Detection of Bladder Cancer Using a Point-of-Care Proteomic Assay

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BLADDER CANCER IS THE FIFTH most common malignancy in the United States. Early detection improves prognosis, treatment options, and quality of life. Although the 5-year survival rate is 95% when tumors are detected while they are confined to the mucosa, up to 25% of the 60,240 bladder tumors predicted to be diagnosed this year will be detected after they have become invasive or metastatic, which lowers 5-year survival to approximately 48% and 10%, respectively. As a result, 13,000 people in the United States will die of bladder cancer this year. The incidence of bladder cancer is higher in men, individuals older than 60 years, and those exposed to carcinogens in their occupation or environment. Cigarette smoking is the most common risk factor and doubles the risk of bladder cancer, accounting for approximately 50% of the bladder cancer deaths in men and 30% in women.

Hematuria and irritative voiding symptoms are the most common symptoms among patients with urinary tract malignancy. Asymptomatic individuals are frequently diagnosed after routine or screening analysis by their primary care physicians has demonstrated hematuria. Hematuria in bladder cancer can be intermittent, and its degree does not correlate with the severity of underlying disease. Consequently, it is recommended that patients with hematuria undergo an evaluation after even a single episode.

A combination of methods is used to evaluate patients at risk for bladder cancer because no single procedure is 100% sensitive. Flexible cystoscopy is an excellent tool because it is low risk and generally can be done in the physician’s office under local anesthesia. However, accuracy can be reduced by poor visualization caused by inflammatory conditions or bleeding, and flat urothelial lesions such as severe dysplasias and carcinoma in situ may be difficult to distinguish from normal bladder tissue. For this reason, voided
urine cytology is frequently used as an adjunctive noninvasive test, but it is expensive, subjective, and has low sensitivity.

We investigated whether a new, noninvasive urine-based test for the nuclear matrix protein NMP22 proteomic marker, using monoclonal antibodies in a point-of-care format, has clinical utility as an aid in diagnosis of bladder cancer and compared its ability to detect cancer with that of voided urine cytology, which must be analyzed in a clinical laboratory.

**METHODS**

**Patients**

Between September 2001 and May 2002, 22 geographically dispersed clinical sites, including academic, veterans', and private practice facilities, prospectively enrolled 1331 consecutive patients with bladder cancer risk factors or symptoms, such as smoking, hematuria, or dysuria (Figure). No individuals had a prior history of bladder malignancy. One additional site recruited 26 patients with active malignancies other than of the bladder to determine the specificity of the NMP22 test for bladder cancer. Information about race was obtained for Food and Drug Administration (FDA) submission purposes from patients by clinical staff at each site. Patients categorized themselves. Institutional review boards reviewed and approved the study protocol for each site, and all participants provided written informed consent.

Patients with cancers other than of the bladder provided a urine specimen for NMP22 protein analysis during a routine visit and did not have endoscopy or voided cytology evaluations. Each patient evaluated for bladder cancer provided a voided urine sample before undergoing cystoscopy. One portion of each sample was sent for routine cytological examination, either within the institution or at a reference laboratory, according to the standard practice at each participating facility. An aliquot of the remaining specimen was tested for the presence of NMP22 protein by a member of the clinic staff. Each device was identified by study identification number so that the physicians who performed the subsequent cystoscopy were blinded to the NMP22 test results, and the staff members who performed the NMP22 assay were blinded to cystoscopy test results. Technicians who conducted the cytological examinations were physically distant from both the cystoscopy and NMP22 evaluations, and laboratory reports arrived after the cystoscopies had been completed and documented.

**NMP22 Assay**

Staff members at each office performed the NMP22 assay per protocol by adding 4 drops of voided urine to the sample well of the point-of-care device. Positive or negative results were read 30 to 50 minutes later in the test window. A built-in control indicated that the assay was complete. There were no other procedural steps.

