



Illustration by Erin Moore

CLINICAL Genitourinary Prostate, Kidney, & Bladder Cancer

Table of Contents

Original Studies

- 301** **Impact of renin-angiotensin system inhibitors on outcomes in patients with metastatic renal cell carcinoma treated with immune-checkpoint inhibitors**
Pier Vitale Nuzzo, Elio Adib, Nicole Weise, Catherine Curran, Tyler Stewart, Dory Freeman, Amin H. Nassar, Sarah Abou Alaiwi, Ziad Bakouny, Bradley A. McGregor, Toni K. Choueiri, Rakesh K. Jain, Rana R. McKay, Guru Sonpavde
 In this multicenter retrospective study, we studied the impact of the concurrent use of renin-angiotensin system inhibitors (RASi) on the outcomes of 229 metastatic renal cell carcinoma (mRCC) patients treated with immunecheckpoint inhibitors (ICI). The findings suggest that RASi could be repurposed to enhance outcomes with ICI in patients with mRCC, which may have a large global impact given their cost-efficacy.
- 307** **Testis Cancer Care in North Carolina: Implications for Real-World Evidence and Cancer Surveillance**
Stephen McMahon, Xi Zhou, Christopher D. Baggett, Marc A. Bjurlin, Ronald C. Chen, Stephen B. Riggs, Mark S. Litwin, Matthew I. Milowsky, Eric M. Wallen, Hung-Jui Tan
 Testis cancer care requires fastidious adherence to clinical guidelines, especially for those pursuing active surveillance. However, quality remains largely unknown. Using linked NC Cancer Registry-insurance claims data, we assessed whether patients received recommended evaluation and monitoring. Among 487 men diagnosed between 2003 and 2013, 18.9% received the recommended monitoring.
- 319** **MRI-Detectability of Clinically Significant Prostate Cancer Relates to Oncologic Outcomes After Prostatectomy**
Andreas G. Wibmer, Robert A. Lefkowitz, Yulia Lakhman, Joshua Chaim, Ines Nikolovski, Evis Sala, Samson W. Fine, Timothy F. Donahue, Michael W. Kattan, Hedvig Hricak, Hebert Alberto Vargas
- 326** **Impact of Metastasectomy on Cancer Specific and Overall Survival in Metastatic Renal Cell Carcinoma: Analysis of the REMARCC Registry**
Margaret F. Meagher, Maria C Mir, Riccardo Autorino, Andrea Minervini, Maximilian Kriegmair, Tobias Maurer, Francesco Porpiglia, Siska Van Bruwaene, Estefania Linares, Vital Hevia, Mireia Musquera, Eduard Roussel, Nicola Pavan, Alessandro Antonelli, Shudong Zhang, Fady Ghali, Devin Patel, Juan Javier-Desloges, Aaron Bradshaw, Jose Rubio, Georgi Guruli, Andrew Tracey, Riccardo Campi, Maarten Albersen, Maria Furlan, Rana R. McKay, Ithaa H. Derweesh
 Role of surgery and metastasectomy in metastatic Renal Cell Carcinoma is in flux. In multicenter comparison of 431 patients who received metastasectomy versus those who did not, metastasectomy was associated with improved cancer-specific survival in favorable-risk and improved overall survival in favorable- and intermediate-risk patients, but not in high-risk patients. These findings point toward refinement of selection criteria for metastasectomy.

