Diagnostic Performance of ^{18}F-DCFPyL in the OSPREY Trial: A Prospective Phase 2/3 Multi-Center Study of ^{18}F-DCFPyL PET/CT Imaging in Patients with Known or Suspected Metastatic Prostate Cancer (NCT02981368)

Michael J. Morris[1,2], Jeremy C. Durack[1], Ajjai S. Alva[3], Herbert A. Vargas[1], Morand Piert[3], Russell K. Pachynski[4] Frederic Pouliot[5], Jean-Mathieu Beauregard[5], Mark A. Preston[6], Atish D. Choudhury[7], Lawrence Saperstein[8], Peter Carroll[9], Steven P. Rowe[10], Kenneth J. Pienta[10,11], Tess Lin[12], Vivien Wong[12], Melissa Nichols[12], Jessica Jensen[12], Barry A. Siegel[13]

[1]Memorial Sloan Kettering Cancer Center and [2]Weill Cornell, New York, NY; [3]University of Michigan, Ann Arbor, MI; [4]Washington University School of Medicine, St. Louis, MO; [5]CHU de Quebec and Laval University, Quebec City, QC; [6]Brigham and Women's Hospital, Boston, MA; [7]Dana-Farber Cancer Institute, Boston, MA; [8]Yale School of Medicine, New Haven, CT; [9]University of California San Francisco, San Francisco, CA; [10]Johns Hopkins University School of Medicine, Baltimore, MD; [11]James Buchanan Brady Urological Institute, Baltimore, MD; [12]Progenics Pharmaceuticals, Inc., New York, NY; [13]Washington University School of Medicine, St. Louis, MO

Abstract # 5012

BACKGROUND AND STUDY PURPOSE

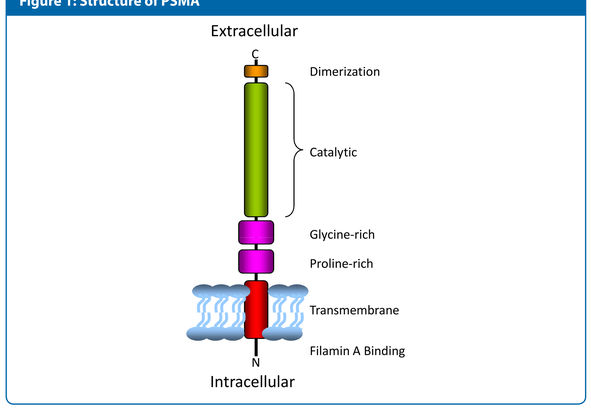
Study Purpose

- Current anatomic and functional imaging methods have poor performance characteristics for disease detection of either locoregional or metastatic prostate cancer
- PSMA-targeted PET imaging is one of the most promising molecular imaging modalities for the detection of prostate cancer to enable more accurate staging and localization of prostate cancer
- ^{18}F-DCFPyL is a PSMA-targeted small molecule radiopharmaceutical PET imaging agent being developed for use in the initial staging of men with high risk prostate cancer, and for the detection of metastatic or recurrent prostate cancer

Prostate-Specific Membrane Antigen (PSMA)

- Dimerized type II transmembrane glycoprotein
- Well established imaging and therapeutic oncology target
- PSMA is expressed in primary and metastatic prostate cancer lesions
- PSMA expression is primarily extracellular enabling diagnostic and therapeutic applications

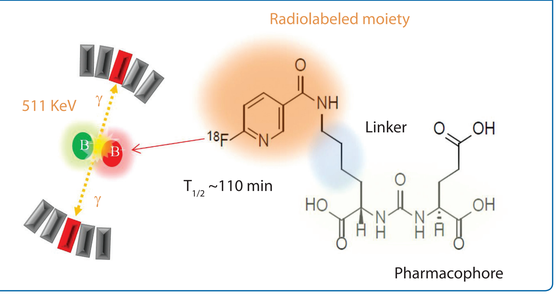
Figure 1: Structure of PSMA



^{18}F-DCFPyL (PyL)

