Practical Guidance on [177Lu]Lu-PSMA-617 Treatment, **Including Radiation Safety, Adverse Event Monitoring,** and Patient Counseling

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BACKGROUND: The approval of the prostatespecific membrane antigen (PSMA)-targeted radioligand therapy [177Lu]Lu-PSMA-617 represents a shift toward precision medicine-based treatments for metastatic castration-resistant prostate cancer.

OBJECTIVES: This review aims to provide practical advice and clinical considerations for working with [177Lu]Lu-PSMA-617; particularly, regarding the role of nurses in managing radiation safety, monitoring and reporting of adverse events, and counseling patients receiving this therapy.

METHODS: Clinical data, protocols, and guidelines are summarized alongside real-world insights to provide practical recommendations for nurses caring for patients treated with [177Lu]Lu-PSMA-617.

FINDINGS: Nurses coordinate safe care for patients receiving [177Lu]Lu-PSMA-617 by facilitating communication among physicians, managing logistic concerns, monitoring for adverse events related to treatment, providing education, and counseling patients and caregivers throughout treatment.

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PROSTATE CANCER IS THE MOST COMMON TYPE OF CANCER among men in the United States, accounting for 14% of all new cancer cases (National Cancer Institute, 2022a). Its incidence is expected to increase by about 23% between 2020 and 2040 (World Health Organization, 2023). The majority of men present with localized prostate cancer (National Cancer Institute, 2022b), but 10%-20% develop castration resistance and some progress to metastatic castration-resistant prostate cancer (mCRPC) (Kirby et al., 2011). Although several different types of therapies are recommended for mCRPC (Lowrance et al., 2020), most are nontargeted therapies associated with modest survival benefits (Henríquez et al., 2021; Staniszewska et al., 2021), off-target effects, and toxicity that can compromise quality of life (Kretschmer et al., 2021).

The treatment of mCRPC is evolving toward precision medicine, with a focus on biomarkers such as prostate-specific membrane antigen (PSMA), mismatch repair deficiency/microsatellite instability, and homologous recombination repair gene mutation (Abida et al., 2019; de Bono et al., 2020; Hofman et al., 2018). PSMA is expressed in the prostatic adenocarcinoma cells of more than 80% of patients with prostate cancer, including those with mCRPC (Hupe et al., 2018; Pomykala et al., 2020; Sartor et al., 2021). PSMA-targeted radioligand imaging and radioligand therapy present a new theranostic approach that targets radiation to PSMA-positive tumors (Current et al., 2020; Zhang et al., 2021). Diagnostic PSMA-targeted radioligand imaging can visualize PSMA expression, which can then be targeted by PSMA-targeted radioligand therapy that delivers cytotoxic radiation to PSMA-expressing cells (Current et al., 2020; Zhang et al., 2021).

Lutetium Lu-177 vipivotide tetraxetan, also known as [177Lu]Lu-PSMA-617, is one such therapeutic radioligand that delivers beta radiation to PSMAexpressing cells (Advanced Accelerator Applications USA, 2022b). Based on results from the prospective, open-label, randomized, phase 3 VISION trial (NCT03511664), in 2022, the U.S. Food and Drug Administration approved [177Lu]Lu-PSMA-617 for the treatment of PSMA-positive mCRPC in adults previously treated with androgen receptor pathway inhibitor and taxane-based chemotherapy. The VISION trial assessed the safety and