Biomarker	Type of sample	Utility assessment	Sample size	Performance	Reference[¶]
Guide Biopsy					
PCA3	Urine after DRE	PSA intermediate zone (2.5–10.0 ng/mL) / Repeated biopsy	N=1024	<u>Cut-off score 20:</u> 69% Sen, 57% Spe 52% reduction of biopsies	Tombal et al.; 2013
PCA3 (+ clinical variables)	Urine after DRE	Full PSA range/ First biopsy	N=594	<u>PCA3/ Cut-off score 35</u> AUC=0.74 (0.70–0.78; 95% CI) 63% Sen, 72% Spe <u>Combination with clinical variables</u> AUC=0.78	Ruffion et al.; 2013
TMPRSS2: ERG, PCA3	Urine after DRE	PSA intermediate zone (2.5-10.0 ng/mL)/ biopsy	N=197	<u>PSA (2.5-10.0 ng/mL)</u> AUC=0.51 (0.44–0.58; 95% CI) <u>PCA3/ Cut-off score 25</u> AUC=0.74 (0.44–0.58; 95% CI) <u>TMPRSS2-ERG</u> AUC=0.66 (0.59–0.73; 95% CI)	Stephan et al.; 2013
TMPRSS2: ERG, PCA3 (+ERSPC)	Urine after DRE	Full PSA range / Biopsy	N=443	<u>PCA3/ Cut-off score 25</u> AUC=0.83 (0.80–0.87; 95% CI) <u>TMPRSS2: ERG; cut-off 10 copies</u> AUC=0.84 (0.81–0.88; 95% CI)	Leyten et al.; 2014

				ERSPC risk calculator AUC=0.80 (0.76–0.84; 95% CI) PCA3+ TMPRSS2: ERG +ERSPC risk calculator AUC=0.84	
miR-148a, miR-375 (+ PSA)	Urine from RP patients (pre-operative catheterised)	Full PSA range/ Grey Zone / First biopsy	N=166	Combination of miRs and PSA: *Full PSA range* AUC=0.85 *PSA range 4-10 ng/ mL* AUC=0.90	Stuopelyte et al.; 2016
CE-MS biomarker panel (+ clinical variables)	Urine	Intermediate PSA range (2–20 ng/mL) / biopsy	Training Set, N=86 Validation Set, N=213	Performance in Validation Set: CE-MS Biomarkers + clinical variables: AUC=0.82 CE-MS Biomarkers: AUC=0.70	Theodorescu D et al.; 2008
CE-MS biomarker panel	Urine	Full PSA range / biopsy	N=184	CE-MS Biomarkers: AUC=0.72 PSA: AUC=0.60	Schiffer E, et al.; 2012
Discrimination of significant and insignificant prostate cancer					
ExoDx + clinical	Urine	PSA intermediate zone (2 -10 ng/mL)	Training Set,	Performance in	McKiernan et al.; 2016

variables		/First biopsy	N=255 Validation Set, N=519	Validation Set: ExoDx + clinical variables AUC=0.73 (0.68–0.77; 95% CI) ExoDx AUC=0.71(0.66–0.76; 95% CI)	
Mi-Prostate Score: PCPThg risk calculator version 1.0 + TMPRSS2: ERG + PCA3	Urine after DRE	Full PSA range/First biopsy	Training Set, N=679 Validation Set, N=1218	Performance in Validation Set: Combination of PCPThg + PCA3+ TMPRSS2: ERG AUC=0.78 PCPThg risk calculator AUC=0.71	Tomlins et al.; 2016
10 genes (UAP1, PDLIM5, IMPDH2, HSPD1, PSA, PCA3, TMPRESS2, ERG, AR, PTEN) + clinical variables	Urine	Full PSA range/Prostatectomy	N=306	For prediction of HG cancer Sensitivity 92% (87–95%)	Albitar et al.; 2018
HOXC6, DLX1 + clinical variables	Urine	Full PSA range/First biopsy	Training Set, N=492 Validation Set, N=371	Performance in Validation Set: HOXC6 and DLX1 AUC=0.73 (0.67–0.78; 95% CI) HOXC6, DLX1 + clinical	Van Neste et al.; 2016

				variables AUC=0.90 (0.85–0.95; 95% CI)	
CE-MS biomarker panel (+ ERSPC risk calculator)	Urine after DRE	Intermediate PSA range (<15 ng/ mL)	Training Set, N=543 Validation Set, N=280	Performance in Validation Set CE-MS Biomarkers + ERSPC AUC=0.82 CE-MS Biomarkers AUC=0.75	Frantzi, Gomez-Gomez et al.; *unpublished data*
Active surveillance					
PCA3	Urine after DRE	Active surveillance	N=90	Discrimination of cancer upgrading at the first repeat biopsy AUC=0.91	Fradet V et al, 2018

Table 1. List of most prominent urinary biomarkers for PCa management. The biomarker characteristics, the purpose of use, along with the performance characteristics are comparatively presented. **Abbreviations:** **AR**=Androgen Receptor; **AUC**=Area Under the ROC curve; **CE**=Capillary Electrophoresis; **DLX1**=Homeobox protein DLX-1; **DRE**=Digital Rectal Examination; **ERG**=Transcriptional regulator ERG; **ERSPC**=European Randomized study of Screening for Prostate Cancer; **HOXC6**=Homeobox protein Hox-C6; **HSPD1**=60 kDa heat shock protein; **IMPDH2**=Inosine-5'-monophosphate dehydrogenase 2; **MS**=Mass Spectrometry; **Sen**=Sensitivity; **Spe**=Specificity, **PCA3**=Prostate cancer antigen 3; **PCPThg**= Prostate Cancer Prevention Trial high grade cancer risk calculator; **PDLIM5**=PDZ and LIM domain protein 5; **PSA**=Prostate-specific antigen; **PTEN**=Phosphatidylinositol 3,4,5-trisphosphate 3-phosphatase and dual-specificity protein phosphatase; **RP**=Radical Prostatectomy; **TMPRSS2**=Transmembrane protease serine 2; **UAP1**=UDP-N-acetylhexosamine pyrophosphorylase

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