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Care Pathway at a Cancer Center for the Administration of Radiometabolic Therapy with 177Lu-PSMA in Patients with Metastatic Castration-resistant Prostate Cancer

Metastatik Kastrasyona Dirençli Prostat Kanserli Hastalarda 177Lu-PSMA ile Radyometabolik Tedavinin Uygulanmasına Yönelik Kanser Merkezinde Bakım Yolu

Carlos Avila[1], *Tatiana Cadavid*[1], *Maria Cristina Martínez*[2], *Humberto Varela*[2], *Nathalie Hernández-Hidalgo*[2]

[1]*Fundación Universitaria Sanitas, Bogotá, Colombia*
[2]*Instituto Nacional de Cancerología, Department of Nuclear Medicine, Bogotá, Colombia*

Abstract

Objectives: To present a clinical care model for the administration of 177Lu-labeled prostate-specific membrane antigen (PSMA) in radiometabolic therapy for metastatic castration-resistant prostate cancer (mCRPC) at the National Cancer Institute (NCI) of Bogotá, Colombia.

Methods: A care model was designed for patients with mCRPC based on the VISION study, a prospective, phase III, multicenter, open-label, randomized study in patients with positive ^{68}Ga-PSMA positron emission tomography/computed tomography who had progressed to taxane and androgen therapy, to receive 177Lu-PSMA-617 combined with the best standard of care vs. the best standard of care alone. The care pathway provided to patients was developed by the Nuclear Medicine Group of the NCI and is the result of adjustments and improvements in the care process and the updating of the literature.

Results: A systematic and efficient care model was formalized and implemented for the administration of 177Lu-PSMA therapy in patients with mCRPC who had previously been treated with at least one androgen receptor pathway inhibitor and one or two taxane regimens, with evidence of disease progression.

Conclusion: An optimized process of care based on the determinants of clinical outcomes was developed for patients who received this type of radiometabolic therapy.

Keywords: Prostatic neoplasms, prostate-specific antigen, lutetium, nuclear medicine radiopharmaceutical delivery of health care, integrated

Address for Correspondence: Nathalie Hernández-Hidalgo MD, Instituto Nacional de Cancerología, Department of Nuclear Medicine, Bogotá, Colombia
Phone: +57 3508919905 **E-mail:** natha8830@gmail.com ORCID ID: orcid.org/0000-0002-7471-9566
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Öz

Amaç: Bogotá, Kolombiya Ulusal Kanser Enstitüsü'nde (NCI) metastatik kastrasyona dirençli prostat kanserinin (mCRPC) radyometabolik tedavisinde 177Lu etiketli prostat spesifik membran antijeninin (PSMA) uygulanmasına yönelik bir klinik bakım modeli sunmaktır.

Yöntem: ^{68}Ga-PSMA pozitron emisyon tomografisi/bilgisayarlı tomografisi pozitif olan ve taksan ve androjen tedavisi almış hastalarda yapılan prospektif, faz III, çok merkezli, açık etiketli, randomize bir çalışma olan VISION çalışmasını temel alarak mCRPC'li hastalar için 177Lu-PSMA-617 ve en iyi bakım standardını tek başına en iyi bakım standardı ile karşılaştıracak bir bakım modeli tasarlandı. Hastalara sağlanan bakım yolu, bakım sürecindeki ayarlamalar ve iyileştirmeler ile literatürün güncellenmesinin sonucunda NCI'nın Nükleer Tıp Grubu tarafından geliştirilmiştir.

Bulgular: Daha önce en az bir androjen reseptör yolağı inhibitörü ve bir veya iki taksan rejimi ile tedavi edilmiş ve hastalık ilerlemesinin kanıtı bulunan mCRPC'li hastalarda 177Lu-PSMA tedavisinin uygulanması için sistematik ve etkili bir bakım modeli şekillendirildi ve uygulandı.

Sonuç: Bu tip radyometabolik tedavi alan hastalar için klinik sonuçların belirleyicilerine dayalı optimize edilmiş bir bakım süreci geliştirilmiştir.

Anahtar kelimeler: Prostat neoplazmaları, prostat spesifik antijen, lutesyum, nükleer tıp radyofarmasötik sağlık hizmeti sunumu, entegre

Introduction

The National Cancer Institute of the United States (NIH) defines prostate cancer as a neoplasm originating in prostate tissues and is the second most commonly diagnosed neoplasm in the male population worldwide (1).

The incidence of prostate cancer diagnosis varies widely between different geographic areas, being highest in Australia/New Zealand and North America, with age-standardized rates of 111.6 and 97.2 per 100,000 population, respectively (1). According to data reported by the NIH, the rate of new cases was 106.8 per 100,000 people in 2018, with an estimated new case rate of 248,530 (13.1%) for 2021 (2). Likewise, the World Health Organization records a worldwide incidence of 30.1 for the year 2020, estimating 1,628,781 new cases in Latin America and 49.8 in Colombia for the same year (3). Regarding the records of the National Cancer Institute (NCI) of Bogotá, patients with prostate cancer (n=5,430) were evaluated between 2017 and 2020, approximately 1,000 patients per year.

