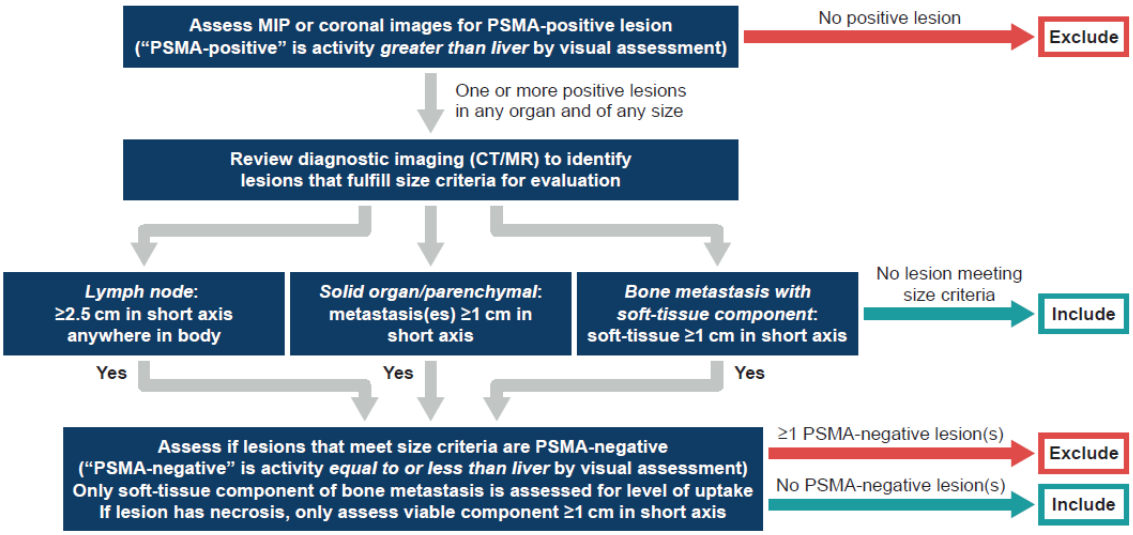
SUPPLEMENTAL DATA

SUPPLEMENTAL FIGURE 1. VISION trial patient selection read methodology



CT, computed tomography; MIP, maximum-intensity projection; MR, magnetic resonance; PSMA, prostate-specific membrane antigen

This figure was originally published in JNM. Kuo PH, et al. Why we did what we did: PSMA-PET/CT selection criteria for the VISION trial. J Nucl Med. 2022;63:816–818. © SNMMI (5).

SUPPLEMENTAL FIGURE 2. Blinded read visual evaluation eCRF

TRID	eCRF details			
eCRF	eCRF name	Visual Assessment of PSMA Imaging		
	Specify relevant trial	Endocyte_PSMA_617_01_VR, Endocyte_PSMA_617_01_Training		
	Relevance	All reads		
	Dependency	All reads		
	Question conformity (applies to required questions only)	Block signoff		
	eCRF question 1:	**Section header:** Visual assessment **Question text:** Does the subject have at least one PSMA-positive lesion (greater than the liver)? **Dependency:** Always required	**Response options:** Single select	• Yes • No
	eCRF question 2:	**Section header:** Visual assessment **Question text:** Is there at least one lymph node ≥2.5 cm (25 mm) in short axis that is PSMA-negative? **Dependency:** Required if: Q1 Field Question: "Does the subject have at least one PSMA-positive lesion (greater than the liver)?" Response option is YES	**Response options:** Single select	• Yes • No
	eCRF question 3:	**Section header:** Visual assessment **Question text:** Is there at least one bone lesion metastasis with a soft tissue component ≥1.0 cm (10 mm) in short axis that is PSMA-negative? **Dependency:** Required if: Q1 Field Question: "Does the subject have at least one PSMA-positive lesion (greater than the liver)?" Response option is YES	**Response options:** Single select	• Yes • No
	eCRF question 4:	**Section header:** Visual assessment **Question text:** Is there at least one solid organ metastases ≥1.0 cm (10 mm) in short axis that is PSMA-negative? **Dependency:** Required if: Q1 Field Question: "Does the subject have at least one PSMA-positive lesion (greater than the liver)?" Response option is YES	**Response options:** Single select	• Yes • No
	eCRF question 5:	**Section header:** Visual assessment **Question text:** Does the subject meet the criteria: Is there at least one PSMA-positive lesion and no PSMA-negative lesion of evaluable size? **Dependency:** Always required	**Response options:** Single select	• Yes • No

eCRF, electronic case report form; PSMA, prostate-specific membrane antigen.

SUPPLEMENTAL TABLE 1. Inter-reader Variability for ^{68}Ga-PSMA-11 PET/CT Scans in the Literature

Reference	Read rules	Readers	Patient population	Kappa/coefficient values	Kappa range and interpretation
(*8*)	Assessed 5 sites of disease: 1. Local (prostatic fossa and surgical anastomosis for patients treated with radical prostatectomy or prostate for patients treated with radiotherapy) 2. Pelvic lymph nodes 3. Distant lymph nodes (any other than pelvic) 4. Bone (any skeletal finding) 5. Other (parenchymal organs and any other soft-tissues) • All areas of increased uptake reported as **anomalous** • All anomalous findings suggestive of recurrent PC (clinical + imaging characteristics) noted as **pathologic**, unless another explanation for increased uptake could be hypothesized • Readers reported exact anatomical localization of finding • Inter-rater agreement calculated with Krippendorff's alpha coefficient	7 expert readers	Biochemical recurrence; 49 patients	Any site • K's alpha anomalous: 0.47 • K's alpha pathologic: 0.64 Local site • K's alpha anomalous: 0.48 • K's alpha pathologic: 0.62 Loco-regional LNs • K's alpha anomalous: 0.63 • K's alpha pathologic: 0.76 Distant LNs • K's alpha anomalous: 0.54 • K's alpha pathologic: 0.75 Bone • K's alpha anomalous: 0.74	0.47–0.79 Moderate-to-substantial

