

Claims

~~1. An antibody molecule which binds programmed death-ligand 1 (PD-L1) and lymphocyte activation gene 3 (LAG-3) for use in a method of treating cancer in a human patient,~~
~~wherein the antibody molecule comprises the heavy chain sequence set forth in SEQ ID NO: 1 and the light chain sequence set forth in SEQ ID NO: 2; and~~
~~wherein the method comprises administering the antibody molecule to the patient once weekly at a dose of 3mg to 20mg per kg of body weight of the patient.~~

~~21. A method of treating cancer in a human patient, wherein the method comprises administering to the patient a therapeutically effective amount of~~ The use of an antibody molecule which binds PD-L1 and LAG-3 in the manufacture of a medicament for treating cancer in a human patient,
 wherein the antibody molecule comprises the heavy chain sequence set forth in SEQ ID NO: 1 and the light chain sequence set forth in SEQ ID NO: 2; and
 wherein ~~the method comprises administering the antibody molecule~~ is to be administered to the patient once weekly at a dose of ~~3mg~~ 10 mg to 20 mg per kg of body weight of the patient.

~~3. The antibody molecule for use, or method, according to claim 1 or 2, wherein the method comprises administering the antibody molecule at a dose of 10mg to 20mg per kg of body weight of the patient.~~

~~42. The antibody molecule for use, or method, according to any one of claims 1 to 3, wherein the method comprises administering the antibody molecule~~ is to be administered at a dose of 10 mg per kg of body weight of the patient.

~~5. The antibody molecule for use, or method, according to claim 1 or 2, wherein the method comprises administering the antibody molecule to the patient at a dose of 210mg to 1400mg.~~

~~63. The antibody molecule for use, or method, according to any one of claims 1 to 3 or 2, or 5, wherein the method comprises administering the antibody molecule~~ is to be administered to the patient at a dose of 700 mg to 1400 mg.

~~74.~~ The antibody molecule for use, or method, according to any one of claims 1 to ~~63~~, wherein ~~the method comprises administering the antibody molecule~~ is to be administered to the patient at a dose of 700 mg.

~~85.~~ The antibody molecule for use, or method, according to any one of claims 1 to ~~74~~, wherein ~~the a~~ tumour is refractive to treatment with one or more checkpoint inhibitors, has relapsed during or following treatment with one or more checkpoint inhibitors, or is responsive to treatment with one or more checkpoint inhibitors.

~~96.~~ The antibody molecule for use, or method, according to claim ~~85~~, wherein the immune checkpoint inhibitor is a programmed cell death protein 1 (PD-1) or PD-L1 inhibitor.

~~10.~~ An antibody molecule which binds PD-L1 and LAG-3 for use in a method of treating cancer in a human patient who has been subjected to treatment with a prior anti-PD-1 or anti-PD-L1 therapy, the antibody molecule comprising the heavy chain sequence set forth in SEQ ID NO: 1 and the light chain sequence set forth in SEQ ID NO: 2;

~~wherein a tumour of the patient has been determined to have an acquired resistance phenotype in respect of the prior anti-PD-1 or anti-PD-L1 therapy, and~~

~~wherein a tumour with an acquired resistance phenotype is a tumour which showed a complete or partial response to treatment with the prior anti-PD-1 or anti-PD-L1 therapy, or showed stable disease for more than 3 months whilst subjected to treatment with the prior anti-PD-1 or anti-PD-L1 therapy.~~

~~117.~~ A method of treating cancer in a human patient who has been subjected to treatment with a prior anti-PD-1 or anti-PD-L1 therapy, the method comprising administering to the patient a therapeutically effective amount of The use of an antibody molecule which binds PD-L1 and LAG-3 and comprises the heavy chain sequence set forth in SEQ ID NO: 1 and the light chain sequence set forth in SEQ ID NO: 2 in the manufacture of a medicament for treating cancer in a human patient who has been subjected to treatment with a prior anti-PD-1 or anti-PD-L1 therapy;

~~wherein a tumour of the patient has been determined to have acquired resistance phenotype in respect of the prior anti-PD-1 or anti-PD-L1 therapy, and~~

~~wherein a tumour with an acquired resistance phenotype is a tumour which showed a complete or partial response to treatment with the prior anti-PD-1 or anti-PD-L1 therapy, or~~

showed stable disease for more than 3 months whilst subjected to treatment with the prior anti-PD-1 or anti-PD-L1 therapy, and

wherein the antibody molecule is to be administered to the patient once weekly at a dose of 10 mg to 20 mg per kg of body weight of the patient.

~~128.~~ The ~~antibody molecule for use, or method,~~ according to ~~any one of claims 10 to 117,~~ wherein at least 15% of tumour cells in a sample of the tumour obtained from the patient prior to treatment with the antibody have been determined to be PD-L1 positive.