Metastatic castration-resistant prostate cancer (mCRPC) is established in patients with suppressed testosterone levels <50 ng/dL with at least one of the following criteria: biochemical progression understood as an increase in prostate-specific antigen (PSA) in studies spaced at least one week apart, with two increases of 50% over the nadir value and with PSA >2 ng/mL (4); or radiological progression with two or more new lesions on bone scan or soft tissue lesions.

Prostate-specific membrane antigen (PSMA) is a transmembrane protein mainly expressed in prostate cancer cells; its high expression is an independent biomarker of poor prognosis during the disease. Most patients with mCRPC have positive PSMA levels, and its high expression has been associated with reduced survival (5).

Radiolabeled PSMA is an effective tool for treating mCRPC. Its usefulness, safety, and low toxicity have been verified because it limits radiation to target organs and reduces the presentation of radiation-related symptoms during tumor cytorduction (5,6,7).

In particular, the use of PSMA radiolabeled with 177Lu has shown an improvement in the overall and progression-free survival of patients and in some cases in tumor regression, both in animal and human studies. Recently, in the VISION study-the only phase III randomized study-it was possible to show the efficacy of 177Lu-PSMA (5), which has led to its inclusion as a therapeutic option in mCRPC after progression despite one or two lines of taxanes according to international guidelines (4).

In the hospital radiopharmacy of NCI (Bogotá, Colombia), radiolabeled PSMA has been developed for the diagnosis and treatment of prostate cancer. In January 2020, 177Lu-PSMA was produced, at which time the first treatment was administered.

To date, 41 therapies have been administered to 19 patients, which has made it possible to adjust an orderly and optimized procedure for the administration of this radionuclide therapy. In Colombia, few institutions have the capacity to administer this type of therapy; thus, this work seeks to document the evolution of a model for the administration of 177Lu-PSMA therapy in patients diagnosed with mCRPC, with the aim that different cancer centers can use it as a guide for the care of this group of patients.

Materials and Methods

To establish a standardized institutional procedure for the administration of 177Lu-PSMA therapies, some key moments were defined (Figure 1).

We don't use statistical analysis in our article.

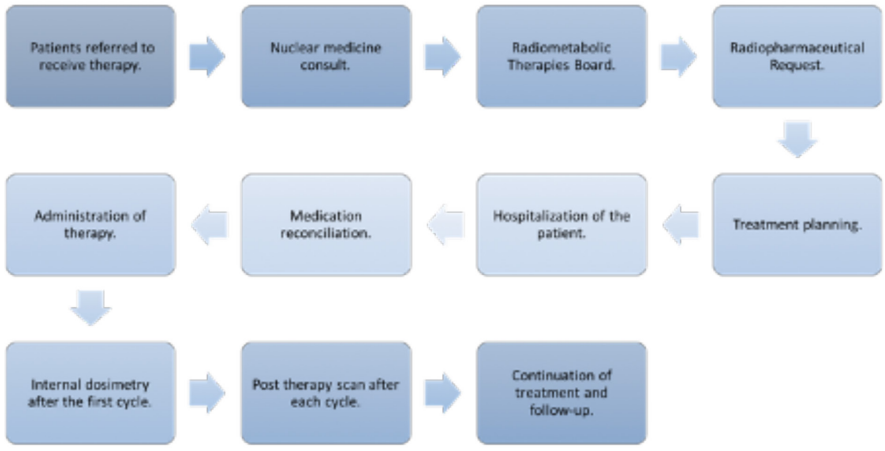

Figure 1. Flowchart 177Lu-PSMA therapy workflow at our institution
177Lu-PSMA: 177Lu-prostate-specific membrane antigen

Results

The Nuclear Medicine Group at NCI has managed to develop a systematic method for the administration of 177Lu-PSMA therapy to patients with mCRPC diagnosis. Figure 2 shows the key stages of the care process in force at the institution.

Patients Eligible for Therapy

Adult patients admitted with a diagnosis of mCRPC, who have been treated with one or two antiandrogens (abiraterone or enzalutamide) and one or two taxane regimens, present biochemical and imaging progression, with evidence of at least one metastatic lesion by computed tomography (CT) scan, magnetic resonance imaging (MRI), or bone scan; additionally, with PSMA-positive metastatic lesions confirmed by positron emission tomography/CT (PET/CT) with ^{68}Ga-PSMA-11 (5,7).

