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Diagnostic Performance of PSMA-Targeted ^{18}F-DCFPyL PET/CT in Men with Biochemically Recurrent Prostate Cancer: Results from the Phase 3, Multicenter CONDOR Study

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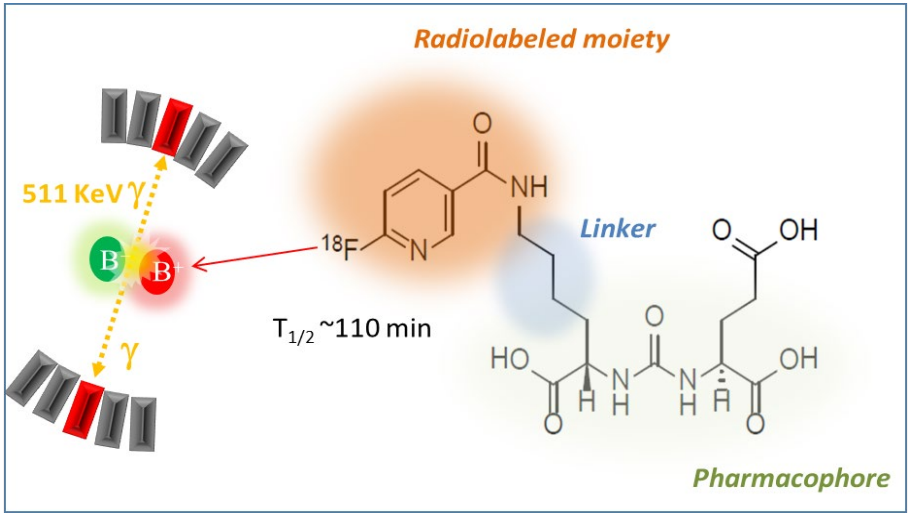
Background

- Currently available imaging modalities are inadequate in reliably localizing occult disease or determining the extent of recurrent prostate cancer, especially in men with low PSA levels
- CONDOR was a registrational phase 3 prospective trial, designed in collaboration with the FDA to demonstrate the diagnostic performance of ^{18}F-DCFPyL
- This is the second of two prospective trials supporting the application for regulatory approval of ^{18}F-DCFPyL in the US

^{18}F-DCFPyL

- Lysine-linked, urea-based small molecule
- Targets the extracellular domain of PSMA
- High specific activity
- 9 (±20%) mCi administered intravenously as bolus injection
- Imaging performed 1-2 hours following administration



Chen et al. Clin Cancer Res 2011; laboratory of Martin G. Pomper, MD, PhD

Select Eligibility Criteria

Inclusion Criteria

- Post-RP: PSA ≥0.2 ng/mL or
- Post-RT or cryotherapy: PSA ≥2 ng/mL above nadir
- Negative or equivocal imaging per institution's SOC work-up (e,g., whole body bone scan, CT, MRI, ^{18}F-fluciclovine or ^{11}C-choline PET, ^{18}F-FDG PET)

Exclusion Criteria

- Ongoing treatment with any systemic therapy
- Treatment with ADT within 3 months prior to ^{18}F-DCFPyL administration

Endpoints

Primary

- **Correct localization rate (CLR)**
  - PPV (TP/[TP+FP]) at the patient level based on anatomic lesion location matching
  - % of subjects with a 1-to-1 correspondence between ^{18}F-DCFPyL PET/CT and the **composite truth standard** for at least one lesion
  - The prespecified success criterion for CLR was if the lower limit of the 95% confidence interval was > 20% for at least 2 of 3 central readers

Secondary

- % of subjects with a change in intended treatment plans as measured by pre- and post-PET questionnaires