- 334 Effect of Testosterone Replacement Therapy on Quality of Life and Sexual Function in Testicular Cancer Survivors With Mild Leydig Cell Insufficiency: Results From a Randomized Double-blind Trial**
Emma Grunwald Højer, Michael Kreiberg, Christian Dehlendorf, Niels Jørgensen, Anders Juul, Jakob Lauritsen, Thomas Wagner, Josephine Rosenvilde, Gedskø Dagaard, Mikkel Bandak
The aim was to evaluate if testosterone replacement therapy (TRT) improves quality of life and sexual function in testicular cancer survivors with mild Leydig cell insufficiency. Sixty-nine patients were randomly assigned to 12 months of testosterone or placebo. Testosterone replacement therapy was not associated with improvement of quality of life and sexual function. Our findings do not support routine use of TRT in these patients.
- 344 Benefit of Metastasectomy in Renal Cell Carcinoma: A Propensity Score Analysis**
Franziska Maisel, Maria A. Smolle, Stefanie Mollnar, Jakob M. Riedl, Dominik A. Barth, Maximilian Seles, Angelika Terbuch, Christopher H. Rossmann, Florian Eisner, Sebastian Mannweiler, Georg Hutterer, Richard Zigeuner, Karl Pummer, Freyja-Maria Smolle-Jüttner, Jörg Lindenmann, Michael Stotz, Armin Gerger, Philipp J. Jost, Thomas Bauernhofer, Martin Pichler, Florian Posch
We performed a propensity score analysis on the role of metastasectomy for patients with metastatic renal cell carcinoma. Our results support the concept that metastasectomy is associated with improved overall survival in this population. This benefit appears to be confined to metastasectomies that achieve complete resection of all known lesions.
- 354 Systemic Therapy in Patients With Metastatic Xp11.2 Translocation Renal Cell Carcinoma**
Xieqiao Yan, Li Zhou, Siming Li, Xiaowen Wu, Chuanliang Cui, Zhihong Chi, Lu Si, Yan kong, Bixia Tang, Caili Li, Lili Mao, Xuan Wang, Bin Lian, Xue Bai, Jie Dai, Jun Guo, Xinan Sheng
- 363 Comparison of 2-Weekly and 3-Weekly Dosing of Docetaxel in Metastatic Prostate Cancer**
Sergio Martinez-Recio, Juan Pablo Perez-Vert, Sara Martinez-Fdez, Diego Jimenez-Bou, Iciar Ruiz-Gutierrez, Jesus Peña, Ana Pertejo, Enrique Espinosa, Alvaro Pinto
In metastatic prostate cancer, 2-weekly docetaxel schedules could be preferred for frail patients. We retrospectively compared 200 patients treated with 2 or 3-weekly schedules. Patients treated with 2-weekly scheme were older and frailer and presented worse outcomes, but survival was not detrimental comparing the schedule chosen after multivariate analyses. The 2-weekly schedule produced less clinically impairing toxicities and toxic deaths.
- 371 Identification and Validation of the Prognostic Impact of Metastatic Prostate Cancer Phenotypes**
Shelby A. Labe, Xi Wang, Eric J. Lehrer, Amar U. Kishan, Daniel E. Spratt, Christine Lin, Alicia K. Morgans, Lee Ponsky, Jorge A. Garcia, Sara Garrett, Ming Wang, Nicholas G. Zaorsky
Our retrospective analysis focuses on improving prognostication. The National Cancer Database was queried from 2010 to 2015 for men diagnosed with castration-sensitive metastatic prostate cancer. We developed and validated several prognostic phenotypes that can aid in risk stratification to potentially personalize therapy. We also performed a literature review of related works. Our nomogram (<https://tinyurl.com/prostate-met>) may be used to predict survival.
- 381 Segmental Ureterectomy Versus Radical Nephroureterectomy in Older Patients Treated for Upper Tract Urothelial Carcinoma**
Alberto Abrate, Francesco Sessa, Maurizio Sessa, Riccardo Campi, Arcangelo Sebastianelli, Virginia Varca, Carlo Pavone, Marco Vella, Riccardo Bartoletti, Vincenzo Ficarra, Sergio Serni, Eugenio Brunocilla, Andrea Gregori, Carlo Trombetta, Andrea Lissiani, Carlo Terrone, Paolo Gontero, Riccardo Schiavina, Mauro Gacci, Alchiede Simonato
Surgery in older patients is associated with higher perioperative morbidity and mortality rates. We compared radical nephroureterectomy and segmental ureterectomy (less invasive) in patients older than 75 years of age with upper tract urothelial carcinoma. Segmental ureterectomy showed lower rates of post-operative complications, without affecting survival; it could be safely indicated in selected older patients with upper tract urothelial carcinoma.

Editor's highlight

388 Molecular Biomarkers of Prognosis in Advanced Renal Cell Carcinoma Patients Treated With Pazopanib Plus Interferon Alpha (INF-2A) in a Phase I/II Study by the Spanish Oncology Genitourinary Group

Xavier García-del-Muro, Ignacio Durán, Jose Luis Perez-Gracia, Miguel Ángel Climent, Begoña Mellado, Juan A. Virizuela, Daniel E. Castellano, Aranzazu González del Alba, Iciar García Carbonero, Carlos Álvarez-Fernández, Jesús García-Donas, Marta Gil-Martin, Alvaro-González Hernández

Phase I/II translational trial evaluating the molecular determinants of pazopanib plus interferon alpha efficacy in advanced renal cell carcinoma. The expression levels of TNF- α , endoglin and PD-L1 correlated with response at eight weeks after treatment initiation. This suggests a crucial role of vascular remodelling and inflammatory-mediated immune cell infiltration for an optimal response to pazopanib plus interferon alpha combination.

