**Study Title:** Study of 18F-DCFPyL PET/CT in the Assessment of Patients with Renal Cell Carcinoma

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**NCT number:** 02687139

**Protocol date:** February 26, 2017

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| Protocol Title: | Study of $^{18}$F-DCFPyL PET/CT in the Assessment of Patients with Renal Cell Carcinoma |
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| eIRB2 ID: | IRB00075596 |
| J Number: | J15145 |
| IND Number: | 121064 |
| Version Date: | February 26, 2017 |

## 1. STUDY SUMMARY

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| PROTOCOL TITLE | Study of $^{18}$F-DCFPyL PET/CT in the Assessment of Patients with Renal Cell Carcinoma |
| IRB NUMBER | IRB00075596 |
| J Number | J15145 |
| IND NUMBER | 121064 |
| INVESTIGATIONAL AGENT | $^{18}$F-DCFPyL |
| PATIENT POPULATION | Patients with localized high-risk (T2-4N0M0) or metastatic ($T_{any}N1M0$ or $T_{any}N_{any}M1$) renal cell carcinoma |
| SAMPLE SIZE | N = 35 |
| OBJECTIVES | • To investigate the sensitivity of $^{18}$F-DCFPyL PET/CT for detecting sites of disease in patients with localized high-risk (T2-4N0M0) or metastatic ($T_{any}N1M0$ or $T_{any}N_{any}M1$) renal cell carcinoma.<br>• To correlate sites of radiotracer uptake on $^{18}$F-DCFPyL PET/CT with conventional imaging findings.<br>• To correlate sites of radiotracer uptake on $^{18}$F-DCFPyL PET/CT with locations of disease recurrence/progression.<br>• To correlate sites of radiotracer uptake on $^{18}$F-DCFPyL PET/CT with the histology of biopsied or resected tissue specimens.<br>• To correlate findings on $^{18}$F-DCFPyL PET/CT with duration of progression-free survival. |

## 2. BACKGROUND & RATIONALE

Renal cell carcinoma (RCC) is the third most common genitourinary malignancy with more than 60,000 new cases diagnosed each year in the United States alone [1]. In the context of metastatic RCC, definitive assessment of small lesions (i.e. <1 cm) as well as response to systemic therapy can be challenging with currently available anatomic imaging modalities such as contrast-enhanced computed tomography (CT) and magnetic resonance imaging (MRI) [2]. In many non-urologic malignancies, these difficult diagnostic tasks are often performed with the quantitative metabolic information available with $^{18}$F-fluorodeoxyglucose (FDG) positron emission tomography (PET)/CT [3]. While $^{18}$F-FDG PET/CT can reliably identify sites of metastatic RCC [4], indeterminate lesions are still common and a role for monitoring treatment response has not been clearly established [5].

One characteristic feature of RCC is that sites of disease are highly vascularized, raising the possibility that a PET radiotracer targeting the tumor neovasculature could reliably image metastatic lesions. One potential target for such a radiotracer is the cell surface protein, prostate-specific membrane antigen (PSMA), which, despite the specificity implied by its name, is highly expressed in the tumor neovasculature of a number of solid tumors including a variety of RCC subtypes [6, 7]. The potential utility of imaging of RCC with PSMA-targeted radiotracers was recently demonstrated in a small series of 5 patients with metastatic clear cell RCC imaged with the $^{18}$F-labeled low-molecular weight PSMA ligand 2-(3-{1-Carboxy-5-[(6-[18F]fluoro-pyridine-3-carbonyl)-amino]-pentyl}-ureido)-pentanedioic acid, more commonly known as $^{18}$F-DCFPyL [8]. In all five patients, sites of putative metastatic disease were readily identified by abnormal $^{18}$F-DCFPyL uptake, with more lesions detected on PET/CT than conventional imaging (18 vs. 28 lesions). These PET detected sites included lesions of the bone, brain, lymph nodes, soft tissue and abdominal viscera. $^{18}$F-DCFPyL uptake ranged from subtle to intense with maximum standardized uptake values ($SUV_{max}$) ranging from 1.6 to 19.3.