PET/CT with ^{68}Ga-PSMA-11 allows defining PSMA-positive and-negative lesions. A positive lesion presents a maximum standardized uptake value higher (1.5 times) than the mean

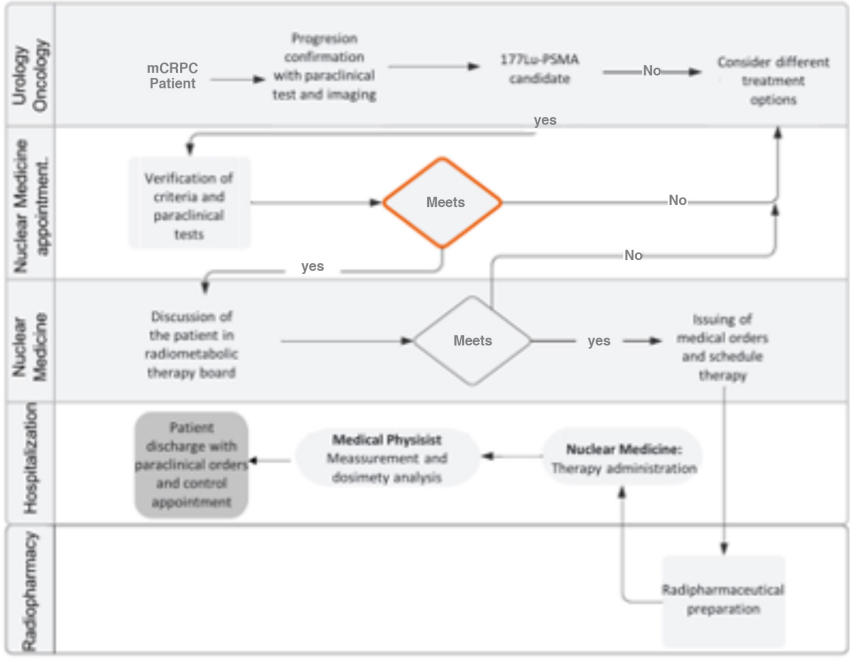

Figure 2. Systematic method for the administration of 177Lu-PSMA therapy
177Lu-PSMA: 177Lu-prostate-specific membrane antigen

standardized uptake value of the liver (7). On the other hand, a PSMA-negative lesion is defined as an uptake equal to or less than that of the liver parenchyma, in any lymph node with a short axis less than 2.5 cm, in any metastatic solid organ tumor with a short axis less than 1 cm, and in any bone lesion with a soft tissue component with a short axis less than 1 cm (Figures 3,4,5,6) (Table 1) (5).

Selection Criteria

Patients with mCRPC and evidence of progression must meet the following criteria to receive 177Lu-PSMA therapy (Tables 2,3).

Nuclear Medicine Consultation

Every patient referred by the oncology or the oncologic urology service undergoes a medical assessment by a

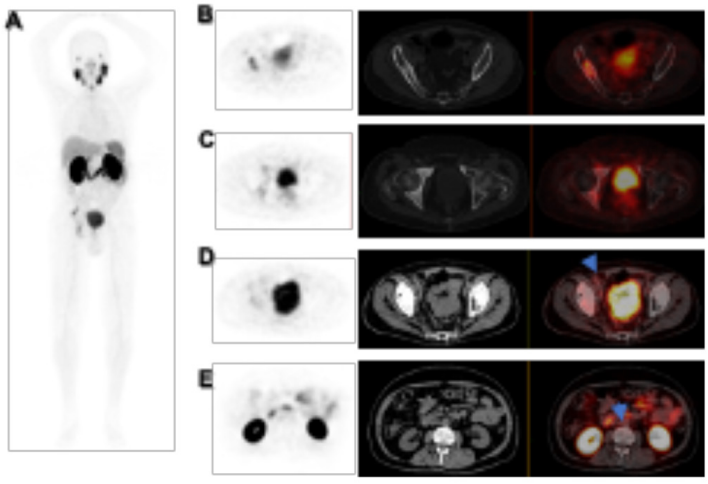

Figure 3. ^{68}Ga-PSMA PET/CT restaging in 70-years-old patient with biochemically recurrent prostate cancer and rising level of prostate-specific antigen: PET maximum intensity projection (A), axial PET/CT shows blast involvement in the right hemipelvis with foci showing moderate PSMA expression (SUV_{max}: 4.6, score 2) (By C), lymph nodes with partial calcification at the level of the aortic bifurcation and in the right external iliac region that do not present PSMA expression, probably post-treatment changes (D), lymph nodes in the inter-aortocaval region (up to 10 mm short diameter) and para-aortics without PSMA expression, score 0 (E)
^{68}Ga-PSMA: ^{68}Ga-prostate-specific membrane antigen, PET/CT: Positron emission tomography/computed tomography, SUV_{max}: Maximum standardized uptake value

