combination with antibody against a tumor surface antigen enhances treatment of the cancer patient, more particularly increases reduction in tumor volume and/or increases survival of the cancer patient.

We claim:

1. Use of a pharmaceutical combination in the manufacture of a medicament for reducing tumor size and/or increasing survival in a cancer patient, the combination comprising:

(a) a recombinant modified vaccinia virus Ankara (MVA), wherein the recombinant MVA is to be administered via intravenous administration to said patient, and wherein the recombinant MVA comprises:

(i) a first nucleic acid encoding a first heterologous tumor-associated antigen (TAA); and

(ii) a second nucleic acid encoding CD40L; and

(b) an antibody, wherein the antibody comprises an Fc domain and is specific to an antigen that is expressed on the cell membrane of a tumor cell;

wherein administration of (a) and (b) to the cancer patient reduces tumor size and/or increases the survival rate of the cancer patient as compared to a non-intravenous administration of (a) or an administration of (b) alone.

2. Use of claim 1, wherein the recombinant MVA further comprises a third nucleic acid encoding a second heterologous TAA.

3. Use of any one of claims 1- 2, wherein the first and/or second TAA is selected from the group consisting of: 5-α-reductase, α-fetoprotein ("AFP"), AM-1, APC, April, B melanoma antigen gene ("BAGE"), β-catenin, Bcl12, bcr-abl, Brachyury, CA-125, caspase-8 ("CASP-8", also known as "FLICE"), Cathepsins, CD19, CD20, CD21/complement receptor 2 ("CR2"), CD22/BL-CAM, CD23/FcεRII, CD33, CD35/complement receptor 1 ("CR1"), CD44/PGP-1, CD45/leucocyte common antigen ("LCA"), CD46/membrane cofactor protein ("MCP"), CD52/CAMPATH-1, CD55/decay accelerating factor ("DAF"), CD59/protectin, CDC27, CDK4, carcinoembryonic antigen ("CEA"), c-myc, cyclooxygenase-2 ("cox-2"), deleted in colorectal cancer gene ("DCC"), DcR3, E6/E7, CGFR, EMBP, Dna78, farnesyl transferase, fibroblast growth factor-8a ("FGF8a"), fibroblast growth factor-8b ("FGF8b"), FLK-1/KDR, folic acid receptor, G250, G melanoma antigen gene family ("GAGE-family"), gastrin 17, gastrin-releasing hormone, ganglioside 2 ("GD2")/ganglioside 3 ("GD3")/ganglioside-monosialic acid-2 ("GM2"),

gonadotropin releasing hormone ("GnRH"), UDP-GlcNAc:R1Man(α1-6)R2 [GlcNAc to Man(α1-6)] β1,6-N¬-acetylglucosaminyltransferase V ("GnT V"), GP1, gp100/Pme117, gp-100-in4, gp15, gp75/tyrosine-related protein-1 ("gp75/TRP-1"), human chorionic gonadotropin ("hCG"), heparanase, HER2, human mammary tumor virus ("HMTV"), 70 kiloDalton heat-shock protein ("HSP70"), human telomerase reverse transcriptase ("hTERT"), insulin-like growth factor receptor-1 ("IGFR-1"), interleukin-13 receptor ("IL-13R"), inducible nitric oxide synthase ("iNOS"), Ki67, KIAA0205, K-ras, H-ras, N-ras, KSA, LKLR-FUT, melanoma antigen-encoding gene 1 ("MAGE-1"), melanoma antigen-encoding gene 2 ("MAGE-2"), melanoma antigen-encoding gene 3 ("MAGE-3"), melanoma antigen-encoding gene 4 ("MAGE-4"), mammaglobin, MAP17, Melan-A/melanoma antigen recognized by T-cells-1 ("MART-1"), mesothelin, MIC A/B, MT-MMPs, mucin, testes-specific antigen NY-ESO-1, osteonectin, p15, P170/MDR1, p53, p97/melanotransferrin, PAI-1, platelet-derived growth factor ("PDGF"), μPA, PRAME, probasin, progenipoietin, prostate-specific antigen ("PSA"), prostate-specific membrane antigen ("PSMA"), RAGE-1, Rb, RCAS1, SART-1, SSX-family, STAT3, STn, TAG-72, transforming growth factor-alpha ("TGF-α"), transforming growth factor-beta ("TGF-β"), Thymosin-beta-15, tumor necrosis factor-alpha ("TNF-α"), TP1, TRP-2, tyrosinase, vascular endothelial growth factor ("VEGF"), ZAG, p16INK4, and glutathione-S-transferase ("GST").

