the graft. IL2 is used post-transfer to reduce anergy of the graft and to propagate it.

With regard to efficacy, room is left for improvement. Increased specificity and sufficient tumor killing ability of cell therapies in general are warranted. In particular, in the ACT of the prior art the transferred cells fail to traffic to tumors, and even if they do, they often quickly become anergic, are otherwise unable to kill tumor cells or fail to propagate resulting in a rapid decline of cell numbers. Furthermore, cancers frequently down-regulate human leukocyte antigen (HLA) – known as major histocompatibility complex in animals - in tumor cells, thus resulting in inability of T-cells to kill, as HLA is required for presentation of tumor epitopes to the T-cell receptor.

The present invention provides efficient tools and methods for cancer therapeutics utilizing adoptive cell transfers.

SUMMARY

An object of the present disclosure is to provide simple methods and tools for overcoming the above problems of inefficient, unsafe and unpredictable cancer therapies. More specifically, the disclosure provides novel methods and means for cell therapy. The objects of the disclosure are achieved by viral vectors, methods and arrangements, which are characterized by what is stated in the independent claims. The specific examples of the disclosure are disclosed in the dependent claims.

The present application describes construction of recombinant viral vectors, methods related to the viral vectors, and their use in tumor cells lines, animal models and cancer patients.

The disclosure is based on the idea of combining oncolytic adenoviral vectors coding for cytokines or adenoviral vectors with adoptive cell therapeutics for cancer treatment in a novel and inventive way. The disclosure is based on surprising effects, i.e. the following improvements in adoptive T-cell therapy: i) recruitment of transferred cells to the tumor, ii) propagation of transferred cells at the tumor, iii) enhanced reactivity of transferred cells at the tumor (Figure 20). Indeed, the said combination of viral vectors and cytokines with adoptive cell therapeutics provides more effective results on wider targets than could have been assumed. Effects of the said combination of viral vectors comprising cytokine transgene with adoptive cell transfer are synergistic com-

pared to the effects of only viral vectors comprising cytokine transgene or only adoptive cell transfers.

It is a further object of the present disclosure to provide a combination of tumor infiltrating lymphocytes (TIL) and transgenic (produced from a virally delivered transgene) interleukin-2 (IL-2) for the treatment of malignancy in humans. The above and various other objects and advantages of the present disclosure are achieved by a method of treating malignancy in humans, comprising administering an effective amount of TIL and IL-2, with or without preconditioning chemotherapy and/or radiotherapy, to a patient afflicted with cancer to cause regression or stabilization of the cancer.

The present disclosure relates to a method of treating cancer in a subject, wherein the method comprises separate administration of adoptive cell therapeutic composition and oncolytic (=replication competent in tumor but not normal cells) adenoviral vectors coding for at least one cytokine to a subject.

The present disclosure further relates to an oncolytic adenoviral vector coding for at least one cytokine together with separate adoptive cell therapeutic composition for use in treatment of cancer.

The present disclosure further relates to a use of an oncolytic adenoviral vector coding for at least one cytokine together with separate adoptive cell therapeutic composition in the manufacture of a medicament for treating cancer in a subject.

The present disclosure also relates to an oncolytic adenoviral vector for use in increasing the efficacy of adoptive cell therapy or T-cell therapy in a subject.

Also, the present disclosure relates to a use of an oncolytic adenoviral vector in the manufacture of a medicament for increasing the efficacy of T-cell therapy in a subject.

Also, the present disclosure relates to a method of increasing the efficacy of adoptive cell therapy or T-cell therapy in a subject by administering an oncolytic adenoviral vector to a subject in need thereof.

The present disclosure also relates to a pharmaceutical kit comprising an adoptive cell therapeutic composition and oncolytic adenoviral vectors coding for at least one cytokine, wherein the adoptive cell therapeutic composition is formulated in a first formulation and the oncolytic adenoviral vectors coding for at least one cytokine are formulated in a second formulation.