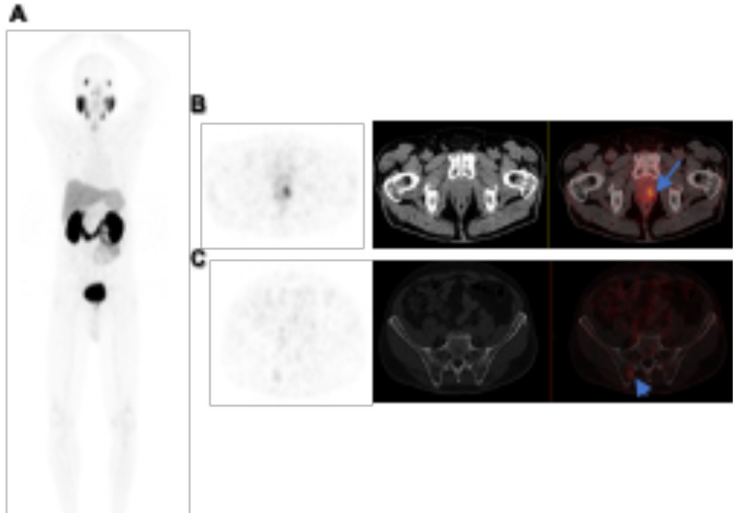

Figure 4. Primary staging using ^{68}Ga-PSMA11 PET/CT in 65-years-old patient with histopathologically proven prostate cancer T3bN0Mx, GG 4, iPSA 7.55 ng/mL: PET maximum intensity projection (A), axial PET/CT showing a focal area of greater intensity at the apex towards the left side with SUV_{max}: 6.4, score 2 (B), focal uptake with low expression of PSMA in the postero-superior region of the right iliac adjacent to the sacroiliac joint (SUV_{max}: 1.6), score 1 (C)
^{68}Ga-PSMA: ^{68}Ga-prostate-specific membrane antigen, PET/CT: Positron emission tomography/computed tomography, SUV_{max}: Maximum standardized uptake value

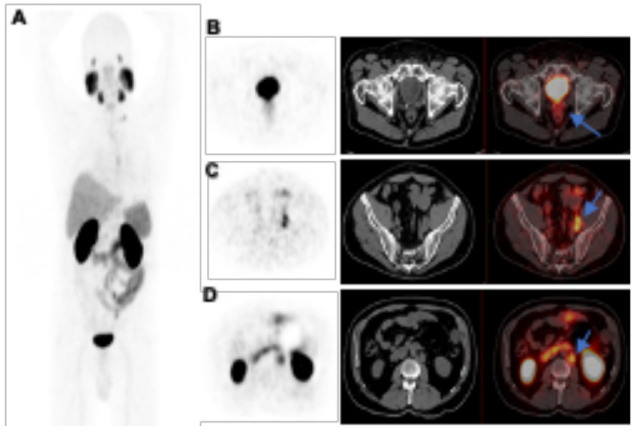

Figure 5. ^{68}Ga-PSMA 11 PET/CT restaging in 62-years-old patient with biochemically recurrent prostate cancer and rising level of prostate-specific antigen: PET maximum intensity projection (A), axial PET/CT post-radical prostatectomy state, low expression of PSMA in the rectovesical septum (SUV_{max}: 3.2, score 1) (B), lymph nodes with moderate expression of PSMA, score 2, in the left internal iliac chain (SUV_{max}: 6) and in the left interiliac region (SUV_{max}: 5.9, score 2) (C), in the left common iliac chain (SUV_{max}: 8.2), para-aortic up to approximately 20 mm in greatest diameter (SUV_{max}: 7.3), interaortocavus (SUV_{max}: 5.3) (D)
^{68}Ga-PSMA: ^{68}Ga-prostate-specific membrane antigen, PET/CT: Positron emission tomography/computed tomography, SUV_{max}: Maximum standardized uptake value

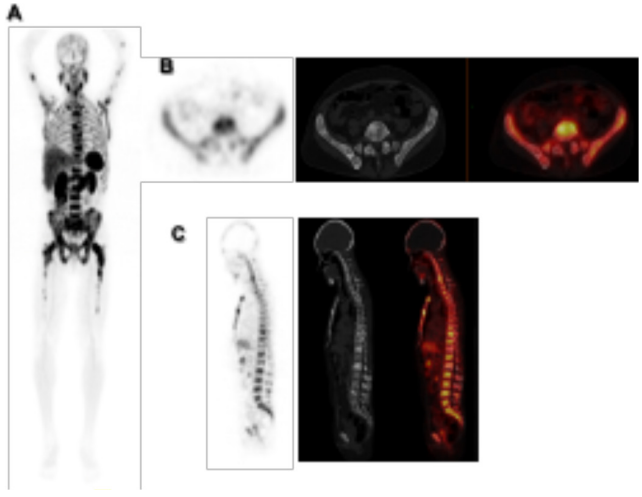

Figure 6. ^{68}Ga-PSMA 11 PET/CT in 73-years-old patient with prostate cancer presenting clinical, biochemical and imaging progression. PET maximum intensity projection (A) axial (B) and sagittal PET/CT (C) osteoblastic polyostotic metastatic compromise with abnormal increased uptake of the radiotracer and high expression of PSMA (score 3) involving the axial and appendicular skeleton, the most dominant located in the left humeral head (SUV_{max}: 6.3), sternal extremity of both clavicles (SUV_{max}: 6.5), manubrium sternal (SUV_{max}: 9.0), left femoral neck (SUV_{max}: 15.5), vertebral body of C6 (SUV_{max}: 9.3)
^{68}Ga-PSMA: ^{68}Ga-prostate-specific membrane antigen, PET/CT: Positron emission tomography/computed tomography, SUV_{max}: Maximum standardized uptake value

