

What is claimed is:

1. A method of treating a patient having cancer, comprising administering to a patient with a cancer identified as having a reduced cyclin dependent kinase inhibitor 1A (CDKN1A) activity as compared to CDKN1A activity in control tissue or cell a therapeutically effective amount of an ATR inhibitor to sensitize the cancer to a DNA damaging agent.
2. The method of claim 1, further comprising administering to the patient a therapeutically effective amount of a DNA damaging agent.
3. The method of any one of claims 1 to 2, wherein the cancer having a reduced CDKN1A activity is characterized by a synergistic growth inhibition response to the ATR inhibitor and the DNA damaging agent.
4. The method of any one of claims 1 to 3, wherein the identifying is by:
measuring the level of cyclin dependent kinase inhibitor 1A (CDKN1A) activity in the cancer; and
comparing the measured CDKN1A activity to CDKN1A activity in a control tissue or cell.
5. The method of any one of claims 1 to 4, further comprising detecting the presence or absence of an activity-attenuating or inactivating mutation in TP53 protein or a gene encoding the TP53 protein, wherein the cancer identified as having a reduced CDKN1A activity level compared to the CDKN1A activity in the control tissue or cell and the presence of an activity-attenuating or inactivating mutation in the TP53 protein or the gene encoding the TP53 protein is administered a therapeutically amount of the ATR inhibitor.
6. The method of claim 5, wherein the activity attenuating or inactivating mutation of TP53 is a loss of function mutation in the DNA binding domain, homo-oligomerization domain, or transactivation domain of TP53.
7. A method of selecting a cancer for treatment with an ATR inhibitor, comprising:
measuring the level of cyclin dependent kinase inhibitor 1A (CDKN1A) activity in a cancer;
comparing the measured CDKN1A activity to CDKN1A activity in a control tissue or cell;
and
selecting the cancer having a reduced CDKN1A activity as compared to CDKN1A activity in a control tissue or cell for treatment with an ATR inhibitor.
8. The method of claim 7, wherein the treatment with the ATR inhibitor is in combination with a DNA damaging agent.

9. The method of claim 7, wherein the cancer having a reduced CDKN1A activity is characterized by a synergistic growth inhibition response to the ATR inhibitor and a DNA damaging agent.

10. The method of any one of claims 7 to 9, further comprising detecting the presence or absence of an activity-attenuating or inactivating mutation in TP53 protein or a gene encoding the TP53 protein, wherein the cancer having a reduced CDKN1A activity compared to the CDKN1A activity in the control tissue or cell, and the presence of an activity-attenuating or inactivating mutation in the TP53 protein or the gene encoding the TP53 protein is selected for treatment with the ATR inhibitor.

11. The method of claim 10, wherein the activity attenuating or inactivating mutation of TP53 is a loss of function mutation in the DNA binding domain, homo-oligomerization domain, or transactivation domain of TP53.

12. A method of selecting a patient with cancer for treatment with an ATR inhibitor, comprising:

measuring the level of CDKN1A activity in a cancer of a patient;

comparing the measured CDKN1A activity to CDKN1A activity in a control tissue or cell;

and

selecting the patient with a cancer identified as having a reduced CDKN1A activity as compared to CDKN1A activity of a control tissue or cell for treatment with the ATR inhibitor.

13. The method of claim 12, wherein the treatment with the ATR inhibitor is in combination with a DNA damaging agent.

14. The method of claim 12, wherein the cancer identified as having a reduced CDKN1A activity is characterized by a synergistic growth inhibition response to the ATR inhibitor and a DNA damaging agent.

15. The method of any one of claims 12 to 14, further comprising detecting the presence or absence of an activity-attenuating or inactivating mutation in TP53 protein or a gene encoding the TP53 protein, and wherein the patient with the cancer having a reduced CDKN1A activity compared to the CDKN1A activity in the control tissue or cell, and the presence of an activity-attenuating or inactivating mutation in the TP53 protein or the gene encoding the TP53 protein is selected for treatment with the ATR inhibitor.

16. The method of claim 15, wherein the activity attenuating or inactivating mutation of TP53 is a loss of function mutation in the DNA binding domain, homo-oligomerization domain, or transactivation domain of TP53.