The NMP22 point-of-care device (NMP22 BladderChek Test, Matritech Inc, Newton, Mass) is a lateral flow immunochromatographic qualitative assay. It detects elevated amounts of the nuclear mitotic apparatus protein, which is an abundant component of the nuclear matrix. Nuclear matrix proteins make up the internal structural framework of the nucleus and are associated with such functions as DNA replication and RNA synthesis, as well as regulation and coordination of gene expression. In tumor cells, nuclear mitotic apparatus protein, which is present in the interphase nucleus and associated with the organization of mitotic spindles during cell division, is elevated concordant with structural/ morphological changes characteristic of malignant cell nuclei. Nuclear matrix protein expression varies with cell type of origin. In individuals with bladder cancer, nuclear mitotic apparatus protein is released into the urine during cell death. Unlike cytological examination, its detection is not dependent on recovery of intact cells. A microtiter plate immunoassay was de-

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**Figure. Flow Diagram of Study**
DETECTION OF BLADDER CANCER WITH A POINT-OF-CARE PROTEOMIC ASSAY

A receiver operating characteristic (ROC) analysis, a plot of the true-positive rate vs the false-positive rate, is a tool for determination of an optimal decision point for sensitivity and specificity and requires quantitative data. An ROC analysis of quantitative data from the microtiter plate format of the NMP22 assay in an evaluation of patients at high risk for bladder cancer had an area under the curve (AUC) of 73%. The 10-U/mL point of determination for the qualitative point-of-care test for NMP22 protein corresponds to the cutoff previously approved by the FDA for the quantitative measurement of NMP22 protein.

Diagnostic Criteria
All patients with risk factors or symptoms of bladder cancer underwent cystoscopy. They were considered positive for malignancy if 1 or more tumors were observed during initial cystoscopy or within the subsequent 3 months. Nine patients with no malignancy found during their initial cystoscopy had a subsequent endoscopy due to continued suspicion, such as increased symptoms. Removed tumors were defined as malignant based on pathological examination. Tumors that were seen endoscopically but not removed were considered positive for malignancy and designated stage (TX) and grade (GX).

Sensitivity of the NMP22 test to detect the presence of bladder cancer was calculated as the number of patients with true-positive test results (positive NMP22 test result and tumor) divided by the total number of patients with malignancy, as detected by endoscopy. Specificity was defined as the percentage of patients with a negative NMP22 test result who were not diagnosed with tumors. Corresponding 95% confidence intervals (CIs) were calculated for both sensitivity and specificity. The sensitivity and specificity of voided cytology were calculated for comparison. A positive cytology test result was defined as one in which malignant or dysplastic cells were present.

Statistical analysis was performed at the M.D. Anderson Cancer Center using S-PLUS version 6.1 (Insightful Corp, Seattle, Wash) and StatXact version 4.0 (Cytel Software Corp, Cambridge, Mass) statistical software.

RESULTS

Characteristics of the Patients
Demographic and baseline characteristics of the individuals with risk factors or symptoms of bladder cancer are summarized in Table 1. Among the 1331 patients who had cystoscopies, 79 (6%) had cancer, 685 (51%) were diagnosed with 1 or more benign urological conditions, and 567 (43%) had no cystoscopic evidence of urinary tract disease. The mean age of the patients with bladder tumors was 65.8 years (range, 21-86 years), and they comprised 3 times as many men as women.

Staging information (Table 2) was available for the 72 cancers that were surgically removed. The 7 tumors seen during cystoscopy but not excised were categorized as TX. Of the cancers with pathological staging data, 62 were superficial (stages Ta, Tis, or T1), and 10 were muscle invasive (T2-T3). Pathological determination of grade was available for 70 of the 72 removed tumors (Table 2). Of these, 27 were well differentiated (low grade), 18 were moderately differentiated (medium grade), and 25 were poorly differentiated (high grade). A total of 27 cancers were...
Detection

Initial cystoscopy alone detected 88.6% (70/79) of the cancers. The remaining 9 malignancies were identified during subsequent cystoscopies conducted due to continued suspicion, such as increased symptoms, within 3 months of the initial evaluation. The NMP22 assay was positive in 55.7% (44/79), and cytology test results of malignant or dysplastic cells were found in 15.8% (12/76).

The NMP22 test was significantly more sensitive than voided urine cytology when compared using the McNemar $\chi^2$ test ($\chi^2=24.7, P<.001$). This difference remains significant after taking into account the inherent variability among the investigational sites using an adjusted McNemar $\chi^2$ test ($\chi^2=7.0, P=.008$). This significant difference is also reflected by the CIs for the sensitivity proportions since they do not overlap, at 55.7% (95% CI, 44.1%-66.7%) for the NMP22 test vs 15.8% (95% CI, 7.6%-24.0%) for cytology. The positive predictive values of the NMP22 assay and cytology were 19.7% (95% CI, 14.5%-25.0%) and 54.6% (95% CI, 32.2%-75.4%), respectively.

