Thanks for 26 great meetings my friend.

Michael Brawer,MD

Sr VP Medical Affairs
Myriad Genetics Laboratories

The CCP score provides significant prognostic information in Gleason score ≤ 6 patients

Jay T. Bishoff[1], Stephen J. Freedland[2], Thorsten Schlomm[3], Julia E. Reid[4], Michael K. Brawer[5], Steven Stone[4], Jack Cuzick[6]

1- Intermountain Urological Institute, Murray, UT
2- Durham VA Medical Center, Durham, NC and Cedars-Sinai Medical Center, Los Angeles, CA
3- University Medical Center Hamburg-Eppendorf, Hamburg, Germany
4- Myriad Genetics, Inc., Salt Lake City
5- Myriad Genetic Laboratories, Inc., Salt Lake City
6- Wolfson Institute of Preventive Medicine, London, United Kingdom

Prolaris Signature is Validated Against Multiple Meaningful Endpoints

	Publication	Sample Type	Patients	Endpoint	Outcome
CLINICAL VALIDATION	Cuzick 2011	RP	353	Biochemical Recurrence	HR = 1.89 per unit Prolaris score, $p=5.6 \times 10^{9}$
	Cuzick 2011	TURP	337	Mortality	HR = 2.92, $p=6.1 \times 10^{-22}$
	Cuzick 2012	Biopsy	349	Mortality	HR = 2.02, $p=8.6 \times 10^{-10}$
	Cooperberg 2013	RP	413	Biochemical Recurrence	HR = 2.10, $p=2.2 \times 10^{-8}$
	Freedland 2013	Biopsy	141	Biochemical Recurrence	HR = 2.55, p=0.0017
	Bishoff 2014	Biopsy	582	Biochemical Recurrence Metastases	HR = 1.6, $p=2.4 \times 10^{-7}$ HR = 5.35, $p=2.1 \times 10^{-8}$
	Cuzick 2015	Biopsy	757	Mortality	HR = 2.32, $p<10^{-17}$

myriad Prolaris

List of cohorts for Gleason ≤ 6 patients with CCP and CAPRA scores

Cohort	Adverse event	Number of patients	Number of adverse events
Trans-Atlantic Prostate Group (TAPG-1)	Death from prostate cancer	53	4 (8%)
Trans-Atlantic Prostate Group (TAPG-2)	Death from prostate cancer	151	4 (3%)
Martini-Clinic, Prostate Cancer Center, University Medical Center, Hamburg-Eppendorf, Hamburg, Germany (MC)	Biochemical recurrence	83	7 (8%)
Durham VA Medical Center, Department of Surgery (Urology), Duke University School of Medicine, Durham, NC (DVA)	Biochemical recurrence	76	36 (47%)
Intermountain Healthcare, Salt Lake City, UT (IHC)	Biochemical recurrence	77	13 (17%)
		440	**64 (15%)**

- This study assessed men with Gleason score ≤ 3+3 in a meta-analysis combining two conservatively managed cohorts, and three cohorts after radical prostatectomy.

Univariate and Bivariate Models

Variable	HR	95% CI	p-value
Univariate			
CCP	1.50	(1.11, 2.03)	0.0099
CAPRA	1.27	(1.03, 1.56)	0.030
CCR	1.83	(1.27, 2.63)	0.0014
Bivariate			
CCP	1.46	(1.08, 1.98)	0.019
CAPRA	1.23	(1.00, 1.53)	0.058

- In univariate analysis, both CCP and CCR scores were significant predictors of outcome.

