CLAIMS

1. A combination of an ATR inhibitor and an immune checkpoint inhibitor for use in the treatment of melanoma in a patient who has previously received immunotherapy.

2. Use of an ATR inhibitor, in combination with an immune checkpoint inhibitor, in the manufacture of a medicament for the treatment of melanoma in a patient, where the patient has previously received immunotherapy.

3. The combination for use according to claim 1 or the use according to claim 3, wherein the ATR inhibitor is selected from the group consisting of AZD6738, M6620 (berzosertib), BAY-1895344, EPT-46464, VE-821 and VX-970.

4. The combination for use or the use according to claim 3 wherein the ATR inhibitor is AZD6738.

5. The combination for use or the use according to any one of claims 1 to 4, wherein the immune checkpoint inhibitor is a PD-1 inhibitor, a PD-L1 inhibitor or a CTLA-4 inhibitor.

6. The combination for use or the use according to any one of claims 1 to 5, wherein the immune checkpoint inhibitor is a PD-L1 inhibitor.

7. The combination for use or the use according to claim 6, wherein the PD-L1 inhibitor is durvalumab or an antigen-binding fragment thereof.

8. The combination for use or the use according to any one of the preceding claims, wherein the melanoma is selected from the group consisting of cutaneous, acral and mucosal melanoma.

9. The combination for use or the use according to any one of the preceding claims, wherein the melanoma is advanced melanoma.

10. The combination for use or the use according to any one of claims 1 to 8, wherein the melanoma is metastatic melanoma.

11. The combination for use or the use according to any one of claims 4 to 10, where AZD6738 is to be administered on days 15 to 28 of a 28-day cycle.

12. The combination for use or the use according to any one of claims 4 to 10, where AZD6738 is to be administered on days 1 to 7 of a 28-day cycle.

13. The combination for use or the use according to any one of claims 4 to 12, where the total daily dose of AZD6738 is between 30 mg and 500 mg.

14. The combination for use or the use according to claim 13, where the total daily dose of AZD6738 is to be administered twice daily in 240 mg doses.

15. The combination for use or the use according to claim 13, where the total daily dose of AZD6738 is to be administered twice daily in 160 mg doses.

16. The combination for use or the use according to any one of claims 7 to 15, where durvalumab is to be administered in an amount of 1500 mg once every 4 weeks from cycle 1 day 1

17. The combination for use or the use according to any one of the preceding claims, where the previous immunotherapy comprises treatment with an immune checkpoint inhibitor.

18. The combination for use or the use according to claim 17, where the previous immunotherapy comprises treatment with an immune checkpoint inhibitor selected from a PD-1 inhibitor, PD-L1 inhibitor and a CTLA-4 inhibitor.

19. The combination for use or the use according to claim 18, where the previous immunotherapy comprises treatment with an immune checkpoint inhibitor selected from the group consisting of pembrolizumab, nivolumab, cemiplimab, spartalizumab, camrelizumab, sintilimab, tislelizumab, toripalimab, AMP-224, AMP-514, atezolizumab, avelumab, durvalumab, KN035, CK-301, AUNP12, CA-170, BMS-986189, ipilimumab and tremelimumab.

20. The combination for use or the use according to claim 19, where the previous immunotherapy comprises treatment with pembrolizumab or nivolumab.

21. The combination for use or the use according to any one of the preceding claims, where the patient has primary resistance to immunotherapy.

22. The combination for use or the use according to any one of claims 1 to 20, where the patient has acquired resistance to immunotherapy.

23. The combination for use or the use according to any one of claims 1 to 21, where the patient received immunotherapy as adjuvant therapy.

24. The combination for use or the use according any one of the preceding claims, where the treatment achieves an objective response rate greater than 30%.

25. The combination for use or the use according any one of the preceding claims, where progression free survival is greater than 3 months, preferably greater than 4 months, preferably greater than 5 months, preferably greater than 6 months, more preferably greater than 7 months.

26. The combination for use or the use according any one of the preceding claims, where overall survival is greater than 10 months, preferably greater than 11 months, preferably greater than 12 months, preferably greater than 13 months, more preferably greater than 14 months.

27. The combination for use or the use according any one of the preceding claims, where duration of response is at least 3 months, preferably at least 4 months, preferably at least 5 months, more preferably at least 6 months.

28. A kit comprising:

a. a first pharmaceutical composition comprising an ATR inhibitor and a pharmaceutically acceptable excipient;

b. a second pharmaceutical composition comprising an immune checkpoint inhibitor and a pharmaceutically acceptable excipient; and

c. instructions for the use of the first and second pharmaceutical compositions in the treatment of melanoma in a patient who has previously received immunotherapy.