CLAIMS

WHAT IS CLAIMED IS:

1. A method of treating cervical cancer in a subject, the method comprising administering to the subject an antibody-drug conjugate that binds to tissue factor (TF), wherein the antibody-drug conjugate is tisotumab vedotin or a biosimilar thereof, and wherein the antibody-drug conjugate is administered at a dose of 2.0 mg/kg once every 3 weeks, wherein the subject has been previously treated with bevacizumab.

2. The method of claim 1, wherein the subject has an ECOG score of 0.

3. The method of claim 1, wherein the subject has an ECOG score of 1.

4. The method of any one of claims 1-3, wherein the subject is less than 65 years old.

5. The method of any one of claims 1-4, wherein the subject has been previously treated with:

a) paclitaxel and cisplatin,

b) paclitaxel and carboplatin, or

c) paclitaxel and topotecan.

6. A method of treating cervical cancer in a subject, the method comprising administering to the subject an antibody-drug conjugate that binds to tissue factor (TF), wherein the antibody-drug conjugate is tisotumab vedotin or a biosimilar thereof, and wherein the antibody-drug conjugate is administered at a dose of 2.0 mg/kg once every 3 weeks, wherein the subject has not been previously treated with bevacizumab.

7. The method of claim 6, wherein the subject has an ECOG score of 0.

8. The method of claim 6, wherein the subject has an ECOG score of 1.

9. The method of any one of claims 6-8, wherein the subject is less than 65 years old.

10. The method of any one of claims 6-9, wherein the subject has been previously treated with:

a) paclitaxel and cisplatin,

b) paclitaxel and carboplatin, or

c) paclitaxel and topotecan.

11. A method of treating cervical cancer in a subject, the method comprising administering to the subject an antibody-drug conjugate that binds to tissue factor (TF), wherein the antibody-drug conjugate is tisotumab vedotin or a biosimilar thereof, and wherein the antibody-drug conjugate is administered at a dose of 2.0 mg/kg once every 3 weeks, wherein the subject has an Eastern Cooperative Oncology Group (ECOG) score of 0.

12. The method of claim 11, wherein the subject is less than 65 years old.

13. The method of any claim 11 or 12, wherein the subject has been previously treated with:

a) paclitaxel and cisplatin,

b) paclitaxel and carboplatin, or

c) paclitaxel and topotecan.

14. A method of treating cervical cancer in a subject, the method comprising administering to the subject an antibody-drug conjugate that binds to tissue factor (TF), wherein the antibody-drug conjugate is tisotumab vedotin or a biosimilar thereof, and wherein the antibody-drug conjugate is administered at a dose of 2.0 mg/kg once every 3 weeks, wherein the subject has an ECOG score of 1.

15. The method of claim 14, wherein the subject is less than 65 years old.

16. The method of any claim 14 or 15, wherein the subject has been previously treated with:

a) paclitaxel and cisplatin,

b) paclitaxel and carboplatin, or

c) paclitaxel and topotecan.

17. A method of treating cervical cancer in a subject, the method comprising administering to the subject an antibody-drug conjugate that binds to tissue factor (TF), wherein the antibody-drug conjugate is tisotumab vedotin or a biosimilar thereof, and wherein the antibody-drug conjugate is administered at a dose of 2.0 mg/kg once every 3 weeks, wherein the subject is less than 65 years old.

18. The method of claim 17, wherein the subject has an ECOG score of 0.

19. The method of claim 17, wherein the subject has an ECOG score of 1.

20. The method of any one of claims 17-19, wherein the subject has been previously treated with:

a) paclitaxel and cisplatin,

b) paclitaxel and carboplatin, or

c) paclitaxel and topotecan.

21. The method of any one of claims 1-20, wherein the objective response rate is between about 13% and about 35%, optionally, wherein the objective response rate is at least about 14%, about 19%, about 21%, 23.8%, about 24%, about 25%, about 26%, about 28%, about 30%, or about 33%.

