wherein the chemotherapeutic agent is delivered continuously to the bladder for at least about 24 hours. In some examples, the tumor cells at the second tumor site are located at a pelvic node. In some examples, the tumor cells at the second tumor site are located at a distant node. In some examples, the tumor cells at the second tumor site are circulating tumor cells. In some examples, the tumor cells at the first tumor site result from metastasis of a primary tumor at the second tumor site. In some examples, the tumor cells at the second site are selected from the group consisting of liver, lung, bone, brain, lymph node, pelvic node, peritoneum, skin, prostate, breast, colon, rectum, and cervix. In some examples, the individual has a urothelial carcinoma of lower tract.

[0014a] In one aspect, the present disclosure refers to use of an effective amount of gemcitabine in the manufacture of a medicament for inhibiting growth of tumor cells at a second tumor site distinct from tumor cells at a first tumor site in the bladder of an individual, wherein the gemcitabine is to be delivered locally and continuously to the bladder for at least 24 hours.

[0015] In some examples, also provided herein is a method of treating or suppressing tumor metastasis at a site distinct from the bladder in an individual having a urothelial carcinoma of lower tract, comprising locally delivering to the bladder an effective amount of a chemotherapeutic agent, wherein the chemotherapeutic agent is delivered continuously to the bladder for at least about 24 hours. In some examples, the tumor metastatic site is at one or more of: liver, lung, bone, brain, lymph node, pelvic node, peritoneum, skin, prostate, breast, colon, rectum, and cervix. In some examples, the tumor metastasis is at two or more different sites.

[0015a] In another example, the present disclosure refers to use of an effective amount of a chemotherapeutic agent in the manufacture of a medicament for treating or suppressing tumor metastasis at a site distinct from the bladder in an individual having a urothelial carcinoma of lower tract, wherein the chemotherapeutic agent is to be delivered locally and continuously to the bladder for at least about 24 hours.

[0016] In some examples according to any of the methods described above, the individual has bladder cancer. In some examples, the individual has muscle invasive bladder cancer or carcinoma in situ (CIS). In some examples, the individual is unfit for or refuses cystectomy.

[0017] In some examples according to any of the methods described above, the individual has not undergone transurethral resection of bladder tumors (TURBT).

[0018] In other examples, the individual has undergone transurethral resection of bladder tumors (TURBT). In some of these examples, the individual has undergone transurethral resection of bladder tumors (TURBT) and has residual tumor at the site of resection.

[0019] In some examples according to any of the methods described above, the chemotherapeutic agent is delivered at a dose of from about 1 mg/day to about 300 mg/day. In some examples, the concentration of the chemotherapeutic agent in the urine is from about 0.1 μg/mL to about 200 μg/mL during the delivery period.

CLAIMS

1. Use of an effective amount of gemcitabine in the manufacture of a medicament for inhibiting growth of tumor cells at a second tumor site distinct from tumor cells at a first tumor site in the bladder of an individual, wherein the gemcitabine is to be delivered locally and continuously to the bladder for at least 24 hours.

2. The use of claim 1, wherein the tumor cells at the second tumor site are located at a pelvic node.

3. The use of claim 1, wherein the tumor cells at the second tumor site are located at a distant node.

4. The use of claim 1, wherein the tumor cells at the second tumor site are circulating tumor cells.

5. The use of claim 1, wherein the tumor cells at the first tumor site result from metastasis of a primary tumor at the second tumor site.

6. The use of claim 5, wherein the second tumor site is selected from the group consisting of liver, lung, bone, brain, lymph node, pelvic node, peritoneum, skin, prostate, breast, colon, rectum, and cervix.

7. The use of any one of claims 1-4, wherein the individual has a urothelial carcinoma of lower tract.

8. The use of any one of claims 1-4, wherein the individual has bladder cancer.

9. The use of claim 8, wherein the individual has muscle invasive bladder cancer or carcinoma in situ (CIS).

10. The use of claim 8 or 9, wherein the individual is unfit for or refuses cystectomy.

11. The use of any one of claims 8-10, wherein the individual has not undergone transurethral resection of bladder tumors (TURBT).

12. The use of any one of claims 8-10, wherein the individual has undergone transurethral resection of bladder tumors (TURBT).

13. The use of claim 12, wherein the individual has residual tumor at the site of resection.

14. The use of any one of claims 1-13, wherein the gemcitabine is to be delivered continuously to the bladder of the individual for a period of 7 days to three weeks.

15. The use of any one of claims 1-14, wherein the use comprises an induction delivery period followed by a maintenance delivery period.

16. The use of claim 15, wherein the induction delivery period and the maintenance delivery period are separated by a rest period of 7 to 14 days or 1 to 4 months.

17. The use of claim 15 or 16, wherein the gemcitabine is to be delivered at a first release rate during the induction delivery period and a second release rate during the maintenance delivery period.

18. The use of any of claims 1-17, wherein the gemcitabine is to be delivered at a dose of from 1 mg/day to 300 mg/day.

19. The use of any of claims 1-18, wherein the concentration of the gemcitabine in the urine is from 0.1 μg/mL to 200 μg/mL during the delivery period.

20. The use of any one of claims 1-19, comprising

a) an induction delivery period, wherein the concentration of gemcitabine in the urine of the individual is at least 0.1 μg/mL;

b) a rest period; and

c) a maintenance delivery period, wherein the concentration of the gemcitabine in the urine of the individual is greater than 0.1 μg/mL.

21. The use of any of claims 1-20, wherein the individual does not receive a radiation therapy.

22. The use of any one of claims 1-21, wherein the gemcitabine is to be delivered with a radiation therapy.

23. The use of any one of claims 1-22, wherein the gemcitabine is to be delivered by an intravesical delivery device.

24. The use of claim 23, wherein the intravesical delivery device contains 100 mg to 500 mg of the gemcitabine.

25. The use of any of claims 23-24, wherein the intravesical delivery device comprises a housing configured for intravesical insertion; and a dosage form comprising gemcitabine, wherein the housing holds the dosage form and is configured to release gemcitabine.

26. The use of any one of claims 23-25, wherein the intravesical delivery device comprises:

a housing defining a reservoir;

a first unit contained within the reservoir, the first unit comprising gemcitabine; and

a second unit contained within the reservoir in a position distinct from the first unit, wherein the second unit comprises a functional agent that facilitates in vivo release of the gemcitabine from the housing.

27. The use of any one of claims 23-26, wherein the intravesical delivery device comprises a housing which contains and controllably releases the gemcitabine and is elastically deformable between a retention shape configured to retain the device in the individual's bladder and a deployment shape for passage of the device through the individual's urethra.

28. The use of any one of claims 23-27, wherein the intravesical delivery device comprises a drug reservoir lumen bounded by a first wall and a second wall, wherein the first wall is impermeable to the drug and the second wall is permeable to the drug, wherein the drug is gemcitabine.

29. The use of any one of claims 23-28 wherein the gemcitabine is released from the intravesical delivery device by osmotic pressure.

30. The use of any one of claims 23-28, wherein the gemcitabine is released from the intravesical delivery device by diffusion.

31. The use of any of claims 25-30, wherein the gemcitabine contained in the housing is in a non-liquid form.

32. The use of claim 31, wherein the non-liquid form is selected from the group consisting of tablets, granules, powders, semisolids, capsules, and combinations thereof.

33. The use of any one of claims 1-32, wherein the individual is human.

34. The use of any one of claims 1-33, wherein the individual is unsuitable for systemic chemotherapy.

35. The use of any one of claims 1-34, wherein the individual has a compromised immune system.

36. The use of any one of claims 1-35, wherein the individual has a high tumor burden.