Table 1. miPSMA expression score. PSMA imaging can be quantified on the basis of the degree of radiotracer uptake. This is visually evaluated relative to uptake by the liver and parotid gland, which both physiologically take up PSMA expression

Score	Reported PSMA expression	Uptake
0	No	Below blood pool
1	Low	Equal to or above blood pool and lower than liver
2	Intermediate	Equal to or above liver and lower than parotid gland
3	High	Equal to or above parotid gland

PSMA: Prostate-specific membrane antigen

Table 2. These threshold criteria are used to evaluate patients before initiating and while monitoring 177Lu-PSMA. Patients with laboratory values outside the threshold values may be treated after discussion and shared
Selection criteria
Have a ^{68}Ga-PSMA 11 PET/CT with PSMA-positive lesions (SUV_{max} 1.5 times greater than the SUV_{mean} of the liver).
Tumor with histopathological confirmation by the pathology service.
Functional status: ECOG ≤2 and a life expectancy of more >6 months.
Safety criteria
Hemoglobin ≥9.0 g/dL.
Bone marrow reserve: leukocytes ≥2,500/µL ($2.5x10^3$/µL), neutrophils ≥1,500/µL platelets >$75x10^3$/µL.
Glomerular filtration > 30 mL/min, with a creatinine ≤1.5.
Total bilirubin ≤1.5x the upper limit of normal for the institution, in case of known Gilbert's syndrome ≤3x the upper limit of normal is allowed.
Alanine aminotransferase or aspartate aminotransferase ≤3.0 and ≤5.0x the upper limit of normal for the institution, in patients with known liver metastases.
Albumin >3.0 g/dL.
Have discontinued myelosuppression therapy at least 6 weeks before the start of lutetium and have recovered from all toxcities related to the previous therapy (equal to or less than grade 2).
177Lu-PSMA:177Lu-prostate-specific membrane antigen, PET/CT: Positron emission tomography/computed tomography, SUV_{max}: Maximum standardized uptake value, SUV_{mean}: Mean standardized uptake value, ECOG: Eastern Cooperative Oncology Group

Table 3. Contraindication for the administration of the therapy
Contraindications
Life expectancy less than 6 months.
Presence or high risk of urinary obstruction.
Progressive deterioration of renal function (GFR <30 mL/min or creatinine >2 times the ULN).
Liver enzymes >5 times the ULN.
Myelosuppression (leukocytes 2,500 mL or platelets <75,000 mL).
Medical condition requiring urgent intervention.
GFR: Glomerular filtration rate, ULN: Upper limit of normal

nuclear medicine professional, who evaluates the patient's general condition and comorbidities, verifies eligibility criteria, and monitors paraclinical findings. The adverse events, benefits, radioprotection measures, and treatment risks are clearly explained to the patient so that they can accept or reject the therapy.

Regarding paraclinical tests, the maximum validity time for them is the following: ≤4 weeks for blood count; <1 week for renal function tests; ≤3 months (preferably 1 month) for CT or MRI of the study area; and ≤3 months for ^{68}Ga-PSMA-11 PET/CT (8).

After this, the informed consent form is filled out and signed by the patient, who is given this document with the recommendations and information necessary for their treatment. The contact information of the patient and one family member is recorded; medical orders are provided to perform the administrative and authorization procedures for subsequent presentation at the Radiometabolic Therapy Board. If the patient is ineligible or does not accept receiving 177Lu-PSMA therapy, their management must be continued by the treating service.

Radiometabolic Therapies Board

Once the patient is evaluated by the nuclear medicine service in the medical consultation, the case is presented to the Radiometabolic Therapies Board in which at least four nuclear physicians participate, who verify the appropriateness of the treatment, the dose to be administered, and discuss possible complications that the patient may present during therapy. After these aspects have been discussed and analyzed, the administration of the treatment is scheduled.

Radiopharmaceutical

For each cycle of therapy, a dose of 200 mCi of 177Lu-PSMA is administered, which can be modified according to medical criteria considering the specific clinical conditions

of each patient. These doses must be administered at intervals of 6-8 weeks until completion of 4-6 doses.

Scheduling

In Colombia, according to current regulations, preparations must be performed in a high-complexity radiopharmacy, which must have an operating license from the Colombian Geological Service and certification of compliance with Resolution 4245 of 2015 on good practices of radiopharmaceutical manufacturing granted by the National Institute for Drug and Food Surveillance (INVIMA) (9). These master preparations must be prepared by pharmaceutical chemists after receiving the medical prescription given by the nuclear physician. Once the application date is assigned, the preparation of the radiopharmaceutical 177Lu-PSMA-I&T is scheduled at least 15 days in advance.

