A Phase 3, Multicenter Study to Assess the Diagnostic Performance and Clinical Impact of ^{18}F-DCFPyL PET/CT in Men with Suspected Recurrence of Prostate Cancer (CONDOR) (NCT03739684)

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Abstract # TPS5093

BACKGROUND

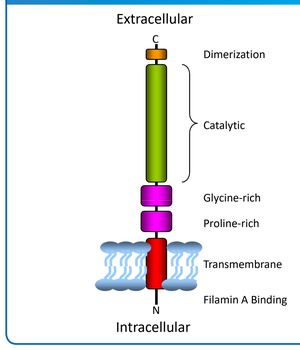
Challenges in early detection/localization of prostate cancer recurrence/metastases

- Men with biochemical relapsed disease (BCR) after initial therapy may receive unnecessary or incomplete local therapy(ies) due to standard imaging modalities failing to correctly identify the distribution of disease
- New positron emission tomography (PET) imaging agents such as ^{11}C-choline and ^{18}F-fluciclovine are FDA-approved options for imaging BCR; however, these have poor performance characteristics in patients with low PSA levels (<2 ng/mL)
- Targeted PET imaging agents with improved detection rates and predictive values are essential to more accurately diagnose, localize, and stage residual, recurrent, and metastatic disease

PSMA is an attractive tumor marker for prostate cancer

- Prostate specific membrane antigen (PSMA) is a well established imaging and therapeutic oncology target **(Figure 1)**
  - PSMA is expressed in primary and metastatic prostate cancer lesions
  - Expression is primarily extracellular enabling diagnostic and therapeutic applications
- PSMA-targeted imaging may more accurately and reliably detect and localize prostate cancer recurrence and metastases as a noninvasive diagnostic modality

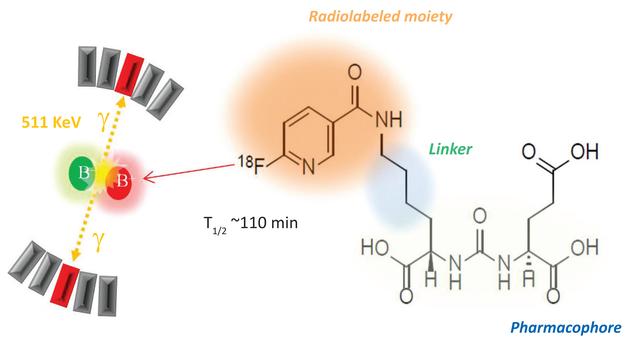
Figure 1: Structure of PSMA



^{18}F-DCFPyL (PyL)

- ^{18}F-DCFPyL is a novel, low-molecular weight, PET radiopharmaceutical that binds selectively to PSMA with high affinity **(Figure 2)**
- The optimal administered activity for ^{18}F-DCFPyL was calculated to be 9 mCi (333 MBq)
- All organ exposures are <50 mGy

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



Summary of clinical experience with ^{18}F-DCFPyL PET/CT imaging in patients with prostate cancer

- ^{18}F-DCFPyL PET/CT imaging was studied in a phase 2/3 trial (OSPREY): A prospective multicenter study examining diagnostic accuracy in patients with prostate cancer (NCT02981368)
- Two patient populations:
  - Cohort A (high risk prostate cancer planned for RP PLND)
    - 40% sensitivity, 98% specificity, 87% PPV and 83% NPV as compared to surgical pathology (AUA 2019: Gorin et al. J Urol 2019 201, Supplement 4; PD60-10)
    - Distant metastatic lesion(s) were detected by ^{18}F-DCFPyL PET/CT in 11.1%
  - Cohort B (radiologic evidence of local recurrence or new/progressive metastasis per conventional imaging)
    - 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 (ASCO 2019: Morris et al. J Clin Oncol 2019, 37, Supplement; abstr 5012))
- Summary:
  - ^{18}F-DCFPyL PET/CT demonstrated high clinically meaningful diagnostic performance characteristics in determining pelvic lymph node metastases
  - Very high standardized uptake values (SUV) even in small lesions, (detect lesions as small as 2 mm)
  - Safe and well tolerated in prior clinical studies

METHODS

Study Population

- Multi-center, multi-reader phase 3 study
- **Patient Population:** Biochemically relapsed prostate cancer (BCR) based on rising PSA after definitive therapy (RP/RT) with negative/equivocal findings for prostate cancer on conventional imaging (including ^{18}F-fluciclovine or ^{11}C-choline PET, CT/MRI bone scintigraphy)
- Total planned subjects enrolled: N~200

Key Study Objectives

Primary Objective

- To determine the Correct Localization Rate (CLR) of ^{18}F-DCFPyL PET/CT imaging in the detection of recurrent prostate cancer at the subject level

Secondary Objectives

- To assess the impact of ^{18}F-DCFPyL PET/CT disease detection on patient's clinical management plans
- To evaluate the safety and tolerability of ^{18}F-DCFPyL

Exploratory Objectives

- To determine detection rates of disease sites with ^{18}F-DCFPyL PET/CT by region (prostatic, pelvic, extra-pelvic) and baseline PSA
- To determine the Positive Predictive Value (PPV) of ^{18}F-DCFPyL PET/CT imaging in the detection of recurrent disease in the prostatic, pelvic, and extra-pelvic regions

Endpoints

Primary endpoint: Correct Localization Rate (CLR)

