PCA3 Surpasses Best Clinical Judgment in Selecting Men Requiring a Repeat Prostate Biopsy: Application of a RAND Decision Model to the REDUCE Trial Placebo Cohort

Introduction & Objective: There is need to better individualize the decision for repeat biopsy (rBx) and to reduce the number of rBx and over-diagnosis of indolent prostate cancer (PCa). Using the RAND Appropriateness Method (RAM), we developed a model to simulate best clinical judgment (BCJ) to select patients for rBx and incorporated the PROGENSA® PCA3 assay. PCA3 has been shown to predict the probability that a rBx will be positive and may be indicative of PCa significance.
Materials and Methods: We have tested our RAM on men of the placebo cohort of the REDUCE study for which PROGENSA® PCA3 scores were available. These men had a baseline PSA 2.5-10 ng/mL, a prior negative Bx, and planned 2-year and 4-year rBx. For each scenario (with and without PCA3), the number of rBx and the number of missed high-grade (Gleason sum ≥7) cancers were assessed.
Results: Data from 1024 subjects were available for analysis. Using BCJ (RAM), incorporating PSA, DRE, number of previous negative Bx, prostate volume and life expectancy, 26% of study-mandated rBx were ruled out while missing 14 high-grade PCa (Table). PCA3 largely surpassed BCJ by ruling out 52% of rBx while missing only 7 high-grade PCa. The most efficient scenario was obtained by combining PCA3 results and BCJ, leading to a 64% reduction in the number of rBx while missing only 8 high-grade PCa.
The sensitivity, specificity, PPV and NPV of the RAM model including PCA3 for Gleason sum ≥7 PCa were superior to the RAM model alone and PCA3 alone.

Scenario	**rBx (n)**	**Reduction (%)**	**Missed high-grade PCa[b] (n)**
REDUCE	1024		0
RAM[a] without PCA3	757	26%	14
PCA3 alone	488	52%	7
RAM[a] with PCA3	368	64%	8

a: expert recommendations; b: out of 55 Gleason sum ≥ 7 cancers
Conclusions: In men with a first negative biopsy, PCA3 alone or in combination with BCJ surpasses BCJ as a strategy to avoid rBx without compromising diagnosis of high-grade cancer.