

What is claimed is:

5 Claim 1: A ~~method of~~combination comprising durvalumab and a chemotherapy for use in preventing a recurrent tumor in a patient in need thereof, ~~comprising administering durvalumab and chemotherapy to the patient,~~ wherein the patient is minimal residual disease-positive (MRD+).

10 Claim 2: The ~~method~~combination for use of claim 1, wherein the chemotherapy comprises at least one of paclitaxel, carboplatin, pemetrexed, or cisplatin.

Claim 3: The ~~method~~combination for use of claim 1, wherein the tumor is a lung tumor, a breast tumor, a colorectal tumor, a prostate tumor, or a melanoma.

15 Claim 4: The ~~method~~combination for use of claim 3, wherein the tumor is a non-small cell lung tumor.

Claim 5: The ~~method~~combination for use of claim 4, wherein the non-small cell lung tumor is a squamous cell carcinoma, an adenocarcinoma, or a large cell carcinoma.

20 Claim 6: The ~~method~~combination for use of claim 4, wherein the patient previously underwent complete resection of a non-small cell lung tumor.

25 Claim 7: The ~~method~~combination for use of claim 6, wherein the non-small cell lung tumor was stage I, stage II, or stage III.

Claim 8: The ~~method~~combination for use of claim 1, wherein the combination of durvalumab and the chemotherapy ~~are~~is to be administered every three weeks.

30 Claim 9: The ~~method~~combination for use of claim 1, wherein the combination of durvalumab and the chemotherapy ~~are~~is to be administered every four weeks.

Claim 10: The ~~method~~combination for use of claim 1, wherein the combination of durvalumab and the chemotherapy ~~are~~is to be administered every three weeks for four doses followed by administration of durvalumab every four weeks.

5 Claim 11: The ~~method~~combination for use of claim 1, wherein the combination of durvalumab and the ~~least one~~ chemotherapy ~~are~~is to be administered simultaneously, separately, or sequentially.

10 Claim 12: The ~~method~~combination for use of any one of claims 1-11, wherein ~~the~~ administration of the combination of durvalumab and the chemotherapy results in increased disease free survival as compared to standard of care.

15 Claim 13: ~~A method of~~Use of a combination of durvalumab and a chemotherapy for the manufacture of a medicament for treating a recurrent tumor in a patient in need thereof, ~~comprising wherein:~~
(a) ~~determining~~ whether the patient is minimal residual disease-positive (MRD+); ~~+~~is to be determined; and
(b) ~~treating or continuing treatment if the patient is~~ to be treated or continued to be ~~treated if he has been identified as MRD+, wherein the treatment comprises treatment with~~
20 ~~durvalumab and chemotherapy.~~+

Claim 14: The ~~method~~use of claim 13, wherein the chemotherapy comprises at least one of paclitaxel, carboplatin, pemetrexed, or cisplatin.

25 Claim 15: The ~~method~~use of claim 13, wherein the tumor is a lung tumor, a breast tumor, a colorectal tumor, a prostate tumor, or a melanoma.

Claim 16: The ~~method~~use of claim 15, wherein the tumor is a non-small cell lung tumor.

30 Claim 17: The ~~method~~use of claim 16, wherein the non-small cell lung tumor is a squamous cell carcinoma, an adenocarcinoma, or a large cell carcinoma.

Claim 18: The ~~method~~use of claim 16, wherein the patient previously underwent complete resection of a non-small cell lung tumor.

5 Claim 19: The ~~method~~use of claim 18, wherein the non-small cell lung tumor was stage I, stage II, or stage III.

Claim 20: The ~~method~~use of claim 13, wherein the combination of durvalumab and the chemotherapy ~~are~~is to be administered every three weeks.

10 Claim 21: The ~~method~~use of claim 13, wherein the combination of durvalumab and the chemotherapy ~~are~~is to be administered every four weeks.

15 Claim 22: The ~~method~~use of claim 13, wherein the combination of durvalumab and the chemotherapy ~~are~~is to be administered every three weeks for four doses followed by administration of durvalumab every four weeks.

20 Claim 23: The ~~method~~use of claim 13, wherein the combination of durvalumab and the ~~least one~~ chemotherapy ~~are~~is to be administered simultaneously, separately, or sequentially.

25 Claim 24: The ~~method of claim 13~~combination for use of any one of claims 1-11, wherein ~~whether~~ the patient is determined to be minimal residual disease-positive (MRD+) ~~is determined~~ by:

(a) sequencing all or part of the genome or exome of a tumor of the patient to define clonal and/or subclonal mutations in the tumor;

(b) defining a set of reagents that will detect the presence of DNA from the tumor via the presence of the clonal and/or subclonal mutations; and

(c) analyzing a sample comprising DNA from the tumor obtained from the patient subsequent to the tumor removal and the defined set of reagents to determine whether the tumor has recurred by detection of the clonal and/or subclonal mutations in the sample.

