METHODS FOR TREATING PROSTATE CANCER WITH BISPECIFIC ANTIBODIES BINDING STEAP1XCD3

FIELD OF THE INVENTION

[0001] The present invention relates to the field of oncology. In particular, the invention relates to the treatment of prostate cancer with a STEAP1 T cell engager (TCE) molecule, either as a monotherapy or in combination with another pharmaceutical agent.

INCORPORATION BY REFERENCE

[0002] This application incorporates by reference International Patent Publication No. WO 2020/010079, filed on July 2, 2019; and International Publication No. WO 2019/157340, filed February 8, 2019, both of which are expressly incorporated herein by reference in their entirety, with particular reference to the figures, legends and claims therein.

[0003] This application contains, as a separate part of the disclosure, a Sequence Listing in computer readable form (Filename: 10649-WO01-SEC_Sequence_Listing.xml; Size: 30,872 bytes; Created: July 25, 2024), which is incorporated by reference in its entirety.

BACKGROUND OF THE INVENTION

[0004] Prostate cancer is one of the most frequently diagnosed noncutaneous cancers and one of the leading causes of cancer deaths in men in the United States (U.S.). In the U.S., an estimated 288,300 new cases of prostate cancer (29% of all new cancer cases in men) and 34,700 prostate cancer related deaths (11% of cancer deaths in men) are expected in 2023 (Siegel et al., Cancer statistics, 2023. CA Cancer J Clin. 2023;73(1):17-48).

[0005] Survival rates vary among men with prostate cancer but are strongly related to disease stage and location of disease (i.e., local vs metastatic). While the 5-year survival rate for men with localized prostate cancer in the US is nearly 100%, the 5-year survival rate drops to as low as 31% for men with metastatic disease (Cancer.Net, 2020). In 2015, there were an estimated 365,000 new cases and 77 000 deaths from prostate cancer in the European Union (10% of total cancer deaths) (EU Science Hub, 2018). In China, there were an estimated 78,300 new cases of prostate cancer, with 33,600 deaths in 2016. During 2000-2016, there was an

increasing trend of incidence rate for prostate cancer. The average annual percentage changed was 7.1% (Zheng et al., Cancer Med., 11:2117-2124, 2022).

[0006] Treatment for patients diagnosed with metastatic prostate cancer has included continuous and intermittent androgen-deprivation therapy (ADT). Docetaxel and the novel hormonal therapies (NHTs), abiraterone, enzalutamide, apalutamide, and darolutamide, are approved therapies. Metastatic prostate cancer often develops resistance to ADT (also known as "castration resistance") due to increased intratumoral steroidogenesis, altered steroid-transporter expression, increased androgen receptor expression (e.g., androgen receptor amplification), and other mechanisms (Galletti et al., Cancer Treat Rev. 2017;57:16-27).

[0007] Since 2010, five new therapeutic agents for metastatic castration resistant prostate cancer (mCRPC) have been approved based on survival benefit: cabazitaxel (Jevtana®), sipuleucel-T (Provenge®), abiraterone (Zytiga®), enzalutamide (Xtandi®), and radium-223 (Xofigo®). However, the optimal sequence or combination of available therapies in mCRPC is largely unknown. Food and Drug Administration (FDA) has also recently approved the following therapies for specific biomarker-defined subgroups of patients with mCRPC: poly ADP ribose polymerase (PARP) inhibitors, olaparib (Lynparza®), rucaparib (Rubraca®); the programmed cell death protein 1 (PD-1) inhibitor, pembrolizumab (Keytruda®); and a radioligand therapeutic targeting prostate-specific membrane antigen, lutetium Lu 177 vipivotide tetraxetan (PLUVICTO®). These therapies are indicated for limited or preselected subgroups of patients; therefore, there remains an unmet need in the late-line mCRPC setting.

[0008] Six-transmembrane epithelial antigen of the prostate 1 (STEAP1), a surface antigen containing 3 short extra-cellular loop regions, is overexpressed in prostate cancer (Hubert et al., Proc Natl Acad Sci USA. 1999;96(25):14523-8) and Ewing sarcoma (Grunewald et al., Mol Cancer Res. 2012 Jan;10(1):52-65), and its expression correlates with prostate cancer disease stage (Gomes et al., Urol Oncol. 2014 Jan;32(1):53.e23-9). Xaluritamig (also known as "AMG 509") is a novel XmAb® 2 + 1 bispecific antibody designed to direct T effector cells (through CD3 binding) to prostate cancer cells expressing STEAP1. In nonclinical studies, xaluritamig demonstrated potent cytotoxicity in prostate cancer cell lines and tumor regression in a preclinical xenograft model (Nolan-Stevaux et al., Cancer Discov. 14(1):90-103, 2024). The

nonclinical evidence supported advancement of xaluritamig to clinical testing in patients with mCRPC.

SUMMARY OF THE INVENTION

[0009] The present invention provides a method of treating a patient having prostate cancer, comprising administering to the patient a pharmaceutical composition comprising an anti-STEAP1 antigen binding protein at a dose of about 0.1 mg to about 2.0 mg.

[0010] The present invention also provides use of an anti-STEAP1 antigen binding protein for preparation of a medicament for treating prostate cancer, wherein the medicament is formulated for administration at a dose of about 0.1 mg to about 2.0 mg.

[0011] The present invention also provides use of an anti-STEAP1 antigen binding protein in the manufacture of a medicament for treating prostate cancer, wherein the medicament is formulated for administration at a dose of about 0.1 mg to about 2.0 mg.

[0012] The present invention also provides an anti-STEAP1 antigen binding protein for treating prostate cancer, wherein the medicament is formulated for administration at a dose of about 0.001 mg to about 2.0 mg.

[0013] An anti-STEAP1 antigen binding protein may be administered to a subject at a dose of about 0.001 mg to about 1.5 mg. In an embodiment, the dose is about 0.1 mg to about 1.5 mg. In an embodiment, the dose is 0.1 mg, 0.2 mg, 0.3 mg, 0.4 mg, 0.5 mg, 0.6 mg, 0.7 mg, 0.75, 0.8 mg, 0.9 mg, 1.0 mg, 1.1 mg, 1.2 mg, 1.3 mg, 1.4 mg, 1.5 mg, 1.6 mg, or 1.7 mg. In an embodiment, the dose is about 0.1 mg. In an embodiment, the dose is about 0.3 mg. In an embodiment, the dose is about 0.75 mg. In an embodiment, the dose is about 1 mg. In an embodiment, the dose is about 1.5 mg. In an embodiment, the dose is 0.1 mg. In an embodiment, the dose is 0.3 mg. In an embodiment, the dose is 0.75 mg. In an embodiment, the dose is 1 mg. In an embodiment, the dose is 1.5 mg. In an embodiment, the dose is administered once per one week. In an embodiment, the dose is administered once per two weeks. In an embodiment, the dose is administered once per three weeks. In an embodiment, the dose is administered once per four weeks. In an embodiment, the dose is administered by intravenous administration. In an embodiment, the dose is administered once per week beginning in cycle one. In an embodiment, the dose is administered once per week beginning in cycle two. In an embodiment, the dose is

administered once per two weeks beginning in cycle two. In an embodiment, the dose is administered once per three weeks beginning in cycle two. In an embodiment, the dose is administered once per four weeks beginning in cycle two. In an embodiment, the dose is administered once per week for the first cycle, and then administered once per two weeks beginning on day one of cycle two. In an embodiment, the dose is administered once per week for the first cycle, and then administered once per two weeks once the target dose has been achieved. In an embodiment, the dose is administered once per week for the first cycle, and then administered once per three weeks once the target dose has been achieved. In an embodiment, the dose is administered once per week for the first cycle, and then administered once per four weeks once the target dose has been achieved. In some embodiments, cycle two is repeated 11 times after cycle 1 has been completed (e.g., for a total treatment period of about 12 months). In some embodiments, cycle 2 is repeated five times after cycle 1 is completed (e.g., for a total treatment period of about six months).

[0014] The present invention also provides a method of treating a patient having prostate cancer, wherein the method comprises administering to the patient a pharmaceutical composition comprising an anti-STEAP1 antigen binding protein at a dose of about 0.1 mg to about 2.0 mg, and further comprising administering to the patient a dose of abiraterone. The present invention provides use of an anti-STEAP1 antigen binding protein for preparation of a medicament for treating prostate cancer, wherein the medicament is formulated for administration at a dose of about 0.001 mg to about 2.0 mg (e.g., about 0.1 mg to about 2.0 mg), and wherein the use further comprises administering to the patient a dose of abiraterone. In an embodiment, the dose of abiraterone is about 500 mg to about 750 mg. In an embodiment, the dose of abiraterone is about 750 mg to about 1000 mg. In an embodiment, the dose of abiraterone is about 1000 mg. In an embodiment, the dose of abiraterone is 1000 mg. In an embodiment, the dose of abiraterone is administered orally. Optionally, abiraterone is administered once a day. In an embodiment, the patient is further administered prednisone (or prednisolone). In various embodiments, the patient is administered 4 mg of prednisone two times per day. In various embodiments, the patient is administered 5 mg of prednisone two times per day. In an embodiment, the patient is further administered 10 mg of prednisolone one time per day. In an embodiment, the patient is orally administered 1000 mg abiraterone once daily and administered prednisone at a dose of 5 mg twice daily or 10 mg once daily. In various aspects, the patient is orally administered 500 mg

abiraterone once daily and administered prednisone at a dose of 4 mg twice daily. In an embodiment, the dose of the anti-STEAP1 antigen binding protein is about 0.1 mg to about 2.0 mg. In an embodiment, the dose of the anti-STEAP1 antigen binding protein is about 0.1 mg to about 1.5 mg. In an embodiment, the dose of the anti-STEAP1 antigen binding protein is about 0.75 mg. In an embodiment, the dose of the anti-STEAP1 antigen binding protein is about 1 mg. In an embodiment, the dose of the anti-STEAP1 antigen binding protein is 1.5 mg. In an embodiment, the dose of the anti-STEAP1 antigen binding protein is administered once per week. In an embodiment, the dose of the anti-STEAP1 antigen binding protein is administered once per two weeks. In an embodiment, the patient is administered a dose of the anti-STEAP1 antigen binding protein and a dose of abiraterone on the same day. In an embodiment, the patient is administered a dose of the anti-STEAP1 antigen binding protein and a dose of abiraterone on cycle 1 day 1. In an embodiment the prostate cancer is chemo-naïve metastatic castration-resistant prostate cancer (mCRPC).

[0015] The present invention also provides a method of treating a patient having prostate cancer, wherein the method comprises administering to the patient a pharmaceutical composition comprising an anti-STEAP1 antigen binding protein at a dose of about 0.1 mg to about 2.0 mg, and further comprising administering to the patient enzalutamide. The present invention provides use of an anti-STEAP1 antigen binding protein for preparation of a medicament for treating prostate cancer, wherein the medicament is formulated for administration at a dose of about 0.001 mg to about 2.0 mg (e.g., about 0.1 mg to about 2.0 mg), and wherein the use further comprises administering to the patient a dose of enzalutamide. In an embodiment, the dose of enzalutamide is about 120 mg to about 160 mg. In an embodiment, the dose of enzalutamide is about 160 mg. In an embodiment, the dose of enzalutamide is 160 mg. In an embodiment, the dose of enzalutamide is administered orally. In an embodiment, the dose of the anti-STEAP1 antigen binding protein is about 0.01 mg to about 2.0 mg. In an embodiment, the dose of the anti-STEAP1 antigen binding protein is about 0.1 mg to about 1.5 mg. In an embodiment, the dose of the anti-STEAP1 antigen binding protein is about 0.75 mg. In an embodiment, the dose of the anti-STEAP1 antigen binding protein is about 1 mg. In an embodiment, the dose of the anti-STEAP1 antigen binding protein is 1.5 mg. In an embodiment, the patient is first administered the anti-STEAP1 antigen binding protein until a target dose of the anti-STEAP1 antigen binding protein is achieved, followed by administering to the patient a dose of enzalutamide. In an

embodiment, the patient is first administered the anti-STEAP1 antigen binding protein until a target dose of the anti-STEAP1 antigen binding protein is achieved, followed by administering to the patient a dose of enzalutamide on the same day as administrating to the patient a dose of the anti-STEAP1 antigen binding protein on cycle 1 day 1. In an embodiment, the prostate cancer is chemo-naïve metastatic castration-resistant prostate cancer (mCRPC).

[0016] The present invention also provides a method of treating a patient having prostate cancer, wherein the method comprises administering to the patient a pharmaceutical composition comprising an anti-STEAP1 antigen binding protein at a dose of about 0.1 mg to about 2.0 mg, and further comprising administering to the patient darolutamide. The present invention provides use of an anti-STEAP1 antigen binding protein for preparation of a medicament for treating prostate cancer, wherein the medicament is formulated for administration at a dose of about 0.001 mg to about 2.0 mg (e.g., about 0.1 mg to about 2.0 mg), and wherein the use further comprises administering to the patient a dose of darolutamide. In an embodiment, the dose of darolutamide is about 450 mg to about 600 mg. In an embodiment, the dose of darolutamide is about 600 mg. In an embodiment, the dose of darolutamide is 600 mg. In an embodiment, the dose of darolutamide is administered orally. In an embodiment, the dose of darolutamide is administered orally, twice daily. In an embodiment, the dose of darolutamide is administered orally, twice daily, by two 300 mg tablets. In an embodiment, the dose of the anti-STEAP1 antigen binding protein is about 0.01 mg to about 2.0 mg. In an embodiment, the dose of the anti-STEAP1 antigen binding protein is about 1.5 mg. In an embodiment, the dose of the anti-STEAP1 antigen binding protein is 1.5 mg.

