POSLUMA®
flotufolastat F 18 injection

Patient Benefit Investigation Form

Phone: 1-855-495-9200 | Fax: 1-877-309-7514 | Email: reimbursement@blueearthdx.com

REQUESTED SERVICE

☐ Benefit investigation only
☐ Prior authorization assistance
☐ Appeal/denial assistance

The following information should be filled out by your healthcare provider

HCPCS: ☐ A9608 POSLUMA (flotufolastat F 18) Injection

CPT® codes: ☐ 78815 ☐ Other: _____

☐ **Diagnosis code C61**
☐ **Diagnosis code Z85.46**
☐ **Diagnosis code R97.21**
☐ Other: _____
☐ **Diagnosis code R97.20**
☐ **Diagnosis code Z19.1**
☐ **Diagnosis code Z19.2**

For new diagnosis of prostate cancer: (please select the risk group that best describes the patient's condition)

☐ **Unfavorable Intermediate** ☐ **High** ☐ **Very High**

Suspicion of recurrent disease after previously treated prostate cancer: ☐ Yes ☐ No

Suspected recurrence based on:

Elevated PSA levels: _____

Prior studies/treatment: _____

Radical prostatectomy ☐ Yes ☐ No Date: _____

Radiation therapy to prostate ☐ Yes ☐ No Date: _____

Other treatments: _____ Date: _____

Previous imaging studies: ☐ CT ☐ MRI ☐ Bone scan
☐ Other: _____

I verify that the patient and physician information contained in this enrollment form is complete and accurate to the best of my knowledge and that I have prescribed POSLUMA based on my professional, independent judgment of medical necessity and it will be used as directed. I certify that I have received the appropriate permission from the patient and met any other applicable requirements imposed under the Health Insurance Portability and Accountability Act of 1996 and/or state law needed to release the above information to Blue Earth Diagnostics and its agents for the purposes of verifying the patient's insurance coverage, on my patient's behalf, and providing information on prior authorization and/or appeals for denials of claims. I authorize the Reimbursement Support Helpline Program to perform a preliminary assessment of insurance and benefit investigation for the above-named patient, and I further authorize and request that the Program provide to me information regarding POSLUMA for my reference in completing documentation as may be required by the patient's health plan. I further authorize POSLUMA Reimbursement Support to submit, at my request, information provided by me on this form and documentation completed by me to applicable health plans.

Prescriber signature required (no stamps) Date

PATIENT DEMOGRAPHIC INFORMATION

First name_____ MI _____
Last name _____
Address _____
City_____ State_____ ZIP _____
Mobile phone #_____ Last 4 of SSN_____
Email_____ DOB_____
Primary insurance_____
Policy holder_____ Group # _____
Policy #_____Phone # _____
Secondary insurance_____
Policy holder_____ Group # _____
Policy #_____Phone # _____

NOTE: Copy of insurance card(s) acceptable in lieu of completing insurance information above. Please include both sides of card.

REFERRING PHYSICIAN INFORMATION

Physician name _____
Physician specialty_____
Practice name _____
Practice address _____
City_____ State_____ ZIP _____
TIN #_____ Medicare PTAN_____
NPI # _____
Contact person _____
Contact phone #_____ Fax # _____
Contact email _____

SITE OF POSLUMA PET/CT SCAN

☐ Hospital outpatient ☐ Physician practice
☐ Independent diagnostic testing facility
☐ Other: _____
Name of facility _____
TIN #_____ Medicare PTAN_____
NPI # _____
Facility contact name _____
Facility contact phone # _____
Facility contact email_____

BLUE EARTH DIAGNOSTICS
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BEDPRC24-0003 01/24