22. The method of any one of claims 1-21, wherein the subject exhibits progression-free survival of at least about 3 months after administration of the antibody-drug conjugate, optionally, wherein the subject exhibits progression-free survival of at least about 4 months, about 5 months, or about 6 months after administration of the antibody-drug conjugate.

23. The method of any one of claims 1-22, wherein the subject exhibits overall survival of at least about 10 months after administration of the antibody-drug conjugate, optionally, wherein

the subject exhibits overall survival of at least about 11 months, about 12 months, about 13 months, or 14 months after administration of the antibody-drug conjugate.

24. The method of any one of claims 1-23, wherein the duration of response to the antibody-drug conjugate is at least about 6 months after administration of the antibody-drug conjugate, optionally, wherein the duration of response to the antibody-drug conjugate is at least about 7 months, about 8 months or about 10 months after administration of the antibody-drug conjugate.

25. The method of any one of claims 1-24, wherein the time to response is less than about 6 months after administration of the antibody-drug conjugate, optionally, wherein the time to response is less than about 4 months, about 2 months, 1.4 months, or about 1.2 months after administration of the antibody-drug conjugate.

26. A method of treating cervical cancer in a subject, the method comprising administering to the subject an antibody-drug conjugate that binds to tissue factor (TF), wherein the antibody-drug conjugate is tisotumab vedotin or a biosimilar thereof, and wherein the antibody-drug conjugate is administered at a dose of 2.0 mg/kg once every 3 weeks, wherein the objective response rate is between about 13% and about 35%, optionally, wherein the objective response rate is at least about 14%, about 19%, about 21%, 23.8%, about 24%, about 25%, about 26%, about 28%, about 30%, or about 33%.

27. The method of claim 26, wherein the subject exhibits progression-free survival of at least about 3 months after administration of the antibody-drug conjugate, optionally, wherein the subject exhibits progression-free survival of at least about 4 months, about 5 months, or about 6 months after administration of the antibody-drug conjugate.

28. The method of claim 26 or 27, wherein the subject exhibits overall survival of at least about 10 months after administration of the antibody-drug conjugate, optionally, wherein the subject exhibits overall survival of at least about 11 months, about 12 months, about 13 months, or 14 months after administration of the antibody-drug conjugate.

29. The method of any one of claims 26-28, wherein the duration of response to the antibody-drug conjugate is at least about 6 months after administration of the antibody-drug conjugate, optionally, wherein the duration of response to the antibody-drug conjugate is at least about 7 months, about 8 months or about 10 months after administration of the antibody-drug conjugate.

30. The method of any one of claims 26-29, wherein the time to response is less than about 6 months after administration of the antibody-drug conjugate, optionally, wherein the time to response is less than about 4 months, about 2 months, 1.4 months, or about 1.2 months after administration of the antibody-drug conjugate.

31. A method of treating cervical cancer in a subject, the method comprising administering to the subject an antibody-drug conjugate that binds to tissue factor (TF), wherein the antibody-drug conjugate is tisotumab vedotin or a biosimilar thereof, and wherein the antibody-drug conjugate is administered at a dose of 2.0 mg/kg once every 3 weeks, wherein the subject exhibits progression-free survival of at least about 3 months after administration of the antibody-drug conjugate, optionally, wherein the subject exhibits progression-free survival of at least about 4 months, about 5 months, or about 6 months after administration of the antibody-drug conjugate.

32. The method of claim 31, wherein the objective response rate is between about 13% and about 35%, optionally, wherein the objective response rate is at least about 14%, about 19%, about 21%, 23.8%, about 24%, about 25%, about 26%, about 28%, about 30%, or about 33%.

33. The method of claim 31 or 32, wherein the subject exhibits overall survival of at least about 10 months after administration of the antibody-drug conjugate, optionally, wherein the subject exhibits overall survival of at least about 11 months, about 12 months, about 13 months, or 14 months after administration of the antibody-drug conjugate.