[0017] The present invention also provides a method of treating a patient having prostate cancer, wherein the method comprises administering to the patient a pharmaceutical composition comprising an anti-STEAP1 antigen binding protein at a dose of about 0.1 mg to about 2.0 mg, and further comprising administering to the patient apalutamide. The present invention provides use of an anti-STEAP1 antigen binding protein for preparation of a medicament for treating prostate cancer, wherein the medicament is formulated for administration at a dose of about 0.001 mg to about 2.0 mg (e.g., about 0.1 mg to about 2.0 mg), and wherein the use further comprises administering to the patient a dose of apalutamide. In an embodiment, the dose of apalutamide is about 180 mg to about 240 mg. In an embodiment, the dose of apalutamide is about 240 mg. In an embodiment, the dose of apalutamide is 240 mg. In an embodiment, the

dose of apalutamide is administered orally. In an embodiment, the dose of apalutamide is administered orally, once daily. In an embodiment, the dose of apalutamide is administered orally, once daily, by four 60 mg tablets. In an embodiment, the dose of the anti-STEAP1 antigen binding protein is about 0.01 mg to about 2.0 mg. In an embodiment, the dose of the anti-STEAP1 antigen binding protein is about 1.5 mg. In an embodiment, the dose of the anti-STEAP1 antigen binding protein is 1.5 mg.

[0018] In an embodiment, the anti-STEAP1 antigen binding protein is administered by step dosing. In an embodiment, the anti-STEAP1 antigen binding protein is administered in two steps. In an embodiment, the anti-STEAP1 antigen binding protein is administered in three steps. In an embodiment, the anti-STEAP1 antigen binding protein is administered on day 1 or day 2 at a dose in the range of 0.1 mg-0.2 mg, day 7, 8, or 9 at a dose in the range of 0.2 mg-0.4 mg, day 14, 15, or 16 at a dose in the range of 0.8 mg-1.2 mg, and day 21, 22, or 23 at a dose in the range of 1.3 mg-1.5 mg. In an embodiment, the anti-STEAP1 antigen binding protein is administered on day 1 at about 0.1 mg, day 8 at about 0.3 mg, day 15 at about 0.75 mg, and day 22 at about 0.75 mg. In an embodiment, the anti-STEAP1 antigen binding protein is administered on day 1 at about 0.1 mg, day 8 at about 0.3 mg, day 15 at about 1.0 mg, and day 22 at about 1.5 mg. In an embodiment, the anti-STEAP1 antigen binding protein is administered on day 1 at 0.1 mg, day 8 at 0.3 mg, day 15 at 0.75 mg, and day 22 at 0.75 mg. In an embodiment, the anti-STEAP1 antigen binding protein is administered on day 1 at 0.1 mg, day 8 at 0.3 mg, day 15 at 1.0 mg, and day 22 at 1.5 mg. In an embodiment, the anti-STEAP1 antigen binding protein is administered on day 1 at 0.1 mg, day 8 at 0.3 mg, day 15 at 0.75 mg, and day 22 at 0.75 mg. In an embodiment, the method further comprises administering to the patient an anti-STEAP1 antigen binding protein once per week, once per two weeks, once per three weeks, or once per four weeks after administration of the step dosing. In an embodiment, the anti-STEAP1 antigen binding protein is administered at 1.5 mg once every two weeks after the step dosing. In an embodiment, the anti-STEAP1 antigen binding protein is administered at 1.5 mg once every three weeks after the step dosing. In an embodiment, the anti-STEAP1 antigen binding protein is administered at 1.5 mg once every four weeks after the step dosing.

[0019] In an embodiment, a dose of anti-STEAP1 antigen binding protein is administered once per week for the first cycle, and then administered once per three weeks once the target dose has been achieved. In an embodiment, a dose of anti-STEAP1 antigen binding protein is

administered once per week for the first cycle, and then administered once per four weeks once the target dose has been achieved.

[0020] In an embodiment, the anti-STEAP1 antigen binding protein is administered in two cycles. In an embodiment, cycle one comprises administering the anti-STEAP1 antigen binding protein on day 1 or day 2 at a dose in the range of about 0.1 mg to about 0.3 mg, day 7, 8, or 9 at a dose in the range of about 0.2 mg to about 0.4 mg, day 14, 15, or 16 at a dose in the range of about 0.8 mg to about 1.2 mg, and day 21, 22, or 23 at a dose in the range of about 1.3 mg to about 1.6 mg. In an embodiment, cycle two, which follows cycle 1, comprises administering the anti-STEAP1 antigen binding protein at 1.5 mg once every two weeks for five months after cycle one is completed. Each cycle is optionally 28 days.

[0021] In an embodiment, cycle one comprises administering the anti-STEAP1 antigen binding protein on day 1 at about 0.1 mg, day 8 at about 0.3 mg, day 15 at about 1.0 mg, and day 22 at about 1.5 mg. In an embodiment, cycle two, which follows cycle 1, comprises administering the anti-STEAP1 antigen binding protein at about 1.5 mg once every two weeks for five months after cycle one is completed. Each cycle is optionally 28 days.

[0022] In an embodiment, cycle one comprises administering the anti-STEAP1 antigen binding protein on day 1 at about 0.1 mg, day 8 at about 0.3 mg, day 15 at about 1.0 mg, and day 22 at about 1.5 mg. In an embodiment, cycle two comprises administering the anti-STEAP1 antigen binding protein at about 1.5 mg once every four weeks for 11 months after cycle one is completed. Each cycle is optionally 28 days.

[0023] In an embodiment, cycle one comprises administering the anti-STEAP1 antigen binding protein on day 1 at 0.1 mg, day 8 at 0.3 mg, day 15 at 1.0 mg, and day 22 at 1.5 mg. In an embodiment, cycle two, which follows cycle one, comprises administering the anti-STEAP1 antigen binding protein at 1.5 mg once every two weeks for five months after cycle one is completed. Each cycle is optionally 28 days.

[0024] In an embodiment, cycle one comprises administering the anti-STEAP1 antigen binding protein on day 1 at 0.1 mg, day 8 at 0.3 mg, day 15 at 1.0 mg, and day 22 at 1.5 mg. In an embodiment, cycle two comprises administering the anti-STEAP1 antigen binding protein at 1.5 mg once every four weeks for 11 months after cycle one is completed. Each cycle is optionally 28 days.

[0025] The disclosure further provides a method of treating a patient having prostate cancer, comprising administering to the patient a pharmaceutical composition comprising xaluritamig over the course of at least two 28 day cycles, wherein (i) Cycle 1 comprises administering about 0.1 mg to about 0.3 mg of xaluritamig on day 1 or day 2, administering about 0.2 mg to about 0.4 mg of xaluritamig on day 7, 8, or 9, administering about 0.8 mg to about 1.2 mg of xaluritamig on day 14, 15, or 16 and administering about 1.3 mg to about 1.6 mg of xaluritamig on day 21, 22, or 23 followed by one or more additional cycles (Cycle 2) comprising administering 1.5 mg of xaluritamig once per two weeks.

[0026] In an embodiment, the anti-STEAP1 antigen binding protein is an XmAb® 2+1 molecule. As used herein, an "XmAb® 2+1" molecule (used interchangeably with a "multichain T cell engager molecule" or "central-scFv" molecule) contains two Fab domains and one scFv domain, wherein each Fab domain binds a target (e.g., STEAP1) and the scFv domain binds another target (e.g., CD3).

[0027] In an embodiment, the anti-STEAP1 antigen binding protein comprises two Fab binding domains, wherein each Fab binding domain binds STEAP1.

[0028] In an embodiment, the anti-STEAP1 antigen binding protein comprises two Fab binding domains, wherein each Fab binding domain binds STEAP1, and wherein each Fab binding domain comprises a variable heavy domain, a variable light domain, a CH1 domain, and a constant light domain, wherein the variable heavy domain comprises HCDR1 comprising SEQ ID NO: 9, HCDR2 comprising SEQ ID NO: 10, and HCDR3 comprising SEQ ID NO: 11; and the variable light domain comprises LCDR1 comprising SEQ ID NO: 12, LCDR2 comprising SEQ ID NO: 13, and LCDR3 comprising SEQ ID NO: 14.

[0029] In an embodiment, the anti-STEAP1 antigen binding protein comprises an scFv binding domain, wherein the scFv binding domain binds CD3.

[0030] In an embodiment, the anti-STEAP1 antigen binding protein comprises an scFv binding domain, wherein the scFv binding domain binds CD3, and wherein the scFv variable heavy domain comprises HCDR1 comprising SEQ ID NO: 1, HCDR2 comprising SEQ ID NO: 2, and HCDR3 comprising SEQ ID NO: 3; an scFv linker; and an scFv variable light domain, wherein the scFv variable light domain comprises LCDR1 comprising SEQ ID NO: 4, LCDR2 comprising SEQ ID NO:5, and LCDR3 comprising SEQ ID NO: 6. In an embodiment, each Fab variable heavy domain comprises an amino acid sequence at least 90% identical to SEQ ID NO:

15; each Fab variable light domain comprises an amino acid sequence at least 90% identical to SEQ ID NO: 16; the scFv variable heavy domain comprises an amino acid sequence at least 90% identical to SEQ ID NO:7; and the scFv variable light domain comprises an amino acid sequence at least 90% identical to SEQ ID NO: 8. In an embodiment, each Fab variable heavy domain comprises SEQ ID NO: 15 or 20; each Fab variable light domain comprises SEQ ID NO: 16; the scFv variable heavy domain comprises SEQ ID NO:7; and the scFv variable light domain comprises SEQ ID NO: 8. In an embodiment, the scFv binding domain which binds CD3 comprises an scFv linker. In an embodiment, each Fab variable heavy domain comprises SEQ ID NO: 15. In an embodiment, each Fab variable heavy domain comprises SEQ ID NO: 20.

[0031] In an embodiment, the anti-STEAP1 antigen binding protein comprises a first Fc domain and a second Fc domain. In an embodiment, the first Fc domain comprises amino acid substitutions E233P, L235V, G236A, S267K, R292C, N297G, V302C, E357Q, and S364K; and the second Fc domain comprises amino acid substitutions N208D, E233P, L235V, G236A, S267K, R292C, Q295E, N297G, V302C, L368D, K370S, N384D, Q418E, and N421D (EU numbering). In an embodiment, the first Fc domain and the second Fc domain each comprise a deletion at position 234.

[0032] In an embodiment, the anti-STEAP1 antigen binding protein comprises a HC (heavy chain) comprising SEQ ID NO: 17, a HC with inserted CD3 scFv comprising SEQ ID NO: 19, and two light chains, each comprising SEQ ID NO: 18. In an embodiment, the anti-STEAP1 antigen binding protein comprises a HC comprising SEQ ID NO: 23, a HC with inserted CD3 scFv comprising SEQ ID NO: 26, and two light chains, each comprising SEQ ID NO: 18. In an embodiment, the anti-STEAP1 antigen binding protein is an XmAb® 2+1 molecule.

[0033] In an embodiment, the anti-STEAP1 antigen binding protein is xaluritamig.

[0034] In an embodiment, the patient has metastatic castration-resistant prostate cancer. In an embodiment, the patient has not previously been treated with chemotherapy. In an embodiment, the patient has previously undergone treatment for prostate cancer, and the patient is suffering from recurrent prostate cancer. In an embodiment, the patient has previously been treated with chemotherapy.

BRIEF DESCRIPTION OF THE DRAWINGS

[0035] **FIG. 1.** Schematic of an XmAb® 2+1 molecule, depicting two Fabs that each bind STEAP1 and an scFv that binds CD3.

[0036] **FIG. 2.** Best percentage change in size of tumor target lesions. Dashed line indicates 30% reduction in tumor SLD from baseline.

[0037] **FIG. 3.** Best PSA percentage change from baseline. Asterisk indicates confirmed PSA responders and dashed lines indicate PSA50 and PSA90 declines.

[0038] **FIG. 4.** Example patient showing response by PSA and radiographic assessments: CT scan and PSA curve over time of a heavily pretreated 65-year old patient with stage IV prostate adenocarcinoma. Patient was enrolled into Cohort 12 (3-step 1.5 mg target dose of xaluritamig). CT scans showed 3 target lesions (2 liver, 1 lymph node) and multiple non-target lesions in the liver as well as 2 lymph nodes during screening. Patient achieved 99% PSA decline from baseline on cycle 1 day 1, and PR (37.3% reduction of target lesions) after 2 cycles which was confirmed at 16 weeks and maintained after 24 weeks. AEs occurred during the first cycle of treatment and included recurrent CRS, tinea grade (both grade 1), rash, and worsening of back pain (both grade 2). During further treatment cycles, rash (grade 1), myalgia, and hyperkalemia (both grade 2) were reported. Patient remains on treatment at the time of this filing.

[0039] **FIG. 5.** Percent change in PSA taken from the patient described in FIG. 4.

DETAILED DESCRIPTION

[0040] Xaluritamig is an XmAb® 2+1 T cell engager (TCE) molecule that is designed to direct T effector cells towards STEAP1 expressing cells. The first in human study of xaluritamig in patients with metastatic castrate resistant prostate cancer (mCRPC) was designed to assess xaluritamig safety, tolerability, pharmacokinetics (PK), and anti-tumor activity, when administered either intravenously or subcutaneously, as monotherapy or in combination with other therapies.

[0041] This first-in-human study reports monotherapy for patients with metastatic castration-resistant prostate cancer (mCRPC). Ninety-seven patients received ≥1 dose ranging from 0.001–2.0 mg IV weekly (QW) or Q2W. The MTD was identified as day 1 (D1) 0.1 mg, D8 0.3 mg, D15 1.0 mg, and D22+ 1.5 mg IV QW. The most common treatment-related adverse

events were cytokine release syndrome (CRS; 72%), fatigue (45%) and myalgia (34%). CRS occurred primarily during cycle 1 and improved with premedication and step-dosing. Prostate specific antigen (PSA) and RECIST responses across cohorts were encouraging (49% PSA50; 24% objective response rate [ORR]) with greater frequency at target doses ≥0.75 mg (59% PSA50; 41% ORR). There were no grade 4 or 5 CRS events. Overall, all CRS events resolved with standard management, using acetaminophen, IV fluids together with tocilizumab and/or corticosteroids. Xaluritamig demonstrated encouraging responses (PSA and RECIST) compared with established treatments and manageable safety for late-line patients with mCRPC.