POSLUMA®
flotufolastat F 18 injection

Patient Benefit Investigation Form

PATIENT AUTHORIZATION TO SHARE HEALTH INFORMATION

I understand that I must authorize the use and disclosure of certain personal health information ("PHI") before I can receive assistance through the Reimbursement Support Helpline Program (the "Program"). I hereby authorize my healthcare providers, pharmacies, and health plan(s) to disclose my PHI related to my medical condition and treatment, and all information provided on this patient enrollment form, to Blue Earth Diagnostics, the manufacturer of POSLUMA, and to its agents and the administrator of the Program (collectively, the "Recipients"). I further authorize the Recipients to use and disclose my PHI for the purposes of establishing my eligibility for benefits from my health plan or other programs, providing educational and reimbursement support, communicating with my healthcare providers and health plan(s), and for Blue Earth Diagnostics' internal business purposes, including quality control and compliance. I understand that signing this authorization is voluntary and that if I were to refuse to sign, that would not affect my eligibility for health plan benefits or ability to obtain treatment by my healthcare providers. I also understand, however, that if I refuse to sign, I will not have access to the services offered by the Program. I also understand that if I sign this authorization, I can cancel it at any time by notifying Blue Earth Diagnostics in writing at reimbursement@blueearthdx.com. Upon receiving my notice of cancellation, Blue Earth Diagnostics would stop using this authorization to access, use, or disclose my PHI, and would notify my healthcare providers and health plan(s) of the cancellation, but the cancellation would not invalidate reliance on the authorization prior to its cancellation. I understand that once disclosures of my PHI pursuant to this authorization have occurred, that PHI may no longer be protected by certain federal or state privacy laws and therefore could potentially be re-disclosed to others.

This authorization will expire 5 years after the date it is signed below or at such earlier time as may be required by applicable state law. I have read this authorization or have had it explained to me. I understand that I will receive a copy of this authorization after I sign it.

Patient signature _____ Date _____

Printed name _____

Abbreviations: CPT, current procedural terminology; HCPCS, Healthcare Common Procedure Coding System.

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HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use POSLUMA® safely and effectively. See full prescribing information for POSLUMA.

POSLUMA (flotufolastat F 18) injection, for intravenous use
Initial U.S. Approval: 2023

----------INDICATIONS AND USAGE----------
POSLUMA is a radioactive diagnostic agent indicated for positron emission tomography (PET) of prostate-specific membrane antigen (PSMA) positive lesions in men with prostate cancer:
- with suspected metastasis who are candidates for initial definitive therapy
- with suspected recurrence based on elevated serum prostate-specific antigen (PSA) level. (1)

----------DOSAGE AND ADMINISTRATION----------
- Recommended amount of radioactivity of POSLUMA is 296 MBq (8 mCi) administered as an intravenous bolus injection. (2.2)
- Initiate imaging approximately 60 minutes after administration. Scanning should start from mid-thigh and proceed to base of skull. (2.4)
- See full prescribing information for additional preparation, handling, administration, imaging, and radiation dosimetry information. (2.3, 2.4)

----------DOSAGE FORMS AND STRENGTHS----------
Injection: 296 MBq/mL to 5,846 MBq/mL (8 mCi/mL to 158 mCi/mL) as flotufolastat F 18 gallium in approximately 25 mL at end of synthesis in a multiple-dose vial. (3)

----------CONTRAINDICATIONS----------
None. (4)

----------WARNINGS AND PRECAUTIONS----------
- Risk of Image Misinterpretation: Image interpretation errors can occur with POSLUMA imaging. Interpretation of POSLUMA PET may differ depending on imaging readers in patients with suspected recurrence of prostate cancer. Consider multidisciplinary consultation and histopathological confirmation. (5.1, 14.2)
- Radiation risk: POSLUMA contributes to a patient's long-term cumulative radiation exposure. Ensure safe handling to protect patients and health care workers from unintentional radiation exposure. (2.1, 5.2)

----------ADVERSE REACTIONS----------
The most common adverse reactions (≥0.4%) are diarrhea, blood pressure increase, and injection site pain. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Blue Earth Diagnostics Ltd at 1-844-POSLUMA (1-844-767-5862) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION

Revised: 5/2023

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

POSLUMA is indicated for positron emission tomography (PET) of prostate-specific membrane antigen (PSMA) positive lesions in men with prostate cancer

- with suspected metastasis who are candidates for initial definitive therapy.
- with suspected recurrence based on elevated serum prostate-specific antigen (PSA) level.

