BC Cancer Protocol Summary for treatment of Metastatic Castration Resistant Prostate Cancer using Lutetium (^{177}Lu) Vipivotide Tetraxetan (PLUVICTO)

Protocol Code	*UGUPLVT*
Tumour Group	*Genitourinary*
Contact Physician	*GU Systemic Therapy*

ELIGIBILITY:

Patients must have:

- Metastatic castration-resistant prostate cancer
- Progressed on an androgen receptor pathway inhibitor, and at least one prior taxane-based chemotherapy regimen, in either metastatic castration-sensitive or castration-resistant setting
- Patients must have at least one prostate specific membrane antigen (PSMA) positive lesion and no PSMA-negative lesions identified on PSMA-PET scan within the last 6 months defined as:
    - All lymph nodes ≥ 2.5 cm in short axis must be 68Ga- PSMA-11 positive.
    - All bone metastases with soft tissue component ≥ 1.0 cm in short axis must be 68Ga-PSMA-11 positive
    - All solid organ metastases ≥ 1.0 cm in short axis must be 68Ga-PSMA-11 positive
- A BC Cancer Compassionate Access Program (CAP) request with appropriate clinical information for each patient must be approved prior to treatment

Patients should have:

- ECOG 0 to 2
- Life expectancy greater than 6 months
- Adequate marrow reserve, renal and hepatic function

Note:

- ^{177}Lu vipivotide tetraxetan (PLUVICTO) must be administered under the supervision of a physician and personnel qualified for administration of radiopharmaceuticals and performed in a facility with valid Canadian Nuclear Safety Commission license for administration of therapeutic ^{177}Lu.
- Use in combination with anticancer therapies other than androgen-deprivation therapy (ADT) will not be funded
- Re-treatment will not be funded

EXCLUSIONS:
Patients must not have:
- Active and/or untreated central nervous system metastases
- Active epidural disease or untreated symptomatic spinal cord compression

TESTS:
- Baseline: CBC & Diff, creatinine, albumin, total bilirubin, ALT, alkaline phosphatase, PSA, testosterone, PSMA-PET
- Prior to each treatment and every 3 weeks: CBC & Diff, creatinine, albumin, total bilirubin, ALT, alkaline phosphatase
- Prior to each treatment: PSA
- If clinically indicated: calcium, sodium, potassium
- Optional: weekly nursing assessment

PREMEDICATIONS:
- Optional: ondansetron 8 mg PO or IV 30 minutes prior to therapy
- Optional: dexamethasone 8 to 12 mg PO or IV 30 minutes prior to therapy

TREATMENT:

Drug	Dose	BC Cancer Administration Guideline
^{177}Lu vipivotide tetraxetan (PLUVICTO)	7.4 GBq/200mCi every 6 weeks	Slow IV push within 1 to 10 minutes* This agent will be administered in an appropriately shielded room under the supervision of a physician and personnel qualified for administration of radiopharmaceuticals.** The infusion must be performed in a facility with valid Canadian Nuclear Safety Commission license for administration of therapeutic ^{177}Lu.

*Prior to administration, flush the intravenous catheter used exclusively for ^{177}Lu vipivotide tetraxetan (PLUVICTO) administration with at least 10 mL of 0.9% sterile sodium chloride solution to assess catheter patency and minimize extravasation risk. Following administration, flush the line with at least 10 mL of 0.9% sterile sodium chloride solution.
***Patient must be kept in **radiation isolation** following administration **and until discharged from the treatment facility.** To be discharged, patient must have a measured dose rate of less than 64 microSv/hr at 1 meter distance.
- Repeat every 6 weeks to a maximum of 6 doses, unless disease progression or unacceptable toxicity.
- Patients with adverse effects related to treatment can extend the dosing interval to 10 weeks between treatments for recovery.

POST-HYDRATION:
- Optional: 500 mL of NS may be infused at a rate of 125 mL/hour after administration of ^{177}Lu vipivotide tetraxetan (PLUVICTO).

DOSE MODIFICATIONS:

- Management of adverse reactions may require temporary dose interruption (extending the dosing interval by up to 4 weeks, from 6 weeks up to 10 weeks), dose reduction or permanent discontinuation of treatment.
- If a treatment delay due to an adverse reaction persists for more than 4 weeks, consider treatment discontinuation at the discretion of treating clinician.
- The dose may be reduced by 20% once and may not be re-escalated. If a patient has further adverse reactions that would require an additional dose reduction, treatment must be discontinued.

1. Hematologic Toxicity:

Grade	ANC ($x10^9$/L)		Platelets ($x10^9$/L)		Hemoglobin (g/L)	Management
1	Greater than or equal to 1.5	and	Greater than or equal to 75	and	Greater than or equal to 100	100% dose: 7.4 GBq (200 mCi)
2	1.0 to less than 1.5	or	50 to less than 75	or	80 to less than 100	• Hold treatment until improvement to Grade 1 or baseline • Perform weekly CBC • Manage as deemed appropriate • Use of growth factors may be considered but should be discontinued once improved to Grade 1 or baseline • Consider checking iron, B12 and folate levels • Consider transfusion if indicated
3 or 4 (first occurrence)	Less than 1.0	or	Less than 50	or	Less than 50 or life-threatening consequences	• Hold treatment until improvement to Grade 1 or baseline • Perform weekly CBC & Diff • Once resolved, restart treatment and reduce dose by 20% to 5.9 GBq (160mCi)
3 or 4 (second occurrence)	Less than 1.0	or	Less than 50	or	Less than 50 or life-threatening consequences	Permanently discontinue

2. **Hepatic Toxicity:** If ALT rises above 5 x ULN in the absence of liver metastases, permanently discontinue ^{177}Lu vipivotide tetraxetan (PLUVICTO).

