NMP22 BladderChek

A new Tumor Marker for Early Detection of Bladder Cancer
Tumor of the Urogenital Tract

• Distribution of the urological tumors

- Prostate 41.6%
- Bladder 33.7%
- Kidney 18.6%
- Testicle 5.5%
- Penis 0.6%
2010 - Bladder Cancer in the USA

- In 2010, an estimated 70,530 adults (52,760 men and 17,770 women) will be diagnosed with bladder cancer in the USA.

- It is estimated that 14,680 people will die from this disease.

- Of newly diagnosed bladder cancer cases, approximately 70%-80% will present with nonmuscle-invasive disease, and despite endoscopic and intravesical treatments, 50%-70% will recur and 10%-30% will progress to muscle-invasive disease.
Incidence & Mortality of Bladder Cancer in Germany in Minutes

<table>
<thead>
<tr>
<th>Minutes</th>
<th>All</th>
<th>Man</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence (25,950)</td>
<td>20</td>
<td>30</td>
<td>75</td>
</tr>
<tr>
<td>Mortality (5,451)</td>
<td>100</td>
<td>150</td>
<td>260</td>
</tr>
</tbody>
</table>
Diagnostic Problems I

- Up to now, there are no special, high-sensitive non-invasive diagnostic examination methods for an early detection of a BT.

- The urine cytology achieves in the area of the non-invasive, good differentiated tumours (pTa, pT1, G1) a very low sensitivity.

- The diagnosis becomes even more difficult due to the fact, that ~ 70%-80 % of all BT are superficial, well differentiated tumors.

- **Consequence:** There is a big diagnostic uncertainty among the greatest group of all bladder tumours.
Diagnostic Problems II

• The bladder cystoscopy is the “Golden Standard” – it is good but not perfect.

• The disadvantage is a “sometimes painful” procedure for the patient and some limitations in the diagnosis of a BT. (CIS, upper UT, occult tumors, early detection)

• The basic problem of the urine diagnostic of proteins is the decomposition of the molecule through proteolytic enzymes.

• A method, which stabilizes the substance of interest or could be used immediately would be of great help for the urologists to get a more accurate biological status of the disease.
A tumor marker like NMP22 is a perfect adjunct to cystoscopy.
NMP22 - a new tumor marker for

- Preventive medical check-up
- Early diagnosis
  (risk groups, symptomatic patients with hematuria,..)
- Monitoring
What is NMP22?

- NMP22 is a nucleus matrix protein, which is expressed very early in tumour cells (10-100 times).

- The test demonstrates a very high sensitivity for superficial tumour compared to cytology.

- The NMP22 test shows no diagnostic gap for the diagnosis of bladder tumours with an high sensitivity and specificity for all tumour stages.

- The test has passed the **FDA registration** regulations in the USA.
What are Nuclear Matrix Proteins?

- Protein framework which organizes DNA
- Control center of cell
- Common to all cells
- NMPs vary by cell type, stage of differentiation, cell cycle and type of cancer
- NMPs are released into blood and urine through apoptosis/cell death
- Applicable to most, if not all forms of cancer
NMP22- Clinical Utility

• NMP22 is not a test which can replace Cystoscopy – it is a perfect adjunct to it.

• NMP22 can possibly help the clinicians to confirm cystoscopies and/or help to optimise the definition of time intervals.

• NMP22 can be used for a screening parameter as confirmation or exclusion test for risk patients, as well as for monitoring of patients after a TURBT.

• NMP22 can detect cancer in the upper urinary tract.

• NMP22 can be used as adjunct to the urological standard diagnostic.
NMP22 - more sensitive as cytology
Sensitivity of NMP22 vs. UC