Furthermore, the present disclosure relates to an oncolytic adenoviral vector comprising

1) an adenovirus serotype 5 (Ad5) nucleic acid backbone comprising a 5/3 chimeric fiber knob:

2) E2F1 promoter for tumor specific expression of E1A;

3) a 24 bp deletion (D24) in the Rb binding constant region 2 of adenoviral E1;

4) a nucleic acid sequence deletion of viral *gp19k* and *6.7k* reading frames; and

5) a nucleic acid sequence encoding at least one cytokine transgene in the place of the deleted *gp19k/6.7K* in the E3 region resulting in replication-associated control of transgene expression under the viral E3 promoter, wherein the cytokine is selected from a group consisting of interferon alpha, interferon beta, interferon gamma, complement C5a, IL-2, TNFalpha, CD40L, IL12, IL-23, IL15, IL17, CCL1, CCL11, CCL12, CCL13, CCL14-1, CCL14-2, CCL14-3, CCL15-1, CCL15-2, CCL16, CCL17, CCL18, CCL19, CCL19, CCL2, CCL20, CCL21, CCL22, CCL23-1, CCL23-2, CCL24, CCL25-1, CCL25-2, CCL26, CCL27, CCL28, CCL3, CCL3L1, CCL4, CCL4L1, CCL5 (=RANTES), CCL6, CCL7, CCL8, CCL9, CCR10, CCR2, CCR5, CCR6, CCR7, CCR8, CCRL1, CCRL2, CX3CL1, CX3CR, CXCL1, CXCL10, CXCL11, CXCL12, CXCL13, CXCL14, CXCL15, CXCL16, CXCL2, CXCL3, CXCL4, CXCL5, CXCL6, CXCL7, CXCL8, CXCL9, CXCL9, CXCR1, CXCR2, CXCR4, CXCR5, CXCR6, CXCR7 and XCL2.

Furthermore, the present disclosure relates to a serotype 3 (Ad3) oncolytic adenoviral vector comprising: a deletion in the E3 area and a tumor specific promoter for expression of a transgene in the place of the deleted area of E3.

In one aspect, the present disclosure refers to use of an oncolytic adenoviral vector coding for at least one cytokine in the manufacture of a medicament for treating cancer in a subject, wherein the medicament is to be administered with separate adoptive T-cell therapeutic composition, wherein said oncolytic adenoviral vector is an adenovirus serotype 3 (Ad3) vector comprising

- a promoter for tumor specific expression of E1A,
- a deletion in the E3 area affecting E3 9 kDa, E3 10.2 kDa, E3 15.2 kDa and E3 15.3 kDa, and
- an exogenous or tumor specific promoter for expression of at least one cytokine in the place of the deleted area of E3.

In another aspect, the present disclosure refers to an oncolytic adenoviral vector coding for at least one cytokine together with separate adoptive T-cell therapeutic composition for use in treatment of cancer, wherein said oncolytic adenoviral vector is an adenovirus serotype 3 (Ad3) vector comprising

- a promoter for tumor specific expression of E1A,
- a deletion in the E3 area affecting E3 9 kDa, E3 10.2 kDa, E3 15.2 kDa and E3 15.3 kDa, and
- an exogenous or tumor specific promoter for expression of at least one cytokine in the place of the deleted area of E3.

In yet another aspect, the present disclosure refers to an oncolytic adenoviral vector for use in increasing the efficacy of separate adoptive T-cell therapy in a tumor of a subject, wherein said oncolytic adenoviral vector is an adenovirus serotype 3 (Ad3) oncolytic adenoviral vector comprising: a promoter for tumor specific expression of E1A, a deletion in the E3 area affecting E3 9 kDa, E3 10.2 kDa, E3 15.2 kDa and E3 15.3 kDa and an exogenous or tumor specific promoter for expression of a transgene in the place of the deleted area of E3, wherein the transgene is a cytokine selected from a group consisting of interferon alpha, interferon beta, interferon gamma, complement C5a, IL-2, TNFalpha, CD40L, IL12, IL-23, IL15, IL17, CCL1, CCL11, CCL12, CCL13, CCL14-1, CCL14-2, CCL14-3, CCL15-1, CCL15-2, CCL16, CCL17, CCL18, CCL19, CCL2, CCL20, CCL21, CCL22, CCL23-1, CCL23-2, CCL24, CCL25-1, CCL25-2, CCL26, CCL27, CCL28, CCL3, CCL3L1, CCL4, CCL4L1, CCL5 (=RANTES), CCL6, CCL7, CCL8, CCL9, CCR10, CCR2, CCR5, CCR6, CCR7, CCR8, CCRL1, CCRL2, CX3CL1, CX3CR, CXCL1, CXCL10, CXCL11, CXCL12, CXCL13, CXCL14, CXCL15, CXCL16, CXCL2, CXCL3, CXCL4, CXCL5, CXCL6, CXCL7, CXCL8, CXCL9, CXCR1, CXCR2, CXCR4, CXCR5, CXCR6, CXCR7 and XCL2.