In this pilot study we aim to expand upon the limited existing data on PSMA PET/CT of RCC by imaging a cohort of patients with kidney cancer over a range of disease stages (stage II-IV) and without restriction to the clear cell histologic type. These preliminary data may then serve to aid in hypothesis generation for the planning of future studies.

## 3. OBJECTIVES

- To investigate the sensitivity of $^{18}$F-DCFPyL PET/CT for detecting sites of disease in patients with localized high-risk (T2-4N0M0) or metastatic ($T_{any}N1M0$ or $T_{any}N_{any}M1$) renal cell carcinoma.

- To correlate sites of radiotracer uptake on $^{18}$F-DCFPyL PET/CT with conventional imaging findings.

- To correlate sites of radiotracer uptake on $^{18}$F-DCFPyL PET/CT with locations of disease recurrence/progression.

- To correlate sites of radiotracer uptake on $^{18}$F-DCFPyL PET/CT with the histology of biopsied or resected tissue specimens collected during the course of routine clinical care.

- To correlate findings on $^{18}$F-DCFPyL PET/CT with duration of progression-free survival.

## 4. PATIENT SELECTION & ELIGIBILITY

### 4.1. NUMBER OF PATIENTS

During the course of this study we aim to enroll 35 patients

### 4.2. INCLUSION CRITERIA

1. Age ≥18 years

2. Clinically diagnosed or histologically proven stage II-IV (T2-4N0M0, $T_{any}N1M_{any}$, $T_{any}N_{any}M1$) renal cell carcinoma

3. Completed staging evaluation with CT or MRI of the chest, abdomen and pelvis ≤90 days prior to study enrollment

### 4.3. EXCLUSION CRITERIA

1. History of other malignancy diagnosed within the last 3 years (with the exception of low risk prostate cancer [Gleason score 6, pretreatment PSA ≤10, cT2a or pT2 if treated], DCIS of the breast, squamous cell carcinoma or basal cell carcinoma of the skin)

2. Administered a radioisotope within 5 physical half-lives prior to study enrollment

3. Pregnancy (as determined in accordance with the policies of the PET center)

4. Intention to enroll in a blinded therapeutic clinical trial following PET/CT

### 4.4. INCLUSION OF WOMEN AND MINORITIES

Men and women of all races and ethnic groups are eligible for this study and encouraged to participate.

## 5. SUBJECT RECRUITMENT AND INFORMED CONSENT

Urologists and medical oncologists at Johns Hopkins will be educated about the study including patient eligibility criteria. At the treating physician's discretion, patients will in turn be informed about the study and their interest in participation assessed. Any patient who expresses interest in participating in the study will then either be directly introduced to the study team staff, who will be present on select clinic days, or their contact information provided to the study coordinator. In all cases, as much time as is needed to consider study participation will be allowed to possible participants; resulting in multiple phone calls, visits, emails, or other communication, as necessary.

The principal investigator or designated individual will discuss the study with interested patients. Patients will be provided with the Institutional Review Board (IRB) approved consent form for review and given sufficient time to consider participation in the study. Once a decision has been made to enter into the study, a signature will be obtained from the patient to confirm consent.

Patients may voluntarily withdraw consent at any point following enrollment in the study. At the time of informed consent patients will be instructed that they may withdraw consent by contacting the principal investigator or study coordinator.

## 6. RISKS & BENEFITS

### 6.1. RISKS

$^{18}$F-DCPyL is a novel imaging agent, which to date, has been studied in <50 patients at Johns Hopkins under existing IRB protocols (IRB00046315, IRB00062296, NA_00092956). Despite this small number, the compound appears to be very well tolerated with no reported serious adverse related events.

