relevant cancer models results resulting in a stimulation of antigen-specific T lymphocytes and significant survival. Oncolytic rhabdovirus specifically infects, replicates in, and kills malignant cells leaving normal tissues unaffected. The oncolytic rhabdovirus (e.g. VSVdelta5 l or Mamba MG 1) expresses a tumor antigen to which the test animal has a preexisting immunity selected from MAGEA3, Human Papilloma Virus E6/E7 fusion protein, human Six-Transmembrane Epithelial Antigen of the Prostate protein, or Cancer Testis Antigen.

A successful therapeutic cancer vaccine will need to target tumour antigens that are expressed on tumours but not on normal tissues. Cancer-germline antigens are an heterologous group of proteins that are physiologically expressed in several types of cancer, but not in differentiated, normal tissues, except for germline cells that are incapable to present antigens to the immune system due to the lack of MHC I molecules. These antigens are encoded by cancer-germline genes. NY-ESO-1 and MAGE-A3 are prototypical MAGE-type antigens being two of the most representative of the group as described in Gnjatic, S. *et al.* (2006) Cancer Res. 95: 1 – 30. Also, Coulie P. G. *et al.* (2014) *supra* which describes responses shown to occur in a number of patients.

SUMMARY

In one aspect, the present disclosure provides a chimpanzee adenovirus (ChAd) vector encapsidating a nucleic acid molecule, the nucleic acid molecule comprising a polynucleotide sequence encoding (i) a MAGE cancer antigen and/or NY-ESO-1 cancer antigen, or immunogenic fragments thereof; or (ii) a MAGE cancer antigen and/or LAGE1 cancer antigen, or immunogenic fragments thereof, operably linked to expression control sequences which direct the translation, transcription and/or expression of the cancer antigen or fragment thereof in an animal cell, and an adenoviral packaging signal sequence. Advantageously such ChAd viral vectors are stable and well-studied, not neutralized by antibodies to human adenovirus and are engineered to be replication deficient. They have high capacity for inserted antigens of interest and can be produced in HEK293 cells containing the adenoviral E1 gene.

MAGE-type antigens are tumour-specific shared human tumour antigens known to induce CD8 T cells in cancer patients. They are expressed in many cancer types and are not expressed in normal tissues, except for male germline cells which have no MHC-1 molecules.

NY-ESO-1 (gene name *CTAG1*) induces a strong CD8 response in many cancer patients and numerous CD8 epitopes can be identified, as presented by multiple HLA class I specificities.

In a particular form the ChAd vector may be (a) ChAdOx1 as disclosed in WO2012/172277; preferably encoded by a polynucleotide of SEQ ID NO: 38 as disclosed in WO2012/172277 or a sequence of at least 80% identity therewith; or (b) ChAdOx2 as disclosed in WO2017/221031; preferably encoded by a polynucleotide of SEQ ID NO: 10 as disclosed in WO2017/221031 or a sequence of at least 80% identity therewith.

In another aspect, the the disclosure refers to a modified vaccinia virus Ankara (MVA) vector encapdisating a nucleic acid molecule, the nucleic acid molecule comprising a polynucleotide sequence encoding (i) a MAGE cancer antigen and/or NY-ESO-1 cancer antigen, or immunogenic fragments thereof; or (ii) a MAGE cancer antigen and/or LAGE1 cancer antigen, or immunogenic fragments thereof, operably linked to expression control sequences which direct the translation, transcription and/or expression of the cancer antigen or fragment thereof in an animal cell. Advantageously, such MVA vectors are not able to replicate in humans and have a long safety track record as smallpox vaccines. MVA provides excellent boosting after priming with ChAd. MVA has no virulence and immune system evasion factors and is highly immunogenic and is readily produced in chicken embryonic fibroblasts or immortalized duck embryonic cell lines.

An MVA vector in more particular form may be as disclosed in WO2011/128704 or EP 2044947 A1.