In a further aspect, the present disclosure refers to use of an oncolytic adenoviral vector in the manufacture of a medicament for increasing the efficacy of adoptive T-cell therapy in a tumor of a subject in need thereof, wherein said oncolytic adenoviral vector is an adenovirus serotype 3 (Ad3) oncolytic

adenoviral vector comprising: a promoter for tumor specific expression of E1A, a deletion in the E3 area affecting E3 9 kDa, E3 10.2 kDa, E3 15.2 kDa and E3 15.3 kDa and an exogenous or ~~a~~ tumor specific promoter for expression of a transgene in the place of the deleted area of E3, wherein the transgene is a cytokine selected from a group consisting of interferon alpha, interferon beta, interferon gamma, complement C5a, IL-2, TNFalpha, CD40L, IL12, IL-23, IL15, IL17, CCL1, CCL11, CCL12, CCL13, CCL14-1, CCL14-2, CCL14-3, CCL15-1, CCL15-2, CCL16, CCL17, CCL18, CCL19, CCL2, CCL20, CCL21, CCL22, CCL23-1, CCL23-2, CCL24, CCL25-1, CCL25-2, CCL26, CCL27, CCL28, CCL3, CCL3L1, CCL4, CCL4L1, CCL5 (=RANTES), CCL6, CCL7, CCL8, CCL9, CCR10, CCR2, CCR5, CCR6, CCR7, CCR8, CCRL1, CCRL2, CX3CL1, CX3CR, CXCL1, CXCL10, CXCL11, CXCL12, CXCL13, CXCL14, CXCL15, CXCL16, CXCL2, CXCL3, CXCL4, CXCL5, CXCL6, CXCL7, CXCL8, CXCL9, CXCR1, CXCR2, CXCR4, CXCR5, CXCR6, CXCR7 and XCL2.

In one aspect, the present disclosure refers to a pharmaceutical kit comprising an adoptive T-cell therapeutic composition and an oncolytic adenoviral vector coding for at least one cytokine, wherein the adoptive cell therapeutic composition is formulated in a first formulation and the oncolytic adenoviral vector coding for at least one cytokine is formulated in a second formulation, wherein said oncolytic adenoviral vector is an adenovirus serotype 3 (Ad3) oncolytic adenoviral vector comprising: a promoter for tumor specific expression of E1A, a deletion in the E3 area affecting E3 9 kDa, E3 10.2 kDa, E3 15.2 kDa and E3 15.3 kDa and an exogenous or ~~a~~ tumor specific promoter for expression of a transgene in the place of the deleted area of E3, wherein the transgene is a cytokine selected from a group consisting of interferon alpha, interferon beta, interferon gamma, complement C5a, IL-2, TNFalpha, CD40L, IL12, IL-23, IL15, IL17, CCL1, CCL11, CCL12, CCL13, CCL14-1, CCL14-2, CCL14-3, CCL15-1, CCL15-2, CCL16, CCL17, CCL18, CCL19, CCL2, CCL20, CCL21, CCL22, CCL23-1, CCL23-2, CCL24, CCL25-1, CCL25-2, CCL26, CCL27, CCL28, CCL3, CCL3L1, CCL4, CCL4L1, CCL5 (=RANTES), CCL6, CCL7, CCL8, CCL9, CCR10, CCR2, CCR5, CCR6, CCR7, CCR8, CCRL1, CCRL2, CX3CL1, CX3CR, CXCL1, CXCL10, CXCL11, CXCL12, CXCL13, CXCL14, CXCL15, CXCL16, CXCL2, CXCL3, CXCL4, CXCL5, CXCL6, CXCL7, CXCL8, CXCL9, CXCR1, CXCR2, CXCR4, CXCR5, CXCR6, CXCR7 and XCL2.