17. The method of any one of claims 1 to 16, wherein the reduced CDKN1A activity is a CDKN1A activity level which is in the lower three quartiles of the CDKN1A activity in the control tissue or cell.

18. The method of claim 17, wherein the reduced CDKN1A activity is a CDKN1A activity level which is in the third or lower quartile of the CDKN1A activity in the control tissue or cell.

19. The method of claim 17, wherein the reduced CDKN1A activity is a CDKN1A activity level which is in the first quartile of the CDKN1A activity in the control tissue or cell.

20. The method of any one of claims 1 to 16, wherein the reduced CDKN1A activity is a CDKN1A activity level which is about 75% or less, about 50% or less, or about 25% or less of the CDKN1A activity of the control tissue or cell.

21. A method of identifying a patient having a cancer contraindicated (not indicated) for treatment with an ATR inhibitor, comprising:

measuring the level of cyclin dependent kinase inhibitor 1A (CDKN1A) activity in a cancer of a patient;

comparing the measured CDKN1A activity to CDKN1A activity in a control tissue or cell;

and

identifying the patient having a cancer with a CDKN1A activity which is substantially similar to CDKN1A activity in control tissue or cell as being contraindicated for treatment with the ATR inhibitor.

22. The method of claim 21, wherein the contraindication is for treatment with the ATR inhibitor in combination with a DNA damaging agent.

23. The method of any one of claims 21 to 22, wherein the patient having a cancer identified as being contraindicated for treatment with the ATR inhibitor is not selected for treatment with the ATR inhibitor.

24. The method of any one of claims 21 to 22, wherein the patient identified as having a cancer as being contraindicated for treatment with the ATR inhibitor is treated with cancer therapy other than treatment with the ATR inhibitor.

25. The method of any one of claims 21 to 24, wherein the cancer contraindicated for treatment with the ATR inhibitor is characterized by a by a non-synergistic growth inhibition response to the ATR inhibitor in combination with a DNA damaging agent.

26. The method of any one of claims 21 to 25, wherein the cancer having substantially similar CDKN1A activity as compared to control tissue or cell is characterized by a non-synergistic growth inhibition response to the ATR inhibitor and a DNA damaging agent.

27. The method of any one of claims 21 to 26, wherein the cancer identified as being contraindicated for treatment with the ATR inhibitor has a measured CDKN1A activity in the fourth quartile of the CDKN1A activity in the control tissue or cell

28. The method of any one of claims 21 to 26, wherein the cancer identified as being contraindicated for treatment with the ATR inhibitor has a measured CDKN1A activity which is greater than 75% of the CDKN1A activity of the control tissue or cell.

29. The method of any one of claims 21 to 28, further comprising detecting the presence or absence of an activity-attenuating or inactivating mutation in TP53 protein or a gene encoding the TP53 protein, wherein the patient with a cancer having a substantially similar CDKN1A activity compared to the CDKN1A activity in the control tissue or cell, and the absence of an activity-attenuating or inactivating mutation in the TP53 protein or the gene encoding the TP53 protein identifies the patient as being contraindicated for treatment with the ATR inhibitor.

30. The method of claim 29, wherein the activity attenuating or inactivating mutation of TP53 is a loss of function mutation in the DNA binding domain, homo-oligomerization domain, or transactivation domain of TP53.

31. The method of claim 30, wherein the cancer contraindicated for treatment with the ATR inhibitor has a wild-type TP53 protein.

32. The method of any one of claims 1 to 31, wherein the control tissue or cell is characterized by a non-synergistic growth inhibition response to the ATR inhibitor and the DNA damaging agent.

33. The method of claim 32, wherein the control tissue or cell is control cancer tissue or cancer cell characterized by a non-synergistic growth inhibition response to the ATR inhibitor in combination with the DNA damaging agent.

