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CLAIMS

1. A method of treating a human patient, said method comprising the steps of:
systemically administering multiple doses of a parenteral formulation of a replication capable oncolytic adenovirus of subgroup B in a single treatment cycle,
wherein the total dose given in each administration is in the range of $1x10^{10}$ to $1x10^{14}$ viral particles per dose, and
wherein each dose of virus is administered such that the rate of viral particle delivery is in the range of $2x10^{10}$ particles per minute to $6x10^{11}$ particles per minute.

2. A method according to claim 1, wherein the total dose given in each administration is in the range of $1x10^{12}$ to $1x10^{13}$ viral particles per dose, for example the total dose given in each administration is in the range of $3x10^{12}$ to $9x10^{12}$ viral particles per dose, in particular wherein the total dose given in each administration is $6x10^{12}$ viral particles per dose.

3. A method according to claims 1 or 2, wherein the period between each dose administration is in the range of 6 hours to 72 hours, such as 48 hours.

4. A method according to any one of claims 1 to 3, wherein the multiple doses are 2, 3, 4, 5, 6 or 7 doses in a single treatment cycle.

5. A method according to any one of claims 1 to 4, wherein the treatment cycle is a period of 14 days or less, such as 7 days or 5 days.

6. A method according to any one of claims 1 to 5, wherein each dose of virus is administered such that the rate of viral particle delivery is in the range of $1x10^{11}$ viral particles per minute to $3x10^{11}$ viral particles per minute, such as $2x10^{11}$ viral particles per minute or $1.67 x10^{11}$ viral particles per minute, per dose, in particular each dose of virus is administered such that the rate of viral particle delivery is $1.5x10^{11}$ viral particles per minute, per dose.

7. A method according to any one of claims 1 to 6, wherein $1 x 10^{13}$ viral particles are administered over a 60 minute period per dose or wherein $6x10^{12}$ viral particles are administered over a 40 minute period per dose.

8. A method according to any one of claims 1 to 7, wherein the plasma level of virus after administration of the second and optionally subsequent doses reaches a level of at least $2x10^{9}$ viral particles per mL.

9. A method according to claim 8, wherein the plasma level of viral particles is maintained for 15 minutes or greater, for example 20, 30, 40, 50 or 60 minutes.

10. A method according to any one of claims 1 to 9, wherein the volume of the formulation administered is 100mL or less, for example 30mLs or less, such as about 3mLs or 5mLs.

11. A method according to any one of claims 1 to 10, wherein a first dose is administered on day 1 and the further therapeutic doses are administered every second day thereafter, for example wherein the first dose is administered on day 1 and the further therapeutic doses are administered on days 3 and 5.

12. A method according to any one of claims 1 to 11, wherein the adenovirus is a chimeric adenovirus, for example wherein the chimeric adenovirus is ColoAd1.

13. A method according to any one of claims 1 to 12, wherein the virus is administered in combination with the administration of any other anti-cancer therapy including a chemotherapeutic agent, an immunotherapeutic agent such as an antibody or fragment thereof, a small molecule inhibitor such as a kinase inhibitor or an mTOR inhibitor, radiotherapy, radio-isotope therapy or any combination thereof.

14. A method according to any one of claims 1 to 13, wherein the virus is administered in combination with the administration of one or more prophylactic agents, for example selected from an antipyretic, an antiemetic, a steroid and an analgesic.

15. A method according to any one of claims 1 to 14 for the treatment of a tumour, for example a solid tumour, such as a colorectal malignancy.

16. A method according to any one of claims 1 to 13 wherein the first and therapeutic dose is in the range 10^9 to 10^{14} viral particles.

17. A method according to any one of claims 1 to 16, wherein the adenovirus is formulated to at least partially avoid the patient's immune system.

18. A method according to any one of claims 1 to 17, wherein the adenovirus contains a transgene.

19. A method according to any one of claims 1 to 18, wherein the treatment results in the necrosis of the cancer cells accompanied by an increase in plasma cytokine levels.

20. A method of treating a patient with a pharmaceutical formulation comprising ColoAd1 comprising the steps of intravenously administering to said patient
a first therapeutic dose on day 1 followed by
a second therapeutic dose on day 3 and
a third therapeutic dose on day 5.

21. A method of treating a human patient, said method comprising systemically administering multiple doses of a parenteral formulation comprising a replication

capable oncolytic adenovirus of subgroup B in a single treatment cycle, wherein the total dose given in each administration is in the range $1x10^{10}$ to $1x10^{13}$ viral particles, and is administered over a period of 1 minute to 90 minutes, for example wherein the total dose given in each administration is $6x10^{12}$ viral particles, and is administered over a period of 40 minutes.

22. A replication capable oncolytic adenovirus of subgroup B for use in treatment of a human patient by systemically administering multiple doses of a parenteral formulation comprising the adenovirus in a single treatment cycle, wherein the total dose given in each administration is in the range $1x10^{10}$ to $1x10^{14}$ or $1x10^{10}$ to $1x10^{13}$ viral particles, and is administered over a period of 1 minute to 90 minutes.

23. A parenteral formulation of a replication capable oncolytic adenovirus of subgroup B, for use according to claim 25, wherein the total dose administered is in the range 1 $x10^{10}$ to 1 $x10^{14}$ viral particles per dose and each dose of virus is administered such that the rate of particle delivery is in the range of $2x10^{10}$ particles per minute to $2x10^{12}$ per minute.

24. Use of a replication capable oncolytic adenovirus of subgroup B for the manufacture of a medicament use in treatment of a human patient by systemically administering multiple doses of a parenteral formulation comprising the adenovirus in a single treatment cycle, wherein the total dose given in each administration is in the range $1x10^{10}$ to $6x10^{12}$ viral particles, and is administered over a period of 1 minute to 90 minutes.

