Claims

1. Use of a recombinant Mycobacterium cell, which is a urease-deficient, recombinant *M. bovis* BCG cell from strain Danish subtype Prague, which comprises a recombinant nucleic acid molecule without functional selection marker encoding a fusion polypeptide comprising:
(a) a domain capable of eliciting an immune response comprising the amino acid sequence from aa.41 to aa.51 in SEQ ID No.2, and
(b) a phagolysosomal escape domain encoded by a nucleic acid molecule selected from
(i) a nucleotide sequence comprising nucleotides 211-1722 as shown in SEQ ID No.1,
(ii) a nucleotide sequence which encodes the same amino acid sequence as the sequence from (i), and
(iii) a nucleotide sequence hybridizing under stringent conditions with the sequence from (i) or (ii), wherein said stringent conditions comprise washing for one hour with 0.2 X or 1X SSC and 0.1% SDS at a temperature of 55 – 68 °C,
in the manufacture of an immunotherapeutic agent for the treatment of non-muscle-invasive bladder carcinoma (NMIBC) of , a subject suffering from recurrent non-muscle-invasive bladder carcinoma, as a second-line therapy, and wherein the human subject has relapsed and/or in whom the bladder carcinoma has progressed after a first-line immunotherapy with standard BCG and wherein the bladder carcinoma recurrence is inhibited for a time period of at least 1 year.

2. The use of claim 1, wherein the administration comprises vesicular instillation into the urinary bladder.

3. The use of claim 1 or 2 in the treatment of a subject having previously undergone at least one unsuccessful first-line therapy of bladder carcinoma comprising an immunotherapy with standard BCG.

4. The use of claim 1, 2 or 3 in the treatment of a subject having previously undergone at least one unsuccessful first-line therapy of bladder carcinoma comprising cystectomy or another local treatment and/or systemic chemotherapy.

5. The use of any one of claims 1-4 in the treatment of a subject having previously undergone at least one unsuccessful first-line therapy of bladder carcinoma selected from the group of cisplatin-based chemotherapy, concomitant chemotherapy and standard BCG.

6. The use of claim 5, wherein the cisplatin-based chemotherapy is followed by bladder surgery and/or radiation therapy.

7. The use of any one of claims 1-6, wherein the subject is a smoker.

8. The use of any one of claims 1-7, wherein the immunotherapeutic agent is administered into the bladder according to a schedule involving weekly instillations

9. The use of any one of claims 1-8, wherein the immunotherapeutic agent is administered into the bladder according to a schedule involving weekly instillations during (i) an induction phase with (ii) a maintenance phase of at least one year, a first maintenance phase after about 3 months with e.g. 3 weekly instillations, a second maintenance phase after about 6 months with e.g. 3 instillations and a third maintenance phase after about 12 months with e.g. 3 instillations.

10. The use of claim 9, wherein the induction phase comprises 6 weekly instillations.

11. The use of claim 9 or 10, wherein the maintenance phase comprises a first maintenance phase after about 3 months with e.g. 3 weekly instillations, a second maintenance phase after about 6 months

with e.g. 3 instillations and a third maintenance phase after about 12 months with e.g. 3 instillations.

12. The use of any one of claims 1-11, wherein the immunotherapeutic agent is administered at a dose of from about 10^7 to 5 x 10^9 CFU.

13. The use of claim 12, wherein the immunotherapeutic agent is administered at a dose of about 2 x 10^9 CFU per administration.

14. The use of any one of claims 1-13, wherein bladder carcinoma recurrence is inhibited for a time period of at least a 2 years, of at least 3 years or of at least 4 years.

15. The use of any one of claims 1-14, wherein the immunotherapy provides a bladder carcinoma -free time period of at least 1 year, of at least 2 years, of at least 3 years or of at least 4 years for at least 30% of the patients.

16. The use of claim 15, wherein the immunotherapy provides a disease-free time period of at least 1 year, of at least 2 years, of at least 3 years or of at least 4 years for at least 45% of the patients.

17. The use of any one of claims 1-16, wherein bladder carcinoma recurrence is blocked for at least one further year in a subject without bladder carcinoma recurrence for a time period of 2 years after treatment start.

18. The use of any one of claims 1-17, wherein overall survival is increased compared to a subject without treatment in a time period of at least 1 year, of at least 2 years, of at least 3 years or of at least 4 years.

19. The use of any one of claims 1-18, wherein the need of cystectomy is reduced or avoided, e.g., for a time period of at least a 1

year, particularly for a time period of at least 2 years, of at least 3 years or of at least 4 years in at least 30% of the patients.

20. The use of claim 19, wherein the need of cystectomy is reduced or avoided, e.g., for a time period of at least a 1 year, of at least 2 years, of at least 3 years or of at least 4 years for at least 45% of the patients.