PRESS RELEASE

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Blue Earth Diagnostics Highlights Results of Studies Evaluating Impact of Urinary Activity on Image Interpretation and Performance of POSLUMA® (Flotufolastat F 18) and ^{18}F-Flotufolastat PET in Prostate Cancer

MONROE TOWNSHIP, N.J. and OXFORD, UK, June 10, 2024 – Blue Earth Diagnostics, a Bracco company and recognized leader in the development and commercialization of innovative PET radiopharmaceuticals, today announced highlights from clinical studies conducted by its collaborators at the Society of Nuclear Medicine and Molecular Imaging (SNMMI) Annual Meeting, June 8-11, 2024. They included interim results of a study by Emory University that evaluated POSLUMA® (flotufolastat F 18) injection PET/CT with and without furosemide in men with biochemically recurrent prostate cancer (BCR), as well as results of a retrospective study conducted by the Technical University of Munich (TUM) that evaluated qualitative and quantitative PET parameters in urinary activity and tumor uptake for ^{18}F-flotufolastat and ^{68}Ga-PSMA-11 in primary prostate cancer. The studies build upon a recently published post-hoc analysis of Blue Earth Diagnostics' clinical studies in which POSLUMA demonstrated low urinary bladder interference that did not impact disease assessment in the vast majority of patients[1]. Links to the abstracts follow below.

POSLUMA is approved and 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. ^{18}F-Flotufolastat produced at TUM is an investigational agent for which the safety and efficacy have not been established by the U.S. Food and Drug Administration.

"The ability to gather actionable information from PSMA PET scans is important for physicians to make informed decisions about patient management for men with prostate cancer," said Eugene Teoh, MBBS, MRCP, FRCR, D.Phil., Chief Medical Officer of Blue Earth Diagnostics. "Activity in the urinary tract, especially in the urinary bladder, is a common feature of FDA-approved PSMA-PET radiopharmaceuticals which are excreted via the urine. High urinary activity can potentially obscure tumors in the prostate region and regional lymph nodes in the pelvis, which are common sites of recurrence, and interfere with accurate image interpretation."

Dr. Teoh continued, "These results reported at SNMMI support our previous experience with POSLUMA and are broadly consistent with results from our clinical trials. A post-hoc analysis of our Phase 3 clinical trials demonstrated that 96% of patients (682/712) exhibited either no urinary activity or activity that was easily distinguishable from disease[1]. Although furosemide usage has been widely described for other PSMA PET imaging agents as a potential means to reduce urinary activity, the POSLUMA Phase 3 trial results were achieved without its use. In cases from this Emory study where furosemide was not used, results also demonstrate the high POSLUMA detection rates in patients with low PSA levels as observed in prior Blue Earth Diagnostics clinical trials."

"These findings from Emory and TUM reinforce important clinical considerations in selecting a precision diagnostic imaging agent for PSMA-PET procedures," said David E. Gauden, D.Phil., Chief Executive Officer of Blue Earth Diagnostics. "POSLUMA provides physicians with useful information based on its performance at low PSA levels, PSMA binding and low urinary bladder activity. It is included in nationally recognized clinical oncology guidelines for prostate cancer and covered by the vast majority of insurance plans. Labeled with the radioisotope fluorine-18 (^{18}F) to leverage high image quality, POSLUMA is widely available through the network of our commercial U.S. manufacturer and distributor, PETNET Solutions Inc, A Siemens Healthineers Company."