The same methods were used to compare the specificity proportions and demonstrated that cytology was significantly more specific than the proteomic assay ($\chi^2=149.6, P<.001$), at 99.2% (95% CI, 98.7%-99.7%) vs 85.7% (95% CI, 83.8%-87.6%), respectively. The difference remains significant after taking variability among the sites into account (adjusted McNemar $\chi^2$ test $\chi^2=9.0, P=.003$). The negative predictive values of the NMP22 assay and cytology were 96.8% (95% CI, 95.6%-97.8%) and 94.9% (95% CI, 93.6%-96.1%), respectively.

Table 1. Patient Demographics and Baseline Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>No Urinary Tract Disease (n = 567)</th>
<th>Benign Disease (n = 685)</th>
<th>Urinary Tract Cancer (n = 79)</th>
<th>Overall (N = 1331)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y Mean (SD)</td>
<td>54.1 (13.8)</td>
<td>61.7 (13.7)</td>
<td>65.8 (13.3)</td>
<td>58.7 (14.3)</td>
</tr>
<tr>
<td>Range</td>
<td>18-91</td>
<td>27-96</td>
<td>21-86</td>
<td>18-96</td>
</tr>
<tr>
<td>No. (% of patients) ≤40</td>
<td>90 (15.9)</td>
<td>50 (7.3)</td>
<td>4 (6.1)</td>
<td>144 (10.8)</td>
</tr>
<tr>
<td>41-60</td>
<td>153 (27.0)</td>
<td>95 (13.9)</td>
<td>5 (6.3)</td>
<td>253 (19.0)</td>
</tr>
<tr>
<td>51-60</td>
<td>146 (25.8)</td>
<td>171 (25.0)</td>
<td>14 (17.7)</td>
<td>331 (24.9)</td>
</tr>
<tr>
<td>61-70</td>
<td>94 (16.6)</td>
<td>167 (24.4)</td>
<td>23 (29.1)</td>
<td>284 (21.3)</td>
</tr>
<tr>
<td>71-80</td>
<td>73 (12.9)</td>
<td>153 (22.3)</td>
<td>26 (32.9)</td>
<td>252 (18.9)</td>
</tr>
<tr>
<td>&gt;80</td>
<td>11 (1.9)</td>
<td>49 (7.2)</td>
<td>7 (8.9)</td>
<td>67 (5.0)</td>
</tr>
<tr>
<td>Sex, No. (% of patients) Male</td>
<td>225 (39.7)</td>
<td>472 (68.9)</td>
<td>62 (8.5)</td>
<td>759 (57.0)</td>
</tr>
<tr>
<td>Female</td>
<td>342 (60.3)</td>
<td>213 (31.1)</td>
<td>17 (2.3)</td>
<td>572 (43.0)</td>
</tr>
<tr>
<td>Race, No. (% of patients) Black, non-Hispanic</td>
<td>54 (9.5)</td>
<td>62 (9.1)</td>
<td>4 (5.1)</td>
<td>120 (9.0)</td>
</tr>
<tr>
<td>White, non-Hispanic</td>
<td>447 (78.3)</td>
<td>572 (83.5)</td>
<td>70 (88.9)</td>
<td>1089 (81.8)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>43 (7.6)</td>
<td>36 (5.3)</td>
<td>5 (6.3)</td>
<td>84 (6.3)</td>
</tr>
<tr>
<td>Asian</td>
<td>15 (2.7)</td>
<td>11 (1.6)</td>
<td>0</td>
<td>26 (2.0)</td>
</tr>
<tr>
<td>Other</td>
<td>5 (0.9)</td>
<td>1 (0.2)</td>
<td>0</td>
<td>6 (0.5)</td>
</tr>
<tr>
<td>Unknown</td>
<td>3 (0.5)</td>
<td>3 (0.4)</td>
<td>0</td>
<td>6 (0.5)</td>
</tr>
</tbody>
</table>