During the course of this study patients will be exposed to 1.59 rem of radiation. The risks related to both $^{18}$F-DCFPyL and radiation exposure will be explained to the patient during the informed consent process.

### 6.2. BENEFITS

There will be no direct medical benefit to participants participating in this study. Rather, their participating may help patients in the future by further our knowledge of RCC.

## 7. STUDY PROCEDURES

1. Eligability screening

2. Informed consent

3. Completion of data collection sheet, KPS score, ECOG performance status and FKSI-19 questionaire

4. $^{18}$F-DCFPyL PET/CT scan

5. Assessment of adverse events via phone call at 1-3 days following PET/CT

6. Treatment per the treating physician including imaging as clinically indicated

7. Collection of clinic notes, surgical reports, imaging test results/images, pathology reports and pathology/tissue specimens in the form of slides or paraffin blocks which are generated as part of routine clinical care for up to five years following study enrollment

## 8. PROTOCOL FOR $^{18}$F-DCFPYL PET/CT

1. Patient will fast for 4 to 6 hours prior to injection of $^{18}$F-DCFPyL

2. An intravenous peripheral intravenous catheter will be placed (or an upper-extremity existing central line accessed) in order to inject the radiotracer

3. Intravenous fluid (5% dextrose + 0.45% normal saline) will be delivered at a low flow rate during the duration of the study (maximum 2 litters)

4. A bolus of less than or equal to 9 mCi (333 MBq) of $^{18}$F-DCPyL will be injected into the IV line by slow push

5. At approximately 60 minutes after the administration of $^{18}$F-DCFPyL, IV fluids will be discontinued and the patient will be asked to void. A whole-body CT and PET scan will then be acquired from the mid-thigh to the vertex of the skull. The PET/CT will be performed on a Discovery DRX PET/CT scanner (GE Healthcare) operating in 3-dimensional emission acquisition mode. Scans will include approximately 8 to 9 fields-of-view, depending on patient height.

6. Temporary IV access will be removed

## 9. STUDY STATISTICS

Descriptive statistics (i.e. proportions/percentages for categorical and medians with interquartile ranges for continuous variables) will be used to describe the study cohort and findings on $^{18}$F-DCFPyL PET/CT scans. More specifically, data will be reported on patient age, race/ethnicity, TNM stage, histologic RCC subtype, Fuhrman grade, surgical margin status, sites/burden of disease, prior cancer treatment and interval treatment following PET/CT scan. Additionally we will report the number and location of putative sites of disease detected on PET/CT. These sites will be correlated to findings on available conventional imaging as well as with histology of biopsied/resected tissue specimens obtained during the course of routine clinical care. Lastly, we will explore the relationship of PET/CT findings with the location and pattern of recurrence/progression as well as duration of progression-free survival. For any analysis of progression-free survival, Kaplan-Meir estimates will be calculated and groups will be compared with the log-rank test. Given the exploratory nature of this study, we do not have any predefined analyses in mind. We do envision, however, comparing the progression-free survival of patients after dichotomization/grouping by a number of different imaging parameters such as number of sites of disease, location of disease sites and mean $SUV_{max}$ values.

## 10. SAFETY MONITORING

Patients will be contacted 1 to 3 days following the $^{18}$F-DCFPyL PET/CT via phone call by a designated study team member to assess for study related adverse events. Any patient experiencing an adverse event will be instructed to go to the nearest emergency room for evaluation by a physician. The outcome of this call with appropriate follow-up will be documented in the medical record as a phone note. All adverse events will be recorded using Common Terminology Criteria for Adverse Events (CTCAE) Version 4.0 and will be submitted to the IRB per policy 103.6b.

## 11. DATA HANDLING AND RECORD KEEPING

Paper consent forms and enrollment check sheets will be kept in a study binder. This binder will be stored in a locked office available only to the study team.

