[0005] The disclosures of all publications, patents, patent applications and published patent applications referred to herein are hereby incorporated herein by reference in their entirety.

SUMMARY

[0006] The present application provides methods, compositions (including pharmaceutical compositions) and kits for treating bladder cancer in an individual comprising intravesical administration of an oncolytic virus, *e.g.*, CG0070.

[0007] In one example, provided herein is a method of treating bladder cancer in an individual, comprising intravesically administering to the individual an effective amount of an oncolytic virus once per week for three weeks during a maintenance phase, wherein the oncolytic virus comprises a viral vector comprising a tumor cell-specific promoter operably linked to a viral gene essential for replication of the oncolytic virus, and a heterologous gene encoding an immune-related molecule.

[0007a] In one example, the present disclosure refers to use of an effective amount of an oncolytic virus in the manufacture of a medicament for treating bladder cancer in an individual having bladder cancer, wherein the medicament is formulated for intravesical administration to the individual once per week for three weeks during a maintenance phase, wherein the oncolytic virus is an adenovirus serotype 5, wherein the endogenous E1a promoter of a native adenovirus is replaced by the human E2F-1 promoter, and the endogenous E3 19kD coding region of the native adenovirus is replaced by a nucleic acid encoding human granulocyte macrophage-colony stimulating factor (GM-CSF).

In one aspect, the present disclosure refers to use of an effective amount of an oncolytic virus in the manufacture of a medicament for treating bladder cancer in an individual or for bladder preservation in an individual having bladder cancer,

wherein the individual is unresponsive or has disease reoccurrence subsequent to a standard therapy for bladder cancer,

wherein the medicament is formulated for intravesical administration to the individual during an induction phase and a maintenance phase,

wherein the medicament is to be administered to the individual during the induction phase once per week for six weeks at a dose of 1×10^{10} to 2×10^{13} viral particles of the oncolytic virus,

wherein the medicament is to be administered to the individual during the maintenance phase once per week for three weeks,

wherein the start of the induction phase and the start of the maintenance phase are separated by 3 months or 6 months, and

wherein the oncolytic virus is an adenovirus serotype 5, wherein the endogenous E1a promoter of a native adenovirus is replaced by the human E2F-1 promoter, and the endogenous E3 19kD coding region of the native adenovirus is replaced by a nucleic acid encoding human granulocyte macrophage-colony stimulating factor (GM-CSF).

[0007b] In one example, the present disclosure refers to use of an effective amount of an oncolytic virus in the manufacture of a medicament for preventing recurrence of bladder cancer in an individual that has achieved a complete or partial response to a prior therapy for bladder cancer, wherein the oncolytic virus comprises a viral vector comprising a tumor cell-specific promoter operably linked to a viral gene essential for replication of the oncolytic virus, and a heterologous gene encoding an immune-related molecule.

[0008] In another example, provided herein is a method of bladder preservation in an individual comprising intravesically administering to the individual an effective amount of an

oncolytic virus once per week for three weeks during a maintenance phase, wherein the oncolytic virus comprises a viral vector comprising a tumor cell-specific promoter operably linked to a viral gene essential for replication of the oncolytic virus, and a heterologous gene encoding an immune-related molecule.

[0009] In some examples, according to any of the methods described above, the oncolytic virus is administered once per week for three weeks every six months during the maintenance phase. In some examples, the method further comprises an induction phase prior to the maintenance phase, wherein the induction phase comprises administering to the induvial an effective amount of oncolytic virus once per week for six weeks. In some examples, the start of the induction phase and the start of the maintenance phase are separated by about 3 months. In some examples, the start of the induction phase and the start of the maintenance phase are separated by about 6 months. In some examples, the induction phase comprises administering to the individual an effective amount of an oncolytic virus once per week for six weeks on month zero and month three of a treatment regimen.