				• K's alpha pathologic: 0.79 Other sites • K's alpha anomalous: 0.67 • K's alpha pathologic: 0.60	
(*9*)	• Recorded SUV_{max} for 1 diseased target region per T (local), N (nodal), Mb (bone), and Mc (visceral) category • Measured background activity by defining SUV_{max} and SUV_{mean} • Overall agreement defined as complete agreement of an observer for all categories	16 readers (various experience)	Biochemical recurrence; 50 patients	All patients (n = 50); Fleiss' Kappa • Local (T): 0.62 (0.59–0.64) • Nodal (N): 0.74 (0.71–0.76) • Bone (Mb): 0.88 (0.86–0.91) • Visceral (Mc): 0.46 (0.44–0.49) BCR and BCP (n = 30) • Local (T): 0.51 (0.48–0.54) • Nodal (N): 0.72 (0.69–0.76) • Bone (Mb): 0.84 (0.80–0.87) • Visceral (Mc): 0.48 (0.44–0.51)	All patients: 0.44–0.91 (with bone) Moderate-to-almost perfect BCR and BCP: 0.44–0.76 (without bone) Moderate-to-substantial
(*7*)	• Interpretation based on PROMISE criteria including miTNM staging and lesions miPSMA expression score visual estimation and PSMA-RADS version 1.0 for a given scan • Agreement between observers was almost perfect for miM (extra pelvic LN and	3 readers (1 resident, 2 very experienced)	Newly diagnosed PC; 43 patients	Agreement K's alpha • miTNM: 0.64 (0.48–0.76) • miT: 0.64 (0.46–0.78) • miN: 0.76 (0.56–0.91)	0.46–1 (with miM) Moderate-to-almost perfect

	distant metastases), substantial for miT (primary tumor), miN (Pelvic LN), PSMA-RADS, and miPSMA (visual assessment) expression score of primary PC lesion and metastases • Agreement was moderate for miPSMA score of positive LNs and detection of PC primary lesions			• miM: 0.94 (0.81–1.00) • PSMA-RADS (0.56–0.90)	
(*11*)	• Lesions were classified as local recurrent, lymphatic mets, bone, mets, or other lesions • Evaluated on 5-point scale 1. Definitely benign 2. Probably benign 3. Equivocal 4. Probably malignant 5. Definitely malignant • Agreement based on malignant vs non-malignant	2 readers + 1 adjudicator for discrepancies (10+ years' experience in hybrid image evaluation with 5+ years' experience in reading PSMA-PET scans); Readers: 1 Radiology NM and 1 NM	Post prostatectomy, PSA recurrent (up to 0.6 ng/ml) PC; 116 patients	• Overall detection rate was 50% • Overall agreement in Cohens Kappa: ○ R1/R2: 0.74 (2 reader agreement) ○ Local: 0.76 ○ Lymphatic: 0.73 ○ Bone sites: 0.58	0.58–0.76 Moderate-to-substantial
(*15*)	Phase 1 • For clinical decision-making, all PET/CT cases were examined by NM physicians Phase 2 • Re-evaluated for primary endpoint analysis (by 2 readers) • Readers evaluated PET images for suspicious findings in the prostate region, regional and non-regional lymph nodes, and osseous and visceral lesions according to a 5-point scale	Experienced (5+ years, > 500 studies) 2 readers for phase 2	Newly diagnosed PC and negative bone scan findings > 10%; 103 patients	• Agreement: k = 0.58	0.58 Moderate
(*6*)	Visual image interpretation • Presence or absence of disease • Number of: ○ prostatic lesions	5 NM expert readers (10+ years)	Newly diagnosed PC; 173 patients	Visual image interpretation • Overall: k = 0.81 (0.61–1.00)	Overall: 0.61–1.00 Substantial-to-almost perfect

	○ regional LN mets ○ distant LN mets ○ bone mets ○ soft-tissue mets			• Primary tumor: k = 0.71 (0.40–1.00) • Regional LN: k = 0.79 (0.70–0.87) • Distant LN: k = 0.77 (0.68–0.86) • Bone mets: k = 0.83 (0.74–0.92) • Soft-tissue: k = 0.63 (0.47–0.80)	By region: 0.40–1.00 Moderate-to-almost perfect
(*10*)	Readers graded images on 2-point scale: A region was judged positive if at least 1 lesion in the region had greater uptake than blood pool (lymph nodes), physiologic background activity of an organ (visceral, prostate, and prostate bed lesions), or background bone marrow uptake (bone lesions)	2 NM physicians (1 year of experience interpreting PSMA-PET scans)	Biochemically recurrent PC; 150 total patients; 72 PET/CT and 78 PET/MRI examinations used for inter-rater reliability	Cohen's Kappa statistic • Prostate bed: k = 0.87 • Pelvic lymph nodes: k = 0.81 • Soft-tissues: k = 0.79 • Bones: k = 0.78 • Overall: k = 0.70	0.70–0.87 Substantial-to-almost perfect

BCP, basal cell carcinoma of the prostate; BCR, biochemical recurrence; CT, computed tomography; K, Kappa; LN, lymph node; mets, metastases; MRI, magnetic resonance imaging; NM, nuclear medicine; PC, prostate cancer; PET, positron-emission tomography; PSA, prostate-specific antigen; PSMA, prostate-specific membrane antigen; RADS, reporting and data system; SUV_{max}, maximum standardized uptake values; SUV_{mean}, mean of standardized uptake values.