[0042] The preliminary efficacy results observed with xaluritamig are numerically higher than those reported for other TCEs in prostate cancer. Efficacy as measured both by PSA and objective response by RECIST (Response Evaluation Criteria in Solid Tumors) were encouraging in this heavily pretreated mCRPC population, and responses occurred with greater frequency in the higher-dose cohorts. PSA declines were seen starting with 0.1 mg xaluritamig, with 49% of patients achieving confirmed PSA50 responses and 28% of patients PSA90 responses. At higher doses, response in RECIST evaluable patients were achieved in 41% of patients. This trial has shown that a high proportion of patients may achieve significant clinical responses which may translate into overall clinical benefit.

[0043] This is the first clinical report of a TCE therapy targeting STEAP1 in prostate cancer. This study provides proof-of-concept for TCEs as a potential therapeutic modality for prostate cancer as supported by the substantial number of radiographic and PSA responses that were observed. The only STEAP1-targeted agent explored in the clinic to date has been a STEAP1-antibody–drug conjugate (ADC) that was limited by toxicities due to the monomethyl auristatin E (MMAE) payload (Maecker et al., MAbs. 2023 Jan-Dec;15(1):2229101).). In summary, the current study demonstrates the feasibility of targeting STEAP1 with TCEs and the potential of xaluritamig as a novel treatment paradigm for patients with mCRPC.

[0044] Targeted immunotherapy with TCEs requires binding to both CD3+ T cells and a tumor-associated antigen. Xaluritamig demonstrated dose-dependent changes in peripheral pharmacodynamic biomarkers of TCE activity, namely T cell margination, T cell activation and cytokine induction. The magnitude of the PD biomarker changes is consistent with the observed PSA declines.

[0045] The overall treatment emergent ADA incidence was 54%, with 8 patients demonstrating a transient antibody response. The ADA response was not dose-dependent and did not result in AEs. With approximately one quarter of patients developing neutralizing and/or PK impacting ADAs, the impact on clinical responses is critical to be assessed. With the onset of neutralizing ADAs being on average after cycle 3, versus responses occurring in the first 2 cycles; an impact on overall response rate is not expected.

[0046] A dosing regimen for an anti-STEAP1 antigen binding protein such as xaluritamig in prostate cancer patients optionally includes step dosing. To help mitigate cytokine release and to achieve treatment with the active dose of an anti-STEAP1 antigen binding protein (e.g., xaluritamig) safely, the step dosing may include two or three steps, each step being a relatively smaller dose increase. The priming dose (initial dose) and target dose are also within a relatively narrow range of one another, while demonstrating efficacy in prostate cancer patients. The doses of the anti-STEAP1 antigen binding protein (xaluritamig) are also relatively low compared to the doses administered in a clinical trial for a bispecific T-cell engager that binds both DLL3 and CD3. Ares et al., J. Clin. Oncol. 2023 Jun 1;41(16):2893-2903 describes that pharmacodynamic responses were greatest after initial administration of 1-mg step dose of a bispecific T-cell engager that binds both DLL3 and CD3, and that the expansion dose was 100 mg (Aggarwal et al., J. Clin. Oncol., 42, Abstract 5012, 2024).

[0047] In prostate cancer, several PSMA-targeted TCEs have entered the clinic but have seen limited success due to minimal efficacy, toxicity, and short duration of response (DOR) (*see* e.g. Sorrentino et al., Cancers (Basel) 2023; 15; Powers et al., J. Hematol Oncol 2020; 13:144; and Tucker et al., Cancer Med 2019;8:4644-55). For example, JNJ-63898081, a PSMA and CD3 bispecific antibody, led to transient declines in prostate specific antigen (PSA) with 2 out of 39 (5%) patients experiencing a confirmed PSA50 response and no radiographic responses in a phase 1 study of patients with mCRPC (Lim et al., Clin Genitourin Cancer 2023;21:366-75). PSMA-targeting TCE HPN424 reported 3 of 63 (5%) patients experiencing a PSA50 response and 1 of 34 (3%) experiencing a confirmed Response Evaluation Criteria in Solid Tumors (RECIST) response with manageable safety (Bono et al., J. Clin. Onc. 2021;39:5013-13).

[0048] The disclosure provides a method wherein an anti-STEAP1 antigen binding protein is administered according to a method of the present disclosure. The present disclosure also provides an anti-STEAP1 antigen binding protein, for use in the treatment of prostate

cancer, wherein the anti-STEAP1 antigen binding protein is formulated for administration according to a method of the present disclosure. In an embodiment, the anti-STEAP1 antigen binding protein is xaluritamig.

[0049] The present disclosure also provides an anti-STEAP1 antigen binding protein for use in the treatment of prostate cancer, wherein the anti-STEAP1 antigen binding protein is formulated for administration at a dose of about 0.1 mg to about 2.0 mg. In an embodiment, the anti-STEAP1 antigen binding protein is xaluritamig.

[0050] The present disclosure also provides an anti-STEAP1 antigen binding protein for use in the treatment of prostate cancer, wherein the anti-STEAP1 antigen binding protein is administered at a dose of about 0.1 mg to about 2.0 mg. In an embodiment, the anti-STEAP1 antigen binding protein is xaluritamig.

[0051] The present disclosure also provides use of an anti-STEAP1 antigen binding protein in the manufacture of a medicament for treating prostate cancer, wherein the medicament is formulated for administration at a dose of about 0.1 mg to about 2.0 mg. A dose of anti-STEAP1 antigen binding protein is about 0.001 mg to about 2 mg, about 0.1 mg to about 1.5 mg, about 0.1 mg to about 2 mg, or about 0.1 mg to about 1.5 mg. In an embodiment, the dose is 0.1 mg, 0.2 mg, 0.3 mg, 0.4 mg, 0.5 mg, 0.6 mg, 0.7 mg, 0.75, 0.8 mg, 0.9 mg, 1.0 mg, 1.1 mg, 1.2 mg, 1.3 mg, 1.4 mg, 1.5 mg, 1.6 mg, or 1.7 mg. In an embodiment, the dose is about 0.1 mg. In an embodiment, the dose is about 0.3 mg. In an embodiment, the dose is about 0.75 mg. In an embodiment, the dose is about 1 mg. In an embodiment, the dose is about 1.5 mg. In an embodiment, the dose is 0.1 mg. In an embodiment, the dose is 0.3 mg. In an embodiment, the dose is 0.75 mg. In an embodiment, the dose is 1 mg. In an embodiment, the dose is 1.5 mg. In an embodiment, the dose is administered once per one week. In an embodiment, the dose is administered once per two weeks. In an embodiment, the dose is administered once per three weeks. In an embodiment, the dose is administered once per four weeks. In an embodiment, the dose is administered by intravenous administration. In an embodiment, the dose is administered once per week beginning in cycle 1. In an embodiment, the dose is administered once per week beginning in cycle 2. In an embodiment, the dose is administered once per two weeks beginning in cycle 2. In an embodiment, the dose is administered once per three weeks beginning in cycle 2. In an embodiment, the dose is administered once per four weeks beginning in cycle 2. In an embodiment, the dose is administered once per week for the first cycle, and then administered

once per two weeks beginning on day one of cycle 2. In an embodiment, the dose is administered once per week for the first cycle, and then administered once per two weeks once the target dose has been achieved, and then administered once per four weeks once the target dose has been achieved. In an embodiment, the anti-STEAP1 antigen binding protein is xaluritamig.

[0052] In an embodiment, the dose is administered once per week for the first cycle, and then administered once per four weeks once the target dose has been achieved. In some embodiments, cycle two is repeated 11 times after cycle 1 has been completed (e.g., for a total treatment period of about 12 months). In some embodiments, cycle 2 is repeated five times after cycle 1 is completed (e.g., for a total treatment period of about six months).

[0053] Combination therapy may further improve efficacy by inducing synergistic effects and/or overcoming mechanisms of resistance. The disclosure contemplates use of xaluritamig in combination with standard of care hormonal and radioligand therapies in patients. In some embodiments, the patient has advanced prostate cancer. In some embodiments, the patient has received prior treatment with 0 or 1 novel hormonal therapy (NHT).

[0054] While NHTs (e.g., abiraterone, enzalutamide, apalutamide, and darolutamide) and taxanes (e.g., docetaxel and cabazitaxel) are standard of care agents for non-metastatic and/or metastatic, castration-resistant prostate cancer, the majority of patients will progress on therapy.

[0055] The disclosure provides a therapeutic regimen wherein an anti-STEAP1 antigen binding protein, such as xaluritamig, is administered according to a method of the present invention, in combination with another agent(s) including abiraterone, enzalutamide, cabazitaxel, darolutamide, apalutamide, PSMA radioligand therapies, PSMA immunotherapies, radium 223, PARP inhibitors, PSMA antibody drug conjugates, B7H3 antibody drug conjugates, radiotherapy and/or standard of care therapies for prostate cancer.

[0056] Abiraterone is a cytochrome P450 (CYP) 17 inhibitor indicated in combination with prednisone (or prednisolone in some regions) for the treatment of patients with mCRPC and, in some regions, metastatic or high risk castration sensitive prostate cancer (CSPC). Disease relapse following abiraterone may result from increased androgen receptor expression (e.g., androgen receptor amplification), among other mechanisms (Galletti et al, Cancer Treat Rev. 2017 Jun;57:16-27).

[0057] Enzalutamide is an androgen receptor inhibitor that acts on different steps in the androgen receptor signaling pathway. Enzalutamide has been shown to competitively inhibit

androgen binding to androgen receptors; and consequently, inhibits nuclear translocation of androgen receptors and their interaction with DNA. Enzalutamide is indicated for the treatment of patients with CRPC and, in some regions, metastatic hormone sensitive prostate cancer. Disease relapse following enzalutamide is due in part to mutations in androgen receptor (like AR V7) and increased androgen receptor expression (e.g., androgen receptor amplification), among other mechanisms (Galletti et al, *supra*).

[0058] However, it is also envisioned that in earlier disease settings xaluritamig may be administered without concurrent ADT. An anti-STEAP1 antigen binding protein (or a STEAP1 antigen binding protein) is a molecule that binds human STEAP1. Such molecule may further bind another target, such as a cell surface antigen such as CD3. Non-limiting examples of formats for such molecules include antibodies (including bispecific antibodies) and fragments thereof and T cell engager molecules including molecules in the XmAb® 2+1 format and bispecific T-cell engager molecules.

[0059] An example of an anti-STEAP1 antigen binding protein is xaluritamig. Xaluritamig is also known as AMG 509. A further description of xaluritamig can be found in International Patent Publication No. WO 2020/010079, which is herein incorporated by reference in its entirety. Xaluritamig sequences are provided in Table 4.

[0060] An anti-STEAP1 antigen binding protein binds to its target(s) when, for example, it binds with a dissociation constant (KD) of $\leq 10^{-7}$ M as measured via a surface plasma resonance technique (e.g., BIACore, GE-Healthcare Uppsala, Sweden) or Kinetic Exclusion Assay (KinExA, Sapidyne, Boise, Idaho).

[0061] Bispecific T-cell engager molecules are recombinant protein constructs made from two flexibly linked antibody derived binding domains. A "bispecific T-cell engager molecule" includes a "BiTE® molecule". One binding domain of bispecific T-cell engager is specific for a selected tumor-associated surface antigen on target cells; the second binding domain is specific for CD3, a subunit of the T cell receptor complex on T cells. By their particular design, bispecific T-cell engager molecules are uniquely suited to transiently connect T cells with target cells and, at the same time, potently activate the inherent cytolytic potential of T cells against target cells (Yang, Fa; Wen, Weihong; Qin, Weijun (2016). "Bispecific Antibodies as a Development Platform for New Concepts and Treatment Strategies". International Journal of Molecular Sciences. 18 (1): 48 (2016)). A bispecific T-cell engager

molecule is bispecific, meaning that it binds two targets on two different types of cells (target antigen such as STEAP1 on a target cell and CD3 on a T cell) at the same time.

[0062] As used herein, an "XmAb® 2+1" molecule (used interchangeably with a "multichain T cell engager molecule" or "central-scFv" molecule) contains two Fab domains and one scFv domain, wherein each Fab domain binds a target (e.g., STEAP1) and the scFv domain binds another target (e.g., CD3). An XmAb® 2+1 molecule format is shown in Figure 1. The scFv domain (e.g., that binds CD3) is inserted between an Fc domain and a CHl-Fv region, thus providing a third antigen binding domain (e.g., two Fabs, each that bind STEAP1, and one scFv that binds CD3). The anti-CD3 scFv is "inserted" in the HC, meaning the scFv is connected by a linker in the HC. In this embodiment, one polypeptide comprises a first heavy chain comprising a first variable heavy domain, a CH1 domain (and optional linker/hinge) and Fc domain, with a scFv comprising a scFv variable light domain, an scFv linker and a scFv variable heavy domain. The scFv is covalently attached between the C-terminus of the CH1 domain of the heavy constant domain and the N-terminus of a first Fc domain using optional domain linkers (VH1-CH1- [optional domain linker] -VH2-scFv linker- VL2 - [optional domain linker including the hinge] -CH2-CH3, or the opposite orientation for the scFv, VH1 -CH1 -[optional domain linker] -VL2-scFv linker- VH2- [optional domain linker including the hinge] -CH2- CH3). In some embodiments, the first polypeptide is VH1- CH1 -domain linker- VH2-scFv linker- VL2-domain linker-CH2-CH3. The other polypeptide is a standard Fab (i.e., VH1-CH1-domain linker (e.g., hinge)-CH2-CH3). This embodiment further utilizes two light chains each comprising a variable light domain and a constant light domain, which associate with the heavy chains to form two identical Fabs that bind a target. In particular embodiments, a STEAP1 Fab CD3 scFv central-scFv molecule (or a STEAP1 Fab CD3 scFv XmAb® 2+1 molecule) comprises two Fab domains, each that bind STEAP1 Fab, and an scFv that binds CD3 scFv. In some particular embodiments, the central-scFv or XmAb® 2+1 molecule is xaluritamig.