3. **Renal Toxicity:**

Serum creatinine		Creatinine Clearance (CrCl)	Management
Less than 1.4 x baseline	and	Greater than or equal to 30 mL/min AND less than 40% decrease from baseline	• 100% dose: 7.4 GBq (200 mCi)
Greater than or equal to 1.4 x baseline (first occurrence)	and	40% or higher decrease from baseline (first occurrence)	• Hold treatment until improvement • Once resolved, restart treatment and reduce dose by 20% to 5.9 GBq (160mCi)
Greater than or equal to 1.4 x baseline (second occurrence)	and	40% or higher decrease from baseline (second occurrence)	• Permanently discontinue

4. **Other Toxicity:**

Toxicity	Severity	Management
Dry mouth	Grade 3	• Reduce dose by 20% to 5.9 GBq (160 mCi).
Gastrointestinal toxicity	Grade 3 or 4 (not amenable to medical intervention)	• Hold treatment until improvement to Grade 2 or baseline. • Once resolved, restart treatment and reduce dose by 20% to 5.9 GBq (160mCi)
Spinal cord compression	Any	• Hold treatment until the compression has been adequately treated and any neurological sequela have stabilized and performance status has stabilized.
Fracture in weight-bearing bones	Any	• Hold treatment until the fracture has been adequately stabilized/treated and performance status has stabilized.

PRECAUTIONS:

1. **Prevention of extravasation** is essential, and the IV-line patency must be tested prior to administration of ^{177}Lu vipivotide tetraxetan (PLUVICTO). Rapid intervention must be implemented if extravasation occurs, per institutional guidelines. If local swelling and pain at the injection site occurs, the infusion must be stopped immediately and the infusion site must be treated with warm packs, compression and elevation. Exercise to increase blood flow to the affected limb may also be useful to reduce the local dose. Infiltration must be reported to the radiation safety officer and nuclear medicine physician for monitoring and calculation of skin dose.
2. **Myelosuppression:** can occur in patients treated with ^{177}Lu vipivotide tetraxetan (PLUVICTO), including anemia, thrombocytopenia, leukopenia, neutropenia, and pancytopenia. Cases of severe and life-threatening myelosuppression have been reported. Monitor patients closely and manage as deemed appropriate based on the severity of myelosuppression. Dose reduction, treatment interruption or permanent treatment discontinuation may be required.
3. **Renal toxicity:** can occur in patients treated with ^{177}Lu vipivotide tetraxetan (PLUVICTO). Cases of severe renal injury have been reported. Patients should be encouraged to increase oral fluid intake and void as often as possible. No dose adjustment is recommended for patients with moderate impairment (CrCl 30 to 59 mL/min) however patients may be at greater risk of toxicity. ^{177}Lu vipivotide tetraxetan (PLUVICTO) has not been studied in patient with severe remain impairment (CrCl less than 29 mL/min) or end-stage renal disease.
4. The room must be monitored for radioactivity contamination after each treatment by qualified nuclear medicine personnel under the supervision of a medical physicist.
5. **Dry mouth:** can occur in patients treated with ^{177}Lu vipivotide tetraxetan (PLUVICTO). This may be managed with sodium bicarbonate mouth rinse, Biotene mouth rinse, xylitol lozenges or gum and frequent fluid intake. Dose reduction, treatment interruption or permanent treatment discontinuation may be required.

Call the GU Systemic Therapy physician at your regional cancer centre or contact Dr. Maryam Soleimani (Medical Oncology), Dr. Scott Tyldesley (Radiation Oncology) or Dr. Don Wilson (Nuclear Medicine) at (604) 877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.

References:

1. Sartor O, de Bono J, Kim NC et al; VISION investigators. Lutetium-177–PSMA-617 for Metastatic Castration-Resistant Prostate Cancer. N Engl J Med. 2021 Sep 16;385(12):1091-1103.
2. Hofman SM, Emmett L, Sandhu S et al; TheraP Trial Investigators and the Australian and New Zealand Urogenital and Prostate Cancer Trials Group. Overall Survival with [^{177}Lu]Lu-PSMA-617 versus Cabazitaxel in Metastatic Castration-Resistant Prostate Cancer (TheraP): Secondary Outcomes of a Randomised, Open-Label, Phase 2 Trial. Lancet Oncol. 2024 Jan;25(1):99-107.
3. Lutetium (177LU) Vipivotide Tetraxetan (Pluvicto) CADTH [Canada's Drug Agency (CDA-AMC)] Reimbursement Recommendation. Canadian Journal of Health Technologies Mar 2023; 3(3): 1-26.