CLAIMS

1. An immunomodulator for use in the treatment, reduction, inhibition or control of a neoplastic disease in a patient intended to undergo checkpoint inhibition therapy simultaneously, separately or sequentially with administration of the immunomodulator.

2. The immunomodulator according to claim 1, wherein said checkpoint inhibition therapy comprises administration of a blocking agent, selected from a cell, protein, peptide, antibody or antigen binding fragment thereof, directed against CTLA-4, PD-1, PD-L1, TIM-3, BTLA, VISTA, LAG-3 and combinations thereof.

3. The immunomodulator according to claim 1 or claim 2, wherein said checkpoint inhibition therapy comprises administration of a sub-therapeutic amount and/or duration of said blocking agent, selected from a cell, protein, peptide, antibody or antigen binding fragment thereof.

4. The immunomodulator according to any of claims 1 to 3, wherein said neoplastic disease is associated with a cancer selected from prostate cancer, liver cancer, renal cancer, lung cancer, breast cancer, colorectal cancer, breast cancer, pancreatic cancer, brain cancer, hepatocellular cancer, lymphoma, leukaemia, gastric cancer, cervical cancer, ovarian cancer, thyroid cancer, melanoma, carcinoma, head and neck cancer, skin cancer and soft tissue sarcoma.

5. The immunomodulator according to claim 4, wherein said neoplastic disease is associated with pancreatic cancer.

6. The immunomodulator according to any of claims 1 to 5, wherein said neoplastic disease is metastatic.

7. The immunomodulator according to any of claims 1 to 6, wherein the immunomodulator comprises a whole cell *Mycobacterium*.

8. The immunomodulator according to claim 7, wherein the *Mycobacterium* is a non-pathogenic heat-killed *Mycobacterium*.

9. The immunomodulator according to claim 8, wherein the non-pathogenic heat-killed *Mycobacterium* is selected from *M. vaccae, M. obuense, M. parafortuitum, M. aurum, M. indicus pranii* and combinations thereof.

10. The immunomodulator according to any of claims 8 or 9, wherein the nonpathogenic heat-killed *Mycobacterium* is preferentially the rough variant.

11. The immunomodulator according to any of claims 8 to 10, wherein the nonpathogenic heat-killed *Mycobacterium* is for administration via the parenteral, oral, sublingual, nasal or pulmonary route.

12. The immunomodulator according to claim 11, wherein the parenteral route is selected from subcutaneous, intradermal, subdermal, intraperitonal, or intravenous.

13. The immunomodulator according to claim 12, wherein the parenteral route does not comprise intratumoural injection.

14. The immunomodulator according to any preceding claim, wherein said checkpoint inhibition therapy comprises administration of a blocking agent, selected from a cell, protein, peptide, antibody or antigen binding fragment thereof, directed against PD-L1 or PD-1.

15. The immunomodulator according to any preceding claim, wherein administration of said immunomodulator is prior to and/or after the checkpoint inhibition therapy.

16. A method of treating, reducing, inhibiting or controlling a neoplasia, tumour or cancer in a subject, wherein said method comprises simultaneously, separately or sequentially administering to the subject, (i) a checkpoint inhibitor,

and (ii) an immunomodulator, wherein said method results in enhanced therapeutic efficacy relative to administration of the checkpoint inhibitor or immunomodulator alone.

17. A method according to claim 16, wherein said checkpoint inhibition therapy comprises administration of a blocking agent, selected from a cell, protein, peptide, antibody or antigen binding fragment thereof, directed against CTLA-4, PD-1, PD-L1, TIM-3, BTLA, VISTA, LAG-3 and combinations thereof.

18. A method according to claim 16 or 17, wherein said checkpoint inhibitor is a blocking agent, selected from a cell, protein, peptide, antibody or antigen binding fragment thereof, directed against PD-1 or PD-L1.

19. A method according to any of claims 16 to 18, wherein said checkpoint inhibition therapy comprises administration of a sub-therapeutic amount of said blocking agent, selected from a cell, protein, peptide, antibody or antigen binding fragment thereof.

20. A method according to any of claims 16 to 19, wherein said neoplasia, tumour or cancer is associated with a cancer selected from prostate cancer, liver cancer, renal cancer, lung cancer, breast cancer, colorectal cancer, breast cancer, pancreatic cancer, brain cancer, hepatocellular cancer, lymphoma, leukaemia, gastric cancer, cervical cancer, ovarian cancer, thyroid cancer, melanoma, carcinoma, head and neck cancer, skin cancer and soft tissue sarcoma.