In one aspect, the present disclosure refers to a serotype 3 (Ad3) oncolytic adenoviral vector comprising: a promoter for tumor specific expression of E1A, a deletion in the E3 area affecting E3 9 kDa, E3 10.2 kDa, E3 15.2 kDa and E3 15.3 kDa and an exogenous or tumor specific promoter for expression of a transgene in the place of the deleted area of E3, wherein the transgene is a cytokine selected from a group consisting of interferon alpha, interferon beta, interferon gamma, complement C5a, IL-2, TNFalpha, CD40L, IL12, IL-23, IL15, IL17, CCL1, CCL11, CCL12, CCL13, CCL14-1, CCL14-2, CCL14-3, CCL15-1, CCL15-2, CCL16, CCL17, CCL18, CCL19, CCL2, CCL20, CCL21, CCL22, CCL23-1, CCL23-2, CCL24, CCL25-1, CCL25-2, CCL26, CCL27, CCL28, CCL3, CCL3L1, CCL4, CCL4L1, CCL5 (=RANTES), CCL6, CCL7, CCL8, CCL9, CCR10, CCR2, CCR5, CCR6, CCR7, CCR8, CCRL1, CCRL2, CX3CL1, CX3CR, CXCL1, CXCL10, CXCL11, CXCL12, CXCL13, CXCL14, CXCL15, CXCL16, CXCL2, CXCL3, CXCL4, CXCL5, CXCL6, CXCL7, CXCL8, CXCL9, CXCR1, CXCR2, CXCR4, CXCR5, CXCR6, CXCR7 and XCL2. In another aspect, the present disclosure refers to a pharmaceutical composition comprising the disclosed oncolytic vector. In yet another aspect, the present disclosure refers to use of the disclosed oncolytic adenoviral vector in the manufacture of a medicament for treating cancer in a subject in need thereof. In a further aspect, the present disclosure refers to the disclosed oncolytic adenoviral vector for use in treatment of cancer.

Still, the present disclosure relates to a pharmaceutical composition comprising an oncolytic vector of the disclosure.

Also, the present disclosure relates to a method of treating cancer in a subject, wherein the method comprises administration of the oncolytic adenoviral vector of the present disclosure to a subject in need thereof.Also, the present disclosure relates to an oncolytic adenoviral vector of the present disclosure for use in treatment of cancer.

Also, the present disclosure relates to a use of an oncolytic adenoviral vector of the present disclosure in the manufacture of a medicament for treating

cancer in a subject.

The advantages of the arrangements of the present disclosure are enhanced therapeutic effect and reduced side effects. Severe adverse events, even deaths are prevented, because enhancements in efficacy, and the anti-suppressive effects of our approach, may reduce the need for preconditioning chemotherapy and/or radiation used in the prior art methods to “make room” for transferred cells and reduce tumor immunosuppression. Also, severe adverse events, even deaths are prevented, because separate addition of IL2 used in the prior art methods to propagate and sustain transferred cells after transferring them into a patient is not needed if the virus produces it while replicating in the tumor. Local production at the tumor can also enhance the sought-after effects of IL-2 (stimulation and propagation of the graft) while reducing systemic exposure which is the cause of adverse events. The present disclosure provides selective treatments, with less toxicity or damage to healthy tissues.

Also, the present disclosure provides surprising therapeutic effects by: i) Providing trafficking signals to the tumor for example by injecting the virus vectors comprising recombinant cytokines into tumor. Virus injection results in production of cytokines relevant for this effect (in reaction to the virus binding to pathogen associated molecular pattern recognition receptors), but much higher effects can be achieved by additional production of the most relevant cytokine as a transgene from the virus. ii) Reducing tolerance by increasing danger signals. Virus injection *per se* can achieve this by binding to pathogen associated molecular pattern recognition receptors, but the effect can be enhanced by additional production of a cytokine as a transgene from the virus. iii) Inducing HLA expression. Virus infection increases HLA expression, since cells attempt to present viral epitopes for mounting an anti-viral T-cell response. Unexpectedly, this can be used to enhance T-cell therapy against tumor epitopes, which requires HLA to work. The effect of the virus on HLA is mediated in part by cytokines; production of said cytokine from the virus can thus induce HLA expression also in nearby tumor cells in a surprising example of the disclosure. iv) Inducing propagation of cells by lifting immunosuppression, mediated by both the presence of the virus *per se* (again through the pathogen associated molecular pattern recognition receptors), but enhanced by production of cytokines (Figure 48). Thus, this approach can solve the critical obstacles currently hindering adaptive cell therapies.