- ^{18}F-DCFPyL is a novel, low-molecular weight, PET radiopharmaceutical that binds selectively to PSMA with high affinity
- The optimal administered activity for ^{18}F-DCFPyL is 9 mCi (333 MBq)
- All organ exposures are <50 mGy

Figure 2: Chemical structure of ^{18}F-DCFPyL



Key Study Endpoints by Cohort

Cohort A (high-risk PCa at diagnosis)

- Sensitivity, specificity, PPV and NPV within the pelvic lymph nodes relative to histology on the patient level

Cohort B (recurrent/metastatic PCa)

- Sensitivity and PPV within metastatic lesions relative to histology on the patient level, and by specific sites of metastases
- Sensitivity and PPV by baseline PSA categories

Previously Reported Data: Cohort A High Risk PCa

- We previously reported the data from Cohort A of this study:
  - Performance characteristics in determining pelvic lymph node metastases: 40% sensitivity, 98% specificity, 87% PPV, and 83% NPV as compared to surgical pathology
    - (AUA 2019: Gorin et al. J Urol 2019 201, Issue Supplement 4; PD60-10)
- Distant metastatic lesion(s) were detected by at least one of the ^{18}F-DCFPyL PET/CT readers in 11.1%
- **Here we present the results of Cohort B: Patients with recurrent/metastatic disease**

Study Objectives

- To prospectively evaluate the performance characteristics of ^{18}F-DCFPyL PET/CT for the detection of regional and distant metastatic lesion(s) in patients with prostate cancer (Pca)

Key Eligibility Criteria (Cohort B)

Inclusion Criteria

- Histologically confirmed adenocarcinoma of the prostate
- Radiologic evidence of local recurrence or new or progressive metastatic disease demonstrated on CT/MRI, ultrasound, or whole-body bone scan
- Evidence of recurrence outside the confines of prior treated site(s)

Exclusion Criteria

- Prior radiation or ablative therapy to intended site of biopsy, if within the prostate bed
- Initiation of new therapy for recurrent and/or progressive metastatic disease since radiographic documentation of recurrence/progression
- Subjects administered:
  - A high-energy (>300 KeV) gamma-emitting radioisotope within five physical half-lives of PyL injection
  - IV iodinated contrast medium within 24 hours of PyL injection
  - Any high density oral contrast medium within 5 days prior to PyL injection

METHODS

- A single dose of ^{18}F-DCFPyL 9±1 mCi (333±37 MBq) IV injection of ^{18}F-DCFPyL is administered 1-2 hours prior to PET/CT imaging on Day 1
- ^{18}F-DCFPyL PET/CT imaging results were evaluated by 3 independent, blinded, central readers
- Image-guided biopsy of at least one amenable lesion
- Pathology review was performed at a local level

Statistical Plan

- Cohort B was initially powered to test the null hypothesis that sensitivity of ^{18}F-DCFPyL PET imaging relative to histopathology is 65%
- The study was thereafter amended to formally test Cohort A hypotheses as primary endpoints; however, Cohort B remained adequately powered
- Point estimates and two-sided 95% CIs are provided for all diagnostic performance parameters relative to histology

Figure 3: Data: Patient disposition

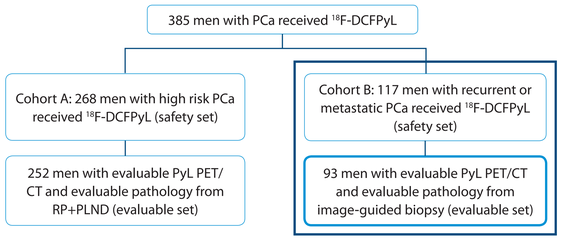


Table 1. Baseline characteristics in men with metastatic/recurrent PCa (Cohort B)

Characteristic	Cohort B (n=93)
Age (years)	
Median (range)	68 (45 – 86)
PSA (ng/mL)	
Median (range)	11.3 (0.03 – 596.9)
PSA (ng/mL), n (%)	
<0.2	5 (5.4)
0.2 to 1.0	8 (8.6)
1.0 to 2.0	6 (6.5)
2.0 to <5.0	16 (17.2)
5.0 to ≤20.0	23 (24.7)
>20	35 (37.6)
Prior PCa therapy n (%)	
Prostatectomy	72 (77.4)
Radiation therapy	58 (62.4)
Systemic therapy	61 (65.6)

