#2483P: PCPro, plasma lipid biomarker, in metastatic hormone-sensitive prostate cancer (mHSPC): from research to clinical implementation in the ENZAMET trial (ANZUP 1304)

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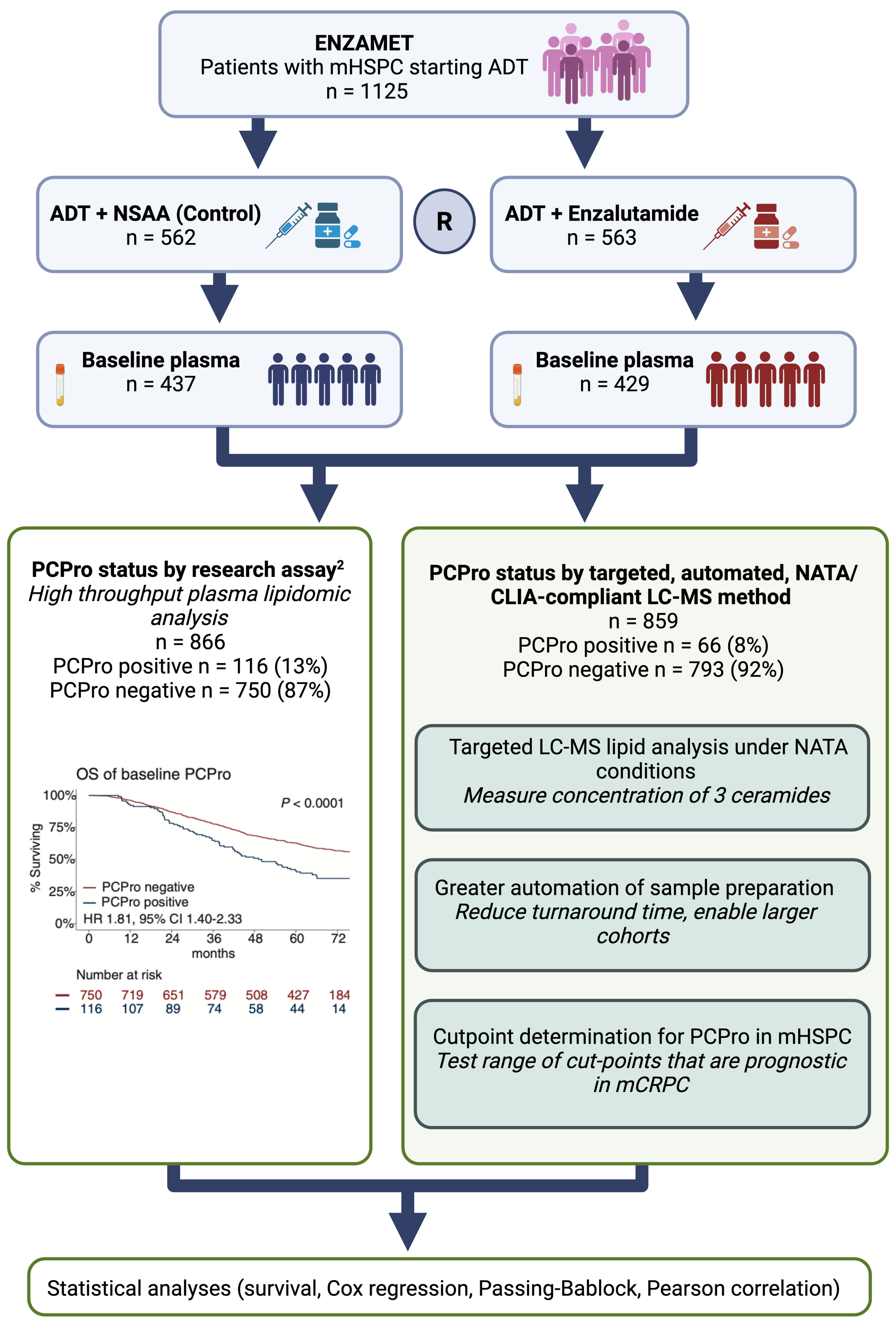
Background

- **Enzalutamide (ENZ)** improves overall survival (OS) in patients with metastatic hormone-sensitive prostate cancer (mHSPC)[1]
- The **ENZAMET phase 3 trial** demonstrated benefit of ENZ plus androgen deprivation therapy (ADT) over non-steroidal anti-androgen (NSAA) plus ADT in mHSPC[1]
- Post-hoc analysis of ENZAMET showed that **PCPro, a circulating lipid biomarker**, is associated with shorter OS in patients with mHSPC treated with ADT + ENZ or NSAA[2]. The analysis used a high-throughput research liquid chromatography-mass spectrometry (LC-MS) approach, which is not validated for clinical practice.

