

A phase 2 trial of darolutamide to enhance prostate-specific membrane antigen expression in patients with localized prostate cancer (Daro-PET).

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PESQUISA E ENSINO

Jéssica Vasconcellos, Camila Mosci, Marcelo Queiroz, Camila Togni, Daniel Moser, Oseas Castro Neves Neto, Felipe M. Cruz, Thiago S. Hemerly, Alexandre K. Taneno, Isabella C. Henriques, Mariana P. de Macedo⁶ Rodrigo N. Ramos, Mariana A. Morini, Isabela W. Cunha, Jose Mauricio Mota.

Instituto D'Or de Pesquisa e Ensino (IDOR), São Paulo, Brazil & Instituto do Câncer do Estado de São Paulo, University of São Paulo, São Paulo, Brazil

BACKGROUND

- Androgen suppression may transiently increase PSMA expression, with potential implications for PSMA PET detection and PSMA-targeted therapies;
- Available evidence predominantly derive from studies in the metastatic castration-resistant setting, with limited or absent data in localized, castration-sensitive disease.

METHODS

- Daro-PET ([NCT05900973](#)) is a phase 2 single-arm trial evaluating if short-course darolutamide increases PSMA expression in high-risk localized prostate cancer;
- Baseline PSMA PET/CT → 7 days of darolutamide 600 mg twice daily → repeat PSMA PET/CT;**
- Two-stage Simon design (80% power, one-sided $\alpha=0.05$): 12 patients in stage 1, expansion to 16 after 1 event, with ≥ 3 events defining a positive trial;
- Primary endpoint:** the proportion of patients with a $\geq 20\%$ increase in SUVmax from PSMA-PET 1 to PSMA-PET 2; **Secondary endpoints:** tumor volume, SUVmean, total lesion PSMA, new metastases, safety, and per-protocol analyses;
- Efficacy analyses were performed in the intention-to-treat (ITT) and per-protocol populations (radiotracer dose of 4.0 ± 1.0 mCi with $\leq 30\%$ variation between PSMA PETs).

RESULTS

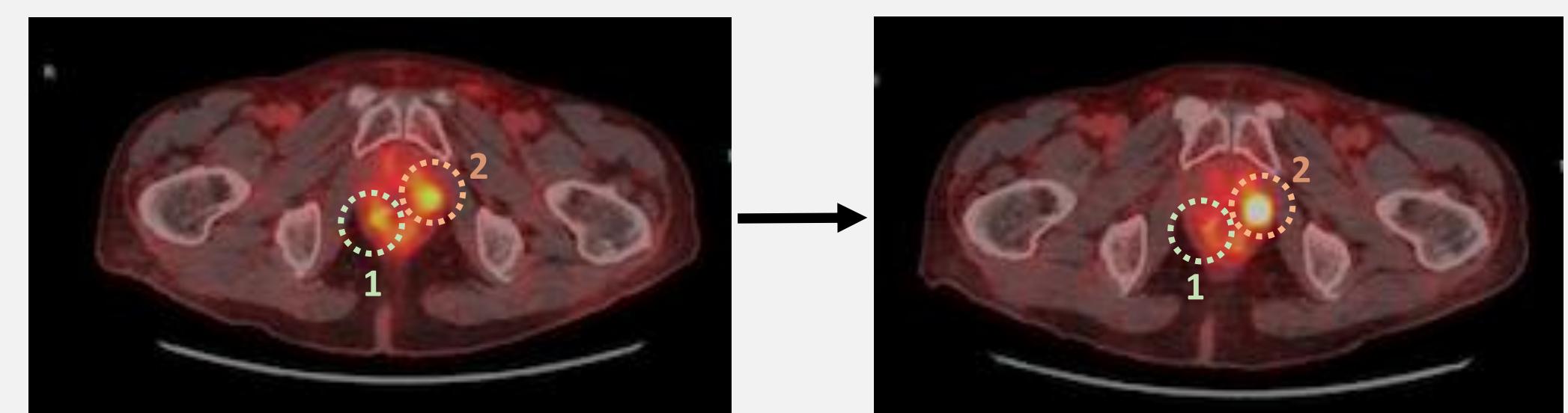
Between July 2023 and March 2025, 16 patients were enrolled.

Table 1. Baseline characteristics.

Characteristic	Cohort, N=16
Age, median (IQR) – years	61 (55.5 – 70.5)
ISUP grade – N (%)	
≥4	9 (56)
Clinical T stage – N (%)	
cT2	6 (37.5)
cT3	10 (62.5)
Total PSA, median (IQR) – ng/ml	10.01 (6.41–11.24)
Total testosterone, median (IQR) – ng/dL	314 (258.3–392.9)
Lymph node involvement at baseline PET, n (%)	
Positive	4 (25)
Negative	12 (75)
Multifocal prostate uptake at baseline PET, n (%)	4 (27)

- All patients completed the protocol with full treatment adherence with no adverse events. Two patients did not undergo prostatectomy by shared decision-making;
- In the ITT population, 5 patients (31%) had any SUVmax increase after darolutamide, with 3 patients (18.8%; 90% CI, 5.3–41.7) achieving a $\geq 20\%$ increase (range: 36.5% to 62%) (Figure 1);**
- Results were similar in the per-protocol population (N=14), with 5 patients (36%) with any SUVmax increase and 3 patients (21%) with an SUVmax $\geq 20\%$ increase;
- Seven patients (50%; 90% CI 26.4–73.6) showed increased tumor volume (range: 6.2% to 98.6%). SUVmean and total lesion PSMA increased in 3 patients (21.4%);**
- No new pelvic or extrapelvic metastases were detected after darolutamide treatment.

Figure 1. PSMA PET scans pre- and post-darolutamide from a representative patient with multifocal disease.



Lesion 1: SUVmax: 9.6; SUVmean: 5.3
Lesion 2: SUVmax: 5.2 ; SUVmean:2.8
Volume: 1.2 mL

SUVmax: 4.6 ($\Delta -52\%$); SUVmean:2.4 ($\Delta -52\%$)
SUVmax: 7.1 ($\Delta +36.5\%$); SUVmean:2.8 ($\Delta +25\%$)
Volume: 2.1 mL ($\Delta +75\%$)

Three patients had 2 prostatic uptake foci, with heterogeneous changes in PSMA uptake after darolutamide (Table 2).

Patient ID	Focus 1: Δ SUVmax (%) / Gleason score	Δ SUVmax (focus 2) (%) / Gleason score
#3	-31.5 (Gleason 3+3)	-8.0 (Gleason 4+3)
#8	-52.0 (Gleason 4+3)	+36.5 (Gleason 4+4)
#12	+62.0 (Gleason 4+4)	+8.3 (Gleason 3+3)

CONCLUSIONS

A 7-day treatment with darolutamide increased PSMA expression in a subset of localized prostate cancer, with notable heterogeneity in response; translational studies are planned to investigate the mechanisms involved.

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