For the ChAd and/or MVA vectors of the disclosure as herein described, the MAGE antigen is preferably MAGE3A and as such has an amino acid sequence of SEQ ID NO: 1 or a sequence of at least 46%; preferably at least 69%; more preferably at least 95% identity therewith; or any immunogenic fragment thereof.

For the ChAd and/or MVA vectors of the disclosure as herein described, the NY-ESO-1 cancer antigen has an amino acid sequence of SEQ ID NO: 3 or a sequence of at least 75%; preferably at least 76.7% identity therewith; or any immunogenic fragment thereof.

For the ChAd and/or MVA vectors of the disclosure as herein described, the LAGE1 antigen has an amino acid sequence of SEQ ID NO: 5, or a sequence of at least 78%; preferably at least 97% identity therewith; or any immunogenic fragment thereof.

In preferred ChAd and/or MVA vectors of the disclosure, the polynucleotide sequence may further encode a human HLA class II histocompatibility antigen gamma chain (hli or li), and li may have an amino acid sequence of SEQ ID NO: 6 or a sequence of at least 79% identity therewith, or a fragment thereof, so that the cancer antigen is expressed in an

animal cell as a fusion with li or fragment thereof; more preferably wherein the fragment is a transmembrane domain; even more preferably wherein the transmembrane domain comprises amino acid residues 30 to 55 or 30 to 61. In a particularly preferred example the transmembrane domain has the amino acid sequence of SEQ ID NO: 7.

In alternatively preferred ChAd and/or MVA vectors of the disclosure, the polynucleotide sequence may further encode tPA which has an amino acid sequence of SEQ ID NO: 8 or a sequence of at least 81% identity therewith, or a fragment thereof; so that the cancer antigen is expressed in an animal cell as a fusion with tPA or a fragment thereof; more preferably wherein the fragment comprises a 21 amino acid leader sequence; even more preferably the 21 amino acid leader sequence is SEQ ID NO: 9.

Advantageously, the inclusion of li or tPA increases immunogenicity of the viral vector produced antigen. This increases the magnitude, breadth and duration of antigen-specific T cell response.

A ChAd vector of the disclosure may be constructed so that it has a polynucleotide sequence encoding (i) a MAGE cancer antigen or immunogenic fragment thereof and a NY-ESO-1 cancer antigen or immunogenic fragment thereof, each as herein defined; or (ii) a MAGE cancer antigen or immunogenic fragment thereof and a LAGE1 cancer antigen or immunogenic fragment thereof, each as herein defined, expressed in an animal cell as a fusion protein.

An MVA vector of the disclosure may be constructed so that it has a polynucleotide sequence encoding (i) a MAGE cancer antigen or immunogenic fragment thereof and/or an NY-ESO-1 cancer antigen or immunogenic fragment thereof each as herein defined; or (ii) a MAGE cancer antigen or immunogenic fragment thereof and/or a LAGE1 cancer antigen or immunogenic fragment thereof each as herein defined, expressed in an animal cell as a fusion protein, wherein at least one of the MAGE cancer antigen, NY-ESO-1 cancer antigen or LAGE1 cancer antigen is a fragment.

The inventors believe that NYESO-1 may be more immunogenic than MAGEA3 in humans. Also, in cancer patients, in certain groups of these, tumours are found more frequently to express MAGEA3 and not NY-ESO-1. Therefore, a possible concern might be in having an MVA boost vector in a prime-boost regimen of the present disclosure, comprising both MAGEA3 and NY-ESO-1 antigens leading to an immunodominant immune response to NY-ESO-1 and ineffective immunization against MAGEA3. Therefore, at least for such particular patient groups, or groups with higher expression of MAGEA3 compared to NY-ESO-1, an MVA vector comprising just MAGEA3 cancer antigen or immunogenic fragment thereof is preferred in the prime-boost regimen. That is to say, in certain examples, the disclosure does not include an MVA vector comprising

any NY-ESO-1 cancer antigen or immunogenic fragment thereof. In a similar way, in certain examples, the disclosure does not include an MVA vector comprising any LAGE1 cancer antigen or immunogenic fragment thereof.