2 DOSAGE AND ADMINISTRATION

2.1 Radiation Safety - Drug Handling

Handle POSLUMA with safety measures to minimize radiation exposure *[*see *Warnings and Precautions (5.2)]*. Use waterproof gloves, effective radiation shielding, including syringe shields, and other appropriate safety measures when handling and administering POSLUMA.

Radiopharmaceuticals should be used by or under the control of physicians who are qualified by specific training and experience in the safe use and handling of radionuclides, and whose experience and training have been approved by the appropriate governmental agency authorized to license the use of radionuclides.

2.2 Recommended Dose and Administration Instructions

Recommended Dose

The recommended amount of radioactivity to be administered in adults is 296 MBq (8 mCi) as an intravenous bolus injection.

Preparation and Administration Instructions

- Inspect POSLUMA visually for particulate matter and discoloration before administration. Do not use the drug if the solution contains particulate matter or is discolored.
- Use aseptic technique and radiation shielding when withdrawing and administering POSLUMA.
- Calculate the necessary volume to administer based on calibration time and required dose.
- The recommended maximum volume of undiluted POSLUMA is 5 mL.
- POSLUMA may be diluted with 0.9% Sodium Chloride Injection, USP.
- Assay the dose in a dose calibrator before administration.

Post Administration Instructions

- After the POSLUMA injection, administer an intravenous flush of sterile 0.9% Sodium Chloride Injection, USP to ensure full delivery of the dose.
- Dispose of any unused drug in a safe manner in compliance with applicable regulations.

2.3 Patient Preparation

Instruct patients to drink water prior to administration of POSLUMA to ensure adequate hydration and to continue drinking and voiding frequently for the first few hours following administration to reduce radiation exposure.

2.4 Image Acquisition

- Patients should void immediately prior to imaging.
- Position the patient supine with arms above the head.
- Begin image acquisition approximately 60 minutes after POSLUMA injection.
- Image acquisition should start from mid-thigh and proceed to the base of the skull.
- Scan duration is approximately 20 minutes depending on the number of bed positions and acquisition time per bed position (typically 3 minutes). Adapt imaging technique according to the equipment used and patient characteristics in order to obtain the best image quality possible.

2.5 Image Display and Interpretation

POSLUMA binds to PSMA. PET images obtained using POSLUMA indicate the presence of PSMA in tissues *[see Clinical Pharmacology (12.1)]*. Lesions should be considered suspicious if uptake is greater than physiologic uptake in that tissue or greater than adjacent background if no physiologic uptake is expected. Tumors that do not express PSMA will not be visualized. Increased uptake in tumors is not specific for prostate cancer *[see Warnings and Precautions (5.1)]*.

2.6 Radiation Dosimetry

Estimated absorbed radiation doses for adult patients following intravenous injection of POSLUMA are shown in Table 1. The effective radiation dose resulting from the administration of the recommended activity of 296 MBq of POSLUMA is 4.1 mSv. The radiation absorbed doses to the critical organs of adrenal glands, kidneys, and submandibular glands for the recommended activity of 296 MBq are 54.3 mGy, 51 mGy, and 43.8 mGy, respectively. When PET/CT is performed, exposure to radiation will increase by an amount dependent on the settings used in the CT acquisition.

Table 1: Estimated Radiation Absorbed Doses in Organs/Tissues in Adults who Received POSLUMA

Organ/Tissue	Absorbed Dose per Unit Administered Activity (mGy/MBq)
	Mean
Adrenal glands	0.184
Brain	0.002
Breasts	0.004
Gallbladder wall	0.017
Lower large intestine wall	0.007
Upper large intestine wall	0.01
Heart wall	0.02
Kidneys	0.172
Lacrimal glands	0.08*
Liver	0.062
Lungs	0.01

Muscle	0.006
Osteogenic cells	0.012
Ovaries	0.005
Pancreas	0.028
Parotid glands	0.114*
Red bone marrow	0.01
Skin	0.002
Small intestine	0.012
Spleen	0.083
Stomach wall	0.012
Sublingual glands	0.065*
Submandibular glands	0.148*
Testes	0.005
Thymus gland	0.01
Thyroid	0.01
Urinary bladder wall	0.006**
Uterus	0.011
Effective dose (mSv/MBq)	**0.014****

*The absorbed dose value reflects self-irradiation only; no dose contribution from other regions to the glands is added. **A 1-hour bladder voiding interval is assumed.

