

Claims

1. An inhibitor of apoptosis protein (IAP) antagonist for use in a method of treating cancer in a human subject, the method comprising:

(i) administering the IAP antagonist during an induction period, wherein the duration of the induction period is selected from the range of 1 to 48 days before first administration of an anti-PD-1 molecule; followed by

(ii) administering an anti-PD-1 molecule after the end of the induction period; wherein:

the anti-PD-1 molecule is Nivolumab, Pembrolizumab, Atezolizumab, Durvalumab, Avelumab, PDR001, IBI-308, Cemiplimab, Camrelizumab, BGB-A317, BCD-100, JS-001, JNJ-3283, MEDI0680, AGEN-2034, TSR-042, Sym-021, PF-06801591, MGD-013, MGA-012, LZM-009, GLS-010, Genolimzumab, BI 754091, AK-104, CX-072, WBP3155, SHR-1316, PD-L1 Inhibitor millamolecule, BMS-936559, M-7824, LY-3300054, KN-035, FAZ-053, CK-301, or CA-170; and

the IAP antagonist administered during the induction period is Debio 1143, GDC-917/CUDC-427, LCL161, GDC-0152, TL-32711/Birinapant, HGS-1029/AEG-40826, BI 891065, ASTX-660 or APG-1387, preferably, the IAP antagonist is Debio 1143, LCL161 or Biranapant.

2. The IAP antagonist for use according to claim 1, wherein:

(a) the human subject is administered with the IAP antagonist during an induction period of 1 to 28 days, followed by the administration of the anti-PD-1 molecule;

(b) the human subject is administered with the IAP antagonist during an induction period of 5 to 28 days, followed by the administration of the anti-PD-1 molecule;

(c) the IAP antagonist is not administered on one or more days during the induction period; and/or

(d) wherein the administration of the IAP antagonist is continued after the administration with the anti-PD-1 molecule has started, or another IAP antagonist is administered concurrently with the anti-PD-1 molecule.

3. The IAP antagonist for use according to claim 1 or 2, wherein:

(a) the cancer is a cancer that is known to be responsive to treatment with an anti-PD-1 molecule in 10% or more of treated patients;

(b) the cancer is head & neck cancer, melanoma, urothelial cancer, non-small cell lung cancer, microsatellite instability (MSI) high tumors from agnostic primary site or kidney cancer;

(c) the cancer is a cancer with a response rate to treatment with an anti-PD-1 molecule of 10% or less, preferably 5% or less; or

(d) the cancer is pancreatic cancer, colorectal cancer, multiple myeloma, small cell lung cancer, hepatocarcinoma or ovarian cancer.

4. The IAP antagonist for use according to any one of the preceding claims, wherein the cancer has been assessed to be poorly immunogenic.

5. The IAP antagonist for use according to claim 4, wherein said assessment consists of an analysis of a marker of immunogenicity in a patient's biological sample taken prior to the induction period and a finding that the marker's presence, expression level or derived score fails a predetermined threshold.

6. The IAP antagonist for use according to claim 5, wherein:

(a) the marker is PD-L1 expressed on cancer cells and/or immune cells; or

(b) the marker is tumor-infiltrating lymphocytes, preferably CD8⁺ cells, or tumor mutation burden.

7. The IAP antagonist for use according to any of the preceding claims, wherein the administering the IAP antagonist during an induction period is continued until the cancer is assessed to be of high immunogenicity.

8. The IAP antagonist for use according to claim 7, wherein said assessment consists of an analysis of a marker of immunogenicity in a patient's biological sample taken after the induction period and a finding that the marker's presence, expression level or derived score exceeds a predetermined threshold.

9. The IAP antagonist for use according to claim 8, wherein:

(a) the marker is PD-L1 expressed on cancer cells and/or immune cells; or

(b) the marker is tumor-infiltrating lymphocytes, preferably CD8⁺ cells, or tumor mutation burden.

10. The IAP antagonist for use according to any one of claims 5, 6, 8 or 9, wherein the biological sample is a tumor or liquid biopsy.

11. The IAP antagonist for use according to any one of the preceding claims, wherein the anti-PD-1 molecule is Nivolumab, Pembrolizumab, Atezolizumab, Durvalumab, Avelumab, PDR001, or BI 754091.

12. The IAP antagonist for use according to any one of claims 1 to 10, wherein the anti-PD-1 molecule is an antibody against PD-1 or PD-L1.

13. The IAP antagonist for use according to any one of the preceding claims, wherein the administration of the anti-PD-1 molecule is combined with one or more other cancer therapies, including another immunotherapy, radiotherapy, chemotherapy, chemioradiotherapy, oncolytic viruses, anti-angiogenic therapies, and/or targeted cancer therapies.

14. The IAP antagonist for use according to any one of the preceding claims, wherein the IAP antagonist is a second mitochondrial-derived activator of caspases (SMAC) mimetic.

15. The IAP antagonist for use according to any one of the preceding claims, wherein the IAP antagonist is Debio 1143.