Claims

1. A vaccine/inhibitor combination comprising:

(i) as vaccine an RNA vaccine comprising at least one RNA, wherein said at least one RNA is an mRNA, comprising at least one open reading frame (ORF) coding for at least one antigen and

(ii) as inhibitor a composition comprising a PD-1 pathway inhibitor~~.~~, wherein the PD-1 pathway inhibitor is an antagonistic antibody directed against PD-L1.

2. The combination according to claim 1, wherein the ~~PD-1 pathway inhibitor is selected from the group consisting of an inhibitor directed against PD-1, PD-L1 or PD-L2.~~

~~3. The combination according to claim 1 or 2, wherein the PD-1 pathway inhibitor is selected from the group consisting of an an antagonistic antibody or a nucleic acid encoded antagonistic antibody, an siRNA, an antisense RNA, a protein comprising or a nucleic acid coding for an amino acid sequence capable of binding to PD-1 but preventing PD-1 pathway signaling, a soluble protein or a nucleic acid coding for a soluble protein competing with PD-1 for binding of its ligands PD-L1 and PD-L2, and a small molecule inhibitor.~~

~~4. The combination according to claim 3, wherein the PD-1 pathway inhibitor is an antibody or a nucleic acid encoded antibody which is directed against PD-1 or PD-1 ligand.~~

~~5. The combination according to claim 4, wherein the antibody directed against PD-1 is Nivolumab (BMS-936558/MDX1106), CT-011 or MK-3475 (SCH 900475).~~

~~6. The combination according to claim 4, wherein the~~ antibody directed against PD-L1 is MDX-1105/BMS-936559, MPDL3280A/RG7446~~,~~ (atezolizumab), or *MEDI4736~~.~~ (durvalumab).*

~~7. The combination according to claim 3, wherein the protein comprising or a nucleic acid coding for an amino acid sequence capable of binding to PD-1 but preventing PD-1 pathway signaling is a fusion protein of a fragment of PD-L1 or PD-L2 ligand.~~

~~8. The combination according to claim 7, wherein the fusion protein is a fusion protein of the extracellular domain of PD-L1 or PD-L2 or a fragment thereof capable of binding to PD-1.~~

~~9. The combination according to claim 8, wherein the fusion protein is a fusion protein of the extracellular domain of PD-L2 and an Fc portion of an immunoglobulin.~~

~~10. The combination according to claim 3, wherein the soluble protein is soluble PD-1 receptor which competes with membrane-bound PD-1 for binding of PD-L1 and/or PD-L2.~~

~~11.~~3. The combination according to any one of claims 1-~~10~~2, wherein the at least one RNA of the RNA vaccine is an isolated RNA.

~~12~~4. The combination according to any one of claims 1- ~~11~~3, wherein the at least one RNA of the RNA vaccine is a stabilized RNA.

~~13~~5. The combination according to any one of claims 1-~~12~~4, wherein the at least one RNA of the RNA vaccine is at least partially G/C modified~~, preferably~~.

6. The combination according to claim 5, wherein the G/C content of the at least one open reading frame of the at least one RNA of the RNA vaccine is increased compared to the wild type open reading frame.

~~14~~7. The combination according to any one of claims 1-~~13~~6, wherein the at least one RNA of the RNA vaccine comprises a codon-optimized region~~, preferably~~.

8. The combination according to claim 7, wherein the at least one open reading frame of the at least one RNA of the RNA vaccine is codon-optimized~~.~~

~~15.~~ 9. The combination according to any one of claims 1-~~14, wherein the at least one RNA of the RNA vaccine is an mRNA.~~

~~16. The combination according to any one of claims 1-15~~8, wherein the at least one RNA of the RNA vaccine is complexed with a carrier.

~~17~~10. The combination according to claim ~~16~~9, wherein the carrier is a cationic or polycationic compound or a polymeric carrier~~, preferably~~ .

11. The combination according to claim 10, wherein the carrier is protamine.

~~18~~12. A pharmaceutical composition comprising:

(i) an RNA vaccine comprising at least one RNA comprising at least one open reading frame coding for at least one antigen as defined in any one of the preceding claims ~~and~~

and

(ii) a PD-1 pathway inhibitor as defined in any one of the preceding claims.

~~19~~13. A kit of parts comprising:

(i) an RNA vaccine comprising an at least one RNA comprising at least one open reading frame coding for at least one antigen as defined in any one of the preceding claims ~~and~~

and

(ii) a composition comprising a PD-1 pathway inhibitor as defined in any one of the preceding claims.

~~20~~14. The combination according to any one of claims 1-~~17~~11, the pharmaceutical composition according to claim ~~18~~12, the kit of parts according to claim ~~19~~13 for medical use.

~~21. The~~ 15. Use of the combination according to ~~any one of claims 1-17 and 20, the pharmaceutical composition according to claim 18 or 20,~~ claim 14 in the ~~kit~~manufacture of ~~parts according to claim 19 or 20 for use in~~ a ~~method of~~medicament for preventing or treating a tumor or cancer disease or an infectious disease.

~~22~~16. The combination or kit of parts for medical use according to claim ~~20~~14 or ~~21~~15, wherein the PD-1 pathway inhibitor and the RNA vaccine are to be administered to a patient in need thereof sequentially or concurrently.

~~23.~~ 17. The combination or kit of parts for use according to claim ~~20 or 21~~16, wherein the PD-1 pathway inhibitor and the RNA vaccine are to be administered ~~to a subject in need thereof concurrently.~~

~~24. The combination or kit of parts according to any one of claims 20-23, wherein the inhibitor and the RNA vaccine are to be administered to a subject in need thereof~~ via different administration routes.

~~25~~18. A PD-1 pathway inhibitor as defined in any one of the preceding claims for use in therapy in combination with an RNA vaccine as defined in any one of the preceding claims.

~~26~~19. An RNA vaccine as defined in any one of the preceding claims for use in therapy in combination with a PD-1 pathway inhibitor as defined in any one of the preceding claims.

~~27. A method of treatment comprising administering to a subject in need thereof a therapeutically effective amount of an RNA vaccine as defined in any one of the preceding claims in combination with a PD-1 pathway inhibitor as defined in any one of the preceding claims.~~

~~28. The method of treatment according to claim 27, wherein the RNA vaccine and the PD-1 pathway inhibitor are administered sequentially and/or via different administration routes.~~