3 DOSAGE FORMS AND STRENGTHS

Injection: 296 MBq/mL to 5,846 MBq/mL (8 mCi/mL to 158 mCi/mL) as flotufolastat F 18 gallium in approximately 25 mL at end of synthesis supplied as a clear, colorless solution in a multiple-dose vial.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Risk of Image Misinterpretation

Image interpretation errors can occur with POSLUMA PET. A negative image does not rule out the presence of prostate cancer and a positive image does not confirm the presence of prostate cancer. The performance of POSLUMA for imaging metastatic pelvic lymph nodes in patients prior to initial definitive therapy seems to be affected by serum PSA levels and risk grouping *[See Clinical Studies (14.1)]*. The performance of POSLUMA for imaging patients with biochemical evidence of recurrence of prostate cancer seems to be affected by serum PSA levels *[See Clinical Studies (14.2)]*. Flotufolastat F 18 uptake is not specific for prostate cancer and may occur in other types of cancer, in non-malignant processes, and in normal tissues. Clinical correlation, which may include histopathological evaluation, is recommended.

Risk of Image Misinterpretation in Patients with Suspected Prostate Cancer Recurrence

The interpretation of POSLUMA PET may differ depending on imaging readers, particularly in the prostate/prostate bed region *[see Clinical Studies (14.2)]*. Because of the associated risk of false positive

interpretation, consider multidisciplinary consultation and histopathological confirmation when clinical decision-making hinges on flotufolastat F18 uptake only in the prostate/prostate bed region or only on uptake interpreted as borderline.

5.2 Radiation Risks

POSLUMA use contributes to a patient's overall long-term cumulative radiation exposure. Long-term cumulative radiation exposure is associated with an increased risk for cancer. Advise patients to hydrate before and after administration and to void frequently after administration. Ensure safe handling to minimize radiation exposure to the patient and health care providers *[see Dosage and Administration (2.1, 2.2)]*.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety of POSLUMA was evaluated in 747 patients with prostate cancer *[see Clinical Studies (14.1,14.2)]*. All patients received a single administration of POSLUMA with an administered radioactivity (mean ± SD) of 307 ± 23 MBq (8.3 ± 0.6 mCi). The mean age of patients was 67 years (range: 43 to 86 years); distribution by race was 78% White, 12% Black or African American, 2% other, and 7% unreported; and distribution by ethnicity was 5% Hispanic/Latino, 87% non-Hispanic/Latino, and 8% unreported.

The adverse reactions reported in ≥ 0.4% of patients are shown in Table 2.

Table 2: Adverse Reactions in ≥ 0.4% of Patients with Prostate Cancer Receiving POSLUMA

Adverse Reaction	**POSLUMA N = 747 n (%)**
Diarrhea	5 (0.7%)
Blood pressure increase	4 (0.5%)
Injection site pain	3 (0.4%)

7 DRUG INTERACTIONS

Androgen deprivation therapy (ADT) and other therapies targeting the androgen pathway, such as androgen receptor antagonists, can result in changes in uptake of flotufolastat F 18 in prostate cancer. The effect of these therapies on performance of POSLUMA PET has not been established.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

POSLUMA is not indicated for use in females. There are no available data on the use of POSLUMA in pregnant women to evaluate for a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. Animal reproduction studies have not been conducted with flotufolastat F 18. Radioactive drugs, including POSLUMA, have the potential to cause fetal harm depending on the fetal stage of development and the magnitude of the radiation dose.

8.2 Lactation

Risk Summary

POSLUMA is not indicated for use in females. There are no data on the presence of flotufolastat F 18 in human milk, the effect on the breastfed infant, or the effect on milk production.