~~4. Use of any one of claims 1–3, wherein the first and/or second TAA comprise one or more mutations to prevent the antibody from binding to the first and/or second TAA.~~

~~5~~4. Use of any one of claims 1-~~4~~3, wherein the first TAA is HER2.

~~6~~5. Use of claim ~~5~~4, wherein the HER2 antigen comprises at least one mutation to: (a) prevent a HER2 antibody binding to the HER2 antigen; (b) prevent extracellular dimerization of the HER2 antigen; (c) prevent tyrosine kinase activity of the HER2 antigen; and/or (d) prevent phosphorylation of the HER2 antigen.

~~7~~6. Use of claim ~~6~~5, wherein the HER2 antigen comprises at least one mutation selected from the group consisting of: E580, D582, P594, F595, K615, and Q624.

87. Use of claim 65, wherein the HER2 antigen comprises at least one mutation selected from the group consisting of: H267, Y274, F279, V308, S310, L317, H318, K333, and P337.

98. Use of claim 4 or 5 or 6, wherein the HER2 antigen comprises at least one mutation selected from the group consisting of:

(a) a mutation that prevents extracellular dimerization of HER2 that is D277R or E280K;

(b) a mutation that prevents tyrosine kinase activity of HER2 that is K753M; and

(c) a mutation that interferes with phosphorylation of HER2 that is Y1023A or is the deletion of residues 1139-1248.

109. Use of claim 1, wherein the first nucleic acid encodes a HER2 antigen having the amino acid sequence set forth in SEQ ID NO:1 or SEQ ID NO: 13.

1110. Use of claim 1, wherein the first nucleic acid encodes a HER2 antigen and the antibody is an anti-HER2 antibody.

1211. Use of any of claims 1-2, wherein the first nucleic acid encodes a HER2 antigen that comprises the sequence set forth in SEQ ID NO: 2 or SEQ ID NO:14.

1312. Use of any of claims 2-1211, wherein the second TAA is Brachyury.

1413. Use of claim 1312, wherein the Brachyury antigen comprises one or more mutations to the nuclear localization domaina deletion of amino acids 286-293.

1514. Use of claim 1412, wherein the second nucleic acid encodes a Brachyury antigen comprising the amino acid sequence set forth in SEQ ID NO:3.

1615. Use of any one of claims 1-1514, wherein the antibody is selected from the group consisting of: Anti-CD20 (e.g., rituximab; ofatumumab; tositumomab), Anti-CD52 (e.g., alemtuzumab Campath®), Anti-EGFR (e.g., cetuximab Erbitux®¸ panitumumab), Anti-CD2 (e.g.,Siplizumab), Anti-CD37 (e.g., BI836826), Anti-CD123 (e.g., JNJ-56022473), Anti-CD30 (e.g., XmAb2513), Anti-CD38 (e.g., daratumumab Darzalex®), Anti-PDL1 (e.g., avelumab, atezolilzumab, durvalumab), Anti-GD2 (e.g., 3F8, ch14.18, KW-2871, dinutuximab), anti-CTLA-4, Anti-CEA, Anti-MUC1, Anti-FLT3, Anti-CD19,

Anti-CD40, Anti-SLAMF7, Anti-CCR4, Anti-B7-H3, Anti-ICAM1, Anti-CSF1R, anti-CA125 (e.g. Oregovomab), anti-FRα (e.g. MOv18-IgG1, Mirvetuximab soravtansine (IMGN853), MORAb-202), anti-mesothelin (e.g. MORAb-009), anti-Trp1, and Anti-HER2.

~~17~~16. Use of claim ~~11~~10, wherein the antibody is selected from Pertuzumab, Trastuzumab, Herzuma, ABP 980, and Ado-trastuzumab emtansine.

~~18~~17. Use of any one of claims 1-~~17~~16, wherein the MVA is MVA-BN.

~~19~~18. Use of any one of claims 1-~~18~~17, wherein (a) is to be administered at the same time as or after (b).

~~20~~19. Use of any one of claims 1-~~19~~18, wherein (a) and (b) are to be administered to the cancer patient in a priming administration followed by one or more boosting administrations of (a) and (b) to be administered to the cancer patient.

~~21~~20. Use of any one of claims 1-~~20~~19, wherein the cancer patient is suffering from and/or is diagnosed with a cancer selected from the group consisting of: breast cancer, lung cancer, head and neck cancer, thyroid, melanoma, gastric cancer, bladder cancer, kidney cancer, liver cancer, melanoma, pancreatic cancer, prostate cancer, ovarian cancer, or colorectal cancer.

~~22~~21. Use of claim ~~21~~20, wherein the cancer patient is suffering from and/or is diagnosed with breast cancer that is HER2 positive.