Exploratory

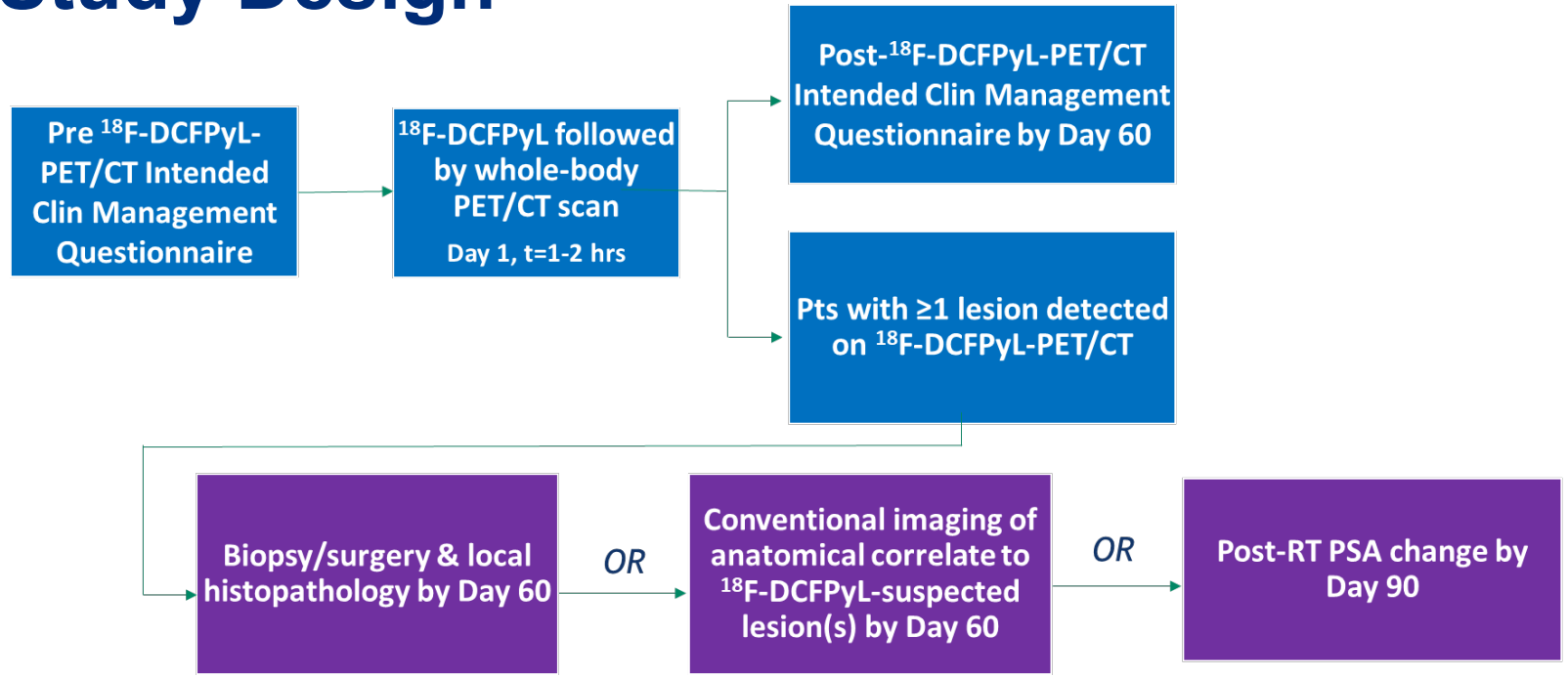
- Detection rate as a function of baseline PSA
- Detection rate at the region level (prostate/prostate bed, pelvis, extra-pelvic regions)
- PPV at the region level (prostate/prostate bed, pelvis, extra-pelvic regions)

Composite Standard of Truth (SOT)

Defined either as:

1) Evaluable local histopathology findings from surgery/biopsy, ***or***
2) Informative conventional imaging (e.g., ^{18}F-fluciclovine PET (preferred if not performed at baseline) or choline PET; targeted MRI/CT), ***or***
3) Confirmed PSA response (decline from baseline of ≥50%) in subjects treated with RT only (no concomitant ADT) following ^{18}F-DCFPyL PET

Study Design



14 sites in the US and Canada
Central imaging core lab

- **Three blinded, independent ^{18}F-DCFPyL PET/CT readers**
- **Two separate truth panel readers, consensus read**

Select Baseline Characteristics

Patients Screened/Consented (N)	**217**
Patients dosed (N)	**208**
Age (years): Median (range)	**68 (43, 91)**
Months from Prostate Cancer Diagnosis: Median (range)	**71 (3, 356)**
Prior Prostate Cancer Therapies, N (%)	
RP only	103 (49.5)
RP and RT	74 (35.6)
RT only	31 (14.9)
At least 1 prior systemic therapy	58 (27.9)
Total Gleason Score, N (%)	
< 8	153 (73.6)
≥ 8	55 (26.4)