Claim 25: The ~~method~~combination for use of claim 24, wherein the sequencing is carried out on a tumor biopsy, all or part of the tumor or one or more subsections of the tumor, cell free DNA (cfDNA), circulating tumor DNA, exosome derived tumor DNA, or circulating tumor cells from the subject.

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Claim 26: The ~~method~~combination for use of claim 25, wherein the sequencing is carried out on the tumor or subsection thereof following removal of the tumor.

Claim 27: The ~~method~~combination for use of claim 24, wherein all or part of the genome or exome of at least two subsections of the tumor is sequenced and clonal and/or subclonal mutations are defined based on which mutations occur in which tumor subsections.

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Claim 28: The ~~method~~combination for use of any one of claims 24-27, wherein the defined set of reagents comprise multiplex PCR primers and the analysis is a multiplex PCR.

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Claim 29: The ~~method~~combination for use of any one of claims 24-27, wherein the sequencing is carried out on blood plasma obtained from the patient, or the sample to be analyzed is a blood plasma sample from the patient.

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Claim 30: The ~~method~~combination for use of any one of claims ~~13-23~~1-11, wherein ~~the treatment is an adjuvant treatment~~ is to be administered to the patient.

Claim 31: The ~~method~~combination for use of any one of claims ~~13-23~~ further comprising administration of 1-11, wherein radiotherapy is to be administered to the patient.

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Claim 32: The ~~method~~use of any one of claims 13-23, wherein ~~the administration of the combination~~ of durvalumab and the chemotherapy results in increased disease free survival as compared to standard of care.

Claim 33: Use of a combination comprising durvalumab and a chemotherapy in the manufacture of a medicament for preventing a recurrent tumor in a patient in need thereof, wherein the patient is minimal residual disease-positive (MRD+).

5 Claim 34: The use of claim 33, wherein the chemotherapy comprises at least one of paclitaxel, carboplatin, pemetrexed, or cisplatin.

Claim 35: The use of claim 33, wherein the tumor is a lung tumor, a breast tumor, a colorectal tumor, a prostate tumor, or a melanoma.

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Claim 36: The use of claim 35, wherein the tumor is a non-small cell lung tumor.

Claim 37: The use of claim 36, wherein the non-small cell lung tumor is a squamous cell carcinoma, an adenocarcinoma, or a large cell carcinoma.

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Claim 38: The use of claim 36, wherein the patient previously underwent complete resection of a non-small cell lung tumor.

Claim 39: The use of claim 38, wherein the non-small cell lung tumor was stage I, stage II, or stage III.

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Claim 40: The use of claim 33, wherein the combination of durvalumab and the chemotherapy is to be administered every three weeks.

25 Claim 41: The use of claim 33, wherein the combination of durvalumab and the chemotherapy is to be administered every four weeks.

Claim 42: The use of claim 33, wherein the combination of durvalumab and the chemotherapy is to be administered every three weeks for four doses followed by administration of durvalumab every four weeks.

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Claim 43: The use of claim 33, wherein the combination of durvalumab and the chemotherapy is to be administered simultaneously, separately, or sequentially.

Claim 44: The use of any one of claims 33-43, wherein administration of the combination of durvalumab and the chemotherapy results in increased disease free survival as compared to standard of care.

Claim 45: The use of any one of claims 33-43, wherein the patient is determined to be minimal residual disease-positive (MRD+) by:

(a) sequencing all or part of the genome or exome of a tumor of the patient to define clonal and/or subclonal mutations in the tumor;

(b) defining a set of reagents that will detect the presence of DNA from the tumor via the presence of the clonal and/or subclonal mutations; and

(c) analyzing a sample comprising DNA from the tumor obtained from the patient subsequent to the tumor removal and the defined set of reagents to determine whether the tumor has recurred by detection of the clonal and/or subclonal mutations in the sample.

Claim 46: The use of claim 45, wherein the sequencing is carried out on a tumor biopsy, all or part of the tumor or one or more subsections of the tumor, cell free DNA (cfDNA), circulating tumor DNA, exosome derived tumor DNA, or circulating tumor cells from the subject.

Claim 47: The use of claim 46, wherein the sequencing is carried out on the tumor or subsection thereof following removal of the tumor.

Claim 48: The use of claim 45, wherein all or part of the genome or exome of at least two subsections of the tumor is sequenced and clonal and/or subclonal mutations are defined based on which mutations occur in which tumor subsections.

Claim 49: The use of any one of claims 45-48, wherein the defined set of reagents comprise multiplex PCR primers and the analysis is a multiplex PCR.

Claim 50: The use of any one of claims 45-48, wherein the sequencing is carried out on blood plasma obtained from the patient, or the sample to be analyzed is a blood plasma sample from the patient.

5 Claim 51: The use of any one of claims 33-43, wherein an adjuvant treatment is to be administered to the patient.

Claim 52: The use of any one of claims 33-43, wherein radiotherapy is to be administered to the patient.

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