CLAIMS

1. Use of an oncolytic adenoviral vector coding for at least one cytokine in the manufacture of a medicament for treating cancer in a subject, wherein the medicament is to be administered with separate adoptive T-cell therapeutic composition, wherein said oncolytic adenoviral vector is an adenovirus serotype 3 (Ad3) vector comprising

- a promoter for tumor specific expression of E1A,
- a deletion in the E3 area affecting E3 9 kDa, E3 10.2 kDa, E3 15.2 kDa and E3 15.3 kDa, and
- an exogenous or tumor specific promoter for expression of at least one cytokine in the place of the deleted area of E3.

2. An oncolytic adenoviral vector coding for at least one cytokine together with separate adoptive T-cell therapeutic composition for use in treatment of cancer, wherein said oncolytic adenoviral vector is an adenovirus serotype 3 (Ad3) vector comprising

- a promoter for tumor specific expression of E1A,
- a deletion in the E3 area affecting E3 9 kDa, E3 10.2 kDa, E3 15.2 kDa and E3 15.3 kDa, and
- an exogenous or tumor specific promoter for expression of at least one cytokine in the place of the deleted area of E3.

3. The use according to claim 1 or the oncolytic adenoviral vector coding for at least one cytokine together with separate adoptive T-cell therapeutic composition for use according to claim 2, wherein the cancer is selected from a group consisting of nasopharyngeal cancer, synovial cancer, hepatocellular cancer, renal cancer, cancer of connective tissues, melanoma, lung cancer, bowel cancer, colon cancer, rectal cancer, colorectal cancer, brain cancer, throat cancer, oral cancer, liver cancer, bone cancer, pancreatic cancer, choriocarcinoma, gastrinoma, pheochromocytoma, prolactinoma, T-cell leukemia/lymphoma, neuroma, von Hippel-Lindau disease, Zollinger-Ellison syndrome, adrenal cancer, anal cancer, bile duct cancer, bladder cancer, ureter cancer, brain cancer, oligodendroglioma, neuroblastoma, meningioma, spinal cord tumor, bone cancer, osteochondroma, chondrosarcoma, Ewing's sarcoma, cancer of unknown primary site, carcinoid, carcinoid of gastrointestinal tract, fibrosarcoma, breast cancer, Paget's disease, cervical cancer, colorectal cancer, rectal cancer, esophagus cancer, gall bladder cancer, head cancer,

eye cancer, neck cancer, kidney cancer, Wilms' tumor, liver cancer, Kaposi's sarcoma, prostate cancer, lung cancer, testicular cancer, Hodgkin's disease, non-Hodgkin's lymphoma, oral cancer, skin cancer, mesothelioma, multiple myeloma, ovarian cancer, endocrine pancreatic cancer, glucagonoma, pancreatic cancer, parathyroid cancer, penis cancer, pituitary cancer, soft tissue sarcoma, retinoblastoma, small intestine cancer, stomach cancer, thymus cancer, thyroid cancer, trophoblastic cancer, hydatidiform mole, uterine cancer, endometrial cancer, vagina cancer, vulva cancer, acoustic neuroma, mycosis fungoides, insulinoma, carcinoid syndrome, somatostatinoma, gum cancer, heart cancer, lip cancer, meninges cancer, mouth cancer, nerve cancer, palate cancer, parotid gland cancer, peritoneum cancer, pharynx cancer, pleural cancer, salivary gland cancer, tongue cancer and tonsil cancer.

4. The use according to claim 1 or 3 or the oncolytic adenoviral vector coding for at least one cytokine together with separate adoptive T-cell therapeutic composition for use according to claim 2 or 3, wherein the subject is a human or an animal.

5. The use according to any one of claims 1, 3 and 4 or the oncolytic adenoviral vector coding for at least one cytokine together with separate adoptive T-cell therapeutic composition for use according to any one of claims 2-4, wherein the adoptive cell therapeutic composition and oncolytic viral vectors coding for at least one cytokine are to be administered to a subject simultaneously or consecutively, in any order.