8.4 Pediatric Use

The safety and effectiveness of POSLUMA have not been established in pediatric patients.

8.5 Geriatric Use

Among the total number of patients receiving POSLUMA in clinical studies of prostate cancer, 463 (62%) were 65 years of age and older, while 118 (16%) were 75 years of age and older *[see Clinical Studies (14.1,14.2)]*. No overall differences in safety or effectiveness were observed between these patients and younger adult patients.

10 OVERDOSAGE

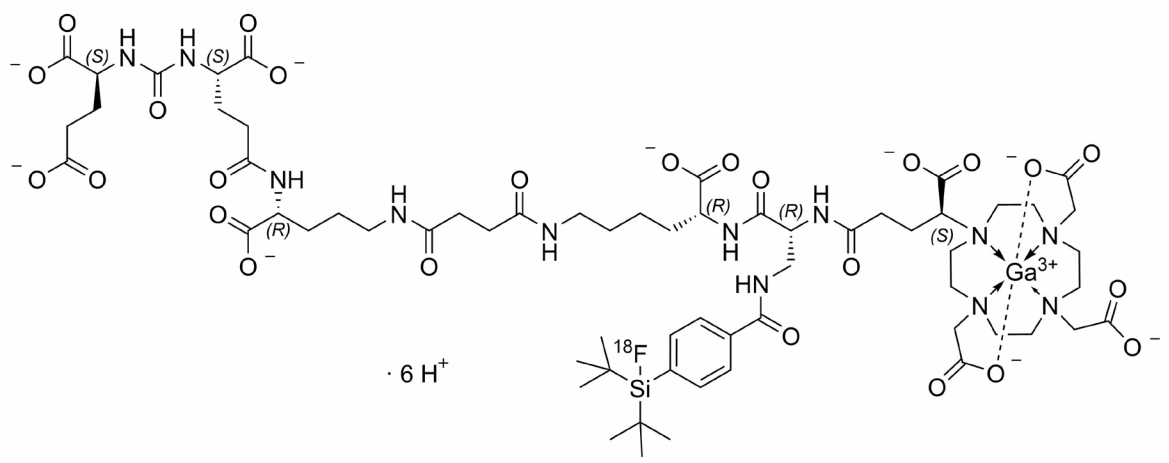
In the event of an overdose of POSLUMA, maintain hydration of the patient and frequent voiding to minimize radiation exposure. A diuretic might also be considered. If possible, an estimate of the radiation effective dose administered to the patient should be made.

11 DESCRIPTION

11.1 Chemical Characteristics

POSLUMA (flotufolastat F 18) injection is a radioactive diagnostic agent for intravenous use. The active ingredient of POSLUMA is flotufolastat F 18 gallium, of which the molecular structure includes a DOTAGA complex with nonradioactive gallium. Radioactive fluorine-18 is covalently bound to silicon.

Chemically, flotufolastat F 18 gallium is gallate(6-), [(4*S*,8*S*,13*R*,27*R*,30*R*,35*S*)-35-[4,10-bis[(carboxy-k*O*)methyl]-7-(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl-kN^1,kN^4,kN^7,kN^{10}]-30-[[[4-[bis(1,1-dimethylethyl)fluoro-^{18}F-silyl]benzoyl]amino]methyl]-1,36-dihydroxy-1,6,11,18,21,29,32,36-octaoxo-5,7,12,17,22,28,31-heptaazahexatriacontane-4,8,13,27-tetracarboxylato(9-)]-, hydrogen (1:6). The molecular weight is 1537.3 g/mol and the structural formula is:



POSLUMA is a sterile, non-pyrogenic, clear, colorless, and isotonic solution. Each mL contains up to 20 mcg of flotufolastat gallium, up to 5,846 MBq (158 mCi) as flotufolastat F 18 gallium at end of synthesis, and the following inactive ingredients: not more than 10% (v/v) alcohol, 1.9 mg anhydrous citric acid, 7.2 mg sodium chloride, and 0.75 mg sodium hydroxide to adjust pH between 4 and 6. POSLUMA contains no preservative.