In preferred examples each of MVA vector, each of the MAGE cancer antigen and NY-ESO-1, or MAGE cancer antigen and LAGE1 are immunogenic fragments.

Where the ChAd and/or MVA vectors of the disclosure are constructed to yield fusions of antigens on expression, the polynucleotide sequence preferably also encodes a suitable polypeptide linker of between 5 and 9 amino acids; more preferably having the amino acid sequence GGGPGGG, which when expressed links the MAGE and NY-ESO-1 or LAGE1 cancer antigens or fragments thereof, in either order, as a fusion protein.

In another aspect, the present disclosure refers to an immunogenic composition comprising a ChAd or MVA vector as claimed in any preceding claim; optionally further comprising an adjuvant. The disclosure therefore also provides an immunogenic composition comprising a ChAd or MVA vector as hereinbefore and as herein described. Such compositions may further comprise a suitable adjuvant.

In another aspect, the present disclosure refers to an isolated polynucleotide comprising a sequence encoding a ChAd vector as disclosed herein; optionally codon optimised for human codon usage. The disclosure further provides an isolated polynucleotide comprising a sequence encoding a fusion protein contained in a ChAd vector or an MVA vector as herein described.

A preferred polynucleotide comprises the nucleic acid sequence SEQ ID NO: 10 encoding a MAGEA3/linker/NY-ESO-1 fusion protein. Also possible are polynucleotides having sequences of at least 70% identity with SEQ ID NO: 10. The translated protein sequence of 501 amino acids is as set forth in SEQ ID NO: 11 or a sequence of at least 70% identity therewith.

Another preferred polynucleotide has the nucleic acid sequence SEQ ID NO: 12 encoding a hli/MAGEA3/linker/NY-ESO-1 fusion protein. Also possible are polynucleotides having sequences of at least 70% identity with SEQ ID NO: 12. The translated protein sequence is set forth in SEQ ID NO: 13 or a sequence of at least 70% identity therewith.

Yet another preferred polynucleotide has the nucleic acid sequence SEQ ID NO: 14 encoding tPA/MAGEA3/linker/NY-ESO-1 fusion protein. Also possible are polynucleotides having sequences of at least 70% identity with SEQ ID NO: 12. The translated protein sequence is set forth in SEQ ID NO: 15 or a sequence of at least 70% identity therewith.

In particular examples the isolated polynucleotide consists of any of the aforementioned sequences or variants thereof.

In all examples of the disclosure, the polynucleotides encoding the antigens are preferably codon optimised for expression in humans. A person of skill in the art will be familiar with a number of available software packages, including for example those described in US Patent No. 8,326,547, or Puigbo, P. et al. (2007) OPTIMIZER: A web server for optimizing

the codon usage of DNA sequences: Nucleic Acids Research, 35:W126-W131. Also, commercially available services and software such as those offered by Integrated DNA Technologies or GenScript.

In another aspect, the present disclosure also includes a Bacterial Artificial Chromosome (BAC) clone comprising a polynucleotide as described herein. Converting the BAC clones of the viral genomes into viruses ("rescue") can be carried out by a well-known process, as described in WO2012/172277 of Isis Innovation Limited, incorporated herein by reference.

In another aspect, the disclosure further includes an isolated host cell comprising a ChAd and/or MVA vector as described herein.

Also, the disclosure provides a method of preventing or treating cancer in an individual, comprising administering an effective amount or a ChAd vector as described herein, and administering an effective amount of an MVA vector as described herein, whereby the adaptive immune system of the individual is stimulated to provide an anti-cancer immune response. Advantageously the method of the disclosure generates a strong T cell immune response, particularly a strong $CD8^+$ immune response leading to protective immunity which is long lasting.

In another aspect, the present disclosure refers to a use of a ChAd vector as disclosed herein for the manufacture of a medicament for preventing or treating of cancer.

In yet another aspect, the present disclosure refers to a use of an MVA vector as disclosed herein for the manufacture of a medicament for preventing or treating of cancer.