The radionuclide 177Lu does not have any therapeutic or diagnostic purpose on its own. Therefore, it is not considered a pharmaceutical product, nor is it suitable for use in humans until it is transformed into a radiopharmaceutical. Therefore, it is necessary to perform biomolecular labeling and finally, transform it into an injectable form called a master formula.

For this master preparation, raw materials and excipients are needed in addition to the radioactive radioisotope; in this case, 2.5-dihydroxybenzoic acid, PSMA I&T peptide, acetate, and acetate buffer, among others, which fulfill different functions such as stabilizing and guaranteeing an adequate pH for the desired chemical reaction and thus obtaining a quality radiopharmaceutical for the patient.

Evaluation of Patient Medications

It is not necessary to discontinue medications before 177Lu-PSMA therapy. In the case of receiving medications to control other pathologies, they must be continued during therapy (7).

Therapy Administration

The 177Lu-PSMA radiopharmaceutical is prepared in the radiopharmacy according to institutional protocol on the same day that it has been scheduled for the administration of the therapy.

The patient should be hospitalized in a single room designed to ensure radiation protection for caregivers, other patients, and the environment. After admission, the nurse records the patient's vital signs and canalizes two veins, one in each arm. The patient is hydrated according to individual conditions; if there is no cardiovascular risk, 1-2 L of normal saline solution is administered at 20 cc/min (7).

To reduce 177Lu-PSMA uptake by the salivary glands, cold packs covered with a dry towel are placed for at least 1 h before and up to 4 h after the end of treatment, replacing them every 30 min. This prevents alterations in the salivary glands, although there is no clear evidence of its usefulness (9).

In patients with brain or spinal cord metastases or at risk of edema and mechanical obstruction, the administration of prophylactic corticosteroids may be considered. Similarly, if the patient presents with alterations in elimination, slow urinary flow, or constipation, diuretics and laxatives can be used after therapy administration, allowing for rapid elimination (7).

After all mentioned above, the radiopharmaceutical is administered by the nuclear physician and the therapy technologist, with support from the nursing staff. A shielded infusion pump is used to administer 177Lu-PSMA intravenously over 1 h.

The nuclear medicine professional should evaluate the patient's condition during the administration of therapy. Once it is completed, the nurse should monitor the patient's vital signs. Subsequently, the physicist in charge of radiological protection must take the necessary measures to guarantee the patient's discharge, with a dose rate <25 μSv/h at a 1-meter distance (Figure 7) (10).

Post-therapy Screening

After the therapy, 120-144 h post-injection, whole-body images should be acquired to evaluate the distribution of the radiopharmaceutical with medium-energy collimators, energy window centered at 208 keV ±10%, velocity 16 cm/min, matrix size 256x1024, and zoom 1.0. This screening should be performed after each dose cycle administered to the patient (Figure 8).

Internal Dosimetry

Whole-body planar imaging, abdominal single photon emission computed tomography (SPECT)/CT, and blood samples were taken 24, 48, and 72-166 h after the application of the first therapy to calculate the doses absorbed in the bone marrow, kidneys, parotids, and other organs of interest. Likewise, the dose absorbed by the highest and most avid tumor lesions was calculated. If dosimetry analyses suggest absorbed doses higher than 27 Gy in the kidneys and 2 Gy in the red bone marrow, a correlation should be made with respective functional tests, and it is analyzed whether to suspend therapy or adjust the interval and activity to be administered. In case of retained whole-body activity at 48 h greater than 120 mCi, the nuclear physician should adjust the dose of 177Lu-PSMA for the remaining cycles.

Figure 7. Timeline of the therapy administration

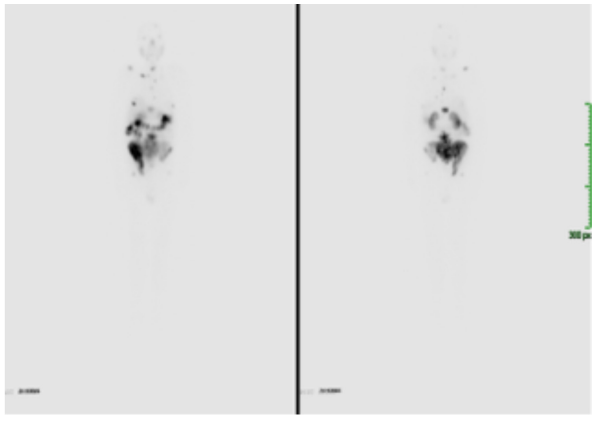

Figure 8. Patient with a history of pT3bN0M1b castration-resistant prostate cancer, with polyostotic bone metastatic involvement and disease in the prostate bed. Two days after administration of 200 mCi of 177Lu-PSMA, a whole body scan was performed in anterior and posterior projections. Physiological distribution of lutetium in liver, spleen and kidneys is observed. In the total body scan, retention of the radiopharmaceutical was observed in multiple bone lesions: right clavicle, thoracic and lumbar vertebral bodies, sacral region, right and left iliac wing, right acetabulum. All the findings show expression of PSMA receptors in the PET/CT ^{68}Ga-PSMA 11
177Lu-PSMA: 177Lu-prostate-specific membrane antigen, PET/CT: Positron emission tomography/computed tomographyc