Electronic data including patient demographics, pathology results, imaging data and treatment details will be housed in a secure password protected REDCap database maintained by the Data Informatics Services Core within the Johns Hopkins Biostatistics Center. Only the study coordinator and investigators will have access to this secure database. Of note, to maintain the protected health information of patients enrolled in this study, only the study Principal Investigator and coordinator will have the ability to export data containing identifying information from this master database. For the purposes of analysis, only de-identified data will be exported.

## 12. DISCLOSURE OF DATA

The results of $^{18}$F-DCFPyL PET/CT scans will be made available to both patients and treating physicians. Because this is a novel diagnostic test which is being studied under an IND, the following statement will appear in all radiology reports:

> $^{18}$F-DCFPyL PET/CT is currently being studied under an Investigational New Drug application from the United States Food and Drug Administration. This scan is considered experimental and the results should be interpreted in this context. Any treatment decisions made based on the results of this study should include a discussion with the patient as to the investigational nature of the scan and the possibility of basing management decisions on falsely positive and/or negative findings.

Additionally, at the time of informed consent, it will be explained to patients that the results of these scans may prompt additional confirmatory imaging and/or invasive procedures that would not have otherwise been contemplated had the patient not participated in this study.

## 13. PATIENT REMUNERATION

Patients will be provided with a voucher for free parking following successful completion of the PET/CT.

## 14. FUNDING

The study will be supported by private philanthropic funds raised by the Johns Hopkins Department of Urology.

## 15. REFERENCES


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3. Wahl RL, Jacene H, Kasamon Y, Lodge MA. From RECIST to PERCIST: evolving considerations for PET response criteria in solid tumors. *J Nucl Med*. 2009; 50 Suppl 1: 122S-150S.

4. Wang HY, Ding HJ, Chen JH, et al. Meta-analysis of the diagnostic performance of [18F]FDG-PET and PET/CT in renal cell carcinoma. *Cancer Imaging.* 2012; 12: 464-474.

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8. Rowe SP, Gorin MA, Hammer HJ, et al. Imaging of metastatic clear cell renal cell carcinoma with PSMA-Targeted 18F-DCFPyL PET/CT. *Ann Nucl Med*. In press.

## APPENDIX A. ELIGIBILITY CHECKLIST

Name _____
Date of Birth _____
Medical Record Number _____
Date Eligibility Screened _____
Person Performing Screening _____

**Gender**: M F

**Race/Ethnicity** (check all that apply):

| | American Indian or Alaskan Native | Asian | Native Hawaiian or Other Pacific Islander | Black or African American | White | Unknown | Other |
|---|---|---|---|---|---|---|---|
| Non-Hispanic | | | | | | | |
| Hispanic or Latino | | | | | | | |
| Unknown | | | | | | | |

| **PATIENT ELIGIBILITY** | | | |
|---|---|---|---|
| **Inclusion Criteria** (Criteria should be answered **YES** for patient to be eligible.) | | **YES** | **NO** |
| 1. | Age ≥18 years | | |
| 2. | Clinically diagnosed or histologically proven stage II-IV (T2-4N0M0, $T_{any}N1M_{any}$, $T_{any}N_{any}M1$) renal cell carcinoma | | |
| 3. | Completed staging evaluation with CT or MRI of the chest, abdomen and pelvis ≤90 days prior to study enrollment | | |

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| **Exclusion Criteria** (Criteria should be answered **NO** for patient to be eligible.) | | **YES** | **NO** |
| 1. | History of other malignancy diagnosed within the last 3 years (with the exception of low risk prostate cancer [Gleason score 6, pretreatment PSA ≤10, cT2a or pT2 if treated], DCIS of the breast, squamous cell carcinoma or basal cell carcinoma of the skin) | | |
| 2. | Administered a radioisotope within 5 physical half-lives prior to study enrollment | | |
| 3. | Pregnancy (as determined in accordance with the policies of the PET center) | | |
| 4. | Intention to enroll in a blinded therapeutic clinical trial following PET/CT | | |