In yet another aspect, the present disclosure refers to a use of a ChAd vector as disclosed herein in the manufacture of a first medicament and use of an MVA vector as disclosed herein in the manufacture of a second medicament, wherein the first and second medicaments are to be used in combination therapy for the prevention or treatment of cancer, wherein the ChAd and MVA vectors are to be administered separately, sequentially or simultaneously to a patient.

In yet another aspect, the present disclosure refers to a use of a ChAd vector as disclosed herein in the manufacture of a first medicament, use of an MVA vector as disclosed herein in the manufacture of a second medicament, use of a chemotherapeutic agent in the manufacture of a third medicament, and use of a checkpoint inhibitor in the manufacture of a fourth medicament wherein the first, second, third and fourth medicaments are to be used in combination therapy for the prevention or treatment of cancer, wherein the ChAd vector, MVA vector, chemotherapeutic agent and checkpoint inhibitor are to be administered separately, sequentially or simultaneously to a patient.

In a preferred method of preventing or treating cancer in accordance with the disclosure, the administration of the ChAd and MVA vectors is carried out separately, sequentially or simultaneously.

In particular methods of preventing or treating cancer in accordance with the disclosure, there is the further administration of an effective amount of one or more immune checkpoint modulators. Such checkpoint modulators may be administered simultaneously, separately or concurrently with the ChAd and MVA vectors.

In the method of preventing or treating cancer aspects of the disclosure, an individual who is being treated may be one who has received, is receiving or will receive a chemotherapy and/or radiotherapy treatment.

In the methods of preventing or treating cancer in accordance with the disclosure, the ChAd vector is preferably administered first. p

In the cancer prevention or treatment methods of the disclosure, the ChAd and MVA vectors may be administered more than once each. In preferred example when the ChAd is used as a priming immunization then there is just one of these, followed by two MVA booster immunizations. Also possible is methods of cancer treatment or prevention in which the ChAd and MVA vectors are administered in alternation.

The period of time between each administration of a vector of the disclosure may be in the range 5 days to 8 weeks; preferably though a period of about 1 week is used between prime and subsequent boost or boosts.

In cancer prevention or treatment methods of the disclosure where a checkpoint modulator is administered and also forms part of the treatment regimen, the checkpoint modulator may be an inhibitor that blocks PD-1, CTLA-4 or PD-L1. Advantageously, using the vectors and immunogenic compositions of the disclosure together with one or more checkpoint modulators can serve to reduce the dosage of checkpoint modulators needed for equivalent effect (i.e. when used alone). The effect is not simply additive but synergistic as between the viral vector treatment regimen of the present disclosure and checkpoint modulators.

Particularly preferred checkpoint modulators may be selected from nivolumab (Opdivo®), pembrolizumab (Keytruda®), ipilimumab (Yervoy®), tremelimumab or atezolizumab (Tecentriq®), durvaliumab (Imfinzi®) or avelumab (Bavencio®).

Methods of preventing or treating cancer in accordance with the disclosure are directed to cancers expressing cancer-germline genes, preferably genes coding MAGE-type, NYESO, and LAGE antigens: preferably directed to particular cancer types, e.g. wherein the cancer is non-small cell lung cancer (NSCLC), melanoma, Hodgkin lymphoma, non-Hodgkin lymphoma, urinary tract (urothelial), esophageal, bladder, small cell lung cancer, renal, head & neck, sarcoma, or breast.

Accordingly, the disclosure includes a ChAd vector of the disclosure for use in the prevention or treatment of cancer. Also, an MVA vector of the disclosure for use in the prevention or treatment of cancer. In respect of such use, each of the various examples of the method of the disclosure applies equally.

Further, the disclosure includes a ChAd vector of the disclosure as herein defined, and an MVA vector of the disclosure as herein defined, for separate, sequential or simultaneous administration to a patient for the prevention or treatment of cancer.