Once each therapy is finished, a nuclear medicine consultation should be scheduled after 4 to 5 weeks to monitor paraclinical findings (blood count, PSA, alkaline phosphatase, lactate dehydrogenase, albumin, and renal and hepatic function tests) to evaluate possible hematotoxicity generated in the patient and, depending on the results, to reschedule the date of the next therapy (Figure 9) (11).

Continuation of Treatment and Follow-up

The duration of therapy depends on each patient's individual clinical condition, which requires careful evaluation of the absorbed doses accumulated by both the salivary glands and kidneys. The patient's clinical condition, paraclinical findings, and inclusion and exclusion criteria for therapy should be reevaluated before proceeding with the next cycle (7).

In recent observational studies, an average of 7 cycles of 177Lu-PSMA therapy have been performed without exceeding toxicity because repeating therapy every 6 to 8 weeks allows hematologic recovery in most cases (7). For this reason, once consultation has been made after administering the first dose, the dates of the following therapies should be scheduled with intervals of 6 to 8 weeks, completing approximately 6 cycles. Likewise, the patient must continue to be monitored by the oncologic urology service during treatment and after its completion, and in 6-monthly controls by the Nuclear Medicine Group, with laboratory tests (to evaluate late toxicity), imaging studies (RECIST), and tumor biomarkers (PSA), to evaluate response to treatment (7).

Complementary imaging with ^{68}Ga-PSMA-11 is performed at the beginning of treatment and 3 months after completion.

The oncologic urology service will evaluate the patient every 3 months from the beginning of therapy, assess the Eastern Cooperative Oncology score and pain scale, resolve symptoms of urinary obstruction, and request complementary images in case of suspected disease progression or complications secondary to metastatic disease.

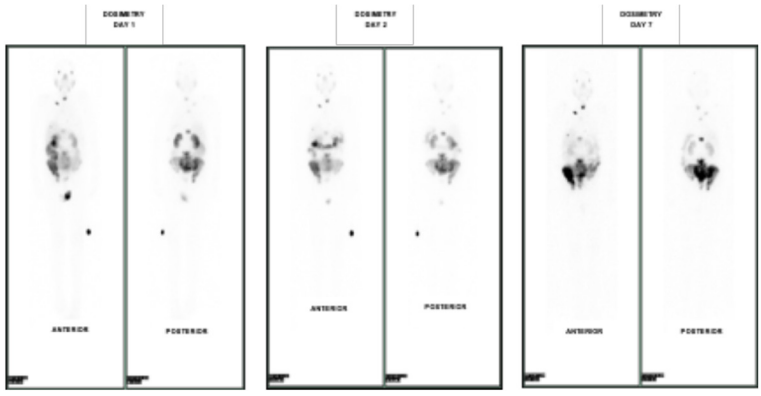

Figure 9. After the administration of 200 mCi of 177Lu-prostate-specific membrane antigen (177Lu-PSMA) I&T therapy, planar images, single photon emission computed tomography (SPECT), and blood samples were acquired at 24, 48, and 170 hours after the administration of the radiopharmaceutical.
• Uptake in the whole body, remnant of the body and parotids, is estimated through planar images following the MIRD 16 methodology.
• The estimation of doses to organs and lesions is estimated with SPECT/computed tomography (CT) and following the MIRD 23 methodology. Regions of interest delimited in CT: liver, kidneys, lumbar and right iliac lesion.
• The estimation of dose to bone marrow follows the methodology described in the European Association of Nuclear Medicine protocol, where the auto-dose in bone marrow is estimated through the dose in blood plasma, and the dose by organs with SPECT/CT and the contribution of the rest of the body with whole body scans.
• S-values are taken from public tabulations of Monte Carlo simulation results for the standardized male (177Lu-PSMA-617 and 177Lu-Octreotate) or female (177Lu-Octreotate) anthropomorphic phantom such as provided, among other dummies, by RADAR and IDAC2.1.
Result:
* Half-life times (bi-exponential fit): Short effective half-life: 0.62 hours. Long effective half-life: 5.27 hours. Whole body retained activity at 48 hours: 30%=59 mCi.
* The doses in Gy, for the organs of main interest due to the therapy with 200 mCi of 177Lu-PSMA, are kidneys: 4.34 Gy, liver: 0.47 Gy, parotids: 1.28 Gy, bone marrow: 1.32 Gy, whole body: 585 mSv.
* Lesion doses, using the sphere method: Right Iliaca (volume =42 cc, density =1.92 g/cm^3): 5.83 Gy, L5 (volume =19 cc, density =1.92 g/cm^3): 5.75 Gy.
Comments:
A high retention of 30% is found at 48 hours, a red bone marrow exposure of 1.32 Gy, generalized bone uptake makes it difficult to estimate the dose to the bone marrow.
The estimated renal dose is 4.34 Gy and 17.4 Gy at the end of treatment, lower than the renal absorbed dose restriction of 23 Gy.
The estimated parotid dose was 1.28 Gy, lower than the dose restriction of 35 Gy.
Dose estimation in SPECT/CT through the sphere method, yields an average dose in bone lesions of 5.78 Gy for the first cycle