[0063] In various aspects of the disclosure, the anti-STEAP1 antigen binding protein comprises two Fab binding domains, wherein each Fab binding domain binds STEAP1, and wherein each Fab binding domain comprises a variable heavy domain, a variable light domain, a CH1 domain, and a constant light domain, wherein the variable heavy domain comprises HCDR1 comprising SEQ ID NO: 9, HCDR2 comprising SEQ ID NO: 10, and HCDR3 comprising SEQ ID NO: 11; and the variable light domain comprises LCDR1 comprising SEQ

ID NO: 12, LCDR2 comprising SEQ ID NO: 13, and LCDR3 comprising SEQ ID NO: 14. The anti-STEAP1 antigen binding protein further comprises an scFv binding domain which binds CD3 and comprises an scFv variable heavy domain comprising HCDR1 comprising SEQ ID NO: 1, HCDR2 comprising SEQ ID NO: 2, and HCDR3 comprising SEQ ID NO: 3; an scFv linker; and an scFv variable light domain comprising LCDR1 comprising SEQ ID NO: 4, LCDR2 comprising SEQ ID NO:5, and LCDR3 comprising SEQ ID NO: 6. In various aspects, each Fab variable heavy domain comprises an amino acid sequence at least 90% identical to SEQ ID NO: 15 or 20; each Fab variable light domain comprises an amino acid sequence at least 90% identical to SEQ ID NO: 16; the scFv variable heavy domain comprises an amino acid sequence at least 90% identical to SEQ ID NO:7; and the scFv variable light domain comprises an amino acid sequence at least 90% identical to SEQ ID NO: 8. For instance, each Fab variable heavy domain may comprise SEQ ID NO: 15 or 20; each Fab variable light domain may comprise SEQ ID NO: 16; the scFv variable heavy domain may comprise SEQ ID NO:7; and the scFv variable light domain may comprise SEQ ID NO: 8. The anti-STEAP1 antigen binding protein may further comprise a first Fc domain and a second Fc domain. In various aspects, the anti-STEAP1 antigen binding protein comprises a heavy chain (HCP comprising SEQ ID NO: 17 or 23, a HC with inserted CD3 scFv comprising SEQ ID NO: 19 or 26, and two light chains (LC), each comprising SEQ ID NO: 18.

[0064] For all positions discussed in the disclosure that relate to antibodies and other antigen-binding proteins, unless otherwise noted, amino acid position numbering is according to the EU index. The EU index or EU index as in Kabat or EU numbering scheme refers to the numbering of the EU antibody (Edelman et al., 1969, Proc Natl Acad Sci USA 63:78-85, hereby entirely incorporated by reference).

[0065] An example of an anti-STEAP1 antigen binding protein is xaluritamig. Xaluritamig sequences are provided in Table 4. Xaluritamig comprises a HC comprising SEQ ID NO: 17, a HC with inserted CD3 scFv comprising SEQ ID NO: 19, and two light chains, each comprising SEQ ID NO: 18. In exemplary aspects, a molecule of the present invention comprises a sequence comprising a C-terminal lysine, as in SEQ ID NOs: 17 or 19. In alternative aspects, the antigen binding protein comprises one or both HC without the C-terminal lysine, as in SEQ ID NOs: 22 and 25. In addition, the HC or HCVR N-terminal glutamine and/or the N-terminal glutamic acid may be converted to pyroglutamic acid, as in SEQ ID NOs: 20, 21, 23, and 24. In

addition, the HC N-terminal glutamine and/or the N-terminal glutamic acid may be converted to pyroglutamic acid, and the sequence may lack a C-terminal lysine, as in SEQ ID NOs: 23 and 26. All forms are envisioned for the antigen binding proteins of the present invention.

[0066] A first Fc domain and a second Fc domain each refer to one half of an Fc (fragment crystallizable) region. An Fc region comprises two CH2 domains and two CH3 domains. Therefore, a first Fc domain and a second Fc domain each comprise a CH2 domain and a CH3 domain.

[0067] The anti-STEAP1 antigen binding protein is generally administered to the patient in a pharmaceutical composition, which can include pharmaceutically-acceptable carriers, excipients, or diluents. "Pharmaceutically-acceptable" refers to molecules, compounds, and compositions that are non-toxic to human recipients at the dosages and concentrations employed and/or do not produce allergic or adverse reactions when administered to humans. In certain embodiments, the pharmaceutical composition may contain formulation materials for modifying, maintaining or preserving, for example, the pH, osmolarity, viscosity, clarity, color, isotonicity, odor, sterility, stability, rate of dissolution or release, adsorption or penetration of the composition. In such embodiments, suitable formulation materials include, but are not limited to, amino acids (such as glycine, glutamine, asparagine, arginine or lysine); antimicrobials; antioxidants (such as ascorbic acid, sodium sulfite or sodium hydrogen-sulfite); buffers (such as borate, bicarbonate, Tris-HCl, citrates, phosphates or other organic acids); bulking agents (such as mannitol or glycine); chelating agents (such as ethylenediamine tetraacetic acid (EDTA)); complexing agents (such as caffeine, polyvinylpyrrolidone, beta-cyclodextrin or hydroxypropyl-betacyclodextrin); fillers; monosaccharides; disaccharides; and other carbohydrates (such as glucose, mannose or dextrins); proteins (such as serum albumin, gelatin or immunoglobulins); coloring, flavoring and diluting agents; emulsifying agents; hydrophilic polymers (such as polyvinylpyrrolidone); low molecular weight polypeptides; salt-forming counterions (such as sodium); preservatives (such as benzalkonium chloride, benzoic acid, salicylic acid, thimerosal, phenethyl alcohol, methylparaben, propylparaben, chlorhexidine, sorbic acid or hydrogen peroxide); solvents (such as glycerin, propylene glycol or polyethylene glycol); sugar alcohols (such as mannitol or sorbitol); suspending agents; surfactants or wetting agents (such as pluronics, PEG, sorbitan esters, polysorbates such as polysorbate 20, polysorbate 80, triton, tromethamine, lecithin, cholesterol, tyloxapal); stability enhancing agents (such as sucrose or

sorbitol); tonicity enhancing agents (such as alkali metal halides, preferably sodium or potassium chloride, mannitol, or sorbitol); delivery vehicles; diluents; excipients and/or pharmaceutical adjuvants. Methods and suitable materials for formulating molecules for therapeutic use are known in the pharmaceutical arts, and are described, for example, in REMINGTON'S PHARMACEUTICAL SCIENCES, 18th Edition, (A.R. Genrmo, ed.), 1990, Mack Publishing Company. In some embodiments, the selection of carriers and excipients for incorporation into the pharmaceutical compositions influences the physical state, stability, rate of in vivo release and rate of in vivo clearance of the anti-STEAP1 antigen binding protein.

[0068] An anti-STEAP1 antigen binding protein, such as xaluritamig, may be formulated as a pre-lyophilized formulation, such as a pre-lyophilized formulation of 0.3 mg/mL to 2.5 mg/mL xaluritamig (e.g., 1 mg/mL) formulated with 10 mM glutamic acid, 9% (w/v) sucrose, 0.01% (w/v) polysorbate 80, pH 4.20 (i.e., xaluritamig is present in a formulation comprising 0.3 mg/mL to 2.5 mg/mL xaluritamig (e.g., 1 mg/mL), 10 mM glutamic acid, 9% (w/v) sucrose, 0.01% (w/v) polysorbate 80, pH 4.20, which is lyophilized). Formulations for an anti-STEAP1 antigen binding protein are also disclosed in PCT Publication No. WO 2019/157340, which is herein incorporated by reference in its entirety.

[0069] The present invention also includes kits for treating prostate cancer in a patient in need thereof. In one embodiment, the kit comprises a pharmaceutical composition of an anti-STEAP1 antigen binding protein and packaging material that provides instructions regarding the use of the pharmaceutical compositions. The pharmaceutical composition of the kit may be present in a container, such as a vial or syringe. The pharmaceutical composition may be provided as a solution, suspension, gel, emulsion, solid, crystal, or as a dehydrated or lyophilized powder. In embodiments in which the pharmaceutical composition is provided as a powder, the kit may also comprise diluents (e.g., water, saline, or phosphate-buffer saline) necessary to reconstitute the pharmaceutical composition as well as instructions for preparing the composition for administration.

[0070] It is intended to be understood that when it referred to herein that a patient is administered a dose of an anti-STEAP1 antigen binding protein that the anti-STEAP1 antigen binding protein is in a pharmaceutical composition.

[0071] In some embodiments, the present invention also provides kits comprising a pharmaceutical composition and instructions for using the pharmaceutical composition for

delivering a therapeutically effective dose, for example, by IV injection for treating prostate cancer in a patient in need thereof. In embodiments in which the pharmaceutical composition is provided in a lyophilized or dry powder form, the kit may comprise a diluent and instructions for reconstituting the pharmaceutical composition prior to administration.

[0072] An anti-STEAP1 antigen binding protein may be administered by means of "step dosing," which refers to increasing the dose administered to a patient before reaching the target dose level (see also e.g., Ball et al., MAbs. 2023 Jan-Dec;15(1):2181016). Step dosing may include one, two, three, four, or five steps (i.e., administration of multiple doses increasing in the amount of therapeutic administered). Each "step" is an increase in the dose administered to the patient from the last dose administered to the patient. Step dosing may include two or three steps. Step dosing may include two steps to reach a target dose of 0.75 mg. Step dosing may include three steps to reach a target dose of 1.5 mg. Step dosing may be implemented to reduce the incidence of cytokine release syndrome. For example, step dosing might begin with a priming dose on cycle 1 day 1 and escalating on day 8 (one step) and continuing at the target dose thereafter. At the conclusion of step dosing, the target dose may be administered (e.g., once per week, once per two weeks, once per three weeks, or once per four weeks). The target dose may be administered at any interval over a desired period of time (e.g., four weeks, five months, or eleven months), providing an overall treatment period of, e.g., two months, six months, or twelve months.

[0073] The anti-STEAP1 antigen binding protein (e.g., xaluritamig) may be first administered by step dosing and then reach the target dose of anti-STEAP1 antigen binding protein (e.g., xaluritamig). Subsequent to reaching the target dose of xaluritamig, a patient may be treated with another therapeutic agent (i.e., combination partner), although the disclosure also contemplates administration of another therapeutic agent prior to reaching the target dose (e.g., administration on C1 D1). Such another therapeutic agent may be administered in a cycle with xaluritamig.

[0074] A "cycle" refers to the repeating pattern of treatment and may be defined by anti-STEAP1 antigen binding protein (e.g., xaluritamig) or a combination partner. A cycle may also provide the basis for follow-up of patients. A cycle may still be present even when a drug is given continuously. A cycle can include a different number of days depending on the treatment. A cycle refers to a period of time in which the actions that need to be taken can be repeated. It is

a standard way of defining treatment duration with defined moments of treatment administration. For example, the anti-STEAP1 antigen binding protein (xaluritamig) cycle may be every 27 days, 28 days, 29 days, 30 days or 31 days.

[0075] The disclosure provides, in various aspects, a method wherein the anti-STEAP1 antigen binding protein (e.g., xaluritamig) is administered to a patient in need thereof over a course of treatment that comprises two or more cycles, each cycle optionally comprising 28 days. Cycle 1 comprises a three-step dosing schedule, wherein the patient is administered a dose of 0.1 mg xaluritamig on day 1 (C1 D1), 0.3 mg xaluritamig on day 8 (C1 D8), 1 mg xaluritamig on day 15 (C1 D15), and 1.5 mg xaluritamig on day 22 (C1 D22). In this scenario, 1.5 mg of xaluritamig is the "target dose." Following cycle 1, one or more additional treatment cycles are performed (i.e., cycle 2, cycle 3, etc.) for a desired period of time. In various aspects, cycles 2 and beyond (i.e., each cycle following cycle 1) comprise administration of 1.5 mg of xaluritamig once every two weeks; for instance, 1.5 mg of xaluritamig is administered on C2 D1 and 1.5 mg of xaluritamig is administered on C2 D15. In alternative aspects, cycle 2 may comprise administering xaluritamig once every three weeks (e.g., 1.5 mg of xaluritamig administered Q3W) or administering xaluritamig once every four weeks (e.g., 1.5 mg of xaluritamig administered Q4W). Cycle 2 may be repeated one or more times. For instance, cycle 2 may be repeated five times, providing treatment to the patient over the course of six months. Alternatively, cycle 2 may be repeated 11 times, providing treatment to the patient over the course of 12 months. In various aspects, the patient is orally administered 1000 mg abiraterone once daily and administered prednisone at a dose of 5 mg twice daily or 10 mg once daily. In various aspects, the patient is orally administered 500 mg abiraterone once daily and administered prednisone at a dose of 4 mg twice daily. In various aspects, the patient is orally administered 160 mg enzalutamide once daily.

[0076] The phrase "with a dose" refers to a dose of a molecule (drug) that can be administered to a patient at the same time (on the same day) as another, different molecule, or administered sequentially (e.g., at least one dose of a molecule administered to a patient is separated in time from at least one dose of another molecule administered to the patient). It is also contemplated herein that a dose of a molecule may be followed by at least one additional dose of the same molecule, followed by at least one dose of a different molecule.

[0077] Generally, intravenous (IV) medications may be administered together on the same day. Administration of oral medication and IV medication may also be administered on the same day. For example, xaluritamig and abiraterone may be administered together on the same day. Medications may also be administered on separate days.

[0078] As used interchangeably herein, "treatment" and/or "treating" and/or "treat" are intended to refer to all processes wherein there may be a slowing, interrupting, arresting, controlling, stopping, or reversing of the progression of the disorders described herein, but does not necessarily indicate a total elimination of all disorder symptoms. Treatment includes administration of an anti-STEAP1 antigen binding protein for treatment of a disease or condition in a human that would benefit from activity of an anti-STEAP1 antigen binding protein, such as prostate cancer, and includes: (a) inhibiting further progression of the disease; and/or (b) relieving the disease, i.e., causing regression of the disease or disorder or alleviating symptoms or complications thereof.

[0079] The present disclosure also provides an anti-STEAP1 antigen binding protein for use in reducing the size of the patient's prostate tumor. In an embodiment, the tumor is reduced by 10%. In an embodiment, the tumor is reduced by 20%. In an embodiment, the tumor is reduced by 30%. In an embodiment, the tumor is reduced by 40%. In an embodiment, the tumor is reduced by 50%. In an embodiment, the tumor is reduced by 60%. In an embodiment, the tumor is reduced by 70%. In an embodiment, the tumor is reduced by 80%. In an embodiment, the tumor is reduced by 90%. In an embodiment, the tumor is no longer present.

