

# Validation of EAU Guideline's Pretreatment Risk Stratification Parameters in Upper Tract Urothelial Carcinoma (UTUC)

Beat Foerster<sup>1,2</sup>, Surena F. Matin<sup>3</sup>, Thomas Seisen<sup>4</sup>, Evangelos Xylinas<sup>5</sup>, Shoji Kimura<sup>6</sup>, Leonardo L. Monteiro<sup>7</sup>, Mounsiif Azizi<sup>8</sup>, Marco Bandini<sup>9</sup>, Timothy Clinton<sup>10</sup>, Kees Hendricksen<sup>11</sup>, Ja H. Ku<sup>12</sup>, Markus Grabbert<sup>13</sup>, Anna K. Czech<sup>14</sup>, Romain Mathieu<sup>15</sup>, Tim Mulwijk<sup>16</sup>, Uzoma Anele<sup>17</sup>, Firas Petros<sup>3</sup>, Laura-Maria Krabbe<sup>10</sup>, Morgan Rouprêt<sup>4</sup>, Alberto Briganti<sup>9</sup>, Axel Heidenreich<sup>13</sup>, Armin Pycha<sup>18</sup>, Riccardo Autorino<sup>17</sup>, Shin Egawa<sup>6</sup>, Philippe E. Spiess<sup>8</sup>, Steven Joniau<sup>16</sup>, Wassim Kassouf<sup>7</sup>, Shahrokh F. Shariat<sup>1, 10, 19, 20</sup>

<sup>1</sup> Department of Urology, Medical University of Vienna, Vienna, Austria.  
<sup>2</sup> Department of Urology, Kantonsspital Winterthur, Winterthur, Switzerland.  
<sup>3</sup> Department of Urology, MD Anderson Cancer Center, Houston, USA.  
<sup>4</sup> Department of Urology, Pitié-Salpêtrière, Faculté de Médecine Pierre et Marie Curie, University Paris VI, Paris, France.  
<sup>5</sup> Department of Urology, Cochin Hospital, Paris Descartes University, Paris, France.  
<sup>6</sup> Department of Urology, Jikei University School of Medicine, Tokyo, Japan.  
<sup>7</sup> Department of Surgery (Division of Urology), McGill University Health Center, Montreal, Canada.  
<sup>8</sup> Department of Genitourinary Oncology, Moffitt Cancer Center, Tampa, USA.  
<sup>9</sup> Department of Urology, Urological Research Institute, Vita-Salute University, San Raffaele Scientific Institute, Milan, Italy.  
<sup>10</sup> Department of Urology, University of Texas Southwestern Medical Center, Dallas, TX, USA.  
<sup>11</sup> Department of Urology, The Netherlands Cancer Institute-Antoni van Leeuwenhoek Hospital, Amsterdam, The Netherlands.  
<sup>12</sup> Department of Urology, Seoul National University Hospital, Seoul, Korea.  
<sup>13</sup> Department of Urology, Uro-Oncology, University Hospital Cologne, Cologne, Germany.  
<sup>14</sup> Department of Urology, Jagiellonian University, Krakow, Poland.  
<sup>15</sup> Department of Urology, University of Rennes, Rennes, France.  
<sup>16</sup> Department of Urology, University Hospitals Leuven, Leuven, Belgium.  
<sup>17</sup> Division of Urology, Virginia Commonwealth University, Richmond.  
<sup>18</sup> Department of Urology, Central Hospital of Bolzano, Bolzano, Italy.  
<sup>19</sup> Department of Urology, Weill Cornell Medical College, New York, USA.  
<sup>20</sup> Karl Landsteiner Institute of Urology and Andrology, Vienna, Austria.

## Aims

- Staging is inaccurate in UTUC.
- EAU pre-treatment risk stratification is necessary for optimal treatment decision-making.
- To validate and assess the additive value of each risk factor for predicting  $\geq pT2$  disease.

## Methods

- Multi-institutional retrospective study
- 406 patients who underwent ureterorenoscopy (URS) with biopsy followed by RNU
- Study period: 2000 - 2017
- Pts with preoperative chemotherapy were excluded