25. Use of a glass or plastic syringe with an internal volume in the range of 3 to 50ml, said syringe containing a parenteral formulation comprising $1x10^{10}$ to $6x10^{12}$ viral particles of a replication capable oncolytic adenovirus of subgroup B, wherein the formulation is sterile and was filled into the syringe under aseptic conditions, for use in treatment, in particular for use in the manufacture of a medicament which is capable of injection or intravenous infusion to a human subject, for example according to any one of claims 1 to 26.

26. ColoAd1 for use in treating ovarian cancer, for example administering a therapeutically effective amount of ColoAd1 to a patient with ovarian cancer, for example employing a dosing regimen described herein.

27. A combination therapy comprising oncolytic type B adenovirus, such as ColoAd1, and a chemotherapeutic agent which does not interfere with the adenovirus activity, such as viral replication *in vivo*.

CLAIMS

1. Use of a parenteral formulation of a replication capable oncolytic adenovirus of subgroup B in the manufacture of a medicament for the treatment of cancer by the administration of multiple doses in a single treatment cycle,

in which the total dose given in each administration is in the range of $1x10^{10}$ to $1x10^{14}$ viral particles per dose, and

in which each dose of virus is administered such that the rate of viral particle delivery is in the range of $2x10^{10}$ particles per minute to $6x10^{11}$ particles per minute.

2. Use according to Claim 1, in which the total dose given in each administration is in the range of $1x10^{12}$ to $1x10^{13}$ viral particles per dose, for example the total dose given in each administration is in the range of $3x10^{12}$ to $9x10^{12}$ viral particles per dose, in particular in which the total dose given in each administration is $6x10^{12}$ viral particles per dose.

3. Use according to Claim 1 or 2, in which the period between each dose administration is in the range of 6 hours to 72 hours.

4. Use according to Claim 3, in which the period between each dose administration is 48 hours.

5. Use according to any preceding claim, in which the multiple doses are 2, 3, 4, 5, 6 or 7 doses in a single treatment cycle.

6. Use according to any preceding claim, in which the treatment cycle is a period of 14 days or less.

7. Use according to Claim 6, in which the treatment cycle is a period of 7 or 5 days.

8. Use according to any preceding claim, in which each dose of virus is administered such that the rate of viral particle delivery is in the range of $1x10^{11}$ viral particles per minute to $3x10^{11}$ viral particles per minute, such as $2x10^{11}$ viral particles per minute or $1.67\ x10^{11}$ viral particles per minute, per dose, in particular each dose of virus is administered such that the rate of viral particle delivery is $1.5x10^{11}$ viral particles per minute, per dose.

9. Use according to Claim 8, in which the rate of viral particle delivery is $2x10^{11}$, $1.67\ x10^{11}$ or $1.5x10^{11}$ viral particles per minute, per dose.

10. Use according to any preceding claim, in which 1 x 10^{13} viral particles are administered over a 60 minute period per dose or in which 6x10^{12} viral particles are administered over a 40 minute period per dose.

11. Use according to any preceding claim, in which the plasma level of virus after administration of the second and optionally subsequent doses reaches a level of at least 2x10^{6} viral particles per mL.

12. Use according to Claim 11, in which the plasma level of viral particles is maintained for 15 minutes or greater.

13. Use according to Claim 12, in which the plasma level of viral particles is maintained for 20, 30, 40, 50 or 60 minutes.

14. Use according to any preceding claim, in which the volume of the formulation administered is 100mL or less, for example 30mLs or less, such as about 3mLs or 5mLs.

15. Use according to any preceding claim, in which a first dose is administered on day 1 and the further therapeutic doses are administered every second day thereafter, for example in which the first dose is administered on day 1 and the further therapeutic doses are administered on days 3 and 5.

16. Use according to any preceding claim, in which the adenovirus is a chimeric adenovirus, for example in which the chimeric adenovirus is ColoAd1.

17. Use according to any preceding claim, in which the virus is administered in combination with the administration of any other anti-cancer therapy including a chemotherapeutic agent, an immunotherapeutic agent such as an antibody or fragment thereof, a small molecule inhibitor such as a kinase inhibitor or an mTOR inhibitor, radiotherapy, radio-isotope therapy or any combination thereof.

18. Use according to any preceding claim, in which the virus is administered in combination with the administration of one or more prophylactic agents.

19. Use according to Claim 18, in which the one or more prophylactic agents is selected from the group consisting of an antipyretic, an antiemetic, a steroid and an analgesic.

20. Use according to any preceding claim for the treatment of a solid tumour.

21. Use according to Claim 20, in which the solid tumour is a colorectal malignancy.

22. Use according to any preceding claim in which the first and therapeutic dose is in the range 10^9 to 10^{14} viral particles.

23. Use according to any preceding claim, in which the adenovirus is formulated to at least partially avoid the patient's immune system.

24. Use according to any preceding claim, in which the adenovirus contains a transgene.

25. Use according to any preceding claim, in which the treatment results in the necrosis of the cancer cells accompanied by an increase in plasma cytokine levels.

26. Use of a pharmaceutical formulation comprising ColoAd1 in the manufacture of a medicament for the treatment of cancer by intravenous administration of

a first therapeutic dose on day 1 followed by

a second therapeutic dose on day 3 and

a third therapeutic dose on day 5.

27. Use of a glass or plastic syringe with an internal volume in the range of 3 to 50ml, the syringe containing a parenteral formulation comprising $1x10^{10}$ to $6x10^{12}$ viral particles of a replication capable oncolytic adenovirus of subgroup B, in which the formulation is sterile and was filled into the syringe under aseptic conditions in the manufacture of a medicament for use in the treatment of cancer.