CELL CYCLE PROGRESSION-COMBINED RISK SCORE STRATIFIES PROSTATE CANCER RISK AND SIGNIFICANTLY MODIFIES TREATMENT DECISIONS IN PROSTATE CANCER

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BACKGROUND

- The cell cycle progression combined risk (CCP-CR) test (Prolaris®, Myriad Genetic Laboratories, Inc.) has been validated in nine cohorts and provides information on the risk of prostate cancer-specific disease progression and disease specific mortality when combined with standard clinicopathologic parameters.[1-6]
- In this analysis, we evaluated how the CCP score modified the AUA risk in results from our initial commercial testing.
- We also queried clinicians' judgment regarding the clinical utility of the CCP-CR test in a prospective registry.

METHODS

- Our current laboratory database was evaluated for patients whose biopsy was tested with the CCP-CR test and whose clinicopathologic data was collected by the ordering physician.
  - Formalin fixed, prostate biopsy tissue from patients diagnosed with adenocarcinoma was analyzed.
- The CCP score was calculated by measuring the RNA expression of 31 cell cycle progression genes normalized to 15 housekeeping genes.
  - A relative classification of cancer aggressiveness was developed to interpret how the patient's CCP score compared to that of patients within the same AUA risk category.
- In addition, clinicians ordering the CCP-CR test commercially were asked to complete a survey regarding their treatment recommendations before and after they received the CCP-CR test result.

RESULTS

COMMERCIAL TESTING

- Test ordered by 457 physicians.
- 2176/2219 (98.1%) samples yielded quality RNA.
- Normal distribution for the CCP score (-2.9 to 3.1).
- Based on the CCP score, 29.1% of men had a less aggressive cancer compared to the clinicopathologic prediction and 26.3% of patients had a more aggressive cancer.

Table 1. Cancer aggressiveness based on CCP scores

AUA Risk Classification	Considerably Less Aggressive	Less Aggressive	Consistent	More Aggressive	Considerably More Aggressive	Totals
Low	15 (1.7%)	229 (26.6%)	406 (47.1%)	193 (22.4%)	19 (2.2%)	862
Intermediate	24 (2.4%)	263 (26.7%)	442 (44.9%)	217 (22.0%)	39 (4.0%)	985
High	14 (4.3%)	88 (26.7%)	123 (37.4%)	76 (23.1%)	28 (8.5%)	329
Totals	53 (2.4%)	580 (26.7%)	971 (44.6%)	486 (22.3%)	86 (4.0%)	2176

PROSPECTIVE REGISTRY

- Currently, 331 patients have been enrolled and 150 clinicians have completed surveys on the influence of the CCP signature test in 305 cases.
- In 65% (198/305) of cases [95% CI: 59%-70%], there was a change recorded between the therapy initially planned and the therapy actually selected.
  - In 122 of 305 (40%) cases, clinicians indicated they would reduce the intended therapeutic burden post-CCP test (Table 2).
- In 88 % (276/315) of cases, the physician felt the CCP score was moderately to very highly influential in their treatment recommendation.

Table 2. Change in therapeutic burden from pre- to post- Prolaris treatment choice

Change in Intended Therapeutic Options (Pre-CCP Test to Post-CCP Test)	Total (n=305)
Reduction	122 (40.0%)
No Change	107 (35.1%)
Increase	76 (24.9%)

Table 3. Influence of the Prolaris test result in treatment selection

Selection	N (%)
None	7 (2.2%)
Low	32 (10.2%)
Moderate	103 (32.7%)
High	136 (43.2%)
Very High	37 (11.7%)
Total	315

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CONCLUSIONS

- The CCP-CR test is a novel assay that can improve risk stratification for men with prostate adenocarcinoma independent of the Gleason score and PSA level.
- Over 50% of men initially tested in the commercial assay were assigned to a different risk category than predicted by their clinicopathologic features alone.
- Based on the judgment of ordering physicians, the CCP-CR score appears to add meaningful new information to risk assessment for localized prostate cancer patients.
- Test results led to major changes in treatment decisions with a significant increase in conservative management options, including active surveillance or watchful waiting.

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