6. The use according to claim 5 or the oncolytic adenoviral vector coding for at least one cytokine together with separate adoptive T-cell therapeutic composition for use according to claim 5, wherein there is a time period of one minute to four weeks between the consecutive administration of adoptive cell therapeutic composition and oncolytic viral vectors coding for at least one cytokine and/or there are several administrations of adoptive cell therapeutic composition and oncolytic viral vectors.

7. The use according to any one of claims 1 and 3-6 or the oncolytic adenoviral vector coding for at least one cytokine together with separate adoptive T-cell therapeutic composition for use according to any one of claims 2-6, wherein the adoptive cell therapeutic composition and/or oncolytic viral vectors coding for at least one cytokine is to be administered through an intratumoral, intra-arterial, intravenous, intrapleural, intravesicular, intracavitary or peritoneal injection, or an oral administration.

8. The use according to any one of claims 1 and 3-7 or the oncolytic adenoviral vector coding for at least one cytokine together with separate adoptive T-cell therapeutic composition for use according to any one of claims 2-7, wherein the cytokine is selected from a group consisting of interferon alpha, interferon beta, interferon gamma, complement C5a, IL-2, TNFalpha, CD40L, IL12, IL-23, IL15, IL17, CCL1, CCL11, CCL12, CCL13, CCL14-1, CCL14-2, CCL14-3, CCL15-1, CCL15-2, CCL16, CCL17, CCL18, CCL19, CCL2, CCL20, CCL21, CCL22, CCL23-1, CCL23-2, CCL24, CCL25-1, CCL25-2, CCL26, CCL27, CCL28, CCL3, CCL3L1, CCL4, CCL4L1, CCL5 (=RANTES), CCL6, CCL7, CCL8, CCL9, CCR10, CCR2, CCR5, CCR6, CCR7, CCR8, CCRL1, CCRL2, CX3CL1, CX3CR, CXCL1, CXCL10, CXCL11, CXCL12, CXCL13, CXCL14, CXCL15, CXCL16, CXCL2, CXCL3, CXCL4, CXCL5, CXCL6, CXCL7, CXCL8, CXCL9, CXCR1, CXCR2, CXCR4, CXCR5, CXCR6, CXCR7 and XCL2.

9. The use according to any one of claims 1 and 3-8 or the oncolytic adenoviral vector coding for at least one cytokine together with separate adoptive T-cell therapeutic composition for use according to any one of claims 2-8, wherein the oncolytic viral vector codes for two or more cytokines.

10. The use according to claim 9 or the oncolytic adenoviral vector coding for at least one cytokine together with separate adoptive T-cell therapeutic composition for use according to claim 9, wherein the oncolytic viral vector codes for any two or more cytokines selected from a cytokine group consisting of interferon alpha, interferon beta, interferon gamma, complement C5a, GMCSF, IL-2, TNFalpha, CD40L, IL12, IL-23, IL15, IL17, CCL1, CCL11, CCL12, CCL13, CCL14-1, CCL14-2, CCL14-3, CCL15-1, CCL15-2, CCL16, CCL17, CCL18, CCL19, CCL2, CCL20, CCL21, CCL22, CCL23-1, CCL23-2, CCL24, CCL25-1, CCL25-2, CCL26, CCL27, CCL28, CCL3, CCL3L1, CCL4, CCL4L1, CCL5 (=RANTES), CCL6, CCL7, CCL8, CCL9, CCR10, CCR2, CCR5, CCR6, CCR7, CCR8, CCRL1, CCRL2, CX3CL1, CX3CR, CXCL1, CXCL10, CXCL11, CXCL12, CXCL13, CXCL14, CXCL15, CXCL16, CXCL2, CXCL3, CXCL4, CXCL5, CXCL6, CXCL7, CXCL8, CXCL9, CXCR1, CXCR2, CXCR4, CXCR5, CXCR6, CXCR7 and XCL2.

11. The use according to claim 9 or 10 or the oncolytic adenoviral vector coding for at least one cytokine together with separate adoptive T-cell therapeutic composition for use according to claim 9 or 10, wherein the adenoviral vector comprises an internal ribosomal entry site (IRES) or optionally a

ribosome shunt site 2A between the two transgenes.