34. The method of claim 33, wherein the control cancer tissue or cancer cell are of the tissue type or cell type determined for the cancer.
35. The method of claim 32, wherein the control tissue or cell is non-cancerous tissue or non-cancerous cell.
36. The method of claim 32, wherein the control tissue or cell is normal tissue or normal cell.
37. The method of claim 36, wherein the normal tissue or normal cell is a tissue type or cell type determined for the cancer.
38. The method of any one of claims 1 to 37, wherein the CDKN1A activity is determined by (a) measuring CDKN1A protein expression, (b) measuring CDKN1A mRNA expression, (c) detecting the presence or absence of activity-attenuating or inactivating mutations in CDKN1A protein or a gene encoding the CDKN1A protein, or (d) combinations thereof.
39. The method of claim 38, wherein the CDKN1A activity is determined by measuring CDKN1A protein expression.
40. The method of claim 39, wherein measuring the CDKN1A protein expression is with an antibody which specifically binds to CDKN1A protein.
41. The method of claim 40, wherein the measuring the CDKN1A protein expression is by an enzyme linked immunosorbent assay (ELISA), immunohistochemistry, Western blotting or fluorescence activated cell sorting (FACS) of cancer cells.
42. The method of claim 38, wherein determining the CDKN1A activity is by measuring CDKN1A mRNA expression.
43. The method of claim 42, wherein measuring the CDKN1A mRNA expression is by polymerase chain reaction (PCR) or hybridization to nucleic acid probes for CDKN1A expressed sequences.
44. The method of claim 43, wherein the PCR is quantitative PCR.
45. The method of claim 43, wherein measuring the CDKN1A mRNA expression is by hybridization to a nucleic acid microarray.

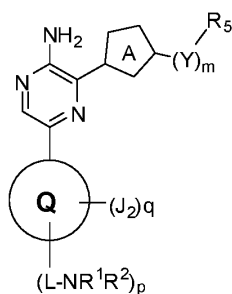
46. The method of claim 38, wherein determining the CDKN1A activity includes detecting the presence or absence of activity attenuating or inactivating mutations in CDKN1A protein or a gene encoding the CDKN1A protein.

47. The method of claim 46, wherein the activity attenuating or inactivation mutation is an inactivating deletion, missense, frame shift, or nonsense mutation.

48. The method of any one of claims 38 to 47, wherein the CDKN1A activity is determined for a biological sample of the cancer obtained from the patient.

49. The method of claim 48, wherein the biological sample comprises a biopsy sample, lymphatic sample, or a blood sample containing the cancer.

50. The method of any one of claims 1 to 49, wherein the ATR inhibitor is compound of Formula IA:

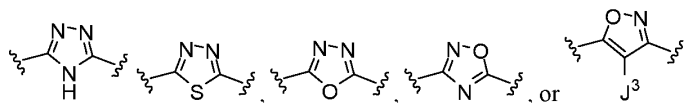


IA

or a pharmaceutically acceptable salt thereof; wherein

Y is a C₁-C₁₀ aliphatic chain wherein up to three methylene units of the aliphatic chain are optionally replaced with O, NR⁰, S, C(O) or S(O)₂;

Ring A is a 5 membered heteroaryl ring selected from



J³ is H or C₁-C₄ alkyl, wherein 1 methylene unit of the alkyl group can optionally be replaced with O, NH, N(C₁-C₄ alkyl), or S and optionally substituted with 1-3 halo;

Q is a 5-6 membered monocyclic aromatic ring containing 0-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur; or an 8-10 membered bicyclic aromatic ring containing 0-6 heteroatoms independently selected from nitrogen, oxygen, and sulfur;

R^5 is H; a 3-7 membered monocyclic fully saturated, partially unsaturated, or aromatic ring containing 0-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur; an 8-10 membered bicyclic fully saturated, partially unsaturated, or aromatic ring containing 0-6 heteroatoms independently selected from nitrogen, oxygen, and sulfur; wherein R^5 is optionally substituted with 1-5 J^5 groups;

L is a C_1 - C_4 alkyl chain wherein up to two methylene units of the alkyl chain are optionally replaced with O, NR^6 , S, $-C(O)-$, $-SO-$, or $-SO_2-$;

R^0 is H or C_1 - C_6 alkyl wherein one methylene unit of the alkyl chain can be optionally replaced with O, NH, $N(C_1-C_4alkyl)$, or S;