PSA: Median (range) ng/mL	**0.8 (0.17, 98.45)**
PSA Group (N=202), N (%)	
<2.0 ng/mL	**139 (68.8)**
<0.5 ng/mL	69 (34.2)
0.5 to <1.0 ng/mL	37 (18.3)
1.0 to <2.0 ng/mL	33 (16.3)
≥2.0 ng/mL	**63 (31.2)**
2.0 to <5.0 ng/mL	33 (16.3)
≥5.0 ng/mL	30 (14.9)

Correct Localization Rate (CLR)

	All Patients (N=208), Median PSA 0.8 ng/mL					
	Reader 1	95% CI (%)	Reader 2	95% CI (%)	Reader 3	95% CI (%)
Negative PyL Scan on Subject Level	71 (34.1%)	(27.7, 40.6)	84 (40.4%)	(33.7, 47.1)	85 (40.9%)	(34.2, 47.5)
Positive PyL Scan on Subject Level	137 (65.9%)	(59.4, 72.3)	124 (59.6%)	(52.9, 66.3)	123 (59.1%)	(52.5, 65.8)
Unevaluable*	33		24		24	
TP/TP+FP	89/104		87/100		84/99	
CLR (95% CI)	85.6%	(78.8, 92.3)	87.0%	(80.4, 93.6)	84.8%	(77.8, 91.9)

*SOT not submitted or false negative at the lesion level

CLR by Baseline Imaging Modality

	All Patients (N=208)	
Uninformative Baseline Imaging Modality	CLR (Range of 3 Readers)	Detection Rate (Range of 3 Readers)
Whole Body Bone Scan and CT/MRI/FDG PET (N=131)	85.1% - 86.3%	58.8% - 66.4%
CT or MRI (N=42)	76.2% - 78.9%	47.6% - 71.4%
Fluciclovine or Choline PET with or without Other Modalities (N=20)	100%	70.0% - 80.0%
Whole Body Bone Scan Only (N=15)	100%	26.7% - 40.0%

CLR by Standard of Truth (SOT)

	All Patients (N=208)	
	CLR (Range of 3 Readers)	PPV (Range of 3 Readers)
Histopathology (N=31)	78.6% - 82.8%	92.9% - 93.3%
Correlative imaging (N=100)	86.1% - 88.6%	87% - 89.5%
PSA response (N=1)	100%	100%