389 Metastasis Within Three Years from Radical Nephroureterectomy as a Potential Surrogate for Overall Survival

Alberto Martini, Chiara Lonati, Andrea Necchi, Matthew D. Galsky, Guillaume Ploussard, Giuseppe Fallara, Antony Pellegrino, Claudio Simeone, Nazareno Suardi, Stefania Zamboni, Wojciech Krajewski, Giuseppe Simone, Alberto Briganti, Francesco Montorsi, Agostino Mattei, Shahrokh F. Shariat, Marco Moschini

Intermediate clinical endpoints (ICE) help expedite approval of novel treatments. We aimed to identify the most informative ICE for predicting overall survival (OS) after radical nephroureterectomy (RNU) for high-grade upper tract urothelial carcinoma. Distant metastases within 3-years from RNU are the most effective surrogates of OS after RNU and could be useful to expedite earlier results of future studies.

390 Axitinib Trough Concentration and its Influence on the Efficacy and Toxicity of Second-line Renal Cell Carcinoma Treatment

Zuzanna Synowiec, Katarzyna Sobańska, Tomasz Synowiec, Artur Teżyk, Piotr Tomczak, Anna Jabłeczka

The aim of the article was to study relationships between the axitinib steady-state trough concentration (C_{trough}) and treatment efficacy and toxicity. There was a statistically significant differences between measured axitinib C_{trough} value and treatment response, median progression-free survival, and toxicity in the group of 35 patients. The data collected may be used to determine indications for axitinib therapy monitoring based on C_{trough} measurements.

Available Exclusively Online at www.clinical-genitourinary-cancer.com

e271 The Role of Bladder Epicheck Test In Follow-Up of Patients with Non-Muscle Invasive Bladder Cancer

Mauro Ragonese, Luca Di Gianfrancesco, Giuseppe Palermo, Francesco Pierconti, Maurizio Martini, Massimiliano Foti, Pierfrancesco Bassi, Marco Racioppi

The need of new non-invasive biomarkers for diagnosis and follow-up of non-muscle invasive bladder cancer is well-known in urological community. The methylation test such as Epicheck could overcome the limits of urinary cytology, particularly in patients treated with Endo vesical therapy. According to our results this test could be included as an adjunctive tool in follow-up of patients.

e276 Prognostic Significance of C-reactive Protein in Patients With Non-metastatic Papillary Renal Cell Carcinoma: Results from the INternational Marker Consortium for Renal Cancer (INMARC) Cohort

Masahiro Toide, Kazutaka Saito, Yosuke Yasuda, Hajime Tanaka, Shohei Fukuda, Dattatraya Patil, Brittney H. Cotta, Sunil H. Patel, Viraj A. Master, Ithaar H. Derweesh, Yasuhisa Fujii

The prognostic value of C-reactive protein was evaluated in patients with non-metastatic papillary renal cell carcinoma undergoing curative surgery using the international multi-institutional cohort. We demonstrated that C-reactive protein was significantly associated with poor recurrence-free survival. C-reactive protein can serve as a useful adjunct biomarker to screen patients with a high risk of recurrence.

