(3*S*)-3-(morpholin-4-ylmethyl)-3,4-dihydroisoquinolin-2(1*H*)-yl]carbonyl}phenyl)-*N*-(5-cyano-1,2-dimethyl-1*H*-pyrrol-3-yl)-*N*-(4-hydroxyphenyl)-1,2-dimethyl-1*H*-pyrrole-3-carboxamide ('Compound A') in combination with azacitidine for use according to claim 30, wherein Compound A and azacitidine are administered during a 28-day cycle as follows:

(i) Compound A is administered on day 1 (D1), day 2 (D2), day 3 (D3), day 4 (D4), day 5 (D5), day 8 (D8) and day 9 (D9) in the two first weeks of the cycle, wherein the single doses administered on D1, D2, D3, D4, D5, D8 and D9 are identical to each other;

(ii) azacitidine is administered according to a 5-2-2 schedule:

- 5-consecutive days (D1-D5) followed by a 2-day break (D6-D7) and then for 2 days (D8-D9),
- followed by a rest period of 19 days.