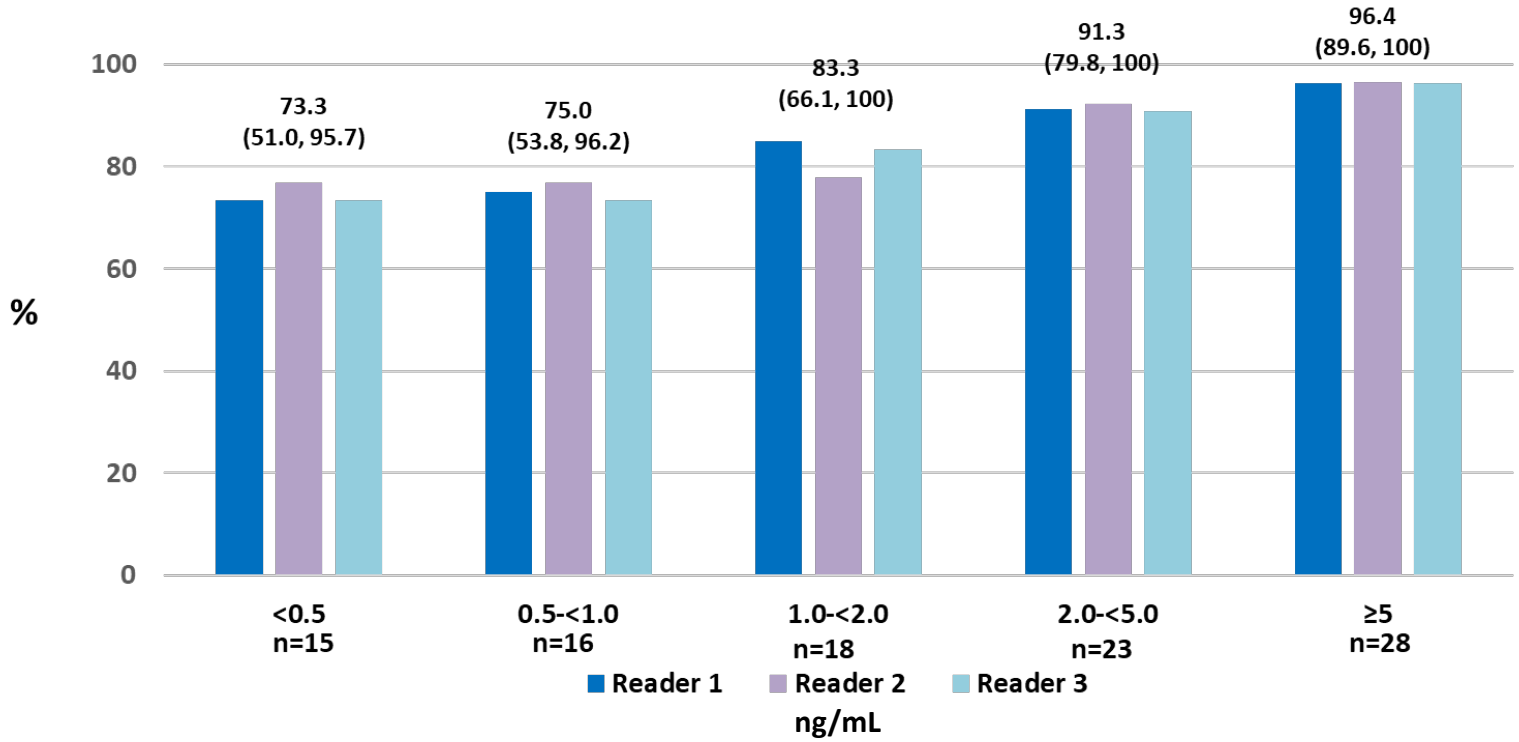
Reader Agreement

Intra-Reader Variability	Concordance (N=42)	Cohen's Kappa (N=42)	(95% CI)	Strength of Agreement*
Reader 1	41 (98%)	0.94	(0.82, 1.0)	Almost Perfect
Reader 2	42 (100%)	1.0		Perfect
Reader 3	38 (91%)	0.81	(0.64, 0.98)	Almost Perfect

Inter-Reader Variability	Concordance (N=208)	Cohen's Kappa (N=208)	(95% CI)	Strength of Agreement**
Between Central Readers	157 (76%)	0.65*	(0.58, 0.73)	Substantial Agreement
Between Central Reader 1 and Local Reader	173 (83%)	0.62	(0.50, 0.73)	Substantial Agreement
Between Central Reader 2 and Local Reader	174 (84%)	0.65	(0.54, 0.75)	Substantial Agreement
Between Central Reader 3 and Local Reader	173 (83%)	0.64	(0.53, 0.74)	Substantial Agreement

*Fleiss Generalized Kappa; **Agreement criteria per: Landis JR, Koch GG. *Biometrics.* 1977;33:159-74.

CLR (%) by PSA groups



Median values for each group of three readers provided

Change in Intended Management

- 63.9% of subjects had a change in intended management as reported by the treating physician

- 78.6% of changes were attributable to positive ^{18}F-DCFPyL scans and 21.4% to negative scans
  - Noncurative systemic therapy to salvage local therapy (n = 43; 21.0%)
  - Salvage local therapy to systemic therapy (n = 58; 28.3%)
  - Observation to initiating therapy (n = 49; 23.9%)
  - Planned treatment to observation (n = 9; 4.4%)

Safety

	All Subjects (N=208) n (%)
Patients who had at least 1 Adverse Event	**14 (6.7%)**
Headache	4 (1.9%)
Fatigue	2 (1.0%)
Hypertension	2 (1.0%)

- **Similar safety profile to prior OSPREY study**
- **Hypersensitivity was the single drug-related Grade 3 AE in a patient with significant allergic history**

Institutions and Collaborators

- Department of Urology, Johns Hopkins University School of Medicine
- Yale School of Medicine
- Cancer Research Center, Centre Hospitalier Universitaire (CHU) de Québec-Université Laval
- Tower Urology
- Department of Urology, University of California San Francisco
- City of Hope
- University of Pennsylvania
- University of Michigan
- Moffitt Cancer Center
- University of Wisconsin School of Medicine
- Stanford University
- Carver College of Medicine, University of Iowa
- Memorial Sloan Kettering Cancer Center
- Siteman Cancer Center/Washington University