9. The use according to any one of claims 1 to 8, further comprising a chemotherapeutic agent that is to be administered to the patient.

10. The use according to claim 9, wherein the chemotherapeutic agent is a taxane, cytotoxic antibiotic, tyrosine kinase inhibitor, PARP inhibitor, B-RAF enzyme inhibitor, HDAC inhibitor, mTOR inhibitor, alkylating agent, platinum analog, nucleoside analog, thalidomide derivative, or antineoplastic chemotherapeutic agent.

11. The use according to claim 10, wherein the chemotherapeutic agent is paclitaxel.

~~1312.~~ A method of determining whether a cancer patient who has been subjected to treatment with a prior anti-PD-1 or anti-PD-L1 therapy is likely to respond to treatment with an antibody molecule which binds PD-L1 and LAG-3 and comprises the heavy chain sequence set forth in SEQ ID NO: 1 and the light chain sequence set forth in SEQ ID NO: 2, the method comprising
determining whether a tumour of the patient has an acquired resistance phenotype or primary resistance phenotype in respect of the prior anti-PD-1 or anti-PD-L1 therapy, wherein a tumour with an acquired resistance phenotype has a higher likelihood of responding to treatment with the antibody than a tumour with a primary resistance phenotype; and

wherein a tumour with an acquired resistance phenotype is a tumour which showed a complete or partial response to treatment with the prior anti-PD-1 or anti-PD-L1 therapy, or showed stable disease for more than 3 months whilst subjected to treatment with the prior anti-PD-1 or anti-PD-L1 therapy, and

a tumour with a primary resistance phenotype is a tumour which achieved stable disease for 3 months or less whilst subjected to treatment with the prior anti-PD-1 or anti-PD-L1 therapy, including a tumour with a best overall response of progressive disease-

~~14. The method according to claim 13, the method further comprising; and~~
determining whether at least 15% of tumour cells in a sample of the tumour obtained from the patient prior to treatment with the antibody are PD-L1 positive,

wherein a tumour with an acquired resistance phenotype comprising at least 15% PD-L1 positive tumour cells has a higher likelihood of responding to treatment with the antibody than a tumour with a primary resistance phenotype, or a tumour with an acquired resistance phenotype comprising less than 15% PD-L1 positive tumour cells.

~~15~~13. The ~~antibody molecule for use, or method,~~ according to any one of claims 1 to ~~14~~12, wherein the cancer is selected from the list consisting of: squamous cell carcinoma of the head and neck (SCCHN), gastric cancer, oesophageal cancer, non-small cell lung cancer (NSCLC), mesothelioma, melanoma, prostate cancer, bladder cancer, breast cancer, colorectal cancer (CRC), adenocarcinoma of the esophagogastric junction (GEJ), renal cell

carcinoma (RCC), hepatocellular carcinoma (HCC), small-cell lung cancer (SCLC), uterine cancer, vulvar cancer, testicular cancer, penile cancer, leukaemia, Merkel cell carcinoma and nasopharyngeal cancer.

~~1614.~~ The ~~antibody molecule for use,~~ or method, according to any one of claims 1 to ~~1412~~, wherein the cancer is selected from the list consisting of: sarcoma, thyroid cancer, glioblastoma multiforme (GBM), ovarian cancer, basal cell carcinoma, MSI-H solid tumours, triple negative breast cancer (TNBC), cervical cancer, oesophageal cancer, multiple myeloma (MM), pancreatic cancer, meningioma, endometrial cancer, thymic carcinoma, gestational trophoblastic neoplasia, lymphomas, peritoneal carcinomatosis, microsatellite stable (MSS) colorectal cancer, and gastrointestinal stromal tumours (GIST).

~~1715.~~ The ~~antibody molecule for use,~~ or method, according to any one of claims 1 to ~~1412~~, wherein the cancer is selected from the list consisting of: head and neck cancer, gastric cancer, oesophageal cancer, NSCLC, mesothelioma, cervical cancer, thyroid cancer and soft-tissue sarcoma; preferably wherein the head and neck cancer is SCCHN.

~~1816.~~ The ~~antibody molecule for use,~~ or method, according to any one of claims 1 to ~~1412~~, wherein the cancer is head and neck cancer, preferably SCCHN.

~~1917.~~ The ~~antibody molecule for use,~~ or method, according to claim ~~1816~~, wherein the SCCHN disease site is the oral cavity, oropharynx, larynx or hypopharynx.

~~20.~~—The ~~antibody molecule for use,~~ or method, according to claim ~~18~~ or ~~19~~ wherein the method comprises administering the antibody molecule to the patient once weekly at a dose of 10mg per kg of body weight of the patient.

~~2118.~~ The ~~antibody molecule for use,~~ or method, according to any one of claims 1 to ~~2011~~, ~~and 13 to 17~~, wherein the antibody molecule is to be administered intravenously.