**A 17-gene genomic prostate score (GPS) as a predictor of biochemical (BCR) and clinical recurrence (CR) in men with surgically treated intermediate- and high-risk prostate cancer (PCa).**

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Background: The biopsy-based GPS (scale 0-100) is validated as a predictor of adverse pathology in men with low- and intermediate-risk PCa. We examined the association of GPS with BCR and CR in higher risk disease. Methods: We performed exploratory analyses in a prior development study of radical prostatectomies (RP) from 441 men with AUA low-, intermediate-, and high-risk PCa, using a cohort sampling design (Klein et al. Eur Urol 2015). Multivariable Cox proportional hazards models were employed with the cohort sampling weights. Since these data were used to select genes and coefficients for GPS, hazard ratios (HR) and other estimates based on GPS were corrected for regression to the mean (RM), and Storey's method was used to control the false discovery rate (FDR). These analyses were confirmed in biopsies from an independent cohort (Cullen et al. Eur Urol 2015) of 139 RP-treated intermediate-risk men. Results: All estimates are RM-corrected. Broad overlapping ranges of GPS values were seen across all 3 risk groups. GPS was strongly associated with BCR (HR 1.6/20 GPS units, p<0.001, FDR q-value <0.1%) and CR (HR 2.8/20 units, p<0.001; FDR q-value <0.1%), after adjusting for risk group. Intermediate-risk men with GPS >40 (41% of all intermediate-risk men) had estimated 3-yr BCR risk and 10-yr CR risk similar to high-risk men (Table). High-risk patients with GPS ≤40, (63% of all high-risk men) had 3-yr BCR risk and 10-yr CR risk similar to intermediate-risk men. High-risk men with GPS >40 had 3-yr BCR risk of almost 50% and 10-yr CR risk of 35%. In the second cohort, intermediate risk men with GPS ≤40 (61% of the cohort) had a 3-yr BCR risk of 8% while men with GPS >40 had a risk of 27%. Conclusions: GPS appears to provide improved risk stratification for BCR and CR in men with AUA intermediate- and high-risk PCa for whom there is an unmet need to inform decisions regarding adjuvant therapy.

| | Intermediate risk | | | High risk | | |
|---|---|---|---|---|---|---|
| **GPS Group** | **Percentage of Men** | **BCR Risk** | **CR Risk** | **Percentage of Men** | **BCR Risk** | **CR Risk** |
| **GPS ≤40** | 59 | 16% | 5% | 63 | 24% | 8% |
| **GPS >40** | 41 | 34% | 17% | 37 | 48% | 35% |
| **All** | 100 | 23% | 10% | 100 | 33% | 18% |

**RM-corrected 3-year BCR and 10-yr CR risk for intermediate- and high-risk men.**