ChAd and MVA vectors for use in prevention or treatment of cancer as herein defined, may further including one or more modulators of cancer-immunity cycle or cancer-immunity set-points as described in Chen, D.S. and Mellman, I. (2013) Immunity 39(1):1-10, and Chen, D.S. and Mellman, I. (2017) Nature 541(7637):321-330; preferably checkpoint inhibitors for administration with the ChAd and MVA vectors for the treatment of cancer.

A large proportion of patients with advanced cancer currently do not respond to immunotherapy based on checkpoint modulators. For example, where an anti-PD1 inhibitor is used in melanoma, renal cell carcinoma, head & neck carcinoma and lung

carcinoma. In one example the disclosure uses a ChAd/MVA vaccine to induce CD8 T cells against MAGE-A3 and NY-ESO-1 in combination with anti-PD1 and chemotherapy. Without wishing to be bound by any particular theory, the inventors expect that what would otherwise be “cold” tumours become infiltrated by tumour-specific CD8 T cells that will be boosted by the anti-PD1.

The inventors have also found that a triple combination of vaccine in accordance with the disclosure, plus chemotherapeutic agent, plus checkpoint inhibitor provides a significantly improved anti-tumour effect, and significant survival times of mice in a mouse model, when compared to vaccine alone or vaccine plus chemotherapeutic agent or vaccine plus checkpoint inhibitor. Indeed the effect of the triple combination is such that it is synergistic. There is a significant depletion of myeloid derived suppressor cell (MDSC) achieved with the triple combination. The disclosure therefore also provides such a triple combination method of treatment and corresponding medical use. Also the disclosure provides a ChAd vector as hereinbefore defined, an MVA vector as hereinbefore defined, a chemotherapeutic agent, and a checkpoint inhibitor, for separate, sequential or simultaneous administration to a patient for the prevention or treatment of cancer.

The chemotherapeutic agent may be selected from (but not limited to) (a) carboplatin or cisplatin in combination with (b) one of paclitaxel, docetaxel, vinorelbine, gemcitabine, etoposide or pemetrexed. For the checkpoint inhibitor this may be PD-1. Such particular triple combinations may provide useful treatments for non-small cell lung cancer (NSCLC) or small cell lung cancer (SCLC) melanoma, Hodgkin lymphoma, non-Hodgkin lymphoma, urinary tract (urothelial), bladder, renal, head & neck, sarcoma or breast cancer.

Also provided as part of the disclosure are kits comprising ChAd and/or MVA vectors as herein described for the prevention or treatment or cancer. Such kits comprise at least one container which holds one of the ChAd and/or MVA vectors of the disclosure. Kits may comprise two or more, i.e. a multiplicity of containers, each with a different viral vector of the disclosure. Kits may include a set of instructions in the use of the vectors as a vaccine, including essential information on the vaccine regimen to be used, e.g. prime-boost, and periods between administrations. In more complex examples the kits may comprise any of the further therapeutic elements, e.g. checkpoint modulators, in accordance with the disclosure described herein.

BRIEF DESCRIPTION OF THE DRAWINGS

Embodiments of the invention are further described hereinafter with reference to the accompanying drawings, in which:

CLAIMS

1. A chimpanzee adenovirus (ChAd) vector encapsidating a nucleic acid molecule, the nucleic acid molecule comprising a polynucleotide sequence encoding (i) a MAGE cancer antigen and/or NY-ESO-1 cancer antigen, or immunogenic fragments thereof; or (ii) a MAGE cancer antigen and/or LAGE1 cancer antigen, or immunogenic fragments thereof, operably linked to expression control sequences which direct the translation, transcription and/or expression of the cancer antigen or fragment thereof in an animal cell, and an adenoviral packaging signal sequence.

2. A ChAd vector as claimed in claim 1, wherein the ChAd vector is (a) ChAdOx1 as disclosed in WO2012/172277; preferably encoded by a polynucleotide of SEQ ID NO: 38 as disclosed in WO2012/172277 or a sequence of at least 80% identity therewith; or (b) ChAdOx2 as disclosed in WO2017/221031; preferably encoded by a polynucleotide of SEQ ID NO: 10 as disclosed in W02017/221031 or a sequence of at least 80% identity therewith.