Table 2. Sensitivity of NMP22 Assay and Voided Cytology by Stage and Grade of Cancer (n = 72)

<table>
<thead>
<tr>
<th>Stage</th>
<th>NMP22 Assay</th>
<th>Voided Cytology</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. With Positive Test Result/Total No. With Bladder Cancer</td>
<td>Sensitivity, % (95% CI)</td>
<td>No. With Positive Test Result/Total No. With Bladder Cancer</td>
</tr>
<tr>
<td>Ta</td>
<td>14/30</td>
<td>48.7 (28.3-65.7)</td>
</tr>
<tr>
<td>Tis</td>
<td>4/5</td>
<td>80.0 (28.4-99.5)</td>
</tr>
<tr>
<td>T1</td>
<td>13/27</td>
<td>48.2 (28.7-68.1)</td>
</tr>
<tr>
<td>T2, T2a</td>
<td>6/6</td>
<td>100 (54.1-100)</td>
</tr>
<tr>
<td>T3a, T3b</td>
<td>3/4</td>
<td>75.0 (19.4-99.4)</td>
</tr>
<tr>
<td>TX</td>
<td>4/7</td>
<td>57.1 (18.4-90.1)</td>
</tr>
<tr>
<td>Noninvasive: Ta-T1</td>
<td>31/62</td>
<td>50.0 (37.0-63.0)</td>
</tr>
<tr>
<td>Muscle invasive: T2-T3</td>
<td>9/10</td>
<td>90.0 (55.5-99.8)</td>
</tr>
</tbody>
</table>

Abbreviation: CI, confidence interval.

Muscle invasive (T2 or T3) and/or poorly differentiated (high grade). No patients had detectable metastases or involvement of regional lymph nodes. The NMP22 test results were available for all patients with risk factors (1331), and cytology test results for 1287 of the patients with risk factors, including 76 of the 79 diagnosed with cancer.

Ten of the 79 malignancies were muscle invasive. Initial cystoscopy visualized 6 (60%) of these, compared with the NMP22 test, which identified 9 (90%) with elevated protein marker. By comparison, voided cytology was positive in only 2 (22%) of the 9 patients with muscle-invasive disease for whom test results were available. The NMP22 assay was also positive for a patient diagnosed with carcinoma in situ after an initial cystoscopic report of benign disease. Thus, a total of 4 potentially life-threatening tumors (T2 G2 of the ureter; T2 G3, Tis G3, and T3 G2 of the bladder) were detected by the NMP22 test but not visualized in the first cystoscopy. One of the 4 tumors was also reflected by the CIs for the sensitivity proportions since they do not overlap, at 55.7% (95% CI, 44.1%-66.7%) for the NMP22 test vs 15.8% (95% CI, 7.6%-24.0%) for cytology. The positive predictive values of the NMP22 assay and cytology were 19.7% (95% CI, 14.5%-25.0%) and 54.6% (95% CI, 32.2%-75.4%), respectively.

The same methods were used to compare the specificity proportions and demonstrated that cytology was significantly more specific than the proteomic assay ($\chi^2=149.6, P<.001$), at 99.2% (95% CI, 98.7%-99.7%) vs 85.7% (95% CI, 83.8%-87.6%), respectively. The difference remains significant after taking variability among the sites into account (adjusted McNemar $\chi^2$ test $\chi^2=9.0, P=.003$). The negative predictive values of the NMP22 assay and cytology were 96.8% (95% CI, 95.6%-97.8%) and 94.9% (95% CI, 93.6%-96.1%), respectively.

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was located in the ureter and therefore outside the viewing area of the cystoscope. Urine tests are often added to an evaluation to identify urinary tract tumors such as this. The combination of the NMP22 test and cystoscopy detected 93.7% of malignancies vs 88.6% for initial cystoscopy alone (P = .26). Cytology detected 2 of the 4 cancers not seen in the initial endoscopy, but which were positive by the NMP22 assay.

