

WHAT IS CLAIMED IS:

Claim 1. — A method of treating a tumor in a subject in need thereof, comprising administering to the subject:

(i) — a therapeutically effective amount of an anti-PD-L1 antibody or an antigen-binding fragment thereof; and

(ii) — an anti-CTLA-4 antibody or an antigen-binding fragment thereof at a dose between 1 mg/kg to 10 mg/kg.

Claim 2. — The method according to claim 1, wherein the anti-CTLA-4 antibody or antigen-binding fragment thereof is administered at a dose of 1 mg/kg.

Claim 3. — The method according to either claim 1 or 2, wherein the anti-PD-L1 antibody or antigen-binding fragment thereof is administered at a dose of between 15 mg/kg to 25 mg/kg.

Claim 4. — The method according to any one of claims 1 to 3, wherein the anti-CTLA-4 antibody or antigen-binding fragment thereof is tremelimumab.

Claim 5. — The method according to any one of claims 1 to 4, wherein the anti-PD-L1 antibody or antigen-binding fragment thereof is durvalumab.

Claim 6. — The method according to any one of claims 1 to 5, wherein the anti-PD-L1 antibody or antigen-binding fragment thereof and the anti-CTLA-4 antibody or antigen-binding fragment thereof are administered every four weeks.

Claim 7. — The method according to claim 6, wherein the anti-PD-L1 antibody or antigen-binding fragment thereof and the anti-CTLA-4 antibody or antigen-binding fragment thereof are administered every four weeks for four doses followed by administration of the anti-PD-L1 antibody or antigen-binding fragment thereof every four weeks.

Claim 8. — The method according to any one of claims 1 to 7, wherein the anti-PD-L1 antibody or antigen-binding fragment thereof and the anti-CTLA-4 antibody or antigen-binding fragment thereof are administered simultaneously, separately, or sequentially.

Claim 9. — ~~The method according to any one of claims 1 to 8, further comprising administering transarterial chemoembolization (TACE).~~

Claim 10. — ~~The method according to any one of claims 1 to 9, wherein the tumor is a hepatocellular carcinoma (HCC).~~

Claim 11. — ~~The method according to any one of claims 1 to 10, wherein the anti-PD-L1 antibody or antigen-binding fragment thereof is durvalumab administered at a dose of 20 mg/kg and the anti-CTLA-4 antibody or antigen-binding fragment thereof is tremelimumab administered at a dose of 1 mg/kg.~~

Claim 12. — ~~A method of treating a tumor in a subject in need thereof, comprising administering to the subject:~~

~~(i) — a therapeutically effective amount of an anti-PD-L1 antibody or an antigen-binding fragment thereof; and~~

~~(ii) — an anti-CTLA-4 antibody or an antigen-binding fragment thereof at a flat dose of between 75 mg to 1120 mg.~~

Claim 13. — ~~The method according to claim 12, wherein the anti-PD-L1 antibody or antigen-binding fragment thereof is administered at a dose of between 1000 mg to 1600 mg.~~

Claim 14. — ~~The method according to claim 12, wherein the anti-CTLA-4 antibody or antigen-binding fragment thereof is administered at a dose of 75 mg.~~

Claim 15. — ~~The method according to claim 12, wherein the anti-CTLA-4 antibody or antigen-binding fragment thereof is administered at a dose of 300 mg.~~

Claim 16. — ~~The method according to any one of claims 12 to 15, wherein the anti-CTLA-4 antibody or antigen-binding fragment thereof is tremelimumab.~~

Claim 17. — ~~The method according to any one of claims 12 to 16, wherein the anti-PD-L1 antibody or antigen-binding fragment thereof is durvalumab.~~

Claim 18.——The method according to any one of claims 12 to 17, wherein the anti-PD-L1 antibody or antigen-binding fragment thereof and the anti-CTLA-4 antibody or the antigen-binding fragment thereof are administered every four weeks.