3. A modified vaccinia virus Ankara (MVA) vector encapdisating a nucleic acid molecule, the nucleic acid molecule comprising a polynucleotide sequence encoding (i) a MAGE cancer antigen and/or NY-ESO-1 cancer antigen, or immunogenic fragments thereof; or (ii) a MAGE cancer antigen and/or LAGE1 cancer antigen, or immunogenic fragments thereof, operably linked to expression control sequences which direct the translation, transcription and/or expression of the cancer antigen or fragment thereof in an animal cell.

4. An MVA vector as claimed in claim 3, wherein the MVA vector is as disclosed in WO2011/128704 or EP 2044947 A1.

5. A ChAd or MVA vector as claimed in any of claims 1 to 4, wherein

(a) the MAGE antigen is MAGE 3A having an amino acid sequence of SEQ ID NO: 1 or a sequence of at least 46%; preferably at least 69%; more preferably at least 95% identity therewith; or any immunogenic fragment thereof; and/or

(b) the NY-ESO-1 cancer antigen has an amino acid sequence of SEQ ID NO: 3 or a sequence of at least 75%; preferably at least 76.7% identity therewith; or any immunogenic fragment thereof; and/or

(c) the LAGE1 cancer antigen has an amino acid sequence of SEQ ID NO: 5, or a sequence of at least 78%; preferably at least 97% identity therewith; or any immunogenic fragment thereof.

6. A ChAd or MVA vector as claimed in any preceding claim, wherein the polynucleotide sequence further encodes a human HLA class II histocompatibility antigen gamma chain (Ii)

with an amino acid sequence of SEQ ID NO: 6 or a sequence of at least 79% identity therewith, or a fragment thereof, so that the cancer antigen is expressed in an animal cell as a fusion with Ii or fragment thereof; preferably wherein the fragment is a transmembrane domain; more preferably wherein the transmembrane domain comprises amino acid residues 30 to 55 or 30 to 61 , even more preferably wherein the transmembrane domain has the amino acid sequence of SEQ ID NO: 7.

7. A ChAd or MVA vector as claimed in any preceding claim, wherein the polynucleotide sequence further encodes tPA with an amino acid sequence of SEQ ID NO: 8 or a sequence of at least 81% identity therewith, or a fragment thereof; so that the cancer antigen is expressed in an animal cell as a fusion with tPA or a fragment thereof; preferably wherein the fragment comprises a 21 amino acid leader sequence; more preferably the 21 amino acid leader sequence is SEQ ID NO: 9.

8. A ChAd vector as claimed in any preceding claim, wherein the polynucleotide sequence encodes (i) a MAGE cancer antigen or immunogenic fragment thereof and a NY-ESO-1 cancer antigen or immunogenic fragment thereof; or (ii) a MAGE cancer antigen or immunogenic fragment thereof and a LAGE1 cancer antigen or immunogenic fragment thereof, expressed in an animal cell as a fusion protein.

9. An MVA vector as claimed in any of claims 1 to 7, wherein the polynucleotide sequence encodes (i) a MAGE cancer antigen or immunogenic fragment thereof and/or an NY-ESO-1 cancer antigen or immunogenic fragment thereof; or (ii) a MAGE cancer antigen or immunogenic fragment thereof and/or a LAGE1 cancer antigen or immunogenic fragment thereof, expressed in an animal cell as a fusion protein, wherein at least one of the MAGE cancer antigen, NY-ESO-1 cancer antigen or LAGE1 cancer antigen is a fragment; optionally wherein the MAGE cancer antigen and NY-ESO-1 or MAGE cancer antigen and LAGE1 are immunogenic fragments.

10. A ChAd or MVA vector as claimed in claim 8 or claim 9, wherein the polynucleotide sequence encodes a linker of between 5 and 9 amino acids; preferably having the amino acid sequence GGGPGGG, which when expressed links the MAGE and NY-ESO-1 or LAGE1 cancer antigens or fragments thereof, in either order, as a fusion protein.