Highlights of the Abstracts

Impact of forced diuresis with furosemide in the evaluation of biochemical recurrence of prostate cancer with ^{18}F-rhPSMA 7.3 PET/CT: Interim analysis of an ongoing prospective trial

Interim results from a prospective study were presented by Ismaheel Lawal, MD, PhD, Resident Physician, Department of Radiology and Imaging Sciences, Emory University, Atlanta Ga. The study investigated the impact of forced diuresis with furosemide during ^{18}F-flotufolastat PET/CT imaging for further improved bladder activity and prostate bed region recurrence detection in BCR. Twelve men had completed both with- and without-furosemide PET/CT scans at the time of the interim analysis. The study assessed bladder activity by SUV, patient-level recurrence and recurrence in the prostate-bed region. The authors concluded that furosemide-augmented bladder activity reduction showed no safety issues and was feasible for ^{18}F-flotufolastat PET/CT imaging. While recognizing detection rates without furosemide remain high and consistent with Phase 3 studies, recurrence detection may be enhanced with the use of furosemide, by further decreasing observed urinary activity, and with no impact on the radiotracer avidity in the recurrent lesion. The full abstract is available here.

Evaluation of qualitative and quantitative PET parameters in primary prostate cancer patients: double-match comparison of ^{18}F-flotufolastat- and ^{68}Ga-PSMA-11-PET

Results from a retrospective study were presented by Isabel Rauscher, MD, Technical University of Munich, School of Medicine, Klinikum rechts der Isar, Department of Nuclear Medicine, Markt Schwaben, Germany. The study evaluated qualitative and quantitative PET parameters in urinary activity and tumor uptake for ^{18}F-flotufolastat and ^{68}Ga-PSMA-11 in a matched cohort of 62 patients staged for primary prostate cancer. Parameters included overall interference from bladder activity, scoring of median semi-quantitative bladder activity, presence of ureteral retention and halo artifacts, and tumor-to-bladder uptake ratio. The authors concluded that interpretation of ^{68}Ga-PSMA-11 PET was significantly more impacted by bladder activity than ^{18}F-flotufolastat PET in the matched populations of primary prostate cancer patients. The full abstract is available here.

Indication and Important Safety Information About POSLUMA

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.

About Blue Earth Diagnostics

Blue Earth Diagnostics, an indirect subsidiary of Bracco Imaging S.p.A., is a growing international molecular imaging company focused on delivering innovative, well-differentiated diagnostic solutions that inform patient care. Formed in 2014, the Company's success is driven by its management expertise and supported by a demonstrated track record of rapid development and commercialization of positron emission tomography (PET) radiopharmaceuticals. Blue Earth Diagnostics' expanding oncology portfolio encompasses a variety of disease states, including prostate cancer and neuro-oncology. Blue Earth Diagnostics is committed to the timely development and commercialization of precision radiopharmaceuticals for potential use in imaging and therapy. For more information, please visit: www.blueearthdiagnostics.com.

About Bracco Imaging

Bracco Imaging S.p.A., part of the Bracco Group, is a world-leading diagnostic imaging provider. Headquartered in Milan, Italy, Bracco Imaging develops, manufactures and markets diagnostic imaging agents and solutions. It offers a product and solution portfolio for all key diagnostic imaging modalities: X-ray imaging (including Computed Tomography-CT, Interventional Radiology, and Cardiac

Catheterization), Magnetic Resonance Imaging (MRI), Contrast Enhanced Ultrasound (CEUS), and Nuclear Medicine through radioactive tracers and novel PET imaging agents to inform clinical management and guide care for cancer patients in areas of unmet medical need. Our continually evolving portfolio is completed by a range of medical devices, advanced administration systems and dose-management software. In 2019 Bracco Imaging enriched its product portfolio by expanding the range of oncology nuclear imaging solutions in the urology segment and other specialties with the acquisition of Blue Earth Diagnostics. In 2021, Bracco Imaging established Blue Earth Therapeutics as a separate, cutting-edge biotechnology vehicle to develop radiopharmaceutical therapies. Visit: www.braccoimaging.com.

[1]Kuo PH, Hermsen R, Penny R, Postem EJ. Post-hoc analysis of the LIGHTHOUSE and SPOTLIGHT studies to assess the impact of urinary activity on interpretation of ^{18}F-rhPSMA-7.3 PET/CT. *Mol Imaging Biol.* 2024 Feb;26(1):53-60. doi: 10.1007/s11307-023-01867-w.

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PP-rh-US-0499