[0080] The present disclosure also provides an anti-STEAP1 antigen binding protein for use in reducing a patient's PSA. The present disclosure contemplates an anti-STEAP1 antigen binding protein for use in slowing or stopping the spread of cancer cells to another part(s) of the patient's body.

[0081] The present disclosure contemplates a method of the present invention used to reduce the size of the patient's prostate tumor. In an embodiment, the tumor is reduced by 10%. In an embodiment, the tumor is reduced by 20%. In an embodiment, the tumor is reduced by 30%. In an embodiment, the tumor is reduced by 40%. In an embodiment, the tumor is reduced by 50%. In an embodiment, the tumor is reduced by 60%. In an embodiment, the tumor is reduced by 70%. In an embodiment, the tumor is reduced by 80%. In an embodiment, the tumor is reduced by 90%. In an embodiment, the tumor is no longer present.

[0082] The present disclosure contemplates a method of the present invention used to reduce the patient's PSA. The present disclosure contemplates a method of the present invention used to slow or stop the spread of cancer cells to another part(s) of the patient's body.
The present disclosure contemplates use of an anti-STEAP1 antigen binding protein in the manufacture of a medicament of the present invention used to reduce the size of the patient's prostate tumor. In an embodiment, the tumor is reduced by 10%. In an embodiment, the tumor is reduced by 20%. In an embodiment, the tumor is reduced by 30%. In an embodiment, the tumor is reduced by 40%. In an embodiment, the tumor is reduced by 50%. In an embodiment, the tumor is reduced by 60%. In an embodiment, the tumor is reduced by 70%. In an embodiment, the tumor is reduced by 80%. In an embodiment, the tumor is reduced by 90%. In an embodiment, the tumor is no longer present.

[0083] The present disclosure contemplates use of an anti-STEAP1 antigen binding protein in the manufacture of a medicament of the present invention used to reduce the patient's PSA. The present disclosure contemplates a method of the present invention used to slow or stop the spread of cancer cells to another part(s) of the patient's body.

[0084] The size of a patient's prostate (and/or metastatic lesions) can be determined by methods known in the art. Such methods include computer tomography (CT), MRI, and/or bone scans. PSA can be determined by a blood test known in the art.

[0085] The present invention contemplates step dosing of an anti-STEAP1 antigen binding protein to reduce cytokine release syndrome (compared to treatment with an anti-STEAP1 antigen binding protein without step dosing) that may result from T-cell engager therapy. Cytokine release syndrome can occur with activation of bystander immune and nonimmune cells, possibly resulting in comorbidities. CRS may be graded according to Lee et al ASTCT Consensus Grading for Cytokine Release Syndrome and Neurologic Toxicity Associated with Immune Effector Cells. Biol Blood Marrow Transplant. 2019;25(4):625 638.

[0086] The term "about" refers to values that are within 10% above or below the referenced value.

EXAMPLES

EXAMPLE 1: PHASE 1 CLINICAL STUDY DESIGN

[0087] This study (NCT04221542) was designed to evaluate the safety, tolerability, pharmacokinetics (PK), and antitumor activity of xaluritamig as monotherapy or in combination in patients (pts) with mCRPC and determine the maximum tolerated dose (MTD) or the recommended phase 2 dose (RP2D). Parts 1 to 3 will evaluate monotherapy with various dosing schedules and target doses and SC administration. Part 4 will evaluate combinations with established standard-of-care mCRPC drugs. Xaluritamig plus abiraterone acetate (4A) or xaluritamig plus enzalutamide (4B) in patients previously treated with 0, 1 or 2 NHT and up to 1 taxane (in hormone sensitive prostate cancer (HSPC) only) in 4A and 4B. Part 5 will be dose expansion in an outpatient setting based on efficacy and toxicity from part 1 dose exploration. Primary endpoints include dose-limiting toxicities, treatment-emergent and -related adverse events, and change in clinical and laboratory parameters. Key secondary endpoints include PK, objective response per RECIST 1.1, prostate-specific antigen response, radiographic progression-free survival per PCWG3, and overall survival. Key inclusion criteria are men with pathologically confirmed mCRPC, evidence of progressive disease, and ECOG performance status of 0 or 1. Key exclusion criteria are small cell or neuroendocrine prostate cancer, untreated CNS metastases or leptomeningeal disease, and a history of or current autoimmune disease or any disease requiring chronic immunosuppressive therapy. In part 1, the dose escalation will be guided by a Bayesian Logistic Regression Model. In parts 2 and 4, doses of AMG 509 will be based on data from the monotherapy parts and dose exploration will be guided by an mTPI-2 design. Investigative sites are in North America, Australia, Asia, and Europe.

[0088] This is an open-label, ascending, multiple dose, phase 1, multi-cohort study evaluating xaluritamig in patients with mCRPC. Up to 441 patients will be enrolled in the study. The study includes the following parts: Part 1: xaluritamig monotherapy administered via IV infusion to patients who have been previously treated with NHT and 1 to 2 prior taxanes; Part 2: xaluritamig monotherapy administered via SC injection to patients who have been previously treated with NHT and 1 to 2 prior taxanes (Part 2 is complete); Part 3: xaluritamig monotherapy administered via IV infusion to patients who have been previously treated with no or 1 NHT (may have been given for hormone sensitive prostate cancer [HSPC]) and no prior taxanes); Part

4: xaluritamig administered via IV infusion in combination with abiraterone acetate (Part 4A) or enzalutamide (Part 4B) to patients who have been previously treated with no or 1 NHT (for hormone sensitive or castration-resistant disease) in Parts 4A and 4B, and 0-2 prior taxane for hormone sensitive disease in Parts 4A and 4B. In Part 4A, xaluritamig is administered IV and abiraterone is administered per the abiraterone label starting on cycle 1 day 1. In Part 4B, xaluritamig is administered IV, and enzalutamide is administered per the enzalutamide label starting one week after the target dose of xaluritamig is reached (or alternative schedules based on emerging safety data). Part 5: xaluritamig monotherapy administered via IV infusion in an outpatient setting to patients who have been previously treated with 1-2 NHT and 1 to 2 prior taxanes.

[0089] In Parts 1, 3, 4, and 5, xaluritamig will be administered every week (QW) or Q2W, as a short-term IV infusion (approximately 60 minutes) with a possible exploration of Q3W or Q4W schedules, based on emerging data and DLRT recommendations. Part 3 and Part 4 dosing regimens and schedules will be adjusted to follow the regimen and schedules that are explored in Part 1, based on emerging data and DLRT recommendations. The Part 5 dosing regimen and schedule will be selected based on emerging data and DLRT recommendations. This may include step dosing. In Part 2, xaluritamig was administered as a deep subcutaneous injection either QW or Q2W. Xaluritamig IV monotherapy dose escalation will occur alongside combination and SC dose escalation, and more than 1 dose regimen may be evaluated in parallel. The dose in Part 3 will be the MTD or RP2D determined in Part 1 dose exploration or expansion. Across all parts, patients are required to be on an ADT while on treatment with AMG 509.

[0090] The dose exploration phase of the Part 1 will enroll up to 100 patients with mCRPC. Dose exploration will be conducted in 2 stages: single-patient cohort(s) followed by multiple-patient cohort(s) (2 to 4 patients per cohort). Planned dose levels are 0.001, 0.003, 0.01, 0.03, 0.1, 0.3, 1, 1.5, and 2 mg IV administered QW. Every 2 weeks (Q2W) schedules may be introduced earlier and the DLRT may recommend exploring every 3 weeks (Q3W) or every 4 weeks (Q4W) schedule starting cycle 2 onwards as well.

Table 1. Xaluritamig doses and dosing regimens in Part 1.

Cohort	N	Step Dosing	Target Dose	Frequency
1	2	None	0.001 mg	QW

2	4	None	0.003 mg	QW
3	4	None	0.01 mg	QW
4	4	None	0.03 mg	QW
5	10	None	0.1 mg	QW
6	6	None	0.3 mg	QW
7a	15	1 step	0.3 mg	QW
7b	12	2 step	1 mg	QW
7c	7	2 step	1 mg	Q2W
8	5	1 step	1mg	QW
9	5	2 step	0.75 mg	QW
10	5	1 step	1 mg	QW
11	6	3 step	1.5 mg	QW
12	6	3 step	1.5 mg	QW
13	7	3 step	2 mg	QW

[0091] Dose escalation/de-escalation decisions in part 1 will be guided by the BLRM model of dose toxicity. The MTD for BLRM is the dose level predicted to have the highest probability of a DLT rate within the target interval of 20% to 33%, subject to overdose control. To control the risk of overdose, the MTD must have less than a 40% predicted probability of overdosing (DLT rate > 33%).

[0092] The MTD for Parts 2 and 4 is the dose level predicted to have the highest probability of a DLT rate within the target interval of 30% to 40%.

[0093] Primary endpoints include dose limiting toxicities, treatment-emergent adverse events, treatment-related adverse events, and changes in vital signs, ECG, and clinical laboratory tests.

[0094] Secondary endpoints include: PK parameters including but not limited to maximum serum concentration (Cmax), time to maximum concentration (Tmax), minimum serum concentration (Cmin), area under the concentration time curve (AUC) over the dosing interval, accumulation following multiple dosing, and, if feasible, half-life (t1/2); objective response (OR) per Response Evaluation Criteria in Solid Tumors (RECIST) 1.1; prostate specific antigen (PSA) response (30%, 50%, 70%, and 90%); PSA50 response at 12 week, duration of response (DOR) per RECIST 1.1; PSA DOR based on PSA50; Time to progression (radiographic and PSA); progression free survival (PFS) (radiographic and PSA); 6 month radiographic PFS1, 2, and 3 year overall survival (OS); Circulating tumor cells (CTCs) – response (CTC0) and rate of CTC conversion; other PCWG3 recommended endpoints (time to

symptomatic skeletal events, alkaline phosphatase [total, bone], lactate dehydrogenase [LDH], hemoglobin, neutrophil to lymphocyte ratio, urine N telopeptide).

[0095] Once the MTD has been identified, enrollment will commence in the dose-expansion phase to confirm the safety and tolerability by evaluating 3 selected dosing regimens and to further evaluate PD and anti-tumor activity to select the most appropriate dose and schedule. These dosing regimens will be pursued in parallel during expansion and will include different dose levels and/or schedules, as shown in Table 2.

Table 2. Clinical trial expansion phase xaluritamig dosing schedules.

Cohort
Xaluritamig 1.5 mg QW (3 step: C1D1 0.1 mg, C1D8 0.3 mg, C1D15 1 mg C1D22 1.5 mg)
Xaluritamig 0.75 mg QW (2 step: C1D1 0.1 mg, C1D8 0.3 mg, C1D15 0.75 mg)
Xaluritamig 1.5 mg Q2W (3 step: C1D1 0.1 mg, C1D8 0.3 mg, C1D15 1 mg, C1D22 1.5 mg)

Patients will be randomized 1:1:1 to the different expansion cohorts. It is anticipated that up to 50 patients (pts) will be enrolled in each expansion cohort.

[0096] As of 23 March 2023, 97 pts had received ≥1 dose of xaluritamig at 15 dose levels/schedules (DLs) (28 [28.3%] pts for ≥ 6 mo); 25 pts remaining on treatment. Median (range) age was 67 (40–86) y; 67 pts (69.1%) had received >3 prior lines of therapy. Treatment-emergent adverse events (TEAEs) were reported in 100% of pts (grade ≥3, 74.2%). The most common AE was cytokine release syndrome (CRS; 72.2%), which was primarily grade 1/2 (cycle 1), one event being grade 3 (no grade 4/5 CRS). In the 2 mg TD cohort, 3/6 DLT evaluable patients experienced DLTs, defining 1.5 mg as the MTD. Treatment-related TEAEs leading to discontinuation occurred in 17.5% of pts. Overall, 89 pts were PSA evaluable; 66 pts were RECIST evaluable. PSA50 (≥50% PSA decline) responses occurred in 42 pts (47.2%); PSA90, in 24 pts (27.0%). PSA responses occurred more at higher DLs (0.75 mg-2 mg) than in lower DLs (0.001-0.3 mg): ≥90% (34.8% vs 18.6%) pts, ≥50% (54.3% vs 39.5%) pts. RECIST responses included 15 (22.7%) confirmed PR and 30 (45.5%) SD. At higher DLs, 14 pts (38.9%) had confirmed PR and 12 (33.3%) SD. Preliminary PK showed dose-proportional increase in exposure ranging from 0.003 mg to 1.5 mg with a mean terminal half-life of approximately 3-4 days.

[0097] Patients were initially enrolled into fixed (non-step) dosing administered intravenously (IV) weekly (QW) in Cohorts 1–6 at 0.001 (n=2), 0.003 (n=4), 0.01 (n=4), 0.03 (n=4), 0.1 (n=10) and 0.3 (n=6) mg, respectively. At 0.3 mg in Cohort 6, 2 of 6 patients experienced dose-limiting toxicities (DLTs) of grade 3 CRS/encephalopathy and back pain, and the dose level was determined to be intolerable and exceeded the maximum tolerated dose (MTD) for cycle 1 day 1. Following adjustments of premedication, the 0.3 mg starting dose (Cohort 8) was still determined intolerable and the MTD for the first dose (priming dose) was confirmed to be 0.1 mg.

[0098] Step dosing started with 0.1 mg on day 1 and used either 1-step (increase on day 8), 2-steps (increases on days 8 and 15) or 3-steps (increases on days 8, 15, and 22) to achieve target dose by days 8, 15 or 22, respectively.

[0099] In Cohorts 7a and 10, 1-step dosing was 0.1 to 0.3 mg or 0.1 to 1.0 mg. The regimen of 0.1 to 0.3 mg (Cohort 7a) was tolerable but the larger step dose of 0.1 to 1.0 mg (Cohort 10) was intolerable due to three of four patients experiencing DLT, consisting of grade 3 atrial fibrillation/QT interval prolongation, grade 3 fasciitis/pharyngitis, and grade 3 arthralgia (one patient each). Based upon the findings of the 1-step dosing, Cohorts 7b, 7c, and 9 evaluated 2-step dosing regimens with a priming dose of 0.1 mg, day 8 dose of 0.3 mg, and day 15 dose of 0.75 or 1.0 mg; all were determined to be tolerable.

