POSLUMA®(flotufolastat F 18) injection

Disease State Overview and Unmet Clinical Need

In 2023, an estimated 288,300 American men will be diagnosed with prostate cancer, making it the most commonly diagnosed non-cutaneous neoplasm in men in the US. The average age at diagnosis is 66 years, and the age-adjusted incidence rate is 1 case per 8 men per year with 6 of 10 new cases occurring in men older than age 65. The American Cancer Society estimates that 34,700 men will die as a result of prostate cancer in 2023.[1] These statistics demonstrate the need for continued advances in prostate cancer diagnosis and therapy. Given this impact on the healthcare system, the importance of successful diagnosis, staging and treatment of this disease cannot be overstated.

For patients at the time of diagnosis of clinically localized disease, imaging is important in treatment planning and prognostication, and may reduce the risk of undertreatment leading to disease spread and overtreatment leading to unnecessary toxicity or surgery. Conventional imaging, which has limited performance for identifying metastatic disease, results in an underestimation of true disease burden.[2] And while bone scans and CT scans can detect bone metastases, specificity and sensitivity is limited for early lesion detection. CT scans and MRIs depend on size to detect lesions, and are therefore limited in their ability to detect metastatic tumors between 4 mm and 8 mm.[3,4] As such, an accurate initial assessment of a patient's disease is critical because intermediate and high-risk prostate cancer is more likely to be advanced at diagnosis and/or relapse than low-risk prostate cancer. PSMA PET is now recognized as a suitable replacement for conventional imaging in men with biopsy-proven, treatment naïve prostate cancer. The superior sensitivity of PSMA PET also enables greater detection of metastatic disease, which can direct treatment planning. The National Comprehensive Cancer Network **(NCCN Guidelines; Version 1.2023; PROS-E)** recommends bone imaging and abdominal/pelvic imaging as the initial work-up in patients newly-diagnosed high- and very high-risk prostate cancer, as well as in a subgroup of patients with unfavorable intermediate-risk prostate cancer. The primary goal of such imaging is to detect extra-prostatic disease (M1: non-regional nodal involvement, bone, or other sites), the identification of which would likely significantly change the planned treatment regimen from locoregional to systemic therapy. As such, conventional imaging offers limited accuracy in prostate cancer assessment, potentially compromising therapeutic decision-making. Current clinical practice guidelines (NCCN and SNMMI) for prostate cancer now include PSMA-PET imaging as a recommendation for patients with newly diagnosed unfavorable intermediate and high-risk prostate cancer.[5,6,7,8]

Despite the fact that most men diagnosed with prostate cancer do not die from the disease, about 40% of patients treated with curative intent following a diagnosis of primary prostate cancer will experience recurrent disease within 10 years following primary treatment. One third of those men who have recurrence will go on to develop metastatic disease within 8 years.[9,10,11,12] In a vast majority of cases, evidence of recurrent disease is based on serial measurement of prostate specific antigen (PSA) alone. This is often referred to as biochemically recurrent (BCR) prostate cancer and is clearly defined within clinical guidelines.[13,14] And despite

extensive efforts during primary staging and intervention, approximately 27–53% of patients with prostate cancer experience recurrence in part due to imperfect conventional staging techniques.[15,16,17] Determining the location of the recurrence is critical, as this guides the optimal choice of therapy. The diagnostic accuracy of conventional imaging tests for the identification of sites of recurrence is low. Almost 90% of the standard battery of imaging tests, for example, CT, MRI and bone scintigraphy, may be negative.[18] These imaging procedures may be unable to detect recurrent prostate tumors <1 cm in size or when PSA levels are <20 ng/mL, when cancer may be more effectively managed or treated with localized therapy.[19-24] As such, conventional imaging modalities have failed to reliably discern disease presence and disease location in the biochemically recurrent setting. For this reason, more accurate, non-invasive imaging techniques for the detection of recurrent cancer are needed. Positron emission tomography (PET) is a well-established, non-invasive, molecular imaging technique. The principle behind the PET radiotracers used in oncology is to image the altered metabolism or receptor profile of tumor cells. Nuclear medicine imaging procedures have been utilized for the detection of recurrent prostate cancer for a number of years, however it is widely recognized that more accurate imaging techniques are needed to improve diagnostic detection rates in these patients. As such, PSMA PET/CT is currently recommended by the NCCN and SNMMI for men with biochemical recurrence after definitive primary local therapy.[5] **(NCCN Guidelines; Version 1.2023; PROS-E)**.

Accurate staging of newly diagnosed prostate cancer, as well as the detection of recurrent disease in those who have had curative intent treatments, can assist in directing appropriate treatment strategies. POSLUMA, a PET ligand for the detection of prostate cancer, allows PET imaging of prostate cancer through binding of prostate-specific membrane antigen (PSMA). This molecule, also known as glutamate carboxypeptidase II or folate hydrolase I, is a type II transmembrane protein with an extracellular enzymatic domain. PSMA is considered to be a promising and specific target for prostate cancer imaging because it can be overexpressed up to 100 to 1000 times on prostate cancer cells. However, PSMA is also expressed in other normal tissues, particularly the glia of the central nervous system where it is involved in glutaminergic neurotransmission, in the renal proximal tubules, in breast epithelium, and in the gut where it may be involved with folate uptake.[25]

POSLUMA has been specifically developed by Blue Earth Diagnostics as a PSMA targeting molecular imaging agent for the detection and localization of men with newly diagnosed prostate cancer and those with biochemically recurrent prostate cancer. POSLUMA was approved by the FDA on May 25, 2023, and its indication is as follows:
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 or with suspected recurrence based on elevated serum prostate-specific antigen (PSA) level.

INDICATION

POSLUMA® (flotufolastat F 18) injection 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

IMPORTANT SAFETY INFORMATION

- 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. The performance of POSLUMA for imaging patients with biochemical evidence of recurrence of prostate cancer seems to be affected by serum PSA levels. 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. Because of the associated risk of false positive interpretation, consider multidisciplinary consultation and histopathological confirmation when clinical decision-making hinges on flotufolastat F 18 uptake only in the prostate/prostate bed region or only on uptake interpreted as borderline.

- 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.

- The adverse reactions reported in ≥0.4% of patients in clinical studies were diarrhea, blood pressure increase and injection site pain.

- Drug Interactions: androgen deprivation therapy (ADT) and other therapies targeting the androgen pathway, such as androgen receptor antagonists, may 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.

To report suspected adverse reactions to POSLUMA, call 1-844-POSLUMA (1-844-767-5862) or contact FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Full POSLUMA prescribing information is available at www.posluma.com/prescribing-information.pdf

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