Among the most aggressive malignancies, those that were poorly differentiated (high grade) and/or muscle invasive (stage T2 or T3), the NMP22 test result was positive in 74% (20/27) compared with cytology, which was positive in 39% (10/26). Of the superficial cancers (Ta, Tis, T1) that were moderately or well differentiated (medium or low grade), the NMP22 assay identified 47% (20/43), compared with 5% (2/41) for cytology. Overall, the point-of-care assay detected 32 malignancies missed by cytology: 11 Ta, 10 T1, 4 T2, 2 T3, 1 CIS, and 4 TX. Voided cytology was positive in only 2 cancer patients for whom the NMP22 test result was negative, both T1 G3.

The specificity of the NMP22 assay was 90.3% among individuals with symptoms but with no evidence of urinary tract disease seen during cystoscopy, and 85.7% overall (Table 3). All risk patients in the study were undergoing an evaluation for bladder cancer that included cystoscopy, so false-positive test results did not require any additional procedures. Cytology demonstrated a specificity of 99.2% among patients with symptoms and was not performed for individuals with non-bladder cancer. Of the 38 patients with active cancers other than bladder, the NMP22 assay was negative in 86.8% (33/38) and positive in 13.2% (5/38).

**COMMENT**

Prognosis and survival of individuals with bladder cancer are related to the stage of the malignancy at the time of detection. Approximately 50% of patients with muscle-invasive disease at first diagnosis demonstrate a recurrence within 2 years of surgery, despite apparently adequate surgical resection. The majority of these patients will experience a cancer-related death within 5 years of diagnosis. By comparison, tumors treated while still confined to the epithelium have lower recurrence rates and progress to higher stages and grades less often, thereby improving patients’ long-term outcome. In addition, early stage disease can be treated by bladder-sparing therapy rather than cystectomy, the standard for advanced disease, which impacts quality of life as well as survival. The direct cost of treatment for patients with metastatic genitourinary cancer has been estimated to be more than 6 times greater than for those patients with localized disease for the same period of time. The challenge, therefore, is to improve detection of bladder cancer without adding increased risk or discomfort to the patient.

Cystoscopy is integral to the diagnosis of bladder cancer, allowing the physician to visualize the bladder wall directly. The sensitivity of cystoscopy is very good, but hematuria and other conditions can obscure lesions, and flat neoplasia can be confused with erythema. As seen in this study, even later-stage cancers are sometimes missed during endoscopy. The precise rate of false-negative cystoscopy test results is difficult to determine, but estimates range from 10% to 40%. In this study it was 11.4%. For this reason, physicians frequently use multiple tools to aid in diagnosis of bladder cancer, including urinalyses and imaging of the upper tract.

Voided cytology has been a widely accepted adjunctive test to cystoscopy because it is noninvasive. This method involves visual assessment of morphological changes and therefore requires intact cells. Small tumors, well-differentiated (low-grade) tumors, or both are less likely to exfoliate cells spontaneously because the strong intercellular attachments are better preserved, and the degree of morphological departure from normal is less, making recognition difficult. This results in low sensitivity, approximately 15% to 30% in early stage cancers. In addition, some inflammatory conditions cause cellular changes that can be confused with neoplastic process, contributing to subjective interpretation. False-positive reports of malignant cells are rare, but ambiguous reports of atypical cells are common. Collecting and analyzing 3 serial first-morning specimens for voided cytology is used by some physicians to improve the detection rate of cancer, but it significantly increases cost, and patient compliance is difficult. Because specially trained technicians are required for the analysis, samples must be stabilized and sent to a laboratory, and test results are not available.

**Table 3.** Specificity of NMP22 Assay

<table>
<thead>
<tr>
<th>Patients With Risk Factors for Bladder Cancer†</th>
<th>No. With Negative Test Result/Total No. Without Bladder Cancer</th>
<th>Specificity, % (95% Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No urinary tract disease (with risk factor)</td>
<td>512/567</td>
<td>90.3 (87.6-92.6)</td>
</tr>
<tr>
<td>Benign prostatic hypertrophy/prostatitis</td>
<td>231/280</td>
<td>82.5 (77.5-86.8)</td>
</tr>
<tr>
<td>Cystitis/inflammation/trigonitis/urinary tract infection</td>
<td>97/125</td>
<td>77.6 (69.3-84.6)</td>
</tr>
<tr>
<td>Erythema</td>
<td>42/51</td>
<td>82.4 (69.1-91.6)</td>
</tr>
<tr>
<td>Hyperplasia/aquamous metaplasia/cysts and polyps</td>
<td>41/53</td>
<td>77.4 (63.8-87.7)</td>
</tr>
<tr>
<td>Calculi</td>
<td>29/40</td>
<td>72.5 (56.1-85.4)</td>
</tr>
<tr>
<td>Trabeculations</td>
<td>175/217</td>
<td>80.7 (74.7-85.7)</td>
</tr>
<tr>
<td>Other benign diseases, kidney and genitourinary</td>
<td>179/220</td>
<td>81.4 (75.6-86.3)</td>
</tr>
<tr>
<td>Other cancer history, nonbladder†</td>
<td>7/8</td>
<td>87.5 (47.3-99.7)</td>
</tr>
<tr>
<td>Other active cancer, nonbladder†</td>
<td>33/38</td>
<td>86.8 (71.9-95.6)</td>
</tr>
</tbody>
</table>