R^1 is H or C_1 - C_6 alkyl;

R^2 is H, C_1 - C_6 alkyl, $-(C_2-C_6alkyl)-Z$ or a 4-8 membered cyclic ring containing 0-2 nitrogen atoms; wherein said ring is bonded via a carbon atom and is optionally substituted with one occurrence of J^Z ;

or R^1 and R^2 , taken together with the atom to which they are bound, form a 4-8 membered heterocyclic ring containing 1-2 heteroatoms selected from oxygen, nitrogen, and sulfur; wherein said heterocyclic ring is optionally substituted with one occurrence of J^{Z1} ;

J^{Z1} is halo, CN, C_1 - C_8 aliphatic, $-(X)_r-CN$, or $-(X)_r-Z$, wherein said up to two methylene units of said C_1 - C_8 aliphatic can be optionally replaced with O, NR, S, $P(O)$, $C(O)$, $S(O)$, or $S(O)_2$, wherein said C_1 - C_8 aliphatic is optionally substituted with halo, CN, or NO_2 ;

X is C_1 - C_4 alkyl;

each t, r and m is independently 0 or 1;

Z is $-NR^3R^4$;

R^3 is H or C_1 - C_2 alkyl;

R^4 is H or C_1 - C_6 alkyl;

or R^3 and R^4 , taken together with the atom to which they are bound, form a 4-8 membered heterocyclic ring containing 1-2 heteroatoms selected from oxygen, nitrogen, and sulfur; wherein said ring is optionally substituted with one occurrence of J^Z ;

R^6 is H, or C_1 - C_6 alkyl;

J^Z is independently NH_2 , $NH(C_1-C_4aliphatic)$, $N(C_1-C_4aliphatic)_2$, halogen, C_1 - C_4 aliphatic, OH, $O(C_1-C_4aliphatic)$, NO_2 , CN, CO_2H , $CO(C_1-C_4aliphatic)$, $CO_2(C_1-C_4aliphatic)$, $O(haloC_1-C_4aliphatic)$, or $haloC_1-C_4aliphatic$;

J^5 is halo, oxo, CN, NO_2 , X^1-R , or $-(X^1)_p-Q^4$;

X^1 is C_1 - C_{10} aliphatic; wherein 1-3 methylene units of said C_1 - C_{10} aliphatic are optionally replaced with $-NR^7$, $-O-$, $-S-$, $C(=NR^7)$, $C(O)$, $S(O)_2$, or $S(O)$, wherein X^1 is optionally and independently substituted with 1-4 occurrences of NH_2 , $NH(C_1-C_4aliphatic)$, $N(C_1-C_4aliphatic)_2$, halogen, C_1 - C_4 aliphatic, OH, $O(C_1-C_4aliphatic)$, NO_2 , CN, CO_2H , $CO_2(C_1-C_4aliphatic)$, $C(O)NH_2$,

C(O)NH(C₁-C₄aliphatic), C(O)N(C₁-C₄aliphatic)₂, SO(C₁-C₄aliphatic), SO₂(C₁-C₄aliphatic), SO₂NH(C₁-C₄aliphatic), NHC(O)(C₁-C₄aliphatic), N(C₁-C₄aliphatic)C(O)(C₁-C₄aliphatic), wherein said C₁-C₄aliphatic is optionally substituted with 1-3 occurrences of halo;

Q⁴ is a 3-8 membered saturated or unsaturated monocyclic ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or a 8-10 membered saturated or unsaturated bicyclic ring having 0-6 heteroatoms independently selected from nitrogen, oxygen, and sulfur; each Q⁴ is optionally substituted with 1-5 J^{Q4};

J^{Q4} is halo, CN, or C₁-C₄alkyl wherein up to 2 methylene units are optionally replaced with O, NR*, S, C(O), S(O), or S(O)₂;

R is H or C₁-C₄alkyl wherein said C₁-C₄alkyl is optionally substituted with 1-4 halo;