11. An immunogenic composition comprising a ChAd or MVA vector as claimed in any preceding claim; optionally further comprising an adjuvant.

12. An isolated polynucleotide comprising a sequence encoding a ChAd vector of any of claims 1 to 8 or 10, or an MVA vector of any of claims 3 to 7 or claim 9 or claim 10; optionally codon optimised for human codon usage.

13. A Bacterial Artificial Chromosome (BAC) clone comprising a polynucleotide of claim 12.

14. An isolated host cell comprising a ChAd and/or MVA vector as set forth in any of claims 1 to 10.

15. Use of a ChAd vector as claimed in any of claims 1, 2, 5 to 8 or 10 for the manufacture of a medicament for preventing or treating of cancer.

16. Use of an MVA vector as claimed in any of claims 3 to 7 or claim 9 or claim 10 for the manufacture of a medicament for preventing or treating of cancer.

17. Use of a ChAd vector as set forth in any of claims 1, 2, 5 to 8 or 10 in the manufacture of a first medicament and use of an MVA vector as set forth in any of claims 3 to 7 or claim 9 or claim 10 in the manufacture of a second medicament, wherein the first and second medicaments are to be used in combination therapy for the prevention or treatment of cancer, wherein the ChAd and MVA vectors are to be administered separately, sequentially or simultaneously to a patient.

18. The use as claimed in claim 17, further including that one or more checkpoint inhibitors are to be administered with the ChAd and MVA vectors for the treatment of cancer; optionally wherein the checkpoint inhibitor is to be administered simultaneously, separately or concurrently with a vector.

19. The use as claimed in any of claims 15 to 17, wherein the patient has received, is receiving or will receive chemotherapy, and/or radiotherapy treatment.

20. The use as claimed in any of claims 17 to 19,

(a) wherein the ChAd vector is to be administered first; and/or

(b) wherein the ChAd and MVA vectors are to be administered more than once each; and/or

(c) wherein the ChAd and MVA vectors are to be administered in alternation; and/or

(d) wherein the period of time between each administration of a vector is in the range 5 days to 8 weeks, preferably 1 week.

21. The use as claimed in any of claims 18 to 20, wherein

(a) the checkpoint inhibitor blocks PD-1, CTLA-4 or PD-L1; or

(b) the checkpoint inhibitor is selected from nivolumab, pembrolizumab, ipilimumab, tremelimumab or atezolizumab, durvaliumab or avelumab.

22. The use as claimed in any of claims 18 to 20, wherein the cancer is non-small cell lung cancer (NSCLC), melanoma, Hodgkin lymphoma, non-Hodgkin lymphoma, urinary tract (urothelial), bladder, small cell lung cancer, renal, head & neck, sarcoma or breast.

23. Use of a ChAd vector as set forth in any of claims 1, 2, 5 to 8 or 10 in the manufacture of a first medicament, use of an MVA vector as set forth in any of claims 3 to 7 or claim 9 or claim 10 in the manufacture of a second medicament, use of a chemotherapeutic agent in the manufacture of a third medicament, and use of a checkpoint inhibitor in the manufacture of a fourth medicament wherein the first, second, third and fourth medicaments are to be used in combination therapy for the prevention or treatment of cancer, wherein the ChAd vector, MVA vector, chemotherapeutic agent and checkpoint inhibitor are to be administered separately, sequentially or simultaneously to a patient.

24. The use as claimed in claim 23, wherein the chemotherapeutic agent is selected from (a) carboplatin or cisplatin in combination with (b) one of paclitaxel, docetaxel, vinorelbine, gemcitabine, etoposide or pemetrexed; optionally

(i) wherein the checkpoint inhibitor is PD-1; and/or

(ii) wherein the cancer is selected from: non-small cell lung cancer (NSCLC) or small cell lung cancer (SCLC), melanoma, Hodgkin lymphoma, non-Hodgkin lymphoma, urinary tract (urothelial), bladder, small cell lung cancer, renal, head & neck, sarcoma or breast cancer.