34. The method of any one of claims 31-33, wherein the duration of response to the antibody-drug conjugate is at least about 6 months after administration of the antibody-drug conjugate,

optionally, wherein the duration of response to the antibody-drug conjugate is at least about 7 months, about 8 months or about 10 months after administration of the antibody-drug conjugate.

35. The method of any one of claims 31-34, wherein the time to response is less than about 6 months after administration of the antibody-drug conjugate, optionally, wherein the time to response is less than about 4 months, about 2 months, 1.4 months, or about 1.2 months after administration of the antibody-drug conjugate.

36. A method of treating cervical cancer in a subject, the method comprising administering to the subject an antibody-drug conjugate that binds to tissue factor (TF), wherein the antibody-drug conjugate is tisotumab vedotin or a biosimilar thereof, and wherein the antibody-drug conjugate is administered at a dose of 2.0 mg/kg once every 3 weeks, wherein the subject exhibits overall survival of at least about 10 months after administration of the antibody-drug conjugate, optionally, wherein the subject exhibits overall survival of at least about 11 months, about 12 months, about 13 months, or 14 months after administration of the antibody-drug conjugate.

37. The method of claim 36, wherein the subject exhibits progression-free survival of at least about 3 months after administration of the antibody-drug conjugate, optionally, wherein the subject exhibits progression-free survival of at least about 4 months, about 5 months, or about 6 months after administration of the antibody-drug conjugate.

38. The method of claim 36 or 37, wherein the objective response rate is between about 13% and about 35%, optionally, wherein the objective response rate is at least about 14%, about 19%, about 21%, 23.8%, about 24%, about 25%, about 26%, about 28%, about 30%, or about 33%.

39. The method of any one of claims 36-38, wherein the duration of response to the antibody-drug conjugate is at least about 6 months after administration of the antibody-drug conjugate, optionally, wherein the duration of response to the antibody-drug conjugate is at least about 7 months, about 8 months or about 10 months after administration of the antibody-drug conjugate.

40. The method of any one of claims 36-39, wherein the time to response is less than about 6 months after administration of the antibody-drug conjugate, optionally, wherein the time to response is less than about 4 months, about 2 months, 1.4 months, or about 1.2 months after administration of the antibody-drug conjugate.

41. A method of treating cervical cancer in a subject, the method comprising administering to the subject an antibody-drug conjugate that binds to tissue factor (TF), wherein the antibody-drug conjugate is tisotumab vedotin or a biosimilar thereof, and wherein the antibody-drug conjugate is administered at a dose of 2.0 mg/kg once every 3 weeks, wherein the duration of response to the antibody-drug conjugate is at least about 6 months after administration of the antibody-drug conjugate, optionally, wherein the duration of response to the antibody-drug conjugate is at least about 7 months, about 8 months or about 10 months after administration of the antibody-drug conjugate.

42. The method of claim 41, wherein the subject exhibits progression-free survival of at least about 3 months after administration of the antibody-drug conjugate, optionally, wherein the subject exhibits progression-free survival of at least about 4 months, about 5 months, or about 6 months after administration of the antibody-drug conjugate.

43. The method of claim 41 or 42, wherein the subject exhibits overall survival of at least about 10 months after administration of the antibody-drug conjugate, optionally, wherein the subject exhibits overall survival of at least about 11 months, about 12 months, about 13 months, or 14 months after administration of the antibody-drug conjugate.

44. The method of any one of claims 41-43, wherein the objective response rate is between about 13% and about 35%, optionally, wherein the objective response rate is at least about 14%, about 19%, about 21%, 23.8%, about 24%, about 25%, about 26%, about 28%, about 30%, or about 33%.

45. The method of any one of claims 41-44, wherein the time to response is less than about 6 months after administration of the antibody-drug conjugate, optionally, wherein the time to

response is less than about 4 months, about 2 months, 1.4 months, or about 1.2 months after administration of the antibody-drug conjugate.