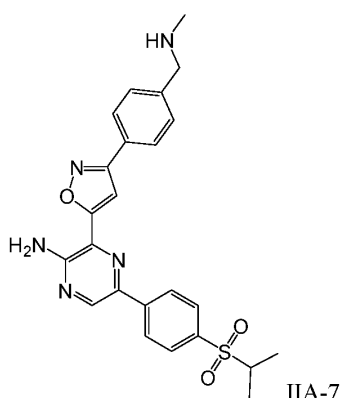
J² is halo; CN; a 5-6 membered aromatic or nonaromatic monocyclic ring having 0-3 heteroatoms selected from oxygen, nitrogen, and sulfur; or a C₁-C₁₀aliphatic group wherein up to 2 methylene units are optionally replaced with O, NR'', C(O), S, S(O), or S(O)₂; wherein said C₁-C₁₀aliphatic group is optionally substituted with 1-3 halo or CN; and said monocyclic ring is optionally substituted with 1-3 occurrences of halo; CN; a C₃-C₆cycloalkyl; a 3-7 membered heterocyclyl containing 0-2 heteroatoms selected from oxygen, nitrogen, and sulfur; or a C₁-C₄alkyl wherein up to one methylene unit of the alkyl chain is optionally replaced with O, NR'', or S; and wherein said C₁-C₄alkyl is optionally substituted with 1-3 halo;

q is 0, 1, or 2;

p is 0 or 1;

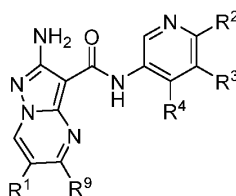
R', R'', and R* are each independently H, C₁-C₄alkyl, or is absent; wherein said C₁-C₄alkyl is optionally substituted with 1-4 halo.

51. The method of claim 50, wherein the ATR inhibitor is compound of the following structure (IIA-7):



or a pharmaceutically acceptable salt thereof.

52. The method of any one of claims 1 to 49, wherein the ATR inhibitor is compound of the ATR inhibitor is a compound of Formula I:



I

or a pharmaceutically acceptable salt thereof, wherein:

R^1 is independently selected from $-C(J^1)_2CN$, halo, $-(L)_k-W$, and M;

R^9 is independently selected from H, $-C(J^1)_2CN$, halo, $-(L)_k-W$, and M;

J^1 is independently selected from H and C_1-C_2 alkyl; or

two occurrences of J^1 , together with the carbon atom to which they are attached, form a 3-4 membered optionally substituted carbocyclic ring;

k is 0 or 1;

M and L are a C_1-C_8 aliphatic, wherein up to three methylene units are optionally replaced with -O-, -NR-, -C(O)-, or -S(O)_n-, each M and L^1 is optionally substituted with 0-3 occurrences of J^{LM} ;

J^{LM} is independently selected from halo, -CN, and a C_1-C_4 aliphatic chain wherein up to two methylene units of the aliphatic chain are optionally replaced with -O-, -NR-, -C(O)-, or -S(O)_n-;

W is independently selected from a 3-7 membered fully saturated, partially unsaturated, or aromatic monocyclic ring having 0-3 heteroatoms selected from oxygen, nitrogen and sulfur; and a 7-12 membered fully saturated, partially unsaturated, or aromatic bicyclic ring having 0-5 heteroatoms selected from oxygen, nitrogen, and sulfur; wherein W is optionally substituted with 0-5 occurrences of J^W ;

J^W is independently selected from -CN, halo, -CF₃; a C_1-C_4 aliphatic wherein up to two methylene units are optionally replaced with -O-, -NR-, -C(O)-, or -S(O)_n-; and a 3-6 membered non-aromatic ring having 0-2 heteroatoms selected from oxygen, nitrogen, and sulfur; or two occurrences of J^W on the same atom, together with atom to which they are joined, form a 3-6 membered ring having 0-2 heteroatoms selected from oxygen, nitrogen, and sulfur; or two occurrences of J^W , together with W, form a 6-10 membered saturated or partially unsaturated bridged ring system;

R^2 is independently selected from H; halo; -CN; NH₂; a C_1-C_2 alkyl optionally substituted with 0-3 occurrences of fluoro; and a C_1-C_3 aliphatic chain wherein up to two methylene units of the aliphatic chain are optionally replaced with -O-, -NR-, -C(O)-, or -S(O)_n;

