

CLAIMS

1. Use of a polypeptide comprising a SIRP α D1 domain variant and an Fc domain variant in the manufacture of a medicament for treating cancer in an individual;
wherein the SIRP α D1 domain variant comprises the amino acid sequence of SEQ ID NO: 81 or SEQ ID NO: 85;
wherein the Fc domain variant is
 - (i) a human IgG1 Fc region comprising L234A, L235A, G237A, and N297A mutations, wherein numbering is according to the EU index of Kabat;
 - (ii) a human IgG2 Fc region comprising A330S, P331S, and N297A mutations, wherein numbering is according to the EU index of Kabat;
 - (iii) a human IgG4 Fc region comprising S228P, E233P, F234V, L235A, and delG236 mutations, wherein numbering is according to the EU index of Kabat; or
 - (iv) a human IgG4 Fc region comprising S228P, E233P, F234V, L235A, delG236, and N297A mutations, wherein numbering is according to the EU index of Kabat;wherein the medicament is to be administered to the individual in combination with (a) a PD-1 inhibitor, (b) an antimetabolite, and (c) a platinum-based chemotherapy agent;
wherein the cancer is head and neck squamous cell carcinoma (HNSCC), and
wherein the individual has not received prior treatment for HNSCC.
2. The use according to claim 1, wherein the HNSCC is advanced and/or metastatic HNSCC.
3. The use according to claim 1 or 2, wherein the PD-1 inhibitor is an anti-PD-1 antibody.
4. The use according to claim 3, wherein the anti-PD-1 antibody is pembrolizumab, nivolumab, pidilizumab, cemiplimab, or BMS-936559.
5. The use according to claim 4, wherein the anti-PD-1 antibody is pembrolizumab.
6. The use according to any one of claims 1-5, wherein the antimetabolite is 5-fluorouracil, 6-mercaptopurine, capecitabine, cytarabine, floxuridine, fludarabine, gemcitabine, hydroxycarbamide, methotrexate, pemetrexed, phototrexate.

7. The use according to claim 6, wherein the antimetabolite is 5-fluorouracil.
8. The use according to any one of claims 1-7, wherein the polypeptide comprising a SIRP α D1 domain variant and an Fc domain variant is to be administered at a dose of 10 mg/kg once a week.
9. The use according to any one of claims 1-7, wherein the polypeptide comprising a SIRP α D1 domain variant and an Fc domain variant is to be administered at a dose of 15 mg/kg once a week.
10. The use according to any one of claims 1-7, wherein the platinum-based chemotherapy agent is carboplatin, cisplatin, oxaliplatin, nedaplatin, triplatin tetranitrate, phenanthriplatin, picoplatin, or satraplatin.
11. The use according to claim 10, wherein the platinum-based chemotherapy agent is cisplatin.
12. The use according to claim 10, wherein the platinum-based chemotherapy agent is carboplatin.
13. The use according to any one of claims 1-12, wherein the SIRP α D1 domain variant comprises the amino acid sequence of SEQ ID NO: 85.
14. The use according to any one of claims 1-12, wherein the SIRP α D1 domain variant comprises the amino acid sequence of SEQ ID NO: 81.
15. The use according to any one of claims 1-14, wherein the Fc domain variant is a human IgG1 Fc region comprising L234A, L235A, G237A, and N297A mutations, wherein numbering is according to the EU index of Kabat.
16. The use according to claim 15, wherein the Fc domain variant comprises the amino acid sequence of SEQ ID NO: 91.

17. The use according to any one of claims 1-13 and 15-16, wherein the polypeptide comprising a SIRP α D1 domain variant and an Fc domain variant comprises the amino acid sequence of SEQ ID NO: 136.
18. The use according to any one of claims 1-12 and 14-16, wherein the polypeptide comprising a SIRP α D1 domain variant and an Fc domain variant comprises the amino acid sequence of SEQ ID NO: 135.
19. The use according to any one of claims 1-18, wherein the polypeptide comprising a SIRP α D1 domain variant and an Fc domain variant forms a homodimer.
20. The use according to any one of claims 1-19, wherein the individual is a human.