Claim 19.——The method according to claim 18, wherein the anti-PD-L1 antibody or antigen-binding fragment thereof and the anti-CTLA-4 antibody or antigen-binding fragment thereof are administered every four weeks for four doses followed by administration of the anti-PD-L1 antibody or antigen-binding fragment thereof every four weeks.

Claim 20.——The method according to any one of claims 12 to 19, wherein the anti-PD-L1 antibody or antigen-binding fragment thereof and the anti-CTLA-4 antibody or the antigen-binding fragment thereof are administered for one dose followed by administration of the anti-PD-L1 antibody or antigen-binding fragment thereof every four weeks.

Claim 21.——The method according to any one of claims 12 to 20, wherein the anti-PD-L1 antibody or antigen-binding fragment thereof and the anti-CTLA-4 antibody or antigen-binding fragment thereof are administered simultaneously, separately, or sequentially.

Claim 22.——The method according to any one of claims 12 to 21, further comprising administering transarterial chemoembolization (TACE).

Claim 23.——The method according to any one of claims 12 to 22, wherein the tumor is a hepatocellular carcinoma (HCC).

Claim 24.——The method according to any one of claims 12 to 23, wherein the anti-PD-L1 antibody or antigen-binding fragment thereof is durvalumab administered at a dose of 1500 mg and the anti-CTLA-4 antibody or antigen-binding fragment thereof is tremelimumab administered at a dose of 75 mg.

Claim 25.——The method according to any one of claims 13 to 25, wherein the anti-PD-L1 antibody or antigen-binding fragment thereof is durvalumab administered at a dose of 1500 mg and the anti-CTLA-4 antibody or antigen-binding fragment thereof is tremelimumab administered at a dose of 300 mg.

Claim 26. — A method of treating a tumor in a subject in need thereof, comprising administering to the subject an anti-CTLA-4 antibody or an antigen-binding fragment thereof at a dose of between 5 mg/kg to 15 mg/kg.

Claim 27. — A method of treating a tumor in a subject in need thereof, comprising administering to the subject an anti-CTLA-4 antibody or an antigen-binding fragment thereof at a flat dose of between 650 mg to 850 mg.

Claim 28. — The method according to claim 26, wherein the anti-CTLA-4 antibody or antigen-binding fragment thereof is administered at a dose of 10 mg/kg.

Claim 29. — The method according to claim 27, wherein the anti-CTLA-4 antibody or antigen-binding fragment thereof is administered at a dose of 750 mg.

Claim 30. — The method according to any one of claims 26 to 29, wherein the anti-CTLA-4 antibody or antigen-binding fragment thereof is tremelimumab.

Claim 31. — The method according to any one of claims 26 to 30, wherein the anti-CTLA-4 antibody or the antigen-binding fragment thereof is administered every four weeks.

Claim 32. — The method according to any one of claims 26 to 30, wherein the anti-CTLA-4 antibody or the antigen-binding fragment thereof is administered every twelve weeks.

Claim 33. — The method according to any one of claims 26 to 30, further comprising administering transarterial chemoembolization (TACE).

Claim 34. — The method according to any one of claims 28 to 33, wherein the tumor is a hepatocellular carcinoma (HCC).

Claim 35. — The method according to claim 27, wherein the anti-CTLA-4 antibody or antigen-binding fragment thereof is tremelimumab administered at a dose of 750 mg every four weeks for seven doses followed by administration of tremelimumab at a dose of 750 mg every twelve weeks.

Claim ~~136~~. A combination for use in the treatment of a tumor in a subject in need thereof, wherein the combination comprises:

(i) ~~20 mg/kg a therapeutically effective amount of an anti-PD-L1 antibody or an antigen-binding fragment thereof on day 1 of treatment followed by administration of 20 mg/kg of the anti-PD-L1 antibody or antigen-binding fragment thereof every 4 weeks; and~~

(ii) ~~4 mg/kg of an anti-CTLA-4 antibody or an antigen-binding fragment thereof as a single dose on day 1 of treatment at a dose between 1 mg/kg to 10 mg/kg,~~

wherein the pharmaceutical combination comprises the anti-PD-L1 antibody or antigen-binding fragment thereof, and the anti-CTLA-4 antibody or antigen-binding fragment thereof.