Poulakis et al. BJU
### Sensitivity in %

<table>
<thead>
<tr>
<th>Sensitivity</th>
<th>NMP22 (n)</th>
<th>Cytology (n) -VUC</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All</strong></td>
<td>85 (347)</td>
<td>62 (253)</td>
</tr>
<tr>
<td>pTa</td>
<td>83 (174)</td>
<td>44 (93)</td>
</tr>
<tr>
<td>pTis</td>
<td>74 (23)</td>
<td>84 (26)</td>
</tr>
<tr>
<td>pT1</td>
<td>85 (40)</td>
<td>70 (33)</td>
</tr>
<tr>
<td>pT2</td>
<td>95 (55)</td>
<td>78 (45)</td>
</tr>
<tr>
<td>pT3</td>
<td>96 (43)</td>
<td>93 (42)</td>
</tr>
<tr>
<td>pT4</td>
<td>100 (9)</td>
<td>89 (8)</td>
</tr>
<tr>
<td><strong>pTa,Tis,T1</strong></td>
<td>83 (237)</td>
<td>53 (152)</td>
</tr>
<tr>
<td>pT2-T4</td>
<td>96 (107)</td>
<td>85 (95)</td>
</tr>
<tr>
<td><strong>G1</strong></td>
<td>82 (106)</td>
<td>38 (49)</td>
</tr>
<tr>
<td>G2</td>
<td>89 (149)</td>
<td>68 (109)</td>
</tr>
<tr>
<td>G3</td>
<td>94 (66)</td>
<td>90 (63)</td>
</tr>
<tr>
<td>Specificity without EC*</td>
<td>68 (226)</td>
<td>96 (253)</td>
</tr>
<tr>
<td><strong>Specificity with EC</strong>*</td>
<td>94 (121)</td>
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*exclusion criteria*
## Various NMP22 studies with NMP22

<table>
<thead>
<tr>
<th>Author</th>
<th>Journal</th>
<th>No. Patients</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>S/M</th>
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<tbody>
<tr>
<td>Soloway</td>
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<td>90</td>
<td>70%</td>
<td>86%</td>
<td>M</td>
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<tr>
<td>Akaza</td>
<td>Jpn J Cancer C 1997</td>
<td>183</td>
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<td>79%</td>
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<tr>
<td>Saad</td>
<td>BJU 2002</td>
<td>120</td>
<td>81%</td>
<td>87%</td>
<td>S/M</td>
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<tr>
<td>Oehr</td>
<td>Tumor Diag&amp;T2006</td>
<td>113</td>
<td>86%</td>
<td>98%</td>
<td>S</td>
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<tr>
<td>Poulakis</td>
<td>BJU 2001</td>
<td>739</td>
<td>85%</td>
<td>68%94%*</td>
<td>S/M</td>
</tr>
<tr>
<td>Mianaga</td>
<td>JoU 1997</td>
<td>300</td>
<td>81%</td>
<td>100%</td>
<td>S/M</td>
</tr>
<tr>
<td>Nero del</td>
<td>Eur Urol 1999</td>
<td>105</td>
<td>83%</td>
<td>87%</td>
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<tr>
<td>Ponsky</td>
<td>JoU 2001</td>
<td>608</td>
<td>88%</td>
<td>84%/99%*</td>
<td>S/M</td>
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<tr>
<td>Lüdecke</td>
<td>CME Program 2007</td>
<td>8871</td>
<td>73%</td>
<td>73%</td>
<td>Meta-analys. Pub.96-02</td>
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<tr>
<td>Hautmann</td>
<td>XX.EAU 2005.</td>
<td>75</td>
<td>85%</td>
<td>91%</td>
<td>S/M</td>
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<tr>
<td>Grossman</td>
<td>JAMA 2006</td>
<td>668</td>
<td>50%&quot;</td>
<td>87%</td>
<td>M</td>
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<tr>
<td>Lüdecke</td>
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<td>517</td>
<td>75%</td>
<td>92%</td>
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<td>Grossman</td>
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<td>56%#</td>
<td>86%</td>
<td>S</td>
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<tr>
<td>Kumar</td>
<td>Jpn J Clin Onc 2006</td>
<td>131</td>
<td>85%/91%*</td>
<td>77%/88%</td>
<td>M</td>
</tr>
</tbody>
</table>

S = Screening
M = Monitoring
* With exc
Use of the NMP22 BladderChek

“The combination of NMP22 and cystoscopy is the most effective method for the early detection of bladder cancer available to the clinician today.”

NMP22 together with white light cystoscopy increases the detection rate for BC up to 96% - 99%.

Diagnostic Work up:
Patients at Risk for Bladder Cancer
Cystoscopy & NMP22

- Initial Evaluation
- Cystoscopy & NMP22

Positive Cystoscopy
- Bladder Cancer Treatment

Negative Cystoscopy & Negative NMP22
- Greater confidence in negative work up

Negative Cystoscopy & Positive NMP22
- Review Risk Profile
- Intensify Surveillance
- Establish NMP baseline

Treat first

Bladder Cancer
Calcui
UTI
Cystitis
NMP22-BladderChek
NMP22 – BladderChek

• Qualitative results in 30 minutes.

• Only 4 drops of urine is needed

• No external lab and shipment of samples.

• clinical utility for diagnosis & monitoring - FDA approved

• Use fresh urine – no freezing

• No interference through hematuria (0.8V%).

• 95% concordance with the quantitative NMP22 version.

• Results are available during the patients visit.