21. A method according to 20, wherein said neoplasia, tumour or cancer is associated with pancreatic cancer.

22. A method according to any of claims 16 to 21, wherein the neoplasia, tumour or cancer is metastatic.

23. A method according to any of claims 16 to 22, wherein the immunomodulator comprises a whole cell *Mycobacterium.*

24. A method according to claim 23, wherein the *Mycobacterium* is a non-pathogenic heat-killed *Mycobacterium.*

25. A method according to claim 24, wherein the non-pathogenic heat-killed *Mycobacterium* is selected from *M. vaccae, M. obuense, M. parafortuitum, M. aurum, M. indicus pranii* and combinations thereof.

26. The method according to claim 24 or 25, wherein the non-pathogenic heat-killed *Mycobacterium* is the rough variant.

27. A method according to claim 25, wherein the non-pathogenic heat-killed *Mycobacterium* is administered via the parenteral, oral, sublingual, nasal or pulmonary route.

28. A method according to claim 27, wherein the parenteral route is selected from subcutaneous, intradermal, subdermal, intraperitonal, or intravenous.

29. A method according to claim 27 or 28, wherein the parenteral route does not comprise intratumoural injection.

30. A method according to any of claims 24 to 29, wherein the amount of non-pathogenic heat-killed *Mycobacterium* administered is from 10^7 to 10^9 cells.

31. A method according to claim 16, wherein enhanced therapeutic efficacy is measured by increased overall survival time.

32. A method according to claim 16, wherein enhanced therapeutic efficacy is measured by increased progression-free survival.

33. A method according to claim 16, wherein enhanced therapeutic efficacy is measured by a decrease or stabilisation of tumour size.

34. A method according to claim 16, wherein enhanced therapeutic efficacy is measured by increased quality of life.

CLAIMS

1. A non-pathogenic heat killed *Mycobacterium* for use in the treatment, reduction, inhibition or control of a neoplastic disease in a patient intended to undergo checkpoint inhibition therapy simultaneously, separately or sequentially with administration of the *Mycobacterium.*

2. The non-pathogenic heat killed *Mycobacterium* for use according to claim 1, wherein said checkpoint inhibition therapy comprises administration of a blocking agent, selected from a cell, protein, peptide, antibody or antigen binding fragment thereof, directed against CTLA-4, PD-1, PD-L1, TIM-3, BTLA, VISTA, LAG-3 and combinations thereof.

3. The non-pathogenic heat killed *Mycobacterium* for use according to claim 1 or claim 2, wherein said checkpoint inhibition therapy comprises administration of a sub-therapeutic amount and/or duration of said blocking agent, selected from a cell, protein, peptide, antibody or antigen binding fragment thereof.

4. The non-pathogenic heat killed *Mycobacterium* for use according to any of claims 1 to 3, wherein said neoplastic disease is associated with a cancer selected from prostate cancer, liver cancer, renal cancer, lung cancer, breast cancer, colorectal cancer, breast cancer, pancreatic cancer, brain cancer, hepatocellular cancer, lymphoma, leukaemia, gastric cancer, cervical cancer, ovarian cancer, thyroid cancer, melanoma, carcinoma, head and neck cancer, skin cancer and soft tissue sarcoma.

5. The non-pathogenic heat killed *Mycobacterium* for use according to claim 4, wherein said neoplastic disease is associated with pancreatic cancer.

6. The non-pathogenic heat killed *Mycobacterium* for use according to any of claims 1 to 5, wherein said neoplastic disease is metastatic.

7. The non-pathogenic heat killed *Mycobacterium* for use according to any of claims 1 to 6, wherein the *Mycobacterium* comprises a whole cell *Mycobacterium.*

8. The non-pathogenic heat killed *Mycobacterium* for use according to claim 7, wherein the non-pathogenic heat-killed *Mycobacterium* is selected from *M. vaccae, M. obuense, M. parafortuitum, M. aurum, M. indicus pranii* and combinations thereof.

9. The non-pathogenic heat killed *Mycobacterium* for use according to claim 8, wherein the nonpathogenic heat-killed *Mycobacterium* is preferentially the rough variant.

10. The non-pathogenic heat killed *Mycobacterium* for use according to any of claims 8 or 9, wherein the nonpathogenic heat-killed *Mycobacterium* is for administration via the parenteral, oral, sublingual, nasal or pulmonary route.

11. The non-pathogenic heat killed *Mycobacterium* for use according to claim 10, wherein the parenteral route is selected from subcutaneous, intradermal, subdermal, intraperitonal, or intravenous.

12. The non-pathogenic heat killed *Mycobacterium* for use according to claim 11, wherein the parenteral route does not comprise intratumoural injection.

13. The non-pathogenic heat killed *Mycobacterium* for use according to any preceding claim, wherein said checkpoint inhibition therapy comprises administration a cell, protein, peptide, antibody or antigen binding fragment thereof, directed against PD-L1 or PD-1.

14. The non-pathogenic heat killed *Mycobacterium* for use according to any preceding claim, wherein administration of said immunomodulator is prior to and/or after the checkpoint inhibition therapy.