Table 2. Imaging to histology correlation: All lesions

All biopsied lesions		Histology (+)	Histology (–)	Total
PyL PET/CT Imaging*	(+)	68	15	83
	(–)	3	7	10
Total		71	22	**93**

Table 3. Imaging to histology correlation: Bone lesions

Bone lesions		Histology (+)	Histology (–)	Total
PyL PET/CT Imaging*	(+)	30	8	38
	(–)	1	4	5
Total		31	12	**43**

Table 4. Imaging to histology correlation: Nodes

Lymph Node lesions		Histology (+)	Histology (–)	Total
PyL PET/CT Imaging*	(+)	29	3	32
	(–)	1	6	7
Total		30	9	**39**

Table 5. Imaging to histology correlation: Viscera/soft tissue

Visceral/ soft tissue		Histology (+)	Histology (–)	Total
PyL PET/CT Imaging*	(+)	9	1	10
	(–)	0	0	0
Total		9	1	**10**

*Median from 3 independent, central readers

Figure 4. Sensitivity and PPV of PyL PET/CT in metastatic PCa relative to histology (cohort B) – Median of three independent readers

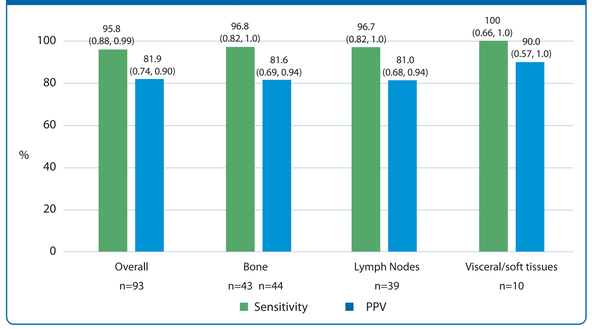
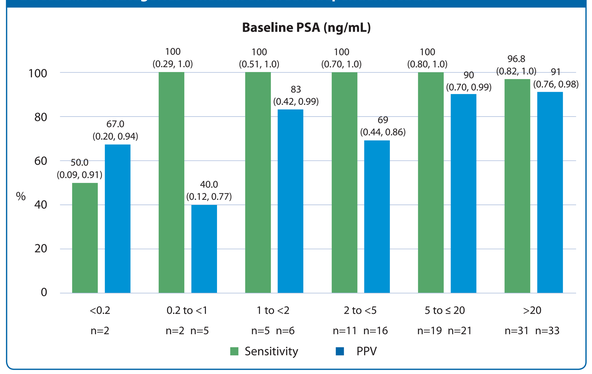


Figure 5. Sensitivity and PPV of 18F-DCFPyL PET/CT in metastatic PCa (cohort B) across all PSA categories – Median of three independent readers



OSPREY: Summary of Safety

- Overall, 385 subjects received ^{18}F-DCFPyL injection in OSPREY
- A total of 27 (7%) subjects experienced at least one drug-related adverse event as determined by the investigator
- There were no serious drug-related adverse events
- The most frequent drug-related AEs were dysgeusia (2.1%) and headache (2.1%)

CONCLUSIONS

- ^{18}F-DCFPyL was safe and well-tolerated
- ^{18}F-DCFPyL PET/CT has excellent performance characteristics in identifying recurrent/metastatic disease:
  - PPV 82% overall, and 82%, 81% and 90% in bone, nodes and viscera
  - Sensitivity 96% overall, and 97%, 97% and 100% in bone, nodes and viscera
- ^{18}F-DCFPyL PET/CT performs well in detecting disease at low PSA values
- ^{18}F-DCFPyL is being further studied as a PET imaging agent in biochemical recurrent (BCR) patients in another prospective, phase 3, multi-center, multi-reader trial (CONDOR; NCT03739684)

Disclosure

- This study was funded by Progenics Pharmaceuticals, Inc., which has a proprietary commercial interest in ^{18}F-DCFPyL (PyL™)

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