[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 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 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).

[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 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).

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 further administered in an induction phase prior to the maintenance phase, wherein, during the induction phase, an effective amount of the medicament is to be administered once per week for six weeks to the individual.

4. The use of claim 3, wherein the start of the induction phase and the start of the maintenance phase are separated by about 3 months or about 6 months.

5. The use of claim 3 or 4, wherein, during the induction phase, an effective amount of the medicament is to be administered to the individual once per week for six weeks on month zero and month three of a treatment regimen.

6. The use of claim 3 or 4, wherein the medicament is to be administered to the individual once per week for six weeks on month zero during the induction phase and is reevaluated at month three.

7. The use of claim 6, wherein the individual begins the maintenance phase at month three.

8. The use of claim 7, wherein, during the maintenance phase, the medicament is to be administered once per week for three weeks every three months for nine months and subsequently once per week for three weeks every six months.

9. The use of claim 6, wherein the individual is to receive a second induction dose of the composition comprising the oncolytic virus once per week for six weeks at month three.

10. The use of claim 9, wherein, during the maintenance phase, the medicament is to be administered once per week for three weeks every three months for six months and subsequently once per week for three weeks every six months.

11. The use of any one of claims 1-10, 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.

12. The use of any one of claims 1-11, wherein the oncolytic virus is CG0070.

13. The use of any one of claims 1-12, wherein the individual has non-muscle-invasive bladder cancer.

14. The use of claim 13, wherein the individual has carcinoma in situ.

15. The use of claim 14, wherein the individual does not have a concurrent papillary carcinoma of Ta or T1 stage.

16. The use of claim 13 or 14, wherein the individual has Ta or T1 stage bladder cancer.

17. The use of any one of claims 1-16, wherein:

(i) the individual is unresponsive to Bacillus Calmette-Guerin (BCG) treatment;

(ii) the individual has disease reoccurrence subsequent to BCG treatment;

(iii) the individual has failed BCG treatment within about 12 months after BCG treatment; and/or

(iv) the individual has not received a cystectomy.

18. The use of claim 17, wherein the individual the individual has refused or is ineligible for a cystectomy.

19. The use of any one of claims 1-18, 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).

20. The use of any one of claims 1-19, the medicament is to be administered at a dose of 1 x 10^8 to 1 x 10^{14} viral particles.

21. The use of any one of claims 1-20, 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.

22. The use of any one of claims 1-21, wherein the individual is human.