# 4Kscore™ Test

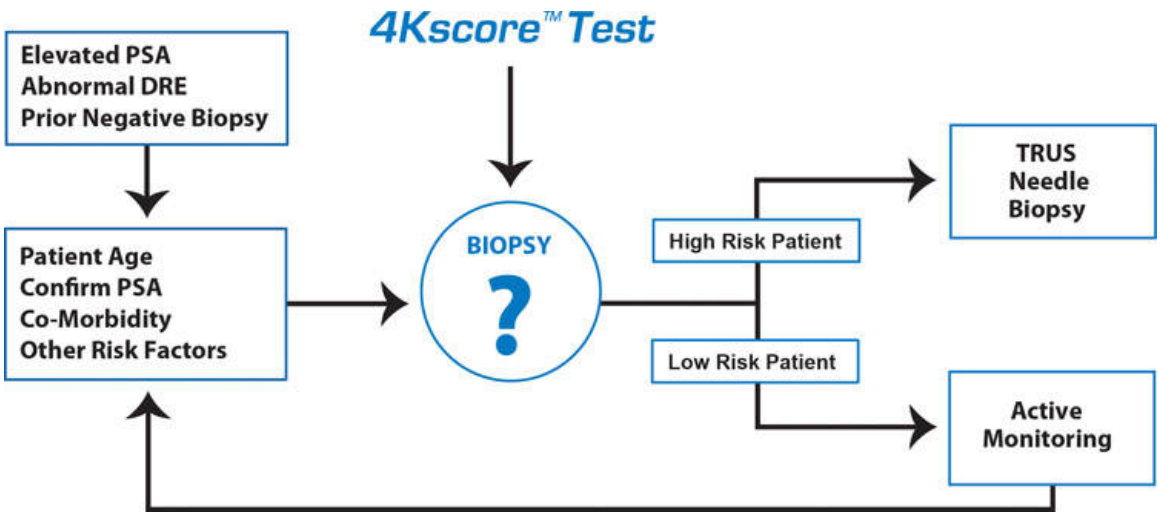
## The Challenge of Prostate Biopsy Decision Making
## The Need for Improved Diagnostic Information

- Provide information to improve decision making before having a prostate biopsy
- Reduce the number of unnecessary biopsies, associated complications, and costs
- Provide diagnostic information from a blood test; no requirement for biopsy tissue
- Demonstrate a potential for a significant health economic benefit

## The OPKO 4Kscore Test - Adding Clarity to Shared Decision Making
## Elements of the 4Kscore Test

The 4Kscore Test relies on the measurement of four prostate-specific kallikreins in blood: Total PSA, Free PSA, Intact PSA, Human Kallikrein 2 (hK2). The blood test results are combined in an algorithm with patient age, DRE (nodules, no nodules), prior negative biopsy (yes/no). The result is a patient specific probability for finding a high-grade, Gleason score 7 or higher prostate cancer upon biopsy. (Low Risk patient example at right)

## 4Kscore Test: Rigorous Clinical Development



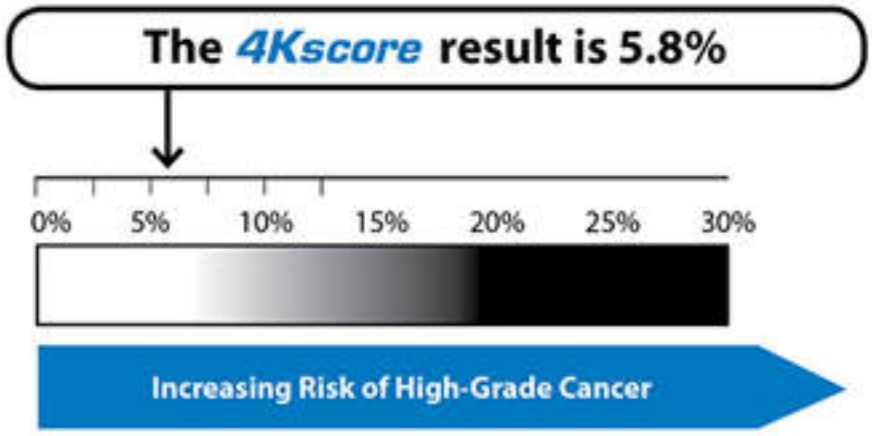

The 4Kscore test was developed by OPKO Lab and is performed by OPKO Lab at its CLIA-accredited laboratory facility. The biomarkers utilized in the 4Kscore Test are based on over a decade of research conducted by scientists at Memorial Sloan Kettering

Cancer Center and leading research centers in Europe on over 10,000 patients. [1-8] The results have recently been replicated in a prospective blinded clinical study conducted at 26 urology centers in the United States on over 663 patients. [9] A recent health economic analysis demonstrated that use of the 4Kscore Test could result in annual savings approaching $1 billion in the US. [10]

## Data from the US Clinical Study

### Clinical Study Design

A total of 663 patients were enrolled from October 2013 to March 2014 in a blinded, prospective clinical study at 26 Urology centers in the US to validate the performance of the 4Kscore Test. In order to obtain a cohort representative of current biopsy selection practice, enrollment was open to all men scheduled for a prostate biopsy, regardless of age, PSA, DRE, or prior biopsy. Each participant underwent a TRUS prostate biopsy of at least 10 cores, and histopathology was conducted according to the established practice at each center. Patients with a treatment history known to influence PSA levels were excluded. A blinded blood sample (K2EDTA) was collected prior to the biopsy and sent to OPKO Lab, Nashville, TN for the four kallikrein testing (Total PSA, Free PSA, Intact PSA and hK2). The four kallikrein results, histopathology, age, DRE, and prior biopsy data were unblinded and analyzed by independent biostatisticians.




**4Kscore Probability Cut Off**

| | 5.0% | 7.5% | 10.0% | 12.5% | 15.0% |
|---|---|---|---|---|---|
| Biopsy Reduction % | 34% | **47%** | 55% | 61% | 67% |
| Delayed diagnosis % | 1.7% | **2.7%** | 3.9% | 5.1% | 6.2% |
| Neg Predictive Value | 95% | **94%** | 93% | 92% | 81% |
| Sensitivity | 92% | **88%** | 82% | 77% | 69% |
| Specificity | 41% | **56%** | 65% | 72% | 81% |

References:
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9 Lin, DW et al. Abstract accepted for Plenary Presentation at American Urological Association Annual Meeting, Orlando, FL, May 18, 2014.
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