Claim ~~37~~. ~~The combination according to claim 36, wherein the dose of the anti-CTLA-4 antibody or antigen-binding fragment thereof is 1 mg/kg.~~

Claim ~~38~~. ~~The combination according to either claim 36 or 37, wherein the dose of the anti-PD-L1 antibody or antigen-binding fragment thereof is between 15 mg/kg to 25 mg/kg.~~

Claim ~~239~~. The combination according to ~~any one of claims 136 to 38~~, wherein the anti-CTLA-4 antibody or antigen-binding fragment thereof is tremelimumab.

Claim ~~340~~. The combination according to ~~any one of claims 1 or 236 to 39~~, wherein the anti-PD-L1 antibody or antigen-binding fragment thereof is durvalumab.

Claim ~~41~~. ~~The combination according to any one of claims 36 to 40, wherein the anti-PD-L1 antibody or antigen-binding fragment thereof and the anti-CTLA-4 antibody or antigen-binding fragment thereof are administered to the subject every four weeks.~~

Claim ~~42~~. ~~The combination according to claim 41, wherein the anti-PD-L1 antibody or antigen-binding fragment thereof and the anti-CTLA-4 antibody or antigen-binding fragment thereof are administered to the subject every four weeks for four doses followed by administration of the anti-PD-L1 antibody or antigen-binding fragment thereof to the subject every four weeks.~~

Claim ~~443~~. The combination according to any one of claims ~~136~~ to ~~342~~, wherein the anti-PD-L1 antibody or antigen-binding fragment thereof and the anti-CTLA-4 antibody or antigen-binding fragment thereof are administered to the subject simultaneously, separately, or sequentially.

Claim ~~544~~. The combination according to any one of claims ~~136~~ to ~~443~~, wherein the combination further comprises administering transarterial chemoembolization (TACE) to the subject.

Claim ~~645~~. The combination according to any one of claims ~~136~~ to ~~544~~, wherein the tumor is a hepatocellular carcinoma (HCC).

~~Claim 46. The combination according to any one of claims 36 to 45, wherein the anti-PD-L1 antibody or antigen-binding fragment thereof is durvalumab at a dose of 20 mg/kg and the anti-CTLA-4 antibody or antigen-binding fragment thereof is tremelimumab at a dose of 1 mg/kg.~~

Claim ~~747~~. A combination for use in the treatment of a tumor in a subject in need thereof, wherein the combination comprises:

(i) ~~1500 mg a therapeutically effective amount of an anti-PD-L1 antibody or an antigen-binding fragment thereof~~ on day 1 of treatment followed by administration of the anti-PD-L1 antibody or antigen-binding fragment thereof every 4 weeks; and

(ii) 300 mg of an anti-CTLA-4 antibody or an antigen-binding fragment thereof as a single dose on day 1 of treatment ~~at a flat dose of between 75 mg to 1120 mg.~~

wherein the pharmaceutical combination comprises the anti-PD-L1 antibody or antigen-binding fragment thereof, and the anti-CTLA-4 antibody or antigen-binding fragment thereof.

~~Claim 48. The combination according to claim 47, wherein the dose of the anti-PD-L1 antibody or antigen-binding fragment thereof is between 1000 mg to 1600 mg.~~

~~Claim 49. The combination according to claim 47, wherein the dose of the anti-CTLA-4 antibody or antigen-binding fragment thereof is 75 mg.~~

Claim 50. — ~~The combination according to claim 47, wherein the dose of the anti-CTLA-4 antibody or antigen-binding fragment thereof is 300 mg.~~

Claim 851. The combination according to ~~any one of claims 747 to 50~~, wherein the anti-CTLA-4 antibody or antigen-binding fragment thereof is tremelimumab.

Claim 952. The combination according to ~~any one of claims 7 or 847 to 51~~, wherein the anti-PD-L1 antibody or antigen-binding fragment thereof is durvalumab.