11.2 Physical Characteristics

POSLUMA contains fluorine-18 (F 18) which is a cyclotron produced radionuclide that decays by positron emission (β+ decay, 96.7%) and orbital electron capture (3.3%) to stable oxygen-18 with a physical half-life of 109.8 minutes (Table 3). The principal photons useful for diagnostic imaging are the coincident pair of 511 keV gamma photons, resulting from the interaction of the emitted positron with an electron (Table 4).

Table 3: Physical Decay Chart for Fluorine-18

Minutes	Fraction Remaining
0	1
15	0.909
30	0.826
60	0.683
110	0.5
220	0.25

Table 4: Principal Radiation Produced from Decay of Fluorine-18

	Energy (keV)	Abundance (%)
Positron	249.8	96.7
Gamma	511	193.5

11.3 External Radiation

The point source air-kerma coefficient for F 18 is 3.75×10^{-17} Gy m^2/(Bq s). The first half-value thickness of lead (Pb) for F 18 gamma rays is approximately 6 mm. The relative reduction of radiation emitted by F 18 that results from various thicknesses of lead shielding is shown in Table 5. The use of 8 cm of Pb will decrease the radiation transmission (i.e., exposure) by a factor of about 10,000.

Table 5: Radiation Attenuation of 511 keV Gamma Rays by Lead Shielding

Shield Thickness cm of Lead (Pb)	Coefficient of Attenuation
0.6	0.5
2	0.1
4	0.01
6	0.001
8	0.0001

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of action

Flotufolastat F 18 binds to PSMA (IC50 = 4.4 nM) expressed on cells, including prostate cancer cells, and is internalized. Prostate cancer cells usually overexpress PSMA. Fluorine-18 is a ß+ emitting radionuclide that can be detected using positron emission tomography.

12.2 Pharmacodynamics

The relationship between flotufolastat F 18 plasma concentrations and image interpretation has not been fully characterized.

12.3 Pharmacokinetics

Distribution

Following intravenous administration, flotufolastat F 18 distributes to liver (15.8% of administered activity), heart blood pool (7.4%), and kidneys (3.2%) and is cleared from the blood.

Elimination

Metabolism

Flotufolastat F 18 does not undergo metabolism up to 50 minutes post injection.

Excretion

Elimination is by urinary excretion. Approximately 7% of the administered activity was excreted in the urine in the first 2 hours post-injection with approximately 15% excreted by 4.5 hours post-injection.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Animal studies to assess the carcinogenicity or mutagenic potential of flotufolastat have not been conducted. However, flotufolastat F 18 has the potential to be mutagenic because of the F 18 radionuclide.

No studies in animals have been performed to evaluate potential impairment of fertility in males or females.

14 CLINICAL STUDIES

14.1 Imaging Prior to Initial Definitive Therapy of Prostate Cancer

The safety and efficacy of POSLUMA were evaluated in LIGHTHOUSE (NCT04186819), a prospective, multicenter, open-label, single-arm study in patients with prostate cancer who were candidates for initial definitive therapy.

The study enrolled 356 patients diagnosed with unfavorable intermediate-risk (32%) or high-/very high-risk prostate cancer (68%) who were candidates for radical prostatectomy and pelvic lymph node dissection (PLND). Unfavorable intermediate-risk was defined as having any ≥ 2 intermediate risk factors [T2b-T2c, Gleason score 7, PSA 10-20], Gleason pattern 4+3=7, or ≥ 50% of biopsy cores positive for prostate cancer. High or very high-risk was defined as having T3 or T4 disease, Gleason score ≥8, primary Gleason pattern 5, and/or PSA >20.

All patients received a single dose of POSLUMA with an administered radioactivity (mean ± SD) of 307 ± 23 MBq (8.3 ± 0.62 mCi), followed by PET/CT scan from mid-thigh to base of the skull. Three central readers blinded to clinical information independently interpreted each scan for lesions considered positive for prostate cancer in pelvic lymph nodes, categorized by subregion and left and right laterality *[see Dosage and Administration (2.5)]*. Positive lesions in the prostate gland, lymph nodes outside the pelvis, soft tissue/parenchyma, and bones were also recorded.