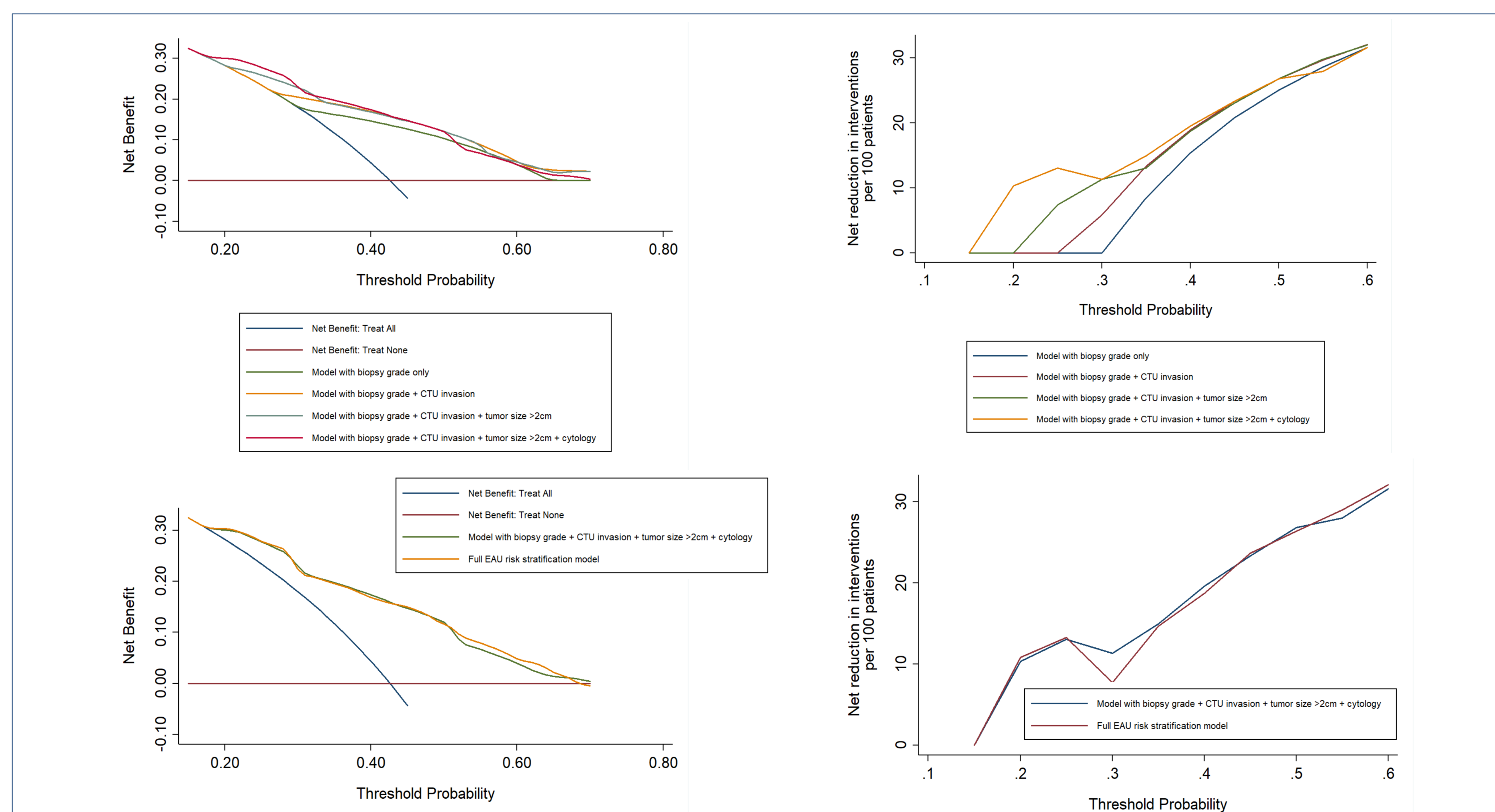
### Characteristics of 406 patients who underwent diagnostic ureterorenoscopy followed by RNU

|                     | All    | $\leq pT1$ | $\geq pT2$ |
|---------------------|--------|------------|------------|
| Total patients      | 406    | 57.4 %     | 42.6 %     |
| High-grade biopsy   | 35.9 % | 22.3 %     | 54.3 %     |
| CTU invasion        | 9.6 %  | 4.3 %      | 16.8 %     |
| Tumor size >2 cm    | 50 %   | 43.3 %     | 59.0 %     |
| High-grade cytology | 23.2 % | 19.7 %     | 27.8 %     |
| Previous cystectomy | 4.4 %  | 3.0 %      | 6.4 %      |
| Multifocality       | 19.7 % | 20.6 %     | 18.5 %     |
| Hydronephrosis      | 27.6 % | 25.8 %     | 39.1 %     |

## Results and Conclusions

- High-grade ureteroscopic biopsy and cytology, CTU invasion and tumor size >2cm seem to be the best factors to identify patients who harbor muscle-invasive disease.
- The additive value of preoperative hydronephrosis, previous cystectomy and tumor multifocality seems limited.
- Further biomarkers are needed to further increase the accuracy to select the patients who could most likely benefit from endoscopic KSS.
- The EAU risk stratification's NPV of 90% is high, therefore allowing accurate selection of patients.

### Decision curve analyses demonstrating the net benefit and RNU avoided of the different models



### Multivariable logistic regression analyses predicting $\geq T2$ disease

| Variables           | Odds Ratio (95% CI) | P-value |
|---------------------|---------------------|---------|
| High-grade biopsy   | 4.44 (2.80 - 7.03)  | <0.001  |
| CTU invasion        | 4.19 (1.88 - 9.36)  | <0.001  |
| Tumor size >2 cm    | 1.75 (1.13 - 2.71)  | 0.013   |
| High-grade cytology | 1.72 (1.03 - 2.89)  | 0.039   |
| Previous cystectomy | 1.86 (0.64 - 5.42)  | 0.3     |
| Multifocality       | 0.84 (0.49 - 1.45)  | 0.5     |
| Hydronephrosis      | 0.98 (0.60 - 1.61)  | 0.9     |

### Performance of the models

| Models         | AUC (%) | NPV (%) | CNB (%) |
|----------------|---------|---------|---------|
| Model 4        | 74      | 89      | 15      |
| Full EAU model | 75      | 90      | 15      |

### Number of RNU avoided per 100 patients

| Threshold Prob | .2   | .25  | .3   | .35  |
|----------------|------|------|------|------|
| Model 4        | 10.3 | 13.1 | 11.3 | 14.9 |
| Full EAU model | 10.8 | 13.3 | 7.7  | 14.6 |

Model 4: Biopsy grade + CTU invasion + tumor size >2cm + cytology; Prob: Probability; TS: Tumor size; AUC: Area under the curve; NPV: Negative predictive value; CNB: Maximum clinical net benefit.