  - CCP: HR = 1.50, p= 0.0099

  - CCR: HR =1.83, p = 0.0014

- CCP remained significant after adjusting for CAPRA (HR = 1.46, p = 0.019).

myriad. Prolaris

. Univariate and Multivariable Models

- CCP also remained significant in a de novo multivariable model adjusting for the components of CAPRA, including PSA, clinical stage, % positive cores and age of diagnosis (HR= 1.47, p = 0.017)

| Covariate	IQR	HR	95% CI	p-value
Univariate				
CCP	1.0	1.50	(1.11, 2.03)	0.0099
PSA levels	2.0	2.12	(1.31, 3.45)	0.0033
Clinical stage				0.035
>T1 vs T1	1.0	1.86	(1.02, 3.40)	
% Positive Cores	33.3	1.05	(0.70, 1.58)	0.80
Age at Diagnosis (yrs)	10.0	1.55	(1.02, 2.35)	0.037
Multivariable				
CCP	1.0	1.47	(1.08, 2.00)	0.017
PSA levels	2.0	2.15	(1.29, 3.60)	0.0045
Clinical stage				0.012
>T1 vs T1	1.0	2.09	(1.14, 3.80)	
% Positive Cores	33.3	0.94	(0.60, 1.46)	0.79
Age at Diagnosis (yrs)	10.0	1.44	(0.95, 2.18)	0.080

myriad® Prolaris®

Univariate and Multivariable Models

- CCP also remained significant in a de novo multivariable model adjusting for the components of CAPRA, including PSA, clinical stage, % positive cores and age of diagnosis (HR= 1.47, p = 0.017)

Covariate	IQR	HR	95% CI	p-value
Univariate				
CCP	1.0	1.50	(1.11, 2.03)	0.0099
PSA levels	2.0	2.12	(1.31, 3.45)	0.0033
Clinical stage				0.035
>T1 vs T1	1.0	1.86	(1.02, 3.40)	
% Positive Cores	33.3	1.05	(0.70, 1.58)	0.80
Age at Diagnosis (yrs)	10.0	1.55	(1.02, 2.35)	0.037
Multivariable				
CCP	1.0	1.47	(1.08, 2.00)	0.017
PSA levels	2.0	2.15	(1.29, 3.60)	0.0045
Clinical stage				0.012
>T1 vs T1	1.0	2.09	(1.14, 3.80)	
% Positive Cores	33.3	0.94	(0.60, 1.46)	0.79
Age at Diagnosis (yrs)	10.0	1.44	(0.95, 2.18)	0.080

myriad®   Prolaris®

Figure 1. Predicted 10-Year Risk from Biopsy Diagnostic Gleason Score 6
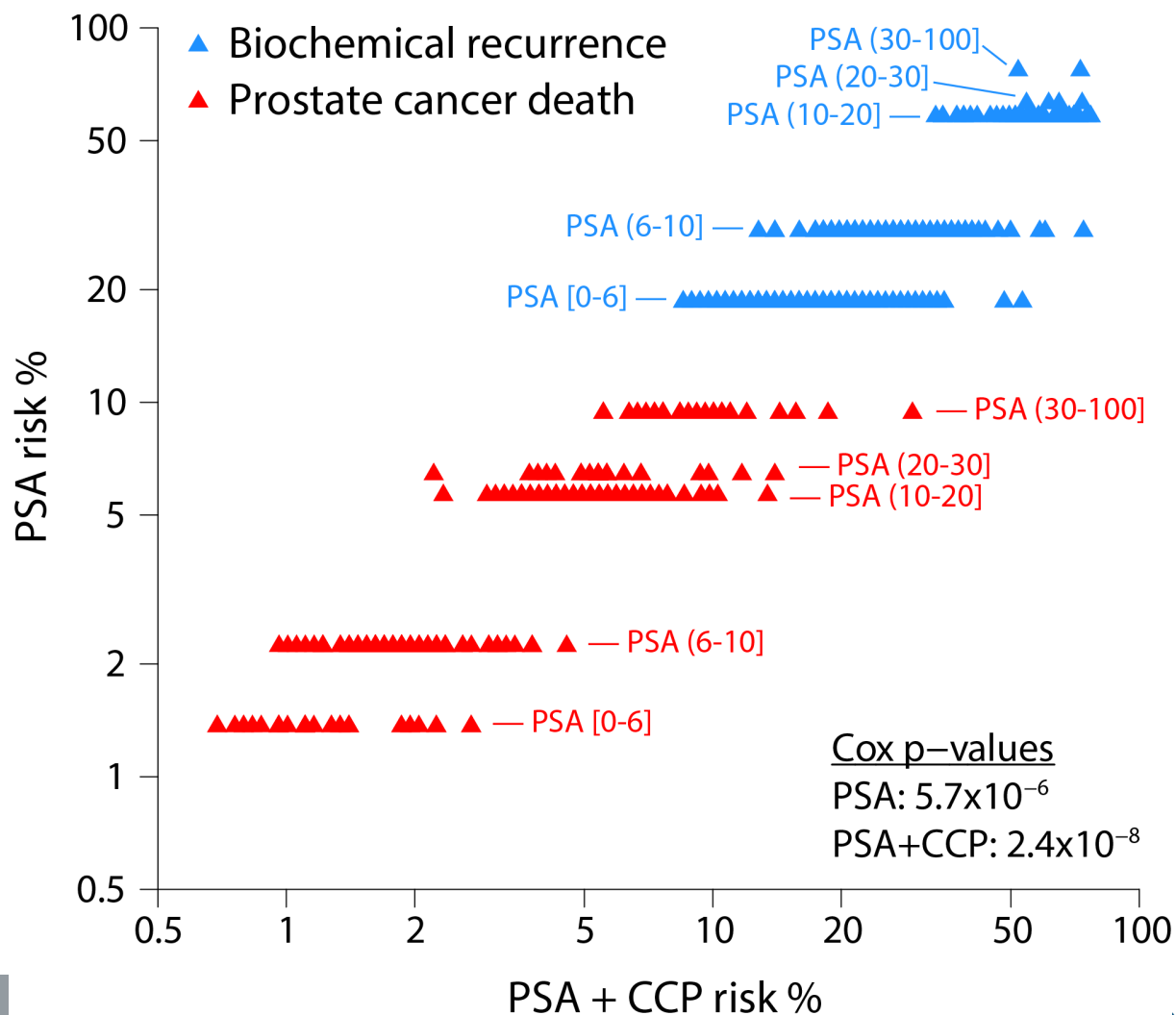
Conclusions