*Other active cancer: breast cancer (n = 14), kidney/renal cancer (n = 5), leukemia/lymphoma (n = 3), lung cancer (n = 1), prostate cancer (n = 12), other types of cancer (n = 3, tongue, testes, spindle-cell [flank]).
1 in 20 patients with hematuria will develop bladder cancer. The sensitivity of urinary dipstick testing is minimal.1 It is important to rule out the presence of the disease in question. Patients enrolled in this investigation were at elevated risk for urological cancer due to behaviors such as smoking or symptoms including hematuria and dysuria. Consequently, the incidence of malignancy in this group was 6%. Currently, 20% or more of symptomatic patients present with disease that is already invasive at the time of first diagnosis. Identifying these malignancies earlier could improve prognosis and reduce the cost of treatment.

Hematuria is the most common symptom of bladder cancer, but it is often intermittent.3 Repetitive home testing of high-risk populations has shown good detection results,2 and the cost of urinary dipstick testing is minimal. However, because hematuria is not specific to cancer, it is estimated that only 1 in 20 patients with hematuria will have bladder cancer.3,4 Positive predictive value, the percentage of times that a positive test result corresponds to the presence of the disease in question, is about 5% for hematuria testing in men for bladder cancer and even lower in women.10 Nevertheless, because the amount of blood in urine is unrelated to stage and grade of cancer, the American Urological Association Best Practice Policy Panel on Asymptomatic Microscopic Hematuria and others have concluded that there is no safe lower limit for hematuria, and high-risk patients should be considered for a urological evaluation after even a single episode.1,3 Among study patients with the highest risk for bladder cancer, men older than 60 years with a history of smoking, the positive predictive value of the NMP22 test was 37%. This is higher than the 20% to 30% predictive value typically reported for prostate-specific antigen in men who have an elevated risk of prostate cancer, those with levels between 4 to 10 ng/mL.38-41

In conclusion, the NMP22 assay may be a useful adjunct to cystoscopy for diagnosing bladder cancer. Studies in different patient populations are necessary to further define the role of this assay in patients with risk factors and symptoms suggestive of possible bladder cancer.

Author Contributions: As principal investigator, Dr Grossman had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Grossman, Messing, Soloway, Katz.

Acquisition of data: Grossman, Messing, Soloway, Tomera, Katz, Berger.

Analysis and interpretation of data: Grossman, Messing, Soloway, Shem.

Drafting of the manuscript: Grossman, Messing.

Critical revision of the manuscript for important intellectual content: Grossman, Messing, Soloway, Tomera, Katz, Berger.

Statistical analysis: Grossman, Shem.

Obtained funding: Grossman, Messing, Soloway, Tomera, Katz, Berger.

Administrative, technical, or material support: Grossman, Messing, Soloway, Tomera, Katz.

Study supervision: Grossman, Messing, Soloway, Katz, Berger.

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Role of the Sponsor: Matritech Inc designed the study, monitored the conduct and collection of data, and reviewed the manuscript for factual accuracy and approved it.

Independent Statistical Analysis: Independent statistical analysis was performed by Yu Shen, PhD, at the University of Texas M. D. Anderson Cancer Center, Department of Biostatistics and Applied Math.

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REFERENCES


DETECTION OF BLADDER CANCER WITH A POINT-OF-CARE PROTEOMIC ASSAY


All adventures, especially into new territory, are scary.
—Sally Ride (1951- )