- Correct localization rate of PyL PET imaging at the subject level, as defined by the % of subjects for whom there is a 1-to-1 correspondence between localization of ≥1 lesion identified on PyL imaging and the composite truth standard of preferably histology if available, follow-up conventional imaging, or treatment response*

Secondary endpoints:

- The percentage of subjects with a change in intended prostate cancer treatment plans due to ^{18}F-DCFPyL PET/CT as measured by comparison of intended management questionnaires completed Pre- and Post- ^{18}F-DCFPyL PET/CT results
- Incidence of adverse events from time of ^{18}F-DCFPyL dosing to 7(±3) days following dosing
- Pre- and post ^{18}F-DCFPyL dosing vital sign changes

Exploratory endpoints:

- Detection rates and PPV of PyL PET by region-level analysis
- The PPV of ^{18}F-DCFPyL PET/CT for prostatic, pelvic, extra-pelvic regions from the composite truth standard in subjects with positive lesion(s) on PyL PET/CT imaging
- Detection rates by baseline PSA groups

***Tiered composite truth standard:**

1. Evaluable histopathology performed within 60 days following PyL PET/CT
2. If histology is not available, informative conventional imaging findings of the anatomical correlate to PyL suspected lesion(s) within 60 days following PyL PET/CT
   - Conventional imaging includes fluciclovine or choline PET, or targeted MRI or CT
   - If neither of the above is available or informative, confirmed PSA response (PSA decline by ≥50%) post-RT (no concomitant ADT) initiated within 60 days following PyL PET/CT

Eligibility Criteria

Inclusion Criteria

- Histopathologically confirmed adenocarcinoma of the prostate, subsequently treated with definitive therapy (RP or RT)
- Rising PSA after definite therapy per AUA or ASTRO/Phoenix criteria
- Negative/equivocal findings for prostate cancer (per investigator's judgement) on conventional imaging performed as standard of care workup within 60 days of study drug injection
- Provide signed informed consent and willing to comply with protocol requirements

Exclusion Criteria

- Administered any high energy (>300 KeV) gamma-emitting radioisotope within 5 physical half-lives prior to study drug injection
- Ongoing treatment with systemic therapy intended for prostate cancer
- Prior treatment with ADT within 3 months before study drug injection
- Receipt of investigational therapy for prostate cancer within 60 days of study drug injection
- Subjects with any other medical conditions/circumstances that, in the opinion of the investigator, compromise the safety or compliance of the subject to produce reliable data or completing the study

Statistics

Primary Endpoint Analysis

- The CLR is computed as 100×TP/(TP+FP); TP = true positives, FP = false positives
- A true positive (TP) result is defined as a subject with both a positive lesion(s) on ^{18}F-DCFPyL PET/CT and a positive result on the composite truth standard
- False positives will be defined as subjects with positive lesion(s) on PyL PET/CT who have negative findings for prostate cancer according to the composite truth standard

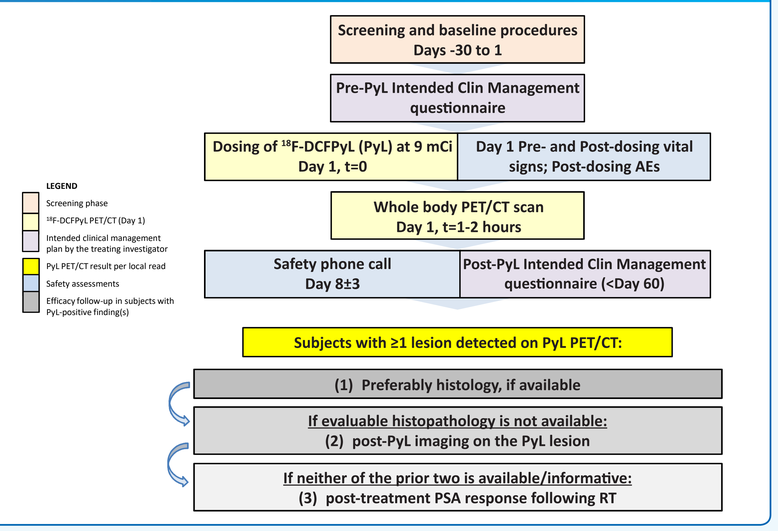
Secondary Endpoint Analysis

- The percentage of subjects with a change in intended prostate cancer treatment plan from Pre- and Post ^{18}F-DCFPyL PET/CT scan evaluated using a one sample binomial test. A summary of shifts in planned management from Pre- and to Post- ^{18}F-DCFPyL imaging evaluations will be presented

Blinding

- Two separate sets of independent central readers from a central imaging core lab will perform PyL PET/CT, biopsy-guided imaging, and post-PyL imaging interpretation
- Central PyL readers will be blinded to all other clinical information and histopathology results (if available)
- Central conventional imaging readers will be blinded to all central PyL reads
- Local pathologists are blinded to central and local imaging results

Figure 3: CONDOR Study Evaluations



SUMMARY

- To determine the Correct Localization Rate (CLR) of ^{18}F-DCFPyL PET/CT imaging in the detection of disease in biochemical recurrent prostate cancer patients
- As of May 2019, 150 subjects have been enrolled in the study
- Key secondary objectives include evaluating the safety and tolerability of PyL, and assessing the impact of ^{18}F-DCFPyL PET/CT disease detection on patient's clinical management plans

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

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