Claims

1. A combination comprising an oncolytic adenovirus, a CDK4/6 inhibitor and nutlin or a derivative of nutlin,

wherein the oncolytic adenovirus is expressing E1A12S protein, is lacking expression of E1A13S protein, is lacking expression of E1B19K, and is replicating in a YB-1 dependent manner in a tumor or cancer containing YB-1 in the cell nucleus independent of the cell cycle; and

wherein the derivative of nutlin induces E2F1 mediated apoptosis, and enhances the oncolytic effect of a combination of the adenovirus and the CDK4/6 inhibitor.

2. The combination of claim 1, wherein the combination comprises a bromodomain inhibitor.

3. The combination of any one of claims 1 and 2, wherein the combination comprises a PARP inhibitor.

4. Use of a combination of any one of claims 1 to 3 in the manufacture of a medicament for the treatment of a tumor or cancer containing YB-1 in the cell nucleus independent of the cell cycle.

5. Use of an oncolytic adenovirus in the manufacture of a medicament for the treatment of a tumor or cancer containing YB-1 in the cell nucleus independent of the cell cycle, wherein the medicament is to be administered with a CDK4/6 inhibitor and nutlin or a derivative of nutlin,

wherein the oncolytic adenovirus is expressing E1A12S protein, is lacking expression of E1A13S protein, is lacking expression of E1B19K, and is replicating in a YB-1 dependent

manner in a tumor or cancer containing YB-1 in the cell nucleus independent of the cell cycle; and

wherein the derivative of nutlin induces E2F1 mediated apoptosis, and enhances the oncolytic effect of a combination of the adenovirus and the CDK4/6 inhibitor.

6. Use of a CDK4/6 inhibitor in the manufacture of a medicament for the treatment of a tumor or cancer containing YB-1 in the cell nucleus independent of the cell cycle, wherein the medicament is to be administered with an oncolytic adenovirus and nutlin or a derivative of nutlin,

wherein the oncolytic adenovirus is expressing E1A12S protein, is lacking expression of E1A13S protein, is lacking expression of E1B19K, and is replicating in a YB-1 dependent manner in a tumor or cancer containing YB-1 in the cell nucleus independent of the cell cycle; and

wherein the derivative of nutlin induces E2F1 mediated apoptosis, and enhances the oncolytic effect of a combination of the adenovirus and the CDK4/6 inhibitor.

7. Use of nutlin or a derivative of nutlin in the manufacture of a medicament for the treatment of a tumor or a cancer containing YB-1 in the cell nucleus independent of the cell cycle, wherein the medicament is to be administered with an oncolytic adenovirus and a CDK4/6 inhibitor,

wherein the oncolytic adenovirus is expressing E1A12S protein, is lacking expression of E1A13S protein, is lacking expression of E1B19K, and is replicating in a YB-1 dependent manner in a tumor or cancer containing YB-1 in the cell nucleus independent of the cell cycle; and

wherein the derivative of nutlin induces E2F1 mediated apoptosis, and enhances the oncolytic effect of a combination of the adenovirus and the CDK4/6 inhibitor.

8. Use of a PARP inhibitor in the manufacture of a medicament for the treatment of a tumor or a cancer containing YB-1 in the cell nucleus independent of the cell cycle, wherein the medicament is to be administered with an oncolytic adenovirus, a CDK4/6 inhibitor and nutlin or a derivative of nutlin,

wherein the oncolytic adenovirus is expressing E1A12S protein, is lacking expression of E1A13S protein, is lacking expression of E1B19K, and is replicating in a YB-1 dependent manner in a tumor or cancer containing YB-1 in the cell nucleus independent of the cell cycle; and

wherein the derivative of nutlin induces E2F1 mediated apoptosis, and enhances the oncolytic effect of a combination of the adenovirus and the CDK4/6 inhibitor.

9. Use of a bromodomain inhibitor in the manufacture of a medicament for the treatment of a tumor or a cancer containing YB-1 in the cell nucleus independent of the cell cycle, wherein the medicament is to be administered with an oncolytic adenovirus, a CDK4/6 inhibitor and nutlin or a derivative of nutlin,

wherein the oncolytic adenovirus is expressing E1A12S protein, is lacking expression of E1A13S protein, is lacking expression of E1B19K, and is replicating in a YB-1 dependent manner in a tumor or cancer containing YB-1 in the cell nucleus independent of the cell cycle; and

wherein the derivative of nutlin induces E2F1 mediated apoptosis, and enhances the oncolytic effect of a combination of the adenovirus and the CDK4/6 inhibitor.

10. The combination of any one of claims 1 to 3, or the use of any one of claims 4 to 9, wherein the adenovirus is replication deficient in cells which lack YB-1 in the nucleus, but is replicating in cells which have YB-1 in the nucleus.

11. The combination of any one of claims 1 to 3 and 10, or the use of any one of claims 4 to 10, wherein the adenovirus is an adenovirus expressing an RGD motif at a fibre.

12. The combination of any one of claims 1 to 3 and 10 to 11, or the use of any one of claims 4 to 11, wherein the adenovirus is XVir-N-31.

13. The combination of any one of claims 1 to 3 and 10 to 12, or the use of any one of claims 4 to 12, wherein the CDK4/6 inhibitor is a CDK4/6 inhibitor arresting cells in the G1 phase and inhibiting E2F1.

14. The combination of any one of claims 1 to 3 and 10 to 13, or the use of any one of claims 4 to 13, wherein the CDK4/6 inhibitor is an ATP-competitive CDK4/6 inhibitor.

15. The combination of any one of claims 1 to 3 and 10 to 14, or the use of any one of claims 4 to 14, wherein the CDK4/6 inhibitor is selected from the group comprising palbociclib which is also referred to as PD 0332991, abemaciclib which is also referred to as LY-2835219, ribociclib which is also referred to as LEE011 and Trilaciclib which is also referred to as G1T28.

16. The combination of any one of claims 1 to 3 and 10 to 15, or the use of any one of claims 4 to 15, wherein nutlin is nutlin-3.

17. The combination of any one of claims 1 to 3, and 10 to 15, or the use of any one of claim 4 to 15, wherein the derivative of nutlin is selected from the group comprising NVP-HDM201, Idasanutlin, AM-8553, SAR405838, Nutlin-3a and AMG232.

18. The use of any one of claims 4 to 17, wherein the tumor or cancer is Rb-negative, is expressing Rb or is Rb-positive.

19. The use of any one of claims 4 to 18, wherein the cells of the tumor cells have a resistance to or are insensitive to one or several pharmaceutically active agents and/or radiation.

20. The use of any one of claims 4 to 19, wherein the tumor or cancer is selected from the group comprising bladder cancer, breast cancer, metastatic breast cancer (mBC), melanoma, glioma, pancreatic cancer, hepatocellular carcinoma, lung adenocarcinoma, sarcoma, ovarian cancer, renal cancer, prostate cancer, and leukemia.