(TPS429) CLARIFY: Positron emission tomography using ^{64}Cu-SAR-bisPSMA in patients with high-risk prostate cancer prior to radical prostatectomy – a phase 3 diagnostic performance study

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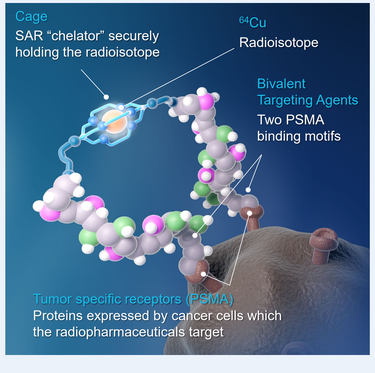
Background

Prostate-specific membrane antigen (PSMA) is used as an imaging target in initial staging of prostate cancer (PC).[1] Current PSMA PET agents have high specificity, but low sensitivity for the detection of pelvic lymph node (LN) involvement.[2-4]

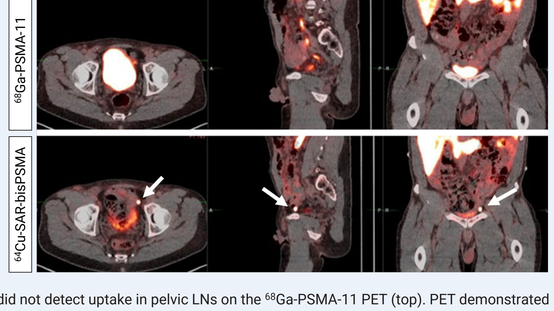
^{64}Cu-SAR-bisPSMA has two distinct advantages over current PSMA positron emission tomography (PET) agents: bivalent structure and longer half-life of ^{64}Cu ($t_{1/2}$ = 12.7 h) compared to monovalent PSMA PET agents utilizing ^{18}F and ^{68}Ga ($t_{1/2}$ < 2 h).[5-7] **(Figure 1)**

Figure 1. ^{64}Cu-SAR-bisPSMA



In the Phase 1 PROPELLER study, ^{64}Cu-SAR-bisPSMA demonstrated 2-3 times higher tumor uptake and detection of additional PC lesions compared to ^{68}Ga-PSMA-11 PET.[8] **(Figure 2)**

Figure 2. ^{64}Cu-SAR-bisPSMA detects LN involvement not identified on ^{68}Ga PSMA-11 PET



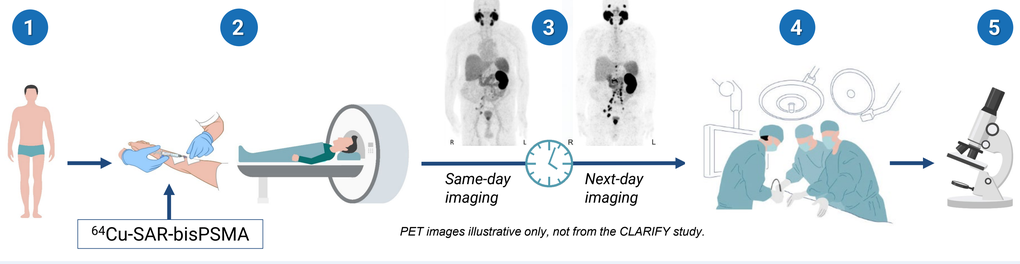
Readers did not detect uptake in pelvic LNs on the ^{68}Ga-PSMA-11 PET (top). PET demonstrated uptake of ^{64}Cu-SAR-bisPSMA (200MBq, Bottom, arrows, same-day imaging post-dose) in a left pelvic LN according to both readers. PC was confirmed via histopathology. Interval between serial imaging: 7 days. Images show PET/computed tomography (CT) fusion (using the same scanner).

Methods

Figure 3. Study Design

CLARIFY is a multi-center, single-arm, non-randomized, open-label, Phase 3 study of ^{64}Cu-SAR-bisPSMA PET in patients with untreated, histopathology-confirmed PC with high-risk features, who are proceeding to radical prostatectomy with pelvic lymph node dissection (RP-LND).

1. Screening
2. ^{64}Cu-SAR-bisPSMA administration followed by PET/CT scan
3. "Same-day" and "next-day" imaging post-dose (Day 1 and Day 2)
4. Surgical removal of the prostate and pelvic LNs
5. Laboratory assessments of the prostate and LNs (histopathology) to confirm the results of the PET scan



Key Eligibility Criteria

- Untreated, histopathology-confirmed prostate adenocarcinoma with high-risk features as defined by National Comprehensive Cancer Network guidelines v1.2023:
  - Clinical stage ≥ T3a, and/or Grade Group ≥ 4, and/or PSA > 20 ng/mL
- Proceeding to RP-LND

Primary Objective

To assess the diagnostic performance of ^{64}Cu-SAR-bisPSMA PET to detect regional nodal metastases

- Independent co-primary endpoints of sensitivity and specificity of same- and next- day ^{64}Cu-SAR-bisPSMA PET compared to standard of truth (SOT)

Secondary Objectives

- Safety and tolerability of ^{64}Cu-SAR-bisPSMA
- Consistency of ^{64}Cu-SAR-bisPSMA PET interpretations for the three central readers
- Positive predictive value (PPV) and negative predictive value (NPV) of ^{64}Cu-SAR-bisPSMA PET to detect PC within pelvic LNs
- Ability of ^{64}Cu-SAR-bisPSMA PET to detect PC
- Diagnostic performance of ^{64}Cu-SAR-bisPSMA PET to detect regional nodal metastases without subregion matching

Study Design

A total of 383 patients will be enrolled. Eligible patients will receive a single administration of ^{64}Cu-SAR-bisPSMA (200 MBq) followed by a PET/CT scan on the same day (1-4 hours post- dose) and on the next day (24 ± 6 hours post-dose). Patients will be assessed for safety and then proceed to RP-PLND **(Figure 3)**.

The same- and next-day ^{64}Cu-SAR-bisPSMA PET/CT scans will be interpreted locally and by three independent, blinded, central readers. The specimens from surgery will be assessed by histopathology to derive the standard of SOT. The diagnostic performance of ^{64}Cu-SAR-bisPSMA will be based on the scan result for the respective day independently (same- and next-day) matched against the SOT.

Study Locations

The study is open for recruitment in the United States and in Australia **(Figure 4).**

Figure 4. Active Sites

For more information on active sites, please visit: https://clinicaltrials.gov/study/NCT06056830

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