Claim 53. — ~~The combination according to any one of claims 47 to 52, wherein the anti-PD-L1 antibody or antigen-binding fragment thereof and the anti-CTLA-4 antibody or the antigen-binding fragment thereof are administered to the subject every four weeks.~~

Claim 54. — ~~The combination according to claim 53, wherein the anti-PD-L1 antibody or antigen-binding fragment thereof and the anti-CTLA-4 antibody or antigen-binding fragment thereof are administered to the subject every four weeks for four doses followed by administration of the anti-PD-L1 antibody or antigen-binding fragment thereof to the subject every four weeks.~~

Claim 55. — ~~The combination according to any one of claims 47 to 54, wherein the anti-PD-L1 antibody or antigen-binding fragment thereof and the anti-CTLA-4 antibody or the antigen-binding fragment thereof are administered to the subject for one dose followed by administration of the anti-PD-L1 antibody or antigen-binding fragment thereof to the subject every four weeks.~~

Claim 1056. The combination according to any one of claims 747 to 955, wherein the anti-PD-L1 antibody or antigen-binding fragment thereof and the anti-CTLA-4 antibody or antigen-binding fragment thereof are administered to the subject simultaneously, separately, or sequentially.

Claim 1157. The combination according to any one of claims 747 to 1056, wherein the combination further comprises administering transarterial chemoembolization (TACE) to the subject.

Claim 1258. The combination according to any one of claims 747 to 1157, wherein the tumor is a hepatocellular carcinoma (HCC).

~~Claim 59. The combination according to any one of claims 47 to 58, wherein the anti-PD-L1 antibody or antigen-binding fragment thereof is durvalumab at a dose of 1500 mg and the anti-CTLA-4 antibody or antigen-binding fragment thereof is tremelimumab at a dose of 75 mg.~~

~~Claim 60. The combination according to any one of claims 48 to 59, wherein the anti-PD-L1 antibody or antigen-binding fragment thereof is durvalumab at a dose of 1500 mg and the anti-CTLA-4 antibody or antigen-binding fragment thereof is tremelimumab at a dose of 300 mg.~~

~~Claim 61. A combination for the treatment of a tumor in a subject in need thereof, wherein the combination comprises an anti-CTLA-4 antibody or an antigen-binding fragment thereof at a dose of between 5 mg/kg to 15 mg/kg.~~

Claim 1362. A composition combination for use in the treatment of a tumor in a subject in need thereof, wherein the composition combination comprises an anti-CTLA-4 antibody or an antigen-binding fragment thereof at a flat dose of between 650 mg to 850 mg.

~~Claim 63. The combination according to claim 61, wherein the dose of the anti-CTLA-4 antibody or antigen-binding fragment thereof is 10 mg/kg.~~

Claim 1464. The composition combination according to claim 1362, wherein the dose of the anti-CTLA-4 antibody or antigen-binding fragment thereof is 750 mg.

Claim 1565. The composition combination according to ~~any one of claims 13 or 1461 to 64~~, wherein the anti-CTLA-4 antibody or antigen-binding fragment thereof is tremelimumab.

Claim 1666. The composition combination according to any one of claims 1361 to 1565, wherein the anti-CTLA-4 antibody or the antigen-binding fragment thereof is administered to the subject every four weeks.

Claim ~~1767~~. The composition combination according to any one of claims ~~1361~~ to ~~1665~~, wherein the anti-CTLA-4 antibody or the antigen-binding fragment thereof is to be administered to the subject every twelve weeks.

Claim ~~1868~~. The composition combination according to any one of claims ~~1361~~ to ~~1765~~, wherein the combination further comprises administering transarterial chemoembolization (TACE) to the subject.

Claim ~~1969~~. The composition combination according to any one of claims ~~1363~~ to ~~1868~~, wherein the tumor is a hepatocellular carcinoma (HCC).

Claim ~~2070~~. The composition combination according to claim ~~1362~~, wherein the anti-CTLA-4 antibody or antigen-binding fragment thereof is tremelimumab administered to the subject at a dose of 750 mg every four weeks for seven doses followed by administration to the subject of tremelimumab at a dose of 750 mg every twelve weeks.