A total of 296 patients (83%) underwent standard-of-care prostatectomy and template PLND and had sufficient histopathology data for evaluation of the pelvic lymph nodes. The mean age was 65 years (range 46 to 82 years); distribution by race was 82% White, 8% Black or African American, 0.3% other, and 10% unreported; and distribution by ethnicity was 5% Hispanic/Latino, 86% non-Hispanic/Latino, and 9% unreported. The median serum PSA was 8.4 ng/mL. The total Gleason score was 7 for 45%, 8 for 26%, and 9 for 25% of the patients, with the remainder of the patients having Gleason scores of 6 or 10. Approximately 24% of patients had pelvic lymph node metastases based on histopathology.

POSLUMA performance was evaluated against histopathology after matching by hemipelvis. Table 6 shows the results, such that at least one true positive hemipelvis region defined a true positive patient.

Table 6: Patient-Level, Hemipelvis Region-Matched Performance of POSLUMA PET for Detection of Pelvic Lymph Node Metastasis (N1) in LIGHTHOUSE

N=296	Reader 1	Reader 2	Reader 3
True Positive	21	19	16

False Positive	16	14	7
True Negative	210	212	219
False Negative	49	51	54
Sensitivity, (%) [95% CI]	30% [20, 42]	27% [17, 39]	23% [14, 35]
Specificity, (%) [95% CI]	93% [89, 96]	94% [90, 97]	97% [94, 99]
Positive Predictive Value, (%) [95% CI]	57% [40, 73]	58% [39, 75]	70% [47, 87]
Negative Predictive Value, (%) [95% CI]	81% [76, 86]	81% [75, 85]	80% [75, 85]

CI= confidence interval

In exploratory analyses, there were numerical trends towards higher sensitivity among patients with PSA greater than or equal to the median value (8.4 ng/mL) and among patients with high-risk or very high-risk categorization.

POSLUMA-positive lesions outside of the prostate gland and pelvic lymph nodes (M1) were also evaluated. As a percentage of the 352 patients with an evaluable POSLUMA scan and of the 61 patients with at least one POSLUMA positive M1 lesion, 10% (95% CI: 7% to 13%) and 56% (95% CI: 42% to 68%), respectively, had at least one matching positive M1 lesion between the POSLUMA majority read and a reference standard consisting of other imaging evaluated by a separate consensus panel or histopathology.

14.2 Imaging for Suspected Recurrence of Prostate Cancer

The safety and efficacy of POSLUMA were evaluated in SPOTLIGHT (NCT04186845), a prospective, multicenter, open-label, single-arm study in patients with biochemical evidence of recurrent prostate cancer.

The study enrolled 391 patients with suspected recurrence defined by either serum PSA of at least 0.2 ng/mL after radical prostatectomy (with confirmatory PSA level also at least 0.2 ng/mL) or by an increase in serum PSA of at least 2 ng/mL above the nadir after other therapies.

All patients received a single dose of POSLUMA with an administered radioactivity (mean ± SD) of 306 ± 22 MBq (8.27 ±0.61 mCi), followed by PET/CT scan from mid-thigh to base of the skull. Three central readers blinded to clinical information independently interpreted each scan by region for the presence and location of lesions considered positive for prostate cancer *[see Dosage and Administration (2.5)]*. The regions interpreted were grouped into three for primary analysis: prostate/prostate bed; pelvic lymph nodes; and other (including extra-pelvic lymph nodes, bone, and soft tissue/parenchyma).

A total of 389 patients had an evaluable POSLUMA PET scan. The mean age was 68 years (range: 43 to 86 years); distribution by race was 75% White, 16% Black or African American, 4% other, and 5% unreported; and distribution by ethnicity 5% was Hispanic/Latino, 87% non-Hispanic/Latino, and 8% unreported. The median baseline serum PSA level was 1.1 ng/mL with 60% of patients having a baseline PSA <2.0 ng/mL. Prior treatment included radical prostatectomy in 79% of the patients.