[0010] Also provided herein is a method of treating Ta or T1 bladder cancer in an individual who has not received a transurothelial resection of bladder tumor (TURBT), comprising intravesically administering to the individual an effective amount of an oncolytic virus, wherein the oncolytic virus comprises a viral vector comprising a tumor cell-specific promoter operably

CLAIMS

What is claimed is:

1. Use of an effective amount of an oncolytic virus in the manufacture of a medicament for treating bladder cancer in an individual or for bladder preservation in an individual having bladder cancer,
wherein the individual is unresponsive or has disease reoccurrence subsequent to a standard therapy for bladder cancer,
wherein the medicament is formulated for intravesical administration to the individual during an induction phase and a maintenance phase,
wherein the medicament is to be administered to the individual during the induction phase once per week for six weeks at a dose of 1×10^{10} to 2×10^{13} viral particles of the oncolytic virus,
wherein the medicament is to be administered to the individual during the maintenance phase once per week for three weeks,
wherein the start of the induction phase and the start of the maintenance phase are separated by 3 months or 6 months, and
wherein the oncolytic virus is an adenovirus serotype 5, wherein the endogenous E1a promoter of a native adenovirus is replaced by the human E2F-1 promoter, and the endogenous E3 19kD coding region of the native adenovirus is replaced by a nucleic acid encoding human granulocyte macrophage-colony stimulating factor (GM-CSF).

2. The use of claim 1, wherein the medicament is to be administered once per week for three weeks every three or six months during the maintenance phase.

3. The use of claim 1 or 2, wherein the medicament is to be administered to the individual once per week for six weeks at month zero during the induction phase, and wherein the individual is to be reevaluated at month three.

4. The use of claim 3, wherein the individual begins the maintenance phase at month three.

5. The use of claim 4, wherein, during the maintenance phase, the medicament is to be administered:
(i) once per week for three weeks every three months for nine months; and subsequently
(ii) once per week for three weeks every six months.

6. The use of claim 3, wherein the medicament is to be administered to the individual during the induction phase once per week for six weeks at month zero and month three.

7. The use of claim 6, wherein, during the maintenance phase, the medicament is to be administered:
(i) once per week for three weeks every three months for six months; and subsequently
(ii) once per week for three weeks every six months.

8. The use of any one of claims 1-7, wherein, during the maintenance phase, the medicament is to be administered :
(i) once per week for three weeks every three months for six to nine months, and subsequently
(ii) once per week for three weeks every six months.

9. The use of any one of claims 1-8, wherein the oncolytic virus is CG0070.

10. The use of any one of claims 1-9, wherein the individual has non-muscle-invasive bladder cancer.

11. The use of claim 10, wherein the individual has carcinoma in situ.

12. The use of claim 11, wherein the individual does not have a concurrent papillary carcinoma of Ta or T1 stage.

13. The use of claim 10 or 11, wherein the individual has Ta or T1 stage bladder cancer.

14. The use of any one of claims 1-13, wherein the standard therapy for bladder cancer is Bacillus Calmette-Guerin (BCG) treatment, and wherein:
(i) the individual is unresponsive to BCG treatment;
(ii) the individual has disease reoccurrence subsequent to BCG treatment;
(iii) the individual has failed BCG treatment within 12 months after BCG treatment; and/or
(iv) the individual has not received a cystectomy.

15. The use of claim 14, wherein the individual has refused or is ineligible for a cystectomy.

16. The use of any one of claims 1-15, wherein a transduction-enhancing agent is to be administered to the individual prior to when the medicament is to be administered to the individual, wherein the transduction enhancing agent is N-Dodecyl-β-D-maltoside (DDM).

17. The use of any one of claims 1-16, wherein the medicament is to be administered at a dose of 1 x 10^{10} to 2 x 10^{13} viral particles of the oncolytic virus during the maintenance phase.

18. The use of any one of claims 1-17, wherein:

(i) the medicament is not to be administered in conjunction with an immune checkpoint modulator; and/or

(ii) the medicament is to be administered as a single therapeutic agent.

19. The use of any one of claims 1-18, wherein the individual is human.