CLAIMS

1. Use of prexasertib or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating cancer, wherein the medicament is to be administered to a subject whose cancer cell tissue sample has been determined to exhibit a Response-Predictive Signature;

wherein the Response-Predictive Signature comprises:

(a) a first biomarker score that is greater than or equal to a first predictive threshold, wherein the first biomarker is Ser296 phosphorylated Chk1;

(b) a second biomarker score that is greater than or equal to a second predictive threshold, wherein the second biomarker is Ser473 phosphorylated Kap1; and

(c) a third biomarker score that is greater than or equal to a third predictive threshold, wherein the third biomarker is total cyclin E1;

and wherein the cancer is selected from ovarian cancer, endometrial cancer, and bladder cancer.

2. The use according to claim 1, wherein at least one of the first biomarker score, the second biomarker score, and the third biomarker score is determined as the percentage of cells positive for the corresponding first biomarker, second biomarker, or third biomarker in the cancer cell tissue sample.

3. The use according to claim 2, wherein each of the first biomarker score, the second biomarker score, and the third biomarker score is determined as the percentage of cells positive for the corresponding first biomarker, second biomarker, and third biomarker in the cancer cell tissue sample.

4. The use according to claim 2, wherein the first predictive threshold is 3% or greater of cells positive for the first biomarker;

the second predictive threshold is 3% or greater of cells positive for the second biomarker; and

the third predictive threshold is 3% or greater of cells positive for the third biomarker.

5. The use according to claim 4 , wherein the first predictive threshold is 5%, 6%, 7%, 8%, 9%, or 10% of cells positive for the first biomarker;

the second predictive threshold is 5%, 6%, 7%, 8%, 9%, or 10% of cells positive for the second biomarker; and

the third predictive threshold is 5%, 6%, 7%, 8%, 9%, or 10% of cells positive for the third biomarker.

6. The use according to claim 1, wherein at least one of the first biomarker score, the second biomarker score, and the third biomarker score is determined from a weighted intensity distribution of the corresponding first biomarker, second biomarker, or third biomarker in the cancer cell tissue sample.

7. The use according to claim 6, wherein each of the first biomarker score, the second biomarker score, and the third biomarker score is determined from a weighted intensity distribution of the corresponding first biomarker, second biomarker, and third biomarker in the cancer cell tissue sample.

8. Use of a therapeutic agent that is an inhibitor of expression or activity of a protein in an ATR/Chk1 signaling pathway in the manufacture of a medicament for treating cancer, wherein the medicament is to be administered to a subject whose cancer cell tissue sample has been determined to exhibit a Response-Predictive Signature;

wherein the Response-Predictive Signature comprises a composite score greater than or equal to a composite threshold, wherein the composite score comprises each of:

(a) a first biomarker score, wherein the first biomarker is Ser296 phosphorylated Chk1;

(b) a second biomarker score, wherein the second biomarker is Ser473 phosphorylated Kap1; and

(c) a third biomarker score, wherein the third biomarker is total cyclin E1;

and wherein the cancer is selected from ovarian cancer, endometrial cancer, and bladder cancer.

9. The use according to claim 8, wherein the composite score is the sum of each of the biomarker scores, optionally wherein the biomarker scores are differentially weighted prior to summing.

10. The use according to claim 8, wherein at least one of the first biomarker score, the second biomarker score, and the third biomarker score is determined as the percentage of cells positive for the corresponding first biomarker, second biomarker, or third biomarker in the cancer cell tissue sample.

11. The use according to claim 10, wherein each of the first biomarker score, the second biomarker score, and the third biomarker score is determined as the percentage of cells positive for the corresponding first biomarker, second biomarker, and third biomarker in the cancer cell tissue sample.

12. The use according to claim 8, wherein at least one of the first biomarker score, the second biomarker score, and the third biomarker score is determined from a weighted intensity distribution of the corresponding first biomarker, second biomarker, or third biomarker in the cancer cell tissue sample.

13. The use according to claim 12, wherein each of the first biomarker score, the second biomarker score, and the third biomarker score is determined from a weighted intensity distribution of the corresponding first biomarker, second biomarker, and third biomarker in the cancer cell tissue sample.

14. The use according to claim 1, wherein the cancer is ovarian cancer.

15. The use according to claim 8, wherein the cancer is ovarian cancer.

16. The use according to claim 14, wherein the ovarian cancer is high grade serous ovarian cancer.

17. The use according to claim 15, wherein the ovarian cancer is high grade serous ovarian cancer.

18. The use according to claim 1, wherein at least one of the first biomarker score, the second biomarker score, and the third biomarker score is determined based on detection of the first biomarker, the second biomarker, or the third biomarker in the nucleus of cells in the cancer cell tissue sample.

19. The use according to claim 18, wherein each of the first biomarker score, the second biomarker score, and the third biomarker score is determined based on detection of the first biomarker, the second biomarker, or the third biomarker in the nucleus of cells in the cancer cell tissue sample.

20. The use according to claim 1, wherein the pharmaceutically acceptable salt of prexasertib administered to the subject is prexasertib (S)-lactate monohydrate.

21. The use according to claim 8, wherein the pharmaceutically acceptable salt of prexasertib administered to the subject is prexasertib (S)-lactate monohydrate.

22. The use according to claim 1, wherein the medicament is to be administered with a second anti-cancer agent to the subject.

23. The use according to claim 8, wherein the medicament is to be administered with a second anti-cancer agent to the subject.

24. The use according to claim 1, wherein the cancer is endometrial cancer.

25. The use according to claim 8, wherein the cancer is endometrial cancer.

26. The use according to claim 1, wherein the cancer is bladder cancer.

27. The use according to claim 8, wherein the cancer is bladder cancer.