46. A method of treating cervical cancer in a subject, the method comprising administering to the subject an antibody-drug conjugate that binds to tissue factor (TF), wherein the antibody-drug conjugate is tisotumab vedotin or a biosimilar thereof, and wherein the antibody-drug conjugate is administered at a dose of 2.0 mg/kg once every 3 weeks, wherein the time to response is less than about 6 months after administration of the antibody-drug conjugate, optionally, wherein the time to response is less than about 4 months, about 2 months, 1.4 months, or about 1.2 months after administration of the antibody-drug conjugate.

47. The method of claim 46, wherein the subject exhibits progression-free survival of at least about 3 months after administration of the antibody-drug conjugate, optionally, wherein the subject exhibits progression-free survival of at least about 4 months, about 5 months, or about 6 months after administration of the antibody-drug conjugate.

48. The method of claim 46 or 47, wherein the subject exhibits overall survival of at least about 10 months after administration of the antibody-drug conjugate, optionally, wherein the subject exhibits overall survival of at least about 11 months, about 12 months, about 13 months, or 14 months after administration of the antibody-drug conjugate.

49. The method of any one of claims 46-48, wherein the duration of response to the antibody-drug conjugate is at least about 6 months after administration of the antibody-drug conjugate, optionally, wherein the duration of response to the antibody-drug conjugate is at least about 7 months, about 8 months or about 10 months after administration of the antibody-drug conjugate.

50. The method of any one of claims 46-49, wherein the objective response rate is at least about between about 13% and about 35%, optionally, wherein the objective response rate is at least about 14%, about 19%, about 21%, 23.8%, about 24%, about 25%, about 26%, about 28%, about 30%, or about 33%.

51. The method of any one of claims 26-50, wherein the subject has been previously treated with bevacizumab.

52. The method of any one of claims 26-50, wherein the subject has not been previously treated with bevacizumab.

53. The method of any one of claims 26-52, wherein the subject has experienced disease progression during or after treatment with:

a) paclitaxel and cisplatin,

b) paclitaxel and carboplatin,

c) paclitaxel and topotecan,

d) bevacizumab, paclitaxel, and cisplatin,

e) bevacizumab, paclitaxel, and carboplatin, or

f) bevacizumab, paclitaxel, and topotecan.

54. The method of any one of claims 26-53, wherein the subject is less than 65 years old.

55. The method of any one of claims 26-54, wherein the subject has an ECOG score of 0.

56. The method of any one of claims 26-54, wherein the subject has an ECOG score of 1.

57. The method of any one of claims 1-56, wherein the cervical cancer is an adenocarcinoma.

58. The method of any one of claims 1-56, wherein the cervical cancer is an adenosquamous carcinoma.

59. The method of any one of claims 1-56, wherein the cervical cancer is a squamous cell carcinoma.

60. The method of any one of claims 1-56, wherein the cervical cancer is a non-squamous cell carcinoma.

61. The method of any one of claims 1-60, wherein the cervical cancer is recurrent or metastatic cervical cancer.

62. The method of any one of claims 1-61, wherein the subject has been previously treated with one or more therapeutic agents and did not respond to the treatment, wherein the one or more therapeutic agents is not the antibody-drug conjugate.

63. The method of any one of claims 1-61, wherein the subject has been previously treated with one or more therapeutic agents and relapsed after the treatment , wherein the one or more therapeutic agents is not the antibody-drug conjugate.

64. The method of any one of claims 1-61, wherein the subject has been previously treated with one or more therapeutic agents and has experienced disease progression during treatment, wherein the one or more therapeutic agents is not the antibody-drug conjugate.

65. The method of any one of claims 62-64, wherein the one or more therapeutic agents is a platinum-based therapeutic agent.

66. The method of any one of claims 62-64, wherein the one or more therapeutic agents is selected from the group consisting of: paclitaxel, cisplatin, carboplatin, topotecan, gemcitabine, fluorouracil, ixabepilone, imatinib mesylate, docetaxel, gefitinib, nab-paclitaxel, pemetrexed, vinorelbine, doxil, cetuximab, pembrolizumab, nivolumab and bevacizumab.