POSLUMA-positive interpretations were compared to a reference standard of either histopathology or other imaging (CT, MRI, Technetium 99m bone scan, or fluciclovine F 18 PET) obtained within 90 days

of the POSLUMA scan using a lesion-to-lesion co-localization method and separate consensus panel. Reference standard information for negative interpretations was not collected.

At least one POSLUMA-positive lesion was detected by at least one reader in 366 patients (94%). Reference standard information consisted of imaging only (n=297) or histopathology (n=69). As a percentage of patients with an evaluable scan, 51% (95% CI: 46% to 56%) for reader 1, 48% (95% CI: 43% to 53%) for reader 2, and 49% (95% CI: 44% to 54%) for reader 3 had at least one matching positive region between the POSLUMA scan and the reference standard. Of all POSLUMA-positive regions, 46% (95% CI: 42% to 50%) for reader 1, 60% (95% CI: 55% to 66%) for reader 2, and 53% (95% CI: 48% to 58%) for reader 3 were categorized as positive by the reference standard.

Table 7 shows patient-level results from the majority read stratified by serum PSA level. Percent PET positivity was calculated as the percentage of patients with POSLUMA-positive lesions out of all patients with an evaluable PET scan. Percent PET positivity includes true and false positives and is not a measure of diagnostic performance.

Table 7: Patient-Level POSLUMA PET Results and Percent PET Positivity Stratified by Serum PSA Level in SPOTLIGHT by Majority Read (N=389)

PSA (ng/mL)	N	PET Positive Patients					PET Negative Patients	Percent PET Positivity [95% CI]
		Total	Histopathology		Imaging only[a]			
			PA	NPA	PA	NPA		
< 0.5	121	77	6	4	27	40	44	64% [54,72]
≥ 0.5 and < 1	67	51	7	3	24	17	16	76% [64,86]
≥ 1 and < 2	45	42	10	2	18	12	3	93% [82, 99]
≥ 2	156	152	33	3	84	32	4	97% [94, 99]
Total	389	322	56	12	153	101	67	83% [79, 86]

PSA = prostate-specific antigen, PA = positive agreement, NPA = no positive agreement, CI = confidence interval
[a]Imaging comprised of one or more of the following: CT, MRI, ^{99m}Tc Bone Scan, fluciclovine F 18 PET

Variable Interpretation in Patients with Suspected Prostate Cancer Recurrence

POSLUMA reader agreement was evaluated for the three central readers and 389 patients. Inter-reader Fleiss κ was 0.41 (95% CI: 0.39-0.43). The three readers agreed on the presence or absence of positive lesions across all five evaluated regions in 118 patients (30% unanimity) *[see Warning and Precautions (5.1)]*.

Given the level of inter-reader agreement observed overall, POSLUMA reader agreement was further evaluated by regional subgroup. The Fleiss κ for was 0.40 (95% CI: 0.33-0.46) in the prostate/prostate bed, 0.73 (95% CI: 0.67-0.78) in the pelvic lymph nodes, and 0.62 (95% CI: 0.58-0.65) across the other regions.

16 HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

POSLUMA injection is supplied as a clear, colorless solution in a multiple-dose glass vial (NDC 69932-002-50) containing 296 MBq/mL to 5,846 MBq/mL (8 mCi/mL to 158 mCi/mL) as flotufolastat F 18 gallium in approximately 25 mL at end of synthesis.

Storage and Handling

Store POSLUMA at 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature]. Store POSLUMA in the original container in radiation shielding. The expiration date and time are provided on the container label. Use POSLUMA within 10 hours from end of synthesis.

Dispose of unused POSLUMA in compliance with applicable regulations.

This preparation is approved for use by persons under license by the Nuclear Regulatory Commission or the relevant regulatory authority of an Agreement State.

17 PATIENT COUNSELING INFORMATION

Adequate Hydration

Instruct patients to drink a sufficient amount of water to ensure adequate hydration before their PET study and urge them to drink and urinate as often as possible during the first hours following the administration of POSLUMA, in order to reduce radiation exposure *[see Dosage and Administration (2.3) and Warnings and Precautions (5.2)]*.

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