Aim

To develop a NATA-compliant PCPro assay for use in prospective clinical trials of precision metabolic therapies in mHSPC

Study design (Fig. 1)



PCPro risk score calculation:
(10.0506 x **Cer(d18:1/18:0)**) + (-0.2783 x total cholesterol) + (-0.2240 x triglycerides) + (-0.2979 x (**Cer(d18:1/24:0)/Cer(d18:1/24:1)**))

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Results

Table 1: Patient characteristics of study cohort by baseline PCPro status

Characteristic	PCPro Negative n = 793	PCPro Positive n = 66	p-value[1]
Treatment arm			0.3
Conventional NSAA	395 (50%)	38 (58%)	
Enzalutamide	398 (50%)	28 (42%)	
Volume of disease			0.2
Low	378 (48%)	25 (38%)	
High	415 (52%)	41 (62%)	
Concurrent docetaxel	359 (45%)	27 (41%)	0.6
ACE-27 score			0.4
0-1	598 (75%)	46 (70%)	
2-3	195 (25%)	20 (30%)	
Region			0.9
Australia/New Zealand	521 (66%)	42 (64%)	
Ireland/UK	96 (12%)	8 (12%)	
North America	176 (22%)	16 (24%)	
Gleason grade			0.09
≤ 7	222 (28%)	15 (23%)	
8-10	466 (59%)	36 (55%)	
Unknown	105 (13%)	15 (23%)	
ECOG performance status			<0.001
0	591 (75%)	33 (50%)	
1-2	202 (25%)	33 (50%)	
Age			0.3
<70	436 (55%)	31 (47%)	
≥ 70	357 (45%)	35 (53%)	
Visceral metastases	89 (11%)	12 (18%)	0.1
Metastatic status at first diagnosis			0.04
M0 (metachronous)/ unknown	310 (39%)	17 (26%)	
M1 (synchronous)	483 (61%)	49 (74%)	

[1]Pearson's Chi-squared test

Table 2: Optimal cutpoint for defining PCPro positive status in mHSPC is -1.38

Cut-point*	Univariate Cox regression		Survival analysis			C-index
	Hazard ratio [95% CI]	p-value	PCPro negative 5yr-survival [95% CI]	PCPro positive 5yr-survival [95% CI]	Log rank p-value	
-1.38	2.23 [1.63 – 3.04]	<0.001	63% [59 – 66%]	31% [22 – 45%]	<0.001	0.532
-1.34	1.99 [1.41 – 2.79]	<0.001	62% [59 – 65%]	34% [24 – 50%]	<0.001	0.524
-1.23	1.66 [1.08 – 2.56]	0.02	61% [58 – 64%]	40% [27 – 60%]	0.02	0.511
-1.19	1.72 [1.07 – 2.76]	0.03	61% [58 – 64%]	36% [22 – 59%]	0.02	0.509
-1.17	1.71 [1.02 – 2.87]	0.04	61% [57 – 64%]	38% [22 – 63%]	0.04	0.508

Range of PCPro cutpoints that were prognostic in studies of mCRPC[3] were explored

Figure 3: NATA-compliant PCPro is prognostic for (A) overall survival and (B) clinical progression-free survival in mHSPC using cutpoint > -1.38