Discussion

The most relevant experience worldwide in the administration of 177Lu-PSMA therapy in patients diagnosed with mCRPC has been developed in Europe; it requires a multidisciplinary team, adequate logistics, and appropriate infrastructure. In Latin America, this therapeutic option is offered in countries such as Mexico, Argentina, Chile, Brazil, and Uruguay; however, no literature has shown standardization in the administration of this therapy. The procedure described above results from several years of work at NCI, which conforms to European standards and seeks excellence in the care of this type of pathology.

Since 2009, the NCI has administered therapies with 177Lu-labeled peptides for the treatment of neuroendocrine neoplasms, such as 177Lu-DOTATATE/DOTATOC, which has made it possible to have adequate rooms for therapy, qualified personnel, and experience necessary for the administration of these radiopharmaceuticals, thus facilitating the incorporation of 177Lu-PSMA therapies for treating patients with mCRPC.

In Colombia, the first 177Lu-PSMA therapy was administered at the NCI, in Bogotá, on January 28, 2020. Since then, different training sessions have been conducted to perfect the administration technique, taking as a reference the more extended experience available worldwide, especially in Europe and Australia, using the therapy and the VISION study. Likewise, during this time, the production and quality control processes have been optimized through continuous improvement, and are now in compliance with Resolution 4245 of 2015.

In Colombia, the regulations for the administration of these therapies and the management of radioactive waste are different from those in other countries, whose health systems, in many cases, have different norms, making it easier to administer this therapy.

Although salivary gland protection is a process that is still under study worldwide, we have not had patients with xerostomia so far with the unproven method of cold gel packs (7,8); thus, we continue to apply this technique.

Uptake in the whole body and parotids is estimated through planar imaging following the MIRD 16 methodology. Estimation of doses to organs and lesions are calculated using SPECT/CT and according to MIRD 23 methodology. Regions of interest delimited by CT are liver, kidneys, sternal and femur injury, and visceral soft tissue injury. Bone marrow dose estimation follows the methodology described in the European Association of Nuclear Medicine protocol, where bone marrow self-dose is estimated through blood plasma dose, organ dose with SPECT/CT, and rest-of-body contribution with whole-body scans. S-values are taken from the public tabulations of the Monte Carlo simulation results for the standardized male (177Lu-PSMA-617 and 177Lu-octreotate) or female (177Lu-octreotate) anthropomorphic phantom as provided, among other phantoms, by RADAR and IDAC2.1.

The standardization of image acquisition techniques for dosimetry and the implementation of tomography-based image quantification techniques have made it possible to quantify volumes of interest in a more precise and reproducible way and provide dosimetric information on exposure to bone marrow, kidneys, salivary glands, and lesions, among other organs of interest.

The goal is to consolidate a multidisciplinary team that participates in the Radiometabolic Therapies Board, including an oncologist, urologist, clinical oncologist, radiologist, and nuclear physician, to complement the selection of the best candidate for the administration of the therapy and continue to build knowledge about the best technique for the management and follow-up of patients, seeking to become a center of excellence in radiometabolic therapies. In addition to the above, it is expected that in the coming years, based on the experience at the NCI, more institutions and therefore more patients may benefit from treatment with 177Lu-PSMA therapy.

Conclusion

The Nuclear Medicine Group of NCI has developed an optimized care process for patients receiving this type of radiometabolic therapy for continuous improvement based on the increasing experience in the multidisciplinary management of these patients. Thus, the learning curve achieved by administering these radiopharmaceutical treatments allows us to share this model so that it can be adjusted to the needs and particularities of each institution that requires administering therapies with 177Lu-PSMA.

Ethics

Ethics Committee Approval: As this is an experience as a Nuclear Medicine Group of the National Cancer Institute of Bogota, Colombia, we do not need approval from the ethics committee.

Informed Consent: Informed consent form is filled out and signed by the patient, who is given this document with the recommendations and information necessary for their treatment.

Authorship Contributions

Surgical and Medical Practices: C.A., T.C., M.C.M., H.V., N.H.-H., Concept: C.A., T.C., M.C.M., N.H.-H., Design: C.A., T.C., N.H.-H., Data Collection or Processing: C.A., T.C., Analysis or Interpretation: C.A., T.C., M.C.M., H.V., N.H.-H., Literature Search: C.A., T.C., Writing: C.A., T.C., H.V., N.H.-H.

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