67. The method of any one of claims 1-66, wherein the subject is not a candidate for curative therapy.

68. The method of claim 67, wherein the curative therapy comprises radiotherapy and/or exenterative surgery.

69. The method of any one of claims 1-66, wherein the subject has received prior radiation to the pelvis.

70. The method of any one of claims 1-66, wherein the subject has not received prior radiation to the pelvis.

71. The method of any one of claims 1-70, wherein the subject has received one prior line of systemic therapy for relapsed, recurrent or metastatic cancer.

72. The method of any one of claims 1-70, wherein the subject has received two prior lines of systemic therapy for relapsed, recurrent or metastatic cancer.

73. The method of any one of claims 71 or 72, wherein the subject did not respond to treatment with the prior systemic therapy.

74. The method of any one of claims 71 or 72, wherein the subject relapsed after treatment with the prior systemic therapy.

75. The method of any one of claims 1-74, wherein the cervical cancer is an advanced stage cervical cancer, such as a stage 3 or stage 4 cervical cancer, such as metastatic cervical cancer.

76. The method of any one of claims 1-75, wherein the cervical cancer is recurrent cervical cancer.

77. The method of any one of claims 1-76, wherein the route of administration for the antibody-drug conjugate is intravenous.

78. The method of any one of claims 1-77, wherein at least about 0.1%, at least about 1%, at least about 2%, at least about 3%, at least about 4%, at least about 5%, at least about 6%, at least about 7%, at least about 8%, at least about 9%, at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at

least about 45%, at least about 50%, at least about 60%, at least about 70%, or at least about 80% of the cervical cancer cells express TF.

79. The method of any one of claims 1-78, wherein the subject has a TF histology score (H-score) of at least 1.

80. The method of any one of claims 1-79, wherein the subject has one or more adverse events and is further administered an additional therapeutic agent to eliminate or reduce the severity of the one or more adverse events.

81. The method of any one of claims 1-79, wherein the subject is at risk of developing one or more adverse events and is further administered an additional therapeutic agent to prevent or reduce the severity of the one or more adverse events.

82. The method of any one of claims 1-80, wherein the subject has one or more adverse events and the dose of the antibody drug conjugate is reduced following the one or more adverse events.

83. The method of claim 82, wherein the dose is reduced from 2.0 mg/kg to 1.3 mg/kg.

84. The method of claim 83, wherein the dose is reduced from 1.3 mg/kg to 0.9 mg/kg.

85. The method of any one of claims 80-84, wherein the one or more adverse events is anemia, abdominal pain, hypokalemia, hyponatremia, epistaxis, fatigue, nausea, alopecia, conjunctivitis, constipation, decreased appetite, diarrhea, vomiting, peripheral neuropathy, or general physical health deterioration.

86. The method of any one of claims 80-85, wherein the one or more adverse events is a grade 3 or greater adverse event.

87. The method of any one of claims 80-85, wherein the one or more adverse events is a serious adverse event.

88. The method of claim 80 or claim 81, wherein the one or more adverse events is conjunctivitis and/or keratitis and the additional agent is a preservative-free lubricating eye drop, an ocular vasoconstrictor and/or a steroid eye drop.

89. The method of any one of claims 1-88, wherein the antibody-drug conjugate is administered as a monotherapy.

90. The method of any one of claims 1-89, wherein the subject is a human.

91. The method of any one of claims 1-90, wherein the antibody-drug conjugate is in a pharmaceutical composition comprising the antibody-drug conjugate and a pharmaceutical acceptable carrier.

92. An antibody-drug conjugate that binds to TF for use in the method of any one of claims 1-91.

93. Use of an antibody-drug conjugate that binds to TF for the manufacture of a medicament for use in the method of any one of claims 1-91.