- e283** **ong-term Health-related Quality of Life (HRQOL) After Radical Cystectomy and Urinary Diversion - A Propensity Score-matched Analysis**
Yannic Volz, Lennert Eismann, Paulo Pfitzinger, Thilo Westhofen, Benedikt Ebner, Jan-Friedrich Jokisch, Alexander Buchner, Gerald B. Schulz, Boris Schlenker, Alexander Karl, Christian G. Stief, Alexander Kretschmer
How urinary diversion affects the patient's health-related quality of life in long-term after radical cystectomy remains unclear. The current study tries to assess quality-of-life up to 4 years after radical cystectomy in a contemporary cohort. However, the choice of urinary diversion does lead to a reduced quality of life of the patients and more attention should be given to co-morbidities.
- e291** **Proposal for a New Vesical Imaging-Reporting and Data System (VI-RADS)-Based Algorithm for the Management of Bladder Cancer: A Paradigm Shift From the Current Transurethral Resection of Bladder Tumor (TURBT)-Dependent Practice**
Satoru Taguchi, Masanaka Watanabe, Mitsuhiro Tambo, Haruhiko Machida, Kenichi Yokoyama, Hiroshi Fukuhara
- e296** **The Distribution of Metastatic Renal Cell Carcinoma by Presenting Tumor Stage in the Modern Era**
Evan Sharp, Anirudh Guduru, Allison M May, Lindsay Lombardo, Sameer A Siddiqui, Zachary A Hamilton
Aim to determine the distribution of metastatic renal cell carcinoma by cT stage over time using the NCDB. There has been a more rapid increase in metastasis of localized renal masses (cT1-T2) as compared to locally advanced disease (cT3-T4). Metastatic kidney cancer is increasingly diagnosed at a lower presenting cT stage. Higher cT stages at diagnosis have worsened survival outcomes.
- e303** **Role of Renin-Angiotensin System Blockers on BCG Response in Nonmuscle Invasive, High Risk Bladder Cancer**
Giovanni Motterle, Alessandro Morlacco, Giulia Giovannini, Elia Vecchiato, Massimo Iafrate, Arturo Calpista, Tommaso Prayer-Galetti, Francesca Martino, Fabrizio Dal Moro, Giacomo Novara
The best treatment option for high-risk non muscle-invasive bladder cancer is BCG immunotherapy. In this study we looked for potential interaction between drugs with known immunomodulatory effects (angiotensin receptor blockers and ACE-inhibitors) and cancer recurrence in patients treated with BCG. Our results show a benefit in patients treated with angiotensin receptor blockers.
- e310** **The Predictive and Prognostic Value of Precystectomy Serum Gamma-Glutamyltransferase Levels in Patients With Invasive Bladder Cancer**
Georgios Gakis, Manuel Alexander Schmid, Fahmy Hassan, Arnulf Stenzl, Markus Renninger
This retrospective analysis investigated the predictive and prognostic value of serum gammaglutamyltransferase (GGT) in 324 patients undergoing RC for invasive bladder cancer (BC). Elevated preoperative serum GGT levels was associated with increased risk of locally advanced BC and mortality after RC. The data suggest that GGT levels may be a useful for improved prognostication in invasive BC.
- e317** **Establishing a Prognostic Model Based on Three Genomic Instability-related LncRNAs for Clear Cell Renal Cell Cancer**
Shen Lulu, Hou Hualing, Zhang Shan, Chen Dianxi, Li Yiqing, Li Qin
In this work, we explored the relationship between genomic instability-related lncRNAs and clinical outcome for clear cell renal cell carcinoma(ccRCC) patients based on TCGA and GEO databases. We successfully established a prognostic risk score model with three genomic instability-related lncRNAs and we further verified the effects of genome instability related lncRNAs on predicting the clinical outcomes of patients. The results will contribute to develop a reliable and referable risk evaluating model and provide new insight into the targeted therapy of clear cell renal carcinoma even though we need more independent data sets to validate GIRS to ensure its robustness and repeatability.

e330 Predictors of Survival in Patients Undergoing Surgery for Renal Cell Carcinoma and Inferior Vena Cava Tumor Thrombus

Alberto C. Pieretti, Manuel Ozambela, Mary E. Westerman, Graciela M. Nogueras-Gonzalez, Luis A. Segarra, Niki M. Zacharias, Ara Vaporciyan, Wayne Hofstetter, Tam Huynh, Saad Aldousari, Surena F. Matin, Jose A. Karam

We assessed preoperative factors associated with overall survival in patients with renal cell carcinoma with IVC thrombus (cT2b, cT3c). We confirmed that cT3c, cN1, and cM1 were independently associated with poor OS. In patients with ≥ 2 risk factors, the median overall survival was 8.9 months. Stratification of patients before surgery allows us to determine whether the benefits of the procedure outweigh the risks.

e339 Comparison Between Micro-Ultrasound and Multiparametric MRI Regarding the Correct Identification of Prostate Cancer Lesions

Vito Lorusso, Boukary Kabre, Geraldine Pignot, Nicolas Branger, Andrea Pacchetti, Jeanne Thomassin-Piana, Serge Brunelle, Andrea Gregori, Naji Salem, Gennaro Musi