12. The use according to any one of claims 1 and 3-11 or the oncolytic adenoviral vector coding for at least one cytokine together with separate adoptive T-cell therapeutic composition for use according to any one of claims 2-11, wherein oncolytic adenoviral vectors coding for at least one cytokine are administered in an amount of $1x10^{10}$- $1x10^{14}$ virus particles.

13. An oncolytic adenoviral vector for use in increasing the efficacy of separate adoptive T-cell therapy in a tumor of a subject, wherein said oncolytic adenoviral vector is an adenovirus serotype 3 (Ad3) oncolytic adenoviral vector comprising: a promoter for tumor specific expression of E1A, a deletion in the E3 area affecting E3 9 kDa, E3 10.2 kDa, E3 15.2 kDa and E3 15.3 kDa and an exogenous or tumor specific promoter for expression of a transgene in the place of the deleted area of E3, wherein the transgene is a cytokine selected from the cytokine group of claim 8.

14. Use of an oncolytic adenoviral vector in the manufacture of a medicament for increasing the efficacy of adoptive T-cell therapy in a tumor of a subject in need thereof, wherein said oncolytic adenoviral vector is an adenovirus serotype 3 (Ad3) oncolytic adenoviral vector comprising: a promoter for tumor specific expression of E1A, a deletion in the E3 area affecting E3 9 kDa, E3 10.2 kDa, E3 15.2 kDa and E3 15.3 kDa and an exogenous or ~~a~~ tumor specific promoter for expression of a transgene in the place of the deleted area of E3, wherein the transgene is a cytokine selected from the cytokine group of claim 8.

15. A pharmaceutical kit comprising an adoptive T-cell therapeutic composition and an oncolytic adenoviral vector coding for at least one cytokine, wherein the adoptive cell therapeutic composition is formulated in a first formulation and the oncolytic adenoviral vector coding for at least one cytokine is formulated in a second formulation, wherein said oncolytic adenoviral vector is an adenovirus serotype 3 (Ad3) oncolytic adenoviral vector comprising: a promoter for tumor specific expression of E1A, a deletion in the E3 area affecting E3 9 kDa, E3 10.2 kDa, E3 15.2 kDa and E3 15.3 kDa and an exogenous or ~~a~~ tumor specific promoter for expression of a transgene in the place of the deleted area of E3, wherein the transgene is a cytokine selected from the cytokine group of claim 8.

16. The pharmaceutical kit according to claim 15, wherein the first and the second formulations are for simultaneous or sequential, in any order,

administration to a subject.

17. Serotype 3 (Ad3) oncolytic adenoviral vector comprising: a promoter for tumor specific expression of E1A, a deletion in the E3 area affecting E3 9 kDa, E3 10.2 kDa, E3 15.2 kDa and E3 15.3 kDa and an exogenous or tumor specific promoter for expression of a transgene in the place of the deleted area of E3, wherein the transgene is a cytokine selected from the cytokine group of claim 8.

18. The oncolytic adenoviral vector according to claim 17, wherein it codes for CD40L.

19. The oncolytic adenoviral vector according to claim 17 or 18, wherein it codes for two or more cytokines.

20. The oncolytic adenoviral vector according to claim 19, wherein it comprises an internal ribosomal entry site (IRES) or optionally a ribosome shunt site 2A between the two transgenes.

21. The oncolytic adenoviral vector according to any one of claims 17-20, wherein the promoter for expression of a transgene in the E3 region is the CMV or E2F promoter.

22. A pharmaceutical composition comprising an oncolytic vector according to any one of claims 17-21.

23. Use of an oncolytic adenoviral vector according to any one of claims 17-21 in the manufacture of a medicament for treating cancer in a subject in need thereof.

24. An oncolytic adenoviral vector according to any one of claims 17-21 for use in treatment of cancer.

25. The use according to any one of claims 1, 3-12, 14 and 23, the oncolytic adenoviral vector coding for at least one cytokine together with separate adoptive T-cell therapeutic composition for use according to any one of claims 2-12, or the oncolytic adenoviral vector for use according to claim 24, wherein the oncolytic adenoviral vector is to be administered with concurrent or sequential radiotherapy, monoclonal antibodies, chemotherapy or other anticancer drugs or interventions to a subject.