[00100] Based upon the findings of the 2-step dosing, Cohorts 11, 12, and 13 evaluated 3-step dosing regimens with a priming dose of 0.1 mg, day 8 dose of 0.3 mg, day 15 dose of either 0.75 or 1.0 mg, and a 22 day dose of either 1.5 or 2 mg. Cohorts 11 (day 15 dose of 0.75 mg) and 12 (day 15 dose of 1.0 mg) had 22 day target doses of 1.5, and both were determined to be tolerable. Cohort 13 tested the highest day 22 dose of 2.0 mg, which was deemed not tolerable due to DLTs in 3 of 4 evaluable patients (grade 3 myalgia [n=2]; grade 3 back pain and arthralgia [n=1]).

[00101] In summary, the maximum tolerated priming dose with the full prophylactic regimen was 0.1 mg, and a 3-step dosing regimen consisting of day 8 0.3 mg, day 15 1.0 mg and day 22+ 1.5 mg IV QW was determined to be the MTD.

[00102] Xaluritamig was tolerable with low-grade CRS (primarily cycle 1) and has encouraging preliminary clinical efficacy in heavily pretreated pts with mCRPC.

[00103] Preliminary efficacy as measured both by PSA and RECIST were encouraging in a heavily pretreated mCRPC population, and responses occurred with greater frequency in the higher-dose cohorts. Consistent with PD markers for T cell activity, PSA declines were seen starting with 0.1 mg xaluritamig, with a significant number of patients achieving confirmed PSA50 and PSA90 responses. At higher doses these translated in ORs with response rates in RECIST evaluable patients observed in 50% of patients.

[00104] The maximum tolerated dose was determined to be 1.5 mg via a three step schedule (cycle 1 day 1 0.1 mg / cycle 1 day 8 0.3 mg / cycle 1 day 15 1 mg / cycle 1 day 22 1.5 mg) with dosing once per week. In the dose expansion a second dosing schedule with 0.75 mg via a 2-step schedule (cycle 1 day 1 0.1 mg / cycle 1 day 8 0.3 mg / cycle 1 day 15 0.75 mg) with dosing once per week will be explored. Dosing of 1.5 mg once per two weeks (Q2W) will also be explored. In this schedule the three step schedule is used. From cycle 2 onwards the target dose of 1.5 mg will be administered Q2W.

[00105] During the study, initial signs of clinical efficacy based in PSA declines were observed across xaluritamig target dose levels of 0.1 mg or higher, with one OR seen in cohorts with 0.3 mg target dose. Among patients in the high dose cohorts (QW administration, target doses above 0.3 mg, deemed safe and tolerable), higher OR rates were seen. Among 67 patients with RECIST-evaluable disease, 16 patients (24%) achieved a confirmed partial response (PR); 32 patients (48%) stable disease (SD), and 13 patients (19%) progressive disease (PD); 6 patients (9%) were not evaluable (Figure 2; Table 3). RECIST ORs were greater at high doses, with 10 patients (50%) achieving confirmed PR. Responses were usually achieved within the first 2 cycles of treatment and duration of response at the higher dose cohorts is still immature. During the study, initial clinical benefit was derived across patients with a diverse range of disease burden, including reduction in bone lesions and imaging responses per RECIST version 1.1.

Table 3. Summary of efficacy data in patients receiving xaluritamig

	All cohorts	**Low dose cohorts**	**High dose cohorts**
PSA evaluable*, n	87	43	44
PSA response, confirmed*, n (%)			
PSA50	43 (49)	17 (40	26 (59)
PSA90	24 (28)	8 (19)	16 (36)
RECIST v1.1 evaluable†, n	67	30	37

RECIST v1.1 response, confirmed, n (%)			
CR	0	0**	0
PR	16 (24)	1 (3)**	15 (41)**
SD	32 (48)	18 (60)**	14 (38)**
PD	13 (19)	6 (20)**	7 (19)**
Not evaluable‡	6 (9)	5 (17)**	1 (3)**

PSA response was defined for ≥50% reduction and ≥90% reduction from the baseline PSA.
*PSA response evaluable analysis set was defined as all patients that were enrolled and received ≥1 dose of xaluritamig, had a measurable (ie, >0) baseline PSA and had the opportunity to be followed for ≥8 weeks starting from day 1. Patients who stopped disease assessment prior to 8 weeks were included in this analysis set if the data cutoff was ≥8 weeks after day 1.
†The RECIST version 1.1 response evaluable analysis set was defined as enrolled patients who had a baseline measurable disease and had the opportunity to be followed for ≥8 weeks starting from the first dose of xaluritamig.
‡Best overall response of not evaluable includes 5 patients without post-baseline scans.
CR, complete response; PD, progressive disease; PR, partial response; PSA, prostate-specific antigen; QW, weekly; RECIST; Response Evaluation Criteria in Solid Tumors; SD, stable disease.

[00106] In the PSA-evaluable analysis set (N=87), confirmed PSA50 responses were reported in 43 patients (49%) and confirmed PSA90 responses were reported in 24 patients (28%) (Figure 3). In the low-dose (n=43 evaluable patients) and high-dose cohorts (n=44), confirmed PSA50 responses were reported in 17 (40%) and 26 (59%) patients, respectively, while confirmed PSA90 responses occurred in 8 (19%) and 16 (36%) patients, respectively. One patient was a 65-year-old man with an initial diagnosis of stage IV adenocarcinoma of the prostate (Gleason score 9). The subject was on androgen deprivation therapy with prior treatments including bicalutamide, abiraterone, docetaxel, cabazitaxel, and carboplatin. Upon receiving IV xaluritamig with a 3-step target dose of 1.5 mg, the subject demonstrated a confirmed PSA50 response with maximum PSA decline from baseline of 99% on Cycle 7 Day 1. CT scans showed 3 target lesions and multiple non-target lesions during screening. Imaging after 2 cycles of treatment showed shrinkage of lesions consistent with PR (37.3% reduction of target lesions) per RECIST 1.1 criteria, which was confirmed at 16 weeks and maintained at 24 weeks (Figure 4 and Figure 5). AEs during the first cycle of treatment were ≤grade 2 and included recurrent CRS, rash, worsening of back pain, and tinea faciei. During further treatment cycles, ≤grade 2 AEs of rash, myalgia, and hyperkalemia were reported.

[00107] Preliminary PK showed dose-proportional increase in exposure over the dose levels explored, with a mean terminal half-life of ~3–4 days. Based on preclinical studies, the

lower and upper black horizontal dashed lines represent the 90% effective concentration (EC90) of the in vitro mediated cell killing assay (74 ng/mL) and half maximal inhibitory concentration (IC50) of the xenograph PK/PD model (259 ng/mL), respectively. Starting at cohort 5 (0.1 mg QW), the observed predose (C_{trough}) concentrations are nearing the predicted minimum efficacious exposure suggesting these doses may lead to clinical response.

[00108] After the first infusion of xaluritamig, a rapid decrease of peripheral T cell counts was observed. Lymphocyte redistribution was accompanied by transient expression of the T cell activation marker, CD69. Measured serum cytokines, including IFN-gamma, IL-2, IL-6, and TNF-alpha, increased from baseline following xaluritamig infusion. Cytokine concentrations peaked within 6–24 hours and returned to baseline prior to subsequent infusions. T cell margination, T cell activation, and cytokine induction were all dose dependent with FDR-corrected P values reaching significance at multiple timepoints post infusion.

[00109] The overall treatment emergent ADA incidence was 49 of 90 evaluable patients (54%), of which 8 patients had a transient antibody response. The median onset of binding ADA was Cycle 2 Day 1. Binding ADA-positive patients were evaluated for ADA impact on drug activity, exposure, and association with safety events. The ADAs observed were not associated with AEs. A subset of binding ADA positive patients was determined to be neutralizing and/or exposure-impacting.

[00110] The safety profile in this study consisted of mostly grade 1 and 2 AEs that were clinically manageable, and no grade 5 events were found to be related to xaluritamig. Nineteen percent of patients discontinued treatment due to a TRAE, partly due to restrictions on the duration of dosing interruption.

[00111] The most frequent TRAE was low-grade CRS occurring primarily in cycle 1. CRS was expected in this study due to the biological mechanism of xaluritamig and clinical experience with other TCEs (11). Three (3%) cases of grade 3 CRS were reported, one was later reduced to grade 1 after data cutoff. The grade 3 events (Cohorts 6 and 7a) occurred prior to the addition of the second pre-dose of dexamethasone and post-dose IV hydration that was initiated in later cohorts. Almost all CRS events manifested in fever with or without hypotension, tachycardia and rarely hypoxia. There were no grade 4 or 5 CRS events. Overall, all CRS events resolved with standard management, using acetaminophen, IV fluids together with tocilizumab and/or corticosteroids.

[00112] A favorable predictable dose-exposure relationship was observed after xaluritamig administration. The preliminary terminal half-life was ~3–4 days and supports a QW dose-schedule. PK suggested that patients at the 0.75 mg target and above would have a trough concentration level at the minimum efficacious exposure based on pre-clinical studies. This allowed further analysis evaluating the clinical outcomes in low (< 0.75 mg) and high dose (≥ 0.75 mg) cohorts.

[00113] Additional analysis was performed in patients with mCRPC in a dose expansion phase that were randomized 1:1:1 to receive IV xaluritamig with target doses of 0.75 mg QW, 1.5 mg QW, or 1.5 mg Q2W, using a 2- or 3-step dosing approach in Cycle 1. Results are provided in the table below.

	0.75 mg QW	**1.5 mg QW**	**1.5 mg Q2W**	**Dose Expansion Total**
PSA evaluable	N = 33	N = 30	N = 32	N = 95
PSA50 response confirmed, n (%)	12 (36.4)	18 (60.0)	17 (53.1)	47 (49.5)
PSA90 response confirmed, n (%)	7 (21.2)	9 (30.0)	11 (34.4)	27 (28.4)
RECIST evaluable	N = 27	N = 21	N = 21	N = 69
Confirmed complete response, n (%)	0 (0.0)	0 (0.0)	1 (4.8)	1 (1.4)
Confirmed partial response, n (%)	4 (14.8%)	4 (19.0)	5 (23.8)	13 (18.8)
Stable disease, n (%)	10 (37.0)	14 (66.7)	10 (47.6)	34 (49.3)
Progressive disease, n (%)	12 (44.4)	1 (4.8)	4 (19.0)	17 (24.6)
Not evaluable, n (%)	1 (3.7)	2 (9.5)	1 (4.8)	4 (5.8)

[00114] While both doses were effective, a target dose of 1.5 mg vs 0.75 mg improved the efficacy of xaluritamig with a manageable side-effect profile in this randomized dose-expansion/optimization study of heavily pretreated patients with mCRPC. A higher target dose of 1.5 mg demonstrated trends toward superior efficacy and similar safety compared to 0.75 mg:

[00115] PSA50 0.75 mg: 36%, 1.5 mg: 53%-60%

[00116] PSA90 0.75 mg: 21%, 1.5 mg: 30%-34%

[00117] ORR 0.75 mg: 15%, 1.5 mg: 19%-29%

[00118] Grade 3 adverse events were mostly transient, manageable, reversible, and allowed treatment continuation in most patients. There were few discontinuations from musculoskeletal inflammatory events or cytokine release syndrome (CRS), with most grade 3 CRS events occurring in Cycle 1 (no grade 4/5 CRS). A Q2W dosing schedule demonstrated an improved adverse event profile with a decreased incidence of overall treatment-related

musculoskeletal inflammatory events (69% vs 74% and 86% in QW dose schedules) and lower number of higher-grade events (grade 2/3 22%/33% vs 31%/37% and 34%/43%).

TABLE 4. SEQUENCES

SEQ ID NO:	Designation	Sequence
1.	Xaluritamig CD3 scFv HCDR1	TYAMN
2.	Xaluritamig CD3 scFv HCDR2	RIRSKYNNYATYYADSVKG
3.	Xaluritamig CD3 scFv HCDR3	HGNFGDSYVSWFAY
4.	Xaluritamig CD3 scFv LCDR1	GSSTGAVTTSNYAN
5.	Xaluritamig CD3 scFv LCDR1	GTNKRAP
6.	Xaluritamig CD3 scFv LCDR1	ALWYSNHWV
7.	Xaluritamig CD3 scFv HCVR	EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQ APGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSK NTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWG QGTLVTVSS
8.	Xaluritamig CD3 scFv LCVR	QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQ QKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISG AQPEDEADYYCALWYSNHWVFGGGTKLTVL
9.	Xaluritamig STEAP1 Fab HCDR1	TYWIE
10.	Xaluritamig STEAP1 Fab HCDR2	EILPGSGQTDFNEKFQG
11.	Xaluritamig STEAP1 Fab HCDR3	WGYYGTRGYFNV
12.	Xaluritamig STEAP1 Fab LCDR1	RASSSVSYMH
13.	Xaluritamig STEAP1 Fab LCDR2	STSNLAS

14.	Xaluritamig STEAP1 Fab LCDR3	QQRRSFPYT
15.	Xaluritamig STEAP1 Fab HCVR	QVQLVQSGAEVKKPGASVKVSCKASGYTFSTYWIEWVRQ APGQRLEWMGEILPGSGQTDFNEKFQGRVTFTADTSSDTA YMELSSLRSEDTAVYYCTRWGYYGTRGYFNVWGQGTLV TVSS
16.	Xaluritamig STEAP1 Fab LCVR	EIVLTQSPATLSLSPGERATLSCRASSSVSYMHWFQQKPG QAPRLLIYSTSNLASGIPARFSGSGSGTDYTLTISSLEPEDFA VYYCQQRRSFPYTFGQGTKLEIK
17.	Xaluritamig STEAP1 HC	QVQLVQSGAEVKKPGASVKVSCKASGYTFSTYWIEWVRQ APGQRLEWMGEILPGSGQTDFNEKFQGRVTFTADTSSDTA YMELSSLRSEDTAVYYCTRWGYYGTRGYFNVWGQGTLV TVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPV TVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT QTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPAPPVA GPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFN WYVDGVEVHNAKTKPCEEEYGSTYRCVSVLTVLHQDWL NGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSR EEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHN HYTQKSLSLSPGK
18.	Xaluritamig STEAP1 LC	EIVLTQSPATLSLSPGERATLSCRASSSVSYMHWFQQKPG QAPRLLIYSTSNLASGIPARFSGSGSGTDYTLTISSLEPEDFA VYYCQQRRSFPYTFGQGTKLEIKRTVAAPSVFIFPPSDEQL KSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVT EQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSP VTKSFNRGEC
19.	Xaluritamig HC with inserted CD3 scFv	QVQLVQSGAEVKKPGASVKVSCKASGYTFSTYWIEWVRQ APGQRLEWMGEILPGSGQTDFNEKFQGRVTFTADTSSDTA YMELSSLRSEDTAVYYCTRWGYYGTRGYFNVWGQGTLV TVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPV TVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT QTYICNVNHKPSNTKVDKKVEPKSCGGGGSGGGGSEVQL VESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGK GLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLY LQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTL VTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEPSLTVSPG GTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTN KRAPGVPARFSGSLLGGKAALTISGAQPEDEADYYCALW YSNHWVFGGGTKLTVLGGGGSGGGGSKTHTCPPCPAPPV AGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKF NWYVDGVEVHNAKTKPCEEQYGSTYRCVSVLTVLHQDW LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPS REQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKT

		TPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEAL HNHYTQKSLSLSPGK
20.	Xaluritamig STEAP1 Fab HCVR pyro-glu	Pyro-gluVQLVQSGAEVKKPGASVKVSCKASGYTFSTYWIEWVR QAPGQRLEWMGEILPGSGQTDFNEKFQGRVTFTADTSSDT AYMELSSLRSEDTAVYYCTRWGYYGTRGYFNVWGQGTL VTVSS
21.	Xaluritamig STEAP1 HC pyro-glu	Pyro-gluVQLVQSGAEVKKPGASVKVSCKASGYTFSTYWIEWVR QAPGQRLEWMGEILPGSGQTDFNEKFQGRVTFTADTSSDT AYMELSSLRSEDTAVYYCTRWGYYGTRGYFNVWGQGTL VTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEP VTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSL GTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPAPP VAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVK FNWYVDGVEVHNAKTKPCEEEYGSTYRCVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLP PSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYK TTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEAL HNHYTQKSLSLSPGK
22.	STEAP1 HC no C-term lysine	QVQLVQSGAEVKKPGASVKVSCKASGYTFSTYWIEWVRQ APGQRLEWMGEILPGSGQTDFNEKFQGRVTFTADTSSDTA YMELSSLRSEDTAVYYCTRWGYYGTRGYFNVWGQGTLV TVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPV TVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT QTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPAPPVA GPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFN WYVDGVEVHNAKTKPCEEEYGSTYRCVSVLTVLHQDWL NGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSR EEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHN HYTQKSLSLSPG
23.	STEAP1 HC pyro-glu and no C-term lysine	Pyro-gluVQLVQSGAEVKKPGASVKVSCKASGYTFSTYWIEWVR QAPGQRLEWMGEILPGSGQTDFNEKFQGRVTFTADTSSDT AYMELSSLRSEDTAVYYCTRWGYYGTRGYFNVWGQGTL VTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEP VTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSL GTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPAPP VAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVK FNWYVDGVEVHNAKTKPCEEEYGSTYRCVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLP PSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYK TTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEAL HNHYTQKSLSLSPG

24.	Xaluritamig HC with inserted CD3 scFv; pyro-glu	Pyro-gluVQLVQSGAEVKKPGASVKVSCKASGYTFSTYWIEWVRQAPGQRLEWMGEILPGSGQTDFNEKFQGRVTFTADTSSDTAYMELSSLRSEDTAVYYCTRWGYYGTRGYFNVWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCGGGGSGGGGSEVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVLGGGGSGGGGSKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPCEEQYGSTYRCVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
25.	Xaluritamig HC with inserted CD3 scFv; no C-term lysine	QVQLVQSGAEVKKPGASVKVSCKASGYTFSTYWIEWVRQAPGQRLEWMGEILPGSGQTDFNEKFQGRVTFTADTSSDTAYMELSSLRSEDTAVYYCTRWGYYGTRGYFNVWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCGGGGSGGGGSEVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVLGGGGSGGGGSKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPCEEQYGSTYRCVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG
26.	Xaluritamig HC with inserted CD3 scFv; pyro-glu and no C-term lysine	Pyro-gluVQLVQSGAEVKKPGASVKVSCKASGYTFSTYWIEWVRQAPGQRLEWMGEILPGSGQTDFNEKFQGRVTFTADTSSDTAYMELSSLRSEDTAVYYCTRWGYYGTRGYFNVWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCGGGGSGGGGSEV

		QLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAP GKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNT LYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQ GTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEPSLTV SPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGG TNKRAPGVPARFSGSLLGGKAALTISGAQPEDEADYYCAL WYSNHWVFGGGTKLTVLGGGGSGGGGSKTHTCPPCPAPP VAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVK FNWYVDGVEVHNAKTKPCEEQYGSTYRCVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLP PSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNY KTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHE ALHNHYTQKSLSLSPG

CLAIMS

What is claimed:

1. A method of treating a patient having prostate cancer, comprising administering to the patient a pharmaceutical composition comprising an anti-STEAP1 antigen binding protein at a dose of about 0.1 mg to about 2.0 mg.
2. The method of claim 1, wherein the dose is about 0.1 mg.
3. The method of claim 1, wherein the dose is about 0.3 mg.
4. The method of claim 1, wherein the dose is about 0.75 mg.
5. The method of claim 1, wherein the dose is about 1 mg.
6. The method of claim 1, wherein the dose is about 1.5 mg.
7. The method of claim 1, wherein the dose is 1.5 mg.
8. The method of any one of claims 1-7, wherein the dose is administered once per one week.
9. The method of any one of claims 1-7, wherein the dose is administered once per two weeks.
10. The method of any one of claims 1-9, wherein the dose is administered by intravenous administration.
11. The method of any one of claims 1-10, comprising administering to the patient a pharmaceutical composition comprising an anti-STEAP1 antigen binding protein at a dose of about 0.1 mg to about 1.5 mg, and the method further comprises administering to the patient a dose of abiraterone.
12. The method of claim 11, wherein the dose of abiraterone is about 1000 mg.
13. The method of claim 11 or 12, wherein the dose of abiraterone is administered orally.
14. The method of any one of claims 11-13, wherein the patient is administered about 5 mg of prednisone two times per day.
15. The method of any one of claims 11-13, wherein the patient is administered about 10 mg of prednisone one time per day.
16. The method of any one of claims 11-15, wherein the dose of the anti-STEAP1 antigen binding protein is about 0.75mg to about 2.0 mg.
17. The method of any one of claims 1-10, comprising administering to the patient a pharmaceutical composition comprising an anti-STEAP1 antigen binding protein at a

dose of about 0.1 mg to about 1.5 mg, and the method further comprises administering to the patient a dose of enzalutamide.

18. The method of claim 17, wherein the dose of enzalutamide is about 160 mg.
19. The method of claim 17 or 18, wherein the dose of enzalutamide is administered orally.
20. The method of any one of claims 17-19, wherein the dose of the anti-STEAP1 antigen binding protein is about 0.75mg to about 2.0 mg.
21. The method of any one of claims 1-20, wherein the anti-STEAP1 antigen binding protein is first administered by step dosing.
22. The method of claim 21, wherein the anti-STEAP1 antigen binding protein is administered by step dosing in two or three steps.
23. The method of claim 21, wherein the anti-STEAP1 antigen binding protein is administered by step dosing on day 1 at 0.1 mg, day 8 at 0.3 mg, day 15 at 1.0 mg, and day 22 at 1.5 mg.
24. The method of claim 21, wherein the anti-STEAP1 antigen binding protein is administered by step dosing on day 1 at 0.1 mg, day 8 at 0.3 mg, day 15 at 0.75 mg, and day 22 at 0.75 mg.
25. The method of any one of claims 21-24, further comprising administering the anti-STEAP1 antigen binding protein according to any one of claims 1-10 to the patient once per week, once per two weeks, once per three weeks, or once per four weeks after administration of the step dosing.
26. The method of claim 25, comprising administering the anti-STEAP1 antigen binding protein at 1.5 mg once every two weeks after the step dosing.
27. The method of any one of claims 1-26, wherein the anti-STEAP1 antigen binding protein comprises two Fab binding domains, each Fab binding domain binds STEAP1, and wherein each Fab binding domain comprises a variable heavy domain, a variable light domain, a CH1 domain, and a constant light domain, which variable heavy domain comprises HCDR1 comprising SEQ ID NO: 9, HCDR2 comprising SEQ ID NO: 10, and HCDR3 comprising SEQ ID NO: 11; and the variable light domain comprises LCDR1 comprising SEQ ID NO: 12, LCDR2 comprising SEQ ID NO: 13, and LCDR3 comprising SEQ ID NO: 14.

28. The method of any one of claims 1-27, wherein the anti-STEAP1 antigen binding protein comprises two Fab domains, each binding STEAP1, and one scFv domain that binds CD3.
29. The method of any one of claims 1-28, wherein the anti-STEAP1 antigen binding protein comprises two Fab binding domains, each Fab binding domain binds STEAP1.
30. The method of any one of claims 1-29, wherein the anti-STEAP1 antigen binding protein comprises two Fab binding domains, each Fab binding domain binds STEAP1, and wherein each Fab binding domain comprises a variable heavy domain, a variable light domain, a CH1 domain, and a constant light domain, which variable heavy domain comprises HCDR1 comprising SEQ ID NO: 9, HCDR2 comprising SEQ ID NO: 10, and HCDR3 comprising SEQ ID NO: 11; and the variable light domain comprises LCDR1 comprising SEQ ID NO: 12, LCDR2 comprising SEQ ID NO: 13, and LCDR3 comprising SEQ ID NO: 14.
31. The method of any one of claims 1-30, wherein the anti-STEAP1 antigen binding protein comprises an scFv binding domain that binds CD3.
32. The method of any one of claims 1-31, wherein the anti-STEAP1 antigen binding protein comprises an scFv binding domain that binds CD3, and the scFv variable heavy domain comprises HCDR1 comprising SEQ ID NO: 1, HCDR2 comprising SEQ ID NO: 2, and HCDR3 comprising SEQ ID NO: 3; an scFv linker; and an scFv variable light domain, that comprises LCDR1 comprising SEQ ID NO: 4, LCDR2 comprising SEQ ID NO:5, and LCDR3 comprising SEQ ID NO: 6.
33. The method of any one of claims 1-32, wherein the anti-STEAP1 antigen binding protein comprises a first Fc domain and a second Fc domain.
34. The method of any one of claims 31-33, wherein each Fab variable heavy domain comprises an amino acid sequence at least 90% identical to SEQ ID NO: 15 or 20; each Fab variable light domain comprises an amino acid sequence at least 90% identical to SEQ ID NO: 16; and the scFv variable heavy domain comprises an amino acid sequence at least 90% identical to SEQ ID NO:7; and the scFv variable light domain comprises an amino acid sequence at least 90% identical to SEQ ID NO: 8.
35. The method of any one of claims 31-34, wherein each Fab variable heavy domain comprises SEQ ID NO: 15 or 20; each Fab variable light domain comprises SEQ ID NO:

16; the scFv variable heavy domain comprises SEQ ID NO:7; and the scFv variable light domain comprises SEQ ID NO: 8.

36. The method of any one of claims 31-35, wherein the scFv binding domain which binds CD3 comprises an scFv linker.
37. The method of any one of claims 33-36, wherein the first Fc domain comprises amino acid substitutions E233P, L235V, G236A, S267K, R292C, N297G, V302C, E357Q, and S364K; and the second Fc domain comprises amino acid substitutions N208D, E233P, L235V, G236A, S267K, R292C, Q295E, N297G, V302C, L368D, K370S, N384D, Q418E, and N421D.
38. The method of any one of claims 33-37, wherein the first Fc domain and the second Fc domain each comprise a deletion at position 234.
39. The method of any one of claims 1-38, wherein the anti-STEAP1 antigen binding protein comprises a HC comprising SEQ ID NO: 17 or 23, a HC with inserted CD3 scFv comprising SEQ ID NO: 19 or 26, and two light chains, each comprising SEQ ID NO: 18.
40. The method of any one of claims 1-39, wherein the anti-STEAP1 antigen binding protein is xaluritamig.
41. The method of any one of claims 1-40, wherein the patient has metastatic castration-resistant prostate cancer.
42. Use of an anti-STEAP1 antigen binding protein for preparation of a medicament for treating prostate cancer, wherein the medicament is formulated for administration at a dose of about 0.1 mg to about 2.0 mg.
43. The use of claim 42, wherein the dose is about 0.1 mg.
44. The use of claim 42, wherein the dose is about 0.3 mg.
45. The use of claim 42, wherein the dose is about 0.75 mg.
46. The use of claim 42, wherein the dose is about 1 mg.
47. The use of claim 42, wherein the dose is about 1.5 mg.
48. The use of claim 42, wherein the dose is 1.5 mg.
49. The use of any one of claims 42-48, wherein the dose is administered once per one week.
50. The use of any one of claims 42-48, wherein the dose is administered once per two weeks.

