Prospective clinical study of a prostate cancer (PCa) rule-out blood test for PSA gray zone patients using a sensitive circulating tumor cell assay.

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Background: The diagnostic confirmation of prostate cancer in patients with a PSA in the gray zone (4–10 ng/ml) is controversial, often leading to unnecessary biopsies. The sensitivity of the PSA test at a 4 ng/mL cut-off can be as low as 21%. We introduce a new test for prostate cancer detection in PSA gray zone patients, with the potential to decrease the number of unnecessary prostate biopsies. Methods: A single-center, multi-year, IRB-approved, prospective, blinded clinical study was conducted in 200 high-risk subjects. 4 mL of blood was drawn and processed for CTC analysis using the CellMax biomimetic platform (CMx). The CMx CTC test uses a proprietary microfluidic biochip that accurately captures and enumerates CTCs with antibodies to EpCAM, CK18 and PSMA. All patients underwent routine screening including PSA and digital rectal exam (DRE). Gray zone and those diagnosed as ‘diseased’ based on PSA & DRE also underwent a biopsy. Multivariate generalized linear models incorporating CMx test results were utilized to derive age adjusted CTC scores predictive of clinical outcomes. Results: A subset of 84 subjects with PSA levels in the gray zone (4–10 ng/ml) were included in this study. Prostate biopsy results were available for 42 patients; 10 had confirmed cancer. A CTC Score was calculated as a nonlinear weighted combination of the CTCs captured with CK18 and PSMA antibodies. After adjustment for age and
PSA, the CTC score remained a significant predictor of clinical outcome in the PSA “gray zone” (likelihood ratio p-value = .015) whereas PSA was not. The sensitivity and specificity of the CTC Score were 80.0% (95% CI: 44.4%, 97.5%) and 93.8% (95% CI: 79.2%, 99.2%). Negative % agreement and Positive % agreement was 93.8% (95% CI: 79.2%, 99.2%) and 80.0% (95% CI: 44.4%, 97.5%). Given the observed odds ratio for CTC score in the study- approximately 0.90 (95% CI 0.79, 0.98), the study is appropriately powered. **Conclusions:** The CMx CTC assay is an accurate, affordable blood based assay, with the potential to reduce unnecessary biopsies in PSA gray-zone patients by up to 90%.