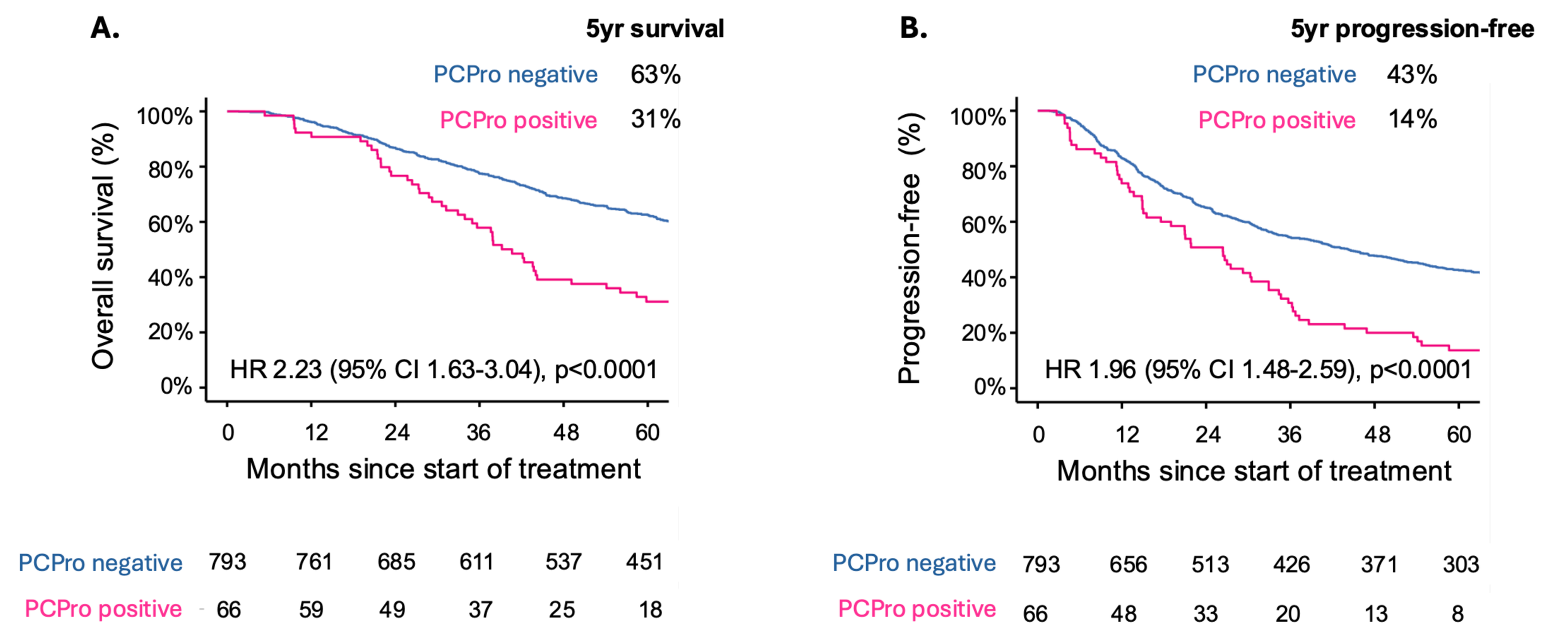


Figure 2. NATA-compliant and research PCPro's final risk scores were highly correlated by Passing-Bablock and by Pearson correlation

Pearson correlation co-efficient 0.85 p < 0.001

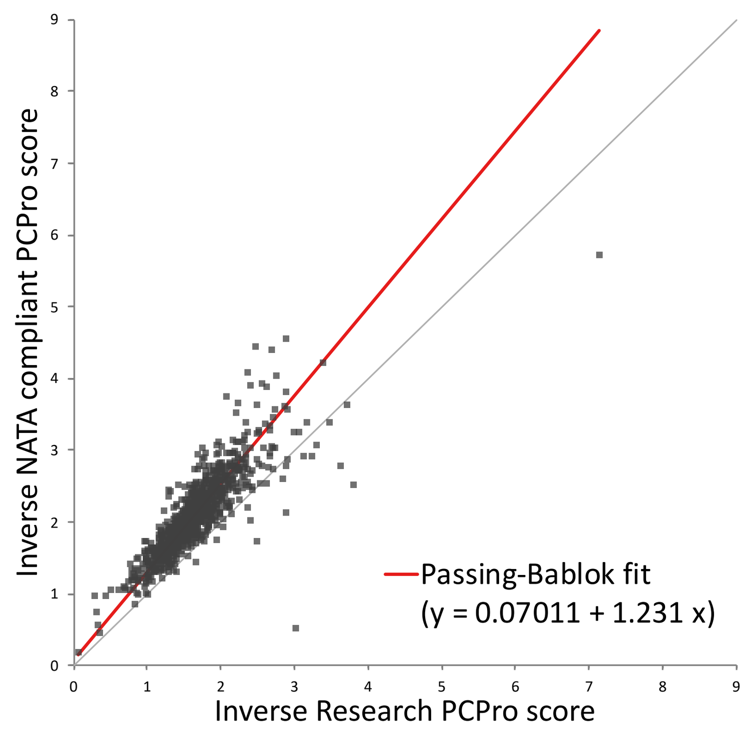
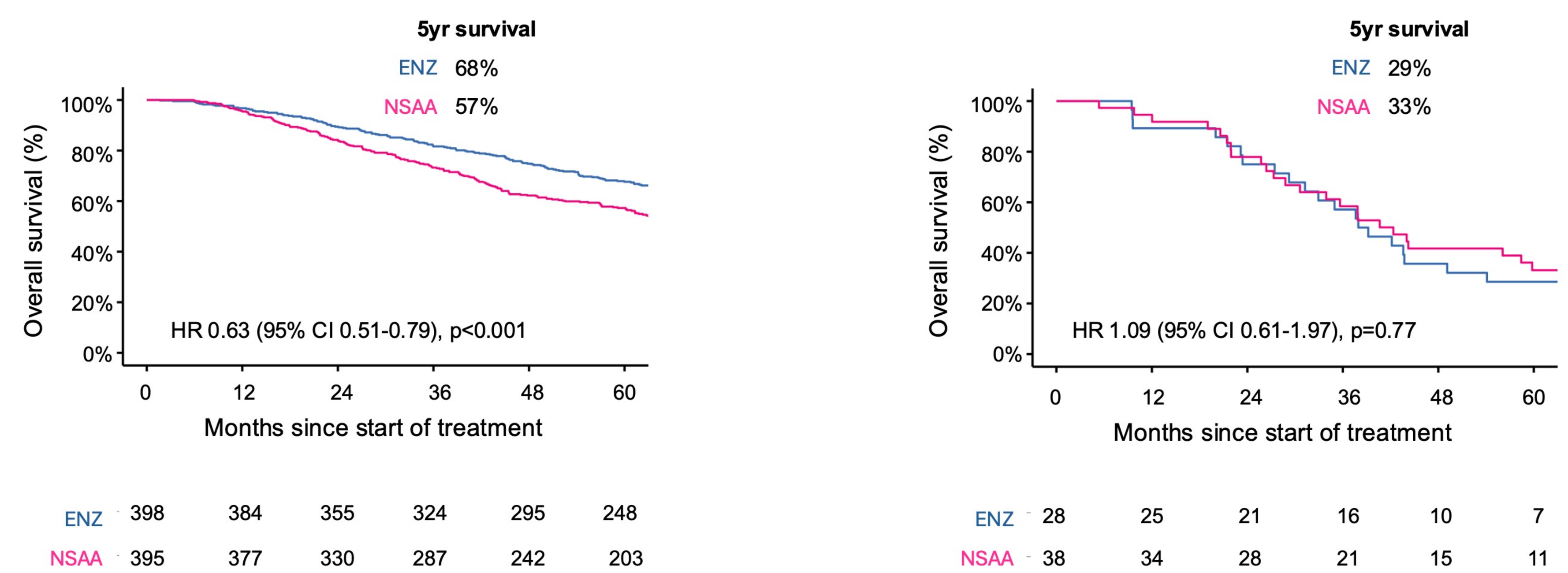


Table 3: NATA-compliant PCPro is prognostic for OS and clinPFS independent of other clinical variables: results of multivariable Cox regression analysis

Variable	OS model		ClinPFS model	
	HR [95% CI]	p-value	HR [95% CI]	p-value
Baseline PCPro (positive vs negative)	1.76 [1.28-2.42]	<0.001	1.53 [1.15-2.03]	0.003
Treatment arm (ENZ vs NSAA)	0.67 [0.54-0.82]	<0.001	0.41 [0.34-0.49]	<0.001
Volume of disease (Low vs High)	0.46 [0.37-0.58]	<0.001	0.49 [0.40-0.59]	<0.001
ECOG (1-2 vs 0)	1.65 [1.33-2.04]	<0.001	1.51 [1.25-1.81]	<0.001
Stage at diagnosis (M1 vs M0)	1.11 [0.89-1.39]	0.4	1.16 [0.96-1.40]	0.1
Concurrent docetaxel (Yes vs No)	0.93 [0.75-1.15]	0.5	0.97 [0.81-1.17]	0.8

Figure 4: Patients who were PCPro-positive had no demonstrable OS benefit with ENZ compared with NSAA. In contrast, OS was significantly improved by ENZ in patients who were PCPro-negative. Interaction p-value 0.09



Conclusion

The optimised, more targeted NATA-compliant assay allows for cheaper, faster, and reproducible PCPro assessment in patients with mHSPC, and can be performed using standard clinical hospital laboratory equipment

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Disclosure statement: R. Mellor (first author and presenter) has no conflicts of interest to declare

References: [1] Sweeney et al (2023) Lancet Oncol 24:323 [2] Lin et al (2025) Ann Oncol 36:1068 [3] Scheinberg et al (2024) Prostate Cancer Prostatic Dis 27:136

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