51. The use of any one of claims 42-50, wherein the dose is administered by intravenous administration.
52. The use of any one of claims 42-51, comprising administering to the patient a dose of a pharmaceutical composition comprising an anti-STEAP1 antigen binding protein at a dose of about 0.1 mg to about 2.0 mg, and wherein the use further comprises administering to the patient a dose of abiraterone.
53. The use of claim 52, wherein the dose of abiraterone is about 1000 mg.
54. The use of claim 52 or 53, wherein the dose of abiraterone is administered orally.
55. The use of any one of claims 52-54, wherein the patient is administered about 5 mg of prednisone two times per day.
56. The use of any one of claims 52-54, wherein the patient is administered about 10 mg of prednisone one time per day.
57. The use of any one of claims 52-55, wherein the dose of the anti-STEAP1 antigen binding protein is about 0.75 mg to about 2.0 mg.
58. The use of any one of claims 42-51, comprising administering to the patient a dose of a pharmaceutical composition comprising an anti-STEAP1 antigen binding protein at a dose of about 0.1 mg to about 1.5 mg, and wherein the method further comprises administering to the patient a dose of enzalutamide.
59. The use of claim 58, wherein the dose of enzalutamide is about 160 mg.
60. The use of claim 58 or 59, wherein the dose of enzalutamide is administered orally.
61. The use of any one of claims 58-60, wherein the dose of anti-STEAP1 antigen binding protein is about 0.75mg to about 2.0 mg.
62. The use of any one of claims 42-61, wherein the anti-STEAP1 antigen binding protein is first administered by step dosing.
63. The use of claim 62, wherein the anti-STEAP1 antigen binding protein is administered by step dosing in two or three steps.
64. The use of claim 62, wherein the anti-STEAP1 antigen binding protein is administered by step dosing on day 1 at 0.1mg, day 8 at 0.3mg, day 15 at 1.0mg, and day 22 at 1.5mg.
65. The use of claim 62, wherein the anti-STEAP1 antigen binding protein is administered by step dosing on day 1 at 0.1mg, day 8 at 0.3mg, day 15 at 0.75mg, and day 22 at 0.75mg.

66. The use of any one of claims 62-65, further comprising administering the anti-STEAP1 antigen binding protein according to any one of claims 52-61 to the patient once per week, once per two weeks, once per three weeks, or once per four weeks after administration of the step dosing.
67. The use of any one of claims 42-66, wherein the anti-STEAP1 antigen binding protein comprises two Fab binding domains, each Fab binding domain binds STEAP1, and each Fab binding domain comprises a variable heavy domain, a variable light domain, a CH1 domain, and a constant light domain, the variable heavy domain comprises HCDR1 comprising SEQ ID NO: 9, HCDR2 comprising SEQ ID NO: 10, and HCDR3 comprising SEQ ID NO: 11; and the variable light domain comprises LCDR1 comprising SEQ ID NO: 12, LCDR2 comprising SEQ ID NO: 13, and LCDR3 comprising SEQ ID NO: 14.
68. The use of any one of claims 42-67, wherein the anti-STEAP1 antigen binding protein comprises two Fab domains, each binding STEAP1, and one scFv domain that binds CD3.
69. The use of any one of claims 42-68, wherein the anti-STEAP1 antigen binding protein comprises two Fab binding domains, each Fab binding domain binds STEAP1.
70. The use of any one of claims 52-69, wherein the anti-STEAP1 antigen binding protein comprises two Fab binding domains, each Fab binding domain binds STEAP1, and each Fab binding domain comprises a variable heavy domain, a variable light domain, a CH1 domain, and a constant light domain, which variable heavy domain comprises HCDR1 comprising SEQ ID NO: 9, HCDR2 comprising SEQ ID NO: 10, and HCDR3 comprising SEQ ID NO: 11; and the variable light domain comprises LCDR1 comprising SEQ ID NO: 12, LCDR2 comprising SEQ ID NO: 13, and LCDR3 comprising SEQ ID NO: 14.
71. The use of any one of claims 42-70, wherein the anti-STEAP1 antigen binding protein comprises an scFv binding domain that binds CD3.
72. The use of any one of claims 42-71, wherein the anti-STEAP1 antigen binding protein comprises an scFv binding domain that binds CD3, and the scFv variable heavy domain comprises HCDR1 comprising SEQ ID NO: 1, HCDR2 comprising SEQ ID NO: 2, and HCDR3 comprising SEQ ID NO: 3; an scFv linker; and an scFv variable light domain

that comprises LCDR1 comprising SEQ ID NO: 4, LCDR2 comprising SEQ ID NO:5, and LCDR3 comprising SEQ ID NO: 6.

73. The use of any one of claims 42-72, wherein the anti-STEAP1 antigen binding protein comprises a first Fc domain and a second Fc domain.
74. The use of any one of claims 71-73, wherein each Fab variable heavy domain comprises an amino acid sequence at least 90% identical to SEQ ID NO: 15; each Fab variable light domain comprises an amino acid sequence at least 90% identical to SEQ ID NO: 16; and the scFv variable heavy domain comprises an amino acid sequence at least 90% identical to SEQ ID NO:7; and the scFv variable light domain comprises an amino acid sequence at least 90% identical to SEQ ID NO: 8.
75. The use of any one of claims 71-74, wherein each Fab variable heavy domain comprises SEQ ID NO: 15; each Fab variable light domain comprises SEQ ID NO: 16; the scFv variable heavy domain comprises SEQ ID NO:7; and the scFv variable light domain comprises SEQ ID NO: 8.
76. The use of any one of claims 71-75, wherein the scFv binding domain which binds CD3 comprises an scFv linker.
77. The use of any one of claims 73-76, wherein the first Fc domain comprises amino acid substitutions E233P, L235V, G236A, S267K, R292C, N297G, V302C, E357Q, and S364K; and the second Fc domain comprises amino acid substitutions N208D, E233P, L235V, G236A, S267K, R292C, Q295E, N297G, V302C, L368D, K370S, N384D, Q418E, and N421D.
78. The use of any one of claims 73-77, wherein the first Fc domain and the second Fc domain each comprise a deletion at position 234.
79. The use of any one of claims 42-78, wherein the anti-STEAP1 antigen binding protein comprises a HC comprising SEQ ID NO: 17, a HC with inserted CD3 scFv comprising SEQ ID NO: 19, and two light chains, each comprising SEQ ID NO: 18.
80. The use of any one of claims 42-79, wherein the anti-STEAP1 antigen binding protein is xaluritamig.
81. The use of any one of claims 42-80, wherein the patient has metastatic castration-resistant prostate cancer.

82. An anti-STEAP1 antigen binding protein for use in treating prostate cancer, wherein the antigen binding protein is formulated for administration at a dose of about 0.1 mg to about 2.0 mg.
83. The anti-STEAP1 antigen binding protein of claim 82, wherein the dose is about 0.1 mg.
84. The anti-STEAP1 antigen binding protein of claim 82, wherein the dose is about 0.3 mg.
85. The anti-STEAP1 antigen binding protein of claim 82, wherein the dose is about 0.75 mg.
86. The anti-STEAP1 antigen binding protein of claim 82, wherein the dose is about 1 mg.
87. The anti-STEAP1 antigen binding protein of claim 82, wherein the dose is about 1.5 mg.
88. The anti-STEAP1 antigen binding protein of claim 82, wherein the dose is 1.5 mg.
89. The anti-STEAP1 antigen binding protein of any one of claims 82-88, wherein the dose is administered once per one week.
90. The anti-STEAP1 antigen binding protein of any one of claims 82-88, wherein the dose is administered once per two weeks.
91. The anti-STEAP1 antigen binding protein of any one of claims 82-90, wherein the dose is administered by intravenous administration.
92. The anti-STEAP1 antigen binding protein of any one of claims 82-91, comprising administering to the patient a dose of a pharmaceutical composition comprising an anti-STEAP1 antigen binding protein at a dose of about 0.1 mg to about 2.0 mg, and wherein the use further comprises administering to the patient a dose of abiraterone.
93. The anti-STEAP1 antigen binding protein of claim 92, wherein the dose of abiraterone is about 1000 mg.
94. The anti-STEAP1 antigen binding protein of claim 92 or claim 93, wherein the dose of abiraterone is administered orally.
95. The anti-STEAP1 antigen binding protein of any one of claims 92-94, wherein the patient is administered about 5 mg of prednisone two times per day.
96. The anti-STEAP1 antigen binding protein of any one of claims 92-95, wherein the patient is administered about 10 mg of prednisone one time per day.
97. The anti-STEAP1 antigen binding protein of any one of claims 82-96, wherein the dose of the anti-STEAP1 antigen binding protein is about 0.75 mg to about 2.0 mg.

98. The anti-STEAP1 antigen binding protein of any one of claims 82-97, comprising administering to the patient a dose of a pharmaceutical composition comprising an anti-STEAP1 antigen binding protein at a dose of about 0.1 mg to about 2.0 mg, and wherein the method further comprises administering to the patient a dose of enzalutamide.
99. The anti-STEAP1 antigen binding protein of claim 98, wherein the dose of enzalutamide is about 160 mg.
100. The anti-STEAP1 antigen binding protein of claim 98 or claim 99, wherein the dose of enzalutamide is administered orally.
101. The anti-STEAP1 antigen binding protein of any one of claims 98-100, wherein the dose of anti-STEAP1 antigen binding protein is about 0.75mg to about 2.0 mg.
102. The anti-STEAP1 antigen binding protein of any one of claims 82-101, wherein the anti-STEAP1 antigen binding protein is first administered by step dosing.
103. The anti-STEAP1 antigen binding protein of claim 102, wherein the anti-STEAP1 antigen binding protein is administered by step dosing in two or three steps.
104. The anti-STEAP1 antigen binding protein of claim 103, wherein the anti-STEAP1 antigen binding protein is administered by step dosing on day 1 at 0.1mg, day 8 at 0.3mg, day 15 at 1.0mg, and day 22 at 1.5mg.
105. The anti-STEAP1 antigen binding protein of claim 103, wherein the anti-STEAP1 antigen binding protein is administered by step dosing on day 1 at 0.1mg, day 8 at 0.3mg, day 15 at 0.75mg, and day 22 at 0.75mg.
106. The anti-STEAP1 antigen binding protein of any one of claims 102-105, further comprising administering the anti-STEAP1 antigen binding protein to the patient once per week, once per two weeks, once per three weeks, or once per four weeks after administration of the step dosing.
107. The anti-STEAP1 antigen binding protein of any one of claims 82-106, wherein the anti-STEAP1 antigen binding protein comprises two Fab binding domains, each Fab binding domain binds STEAP1, and each Fab binding domain comprises a variable heavy domain, a variable light domain, a CH1 domain, and a constant light domain, the variable heavy domain comprises HCDR1 comprising SEQ ID NO: 9, HCDR2 comprising SEQ ID NO: 10, and HCDR3 comprising SEQ ID NO: 11; and the variable light domain

comprises LCDR1 comprising SEQ ID NO: 12, LCDR2 comprising SEQ ID NO: 13, and LCDR3 comprising SEQ ID NO: 14.

108. The anti-STEAP1 antigen binding protein of any one of claims 82-107, wherein the anti-STEAP1 antigen binding protein is an XmAb® 2+1 molecule comprises two Fab domains, each binding STEAP1, and one scFv domain that binds CD3.

109. The anti-STEAP1 antigen binding protein of any one of claims 82-108, wherein the anti-STEAP1 antigen binding protein comprises two Fab binding domains, each Fab binding domain binds STEAP1.

110. The anti-STEAP1 antigen binding protein of any one of claims 82-109, wherein the anti-STEAP1 antigen binding protein comprises two Fab binding domains, each Fab binding domain binds STEAP1, and each Fab binding domain comprises a variable heavy domain, a variable light domain, a CH1 domain, and a constant light domain, which variable heavy domain comprises HCDR1 comprising SEQ ID NO: 9, HCDR2 comprising SEQ ID NO: 10, and HCDR3 comprising SEQ ID NO: 11; and the variable light domain comprises LCDR1 comprising SEQ ID NO: 12, LCDR2 comprising SEQ ID NO: 13, and LCDR3 comprising SEQ ID NO: 14.

111. The anti-STEAP1 antigen binding protein of any one of claims 82-110, wherein the anti-STEAP1 antigen binding protein comprises an scFv binding domain that binds CD3.

112. The anti-STEAP1 antigen binding protein of any one of claims 82-111, wherein the anti-STEAP1 antigen binding protein comprises an scFv binding domain that binds CD3, and the scFv variable heavy domain comprises HCDR1 comprising SEQ ID NO: 1, HCDR2 comprising SEQ ID NO: 2, and HCDR3 comprising SEQ ID NO: 3; an scFv linker; and an scFv variable light domain, which scFv variable light domain comprises LCDR1 comprising SEQ ID NO: 4, LCDR2 comprising SEQ ID NO:5, and LCDR3 comprising SEQ ID NO: 6.

113. The anti-STEAP1 antigen binding protein of any one of claims 82-112, wherein the anti-STEAP1 antigen binding protein comprises a first Fc domain and a second Fc domain.

114. The anti-STEAP1 antigen binding protein of any one of claims 111-113, wherein each Fab variable heavy domain comprises an amino acid sequence at least 90% identical to SEQ ID NO: 15; each Fab variable light domain comprises an amino acid sequence at least 90% identical to SEQ ID NO: 16; and the scFv variable heavy domain comprises an

amino acid sequence at least 90% identical to SEQ ID NO:7; and the scFv variable light domain comprises an amino acid sequence at least 90% identical to SEQ ID NO: 8.

115. The anti-STEAP1 antigen binding protein of any one of claims 111-114, wherein each Fab variable heavy domain comprises SEQ ID NO: 15; each Fab variable light domain comprises SEQ ID NO: 16; the scFv variable heavy domain comprises SEQ ID NO:7; and the scFv variable light domain comprises SEQ ID NO: 8.
116. The anti-STEAP1 antigen binding protein of any one of claims 111-115, wherein the scFv binding domain which binds CD3 comprises an scFv linker.
117. The anti-STEAP1 antigen binding protein of any one of claims 111-116, wherein the first Fc domain comprises amino acid substitutions E233P, L235V, G236A, S267K, R292C, N297G, V302C, E357Q, and S364K; and the second Fc domain comprises amino acid substitutions N208D, E233P, L235V, G236A, S267K, R292C, Q295E, N297G, V302C, L368D, K370S, N384D, Q418E, and N421D.
118. The anti-STEAP1 antigen binding protein of any one of claims 111-116, wherein the first Fc domain and the second Fc domain each comprise a deletion at position 234.
119. The anti-STEAP1 antigen binding protein of any one of claims 82-118, wherein the anti-STEAP1 antigen binding protein comprises a HC comprising SEQ ID NO: 17, a HC with inserted CD3 scFv comprising SEQ ID NO: 19, and two light chains, each comprising SEQ ID NO: 18.
120. The anti-STEAP1 antigen binding protein of any one of claims 82-119, wherein the anti-STEAP1 antigen binding protein is xaluritamig.
121. The anti-STEAP1 antigen binding protein of any one of claims 82-120, wherein the patient has metastatic castration-resistant prostate cancer.