- R^3 is independently selected from H; halo; C_1 - C_4 alkyl optionally substituted with 1-3 occurrences of halo; C_3 - C_4 cycloalkyl; 3-4 membered heterocyclyl; -CN; and a C_1 - C_3 aliphatic chain wherein up to two methylene units of the aliphatic chain are optionally replaced with -O-, -NR-, -C(O)-, or -S(O)_n;
- R^4 is independently selected from Q^1 and a C_1 - C_{10} aliphatic chain wherein up to four methylene units of the aliphatic chain are optionally replaced with -O-, -NR-, -C(O)-, or -S(O)_n-; each R^4 is optionally substituted with 0-5 occurrences of J^Q ; or
- R^3 and R^4 , taken together with the atoms to which they are bound, form a 5-6 membered aromatic or non-aromatic ring having 0-2 heteroatoms selected from oxygen, nitrogen and sulfur; the ring formed by R^3 and R^4 is optionally substituted with 0-3 occurrences of J^Z ;
- Q^1 is independently selected from a 3-7 membered fully saturated, partially unsaturated, or aromatic monocyclic ring, the 3-7 membered ring having 0-3 heteroatoms selected from oxygen, nitrogen and sulfur; and an 7-12 membered fully saturated, partially unsaturated, or aromatic bicyclic ring having 0-5 heteroatoms selected from oxygen, nitrogen, and sulfur;
- J^Z is independently selected from C_1 - C_6 aliphatic, =O, halo, and $\rightarrow O$;
- J^Q is independently selected from -CN; halo; =O; Q^2 ; and a C_1 - C_8 aliphatic chain wherein up to three methylene units of the aliphatic chain are optionally replaced with -O-, -NR-, -C(O)-, or -S(O)_n-; each occurrence of J^Q is optionally substituted by 0-3 occurrences of J^R ; or two occurrences of J^Q on the same atom, taken together with the atom to which they are joined, form a 3-6 membered ring having 0-2 heteroatoms selected from oxygen, nitrogen, and sulfur; wherein the ring formed by two occurrences of J^Q is optionally substituted with 0-3 occurrences of J^X ; or two occurrences of J^Q , together with Q^1 , form a 6-10 membered saturated or partially unsaturated bridged ring system;
- Q^2 is independently selected from a 3-7 membered fully saturated, partially unsaturated, or aromatic monocyclic ring having 0-3 heteroatoms selected from oxygen, nitrogen, and sulfur; and an 7-12 membered fully saturated, partially unsaturated, or aromatic bicyclic ring having 0-5 heteroatoms selected from oxygen, nitrogen, and sulfur;
- J^R is independently selected from -CN; halo; =O; $\rightarrow O$; Q^3 ; and a C_1 - C_6 aliphatic chain wherein up to three methylene units of the aliphatic chain are optionally replaced with -O-, -NR-, -C(O)-, or -S(O)_n-; each J^R is optionally substituted with 0-3 occurrences of J^T ; or two occurrences of J^R on the same atom, together with the atom to which they are joined, form a 3-6 membered ring having 0-2 heteroatoms selected from oxygen, nitrogen, and sulfur; wherein the ring formed by two occurrences of J^R is optionally substituted with 0-3 occurrences of J^X ; or two occurrences of J^R , together with Q^2 , form a 6-10 membered saturated or partially unsaturated bridged ring system;
- Q^3 is a 3-7 membered fully saturated, partially unsaturated, or aromatic monocyclic ring having 0-3 heteroatoms selected from oxygen, nitrogen, or sulfur; or an 7-12 membered fully saturated,

partially unsaturated, or aromatic bicyclic ring having 0-5 heteroatoms selected from oxygen, nitrogen, and sulfur;

J^X is independently selected from -CN; =O; halo; and a C_1 - C_4 aliphatic chain, wherein up to two methylene units of the aliphatic chain are optionally replaced with -O-, -NR-, -C(O)-, or -S(O)_n-;
 J^T is independently selected from halo, -CN; $\rightarrow$ O; =O; -OH; a C_1 - C_6 aliphatic chain wherein up to two methylene units of the aliphatic chain are optionally replaced with -O-, -NR-, -C(O)-, or -S(O)_n-; and a 3-6 membered non-aromatic ring having 0-2 heteroatoms selected from oxygen, nitrogen, and sulfur; each occurrence of J^T is optionally substituted with 0-3 occurrences of J^M ; or two occurrences of J^T on the same atom, together with the atom to which they are joined, form a 3-6 membered ring having 0-2 heteroatoms selected from oxygen, nitrogen, and sulfur; or two occurrences of J^T , together with Q^3 , form a 6-10 membered saturated or partially unsaturated bridged ring system;

J^M is independently selected from halo and C_1 - C_6 aliphatic;

n is 0, 1 or 2; and

R is independently selected from H and C_1 - C_4 aliphatic.

53. The method of any one of claims 1 to 52, wherein the DNA damaging agent when present comprises ionizing radiation, platinating agent, topoisomerase I (Topo I) inhibitor, topoisomerase II (Topo II) inhibitor, anti-metabolite, alkylating agent, anti-cancer antibiotic, or combinations thereof.

54. The method of claim 53, wherein the DNA damaging agent comprises a platinating agent.

55. The method of claim 54, wherein the platinating agent comprises cisplatin, oxaliplatin, or carboplatin.

56. The method of claim 53, wherein the DNA damaging agent comprises an antimetabolite.

57. The method of claim 56, wherein the anti-metabolite comprises cytarabine, gemcitabine, capecitabine, or 5-fluorouracil (5-FU).

58. The method of any one of claims 1 to 57, wherein the DNA damaging agent, when present, comprises a DNA damage enhancing agent.

59. The method of claim 58, wherein the DNA damage enhancing agent is a PARP inhibitor.

60. The method of claim 59, wherein the DNA damage enhancing agent is a Chk1 inhibitor.
61. The method of any one of claims 1 to 60, wherein the cancer is lung cancer, ovarian cancer, endometrial cancer, pancreatic cancer, head and neck cancer, esophageal cancer, breast cancer and colorectal cancer.
62. The method of any one of claims 1 to 60, wherein the cancer is a hematologic cancer.
63. The method of claim 62, wherein the hematological cancer is a lymphoma or a leukemia.
64. A method of selecting a cancer treatment regimen for a patient having a cancer, comprising:
measuring the level of cyclin dependent kinase inhibitor 1A (CDKN1A) activity in a cancer of a patient;
comparing the measured CDKN1A activity to CDKN1A activity in a control tissue or cell;
and
(a) selecting a cancer treatment regimen that does not include treatment with an ATR inhibitor in combination with a DNA damaging agent if the cancer is identified as having a CDKN1A activity which is substantially similar to CDKN1A activity in control tissue or cell; and
(b) selecting a cancer treatment regimen that includes treatment with an ATR inhibitor in combination with a DNA damaging agent if the cancer is identified as having a CDKN1A activity which is reduced as compared to CDKN1A activity of control tissue or cell.
65. A method of treating a patient having a cancer, comprising:
measuring the level of cyclin dependent kinase inhibitor 1A (CDKN1A) activity in a cancer of a patient;
comparing the measured CDKN1A activity to CDKN1A activity in a control tissue or cell;
and
(a) treating the patient with a cancer treatment regimen which does not include treatment with an ATR inhibitor in combination with a DNA damaging agent if the cancer is identified as having a CDKN1A activity which is substantially similar to CDKN1A activity in control tissue or cell; and
(b) treating the patient with a cancer treatment regimen which includes treatment with an ATR inhibitor in combination with a DNA damaging agent if the cancer is identified as having a CDKN1A activity which is reduced as compared to CDKN1A activity in control tissue or cell.

66. An article of manufacture comprising:
- (a) a packaging material;
 - (b) an ATR inhibitor, or a pharmaceutically acceptable salt thereof; and
 - (c) a label, a package insert, or directions for obtaining the label or the package insert,
- contained within the packaging material, wherein the label or package insert provides prescribing information based on level of CDKN1A activity, or based on the level of CDKN1A activity and TP53 mutations status, determined for the cancer in a patient.