- The CCP score predicts oncologic outcomes in Gleason 6 or less prostate cancer patients.

- This meta-analysis adds to the evidence that CCP score provides significant prognostic discrimination to patients with low-risk localized disease.

What should you ask of your prostate cancer prognostic test

1. Analytic Validity
2. Clinical Validity (in the setting you are counseling the patient for ie. AS, RadP, EBRT
3. Real Oncologic Endpoints (BCR, Mets,DSM)
4. Applicable across all Risk Groups
5. Clinical Utility

CCP Score Correlation with Gleason Score and PSA

Study	CCP Score vs Gleason Score†	CCP Score vs log PSA
TURP conservatively managed	0.57	0.27
Needle Biopsy conservatively managed	0.37	0.14
RP 1	0.22	0.21
RP 2	0.18	0.11
EBRT	0.23	0.31
Biopsy-RP 1	0.27	0.13
Biopsy-RP 2	0.18	0.09
Biopsy-RP 3	0.30	0.13

- Pearson correlation (all coefficients are significant at 0.05 level).
† Diagnostic for biopsy samples; pathologic for surgery tumor samples; treated as integers (1 for <7, 2 for 7, and 3 for >7).

myriad. Prolaris

Multivariate Analysis in Multiple Cohorts Demonstrates that Prolaris Performs Well in Gleason Score 6

	Covariate	TAPG Needles	Biopsy-RP 1	Biopsy-RP 2	Biopsy-RP 3	TOTAL	TOTAL	HR	95% CI	p-value
		DSM	Biochemical recurrence			N	events			
UNIVARIATE	CCP	204	83	76	77	440	64	1.5	(1.11, 2.03)	0.0099
	CAPRA	204	83	76	77	440	64	1.27	(1.03, 1.56)	0.03
	CCR	204	83	76	77	440	64	1.83	(1.27, 2.63)	0.0014
BIVARIATE	CAPRA	204	83	76	77	440	64	1.23	(1.00, 1.53)	0.058
	CCP							1.46	(1.08, 1.98)	0.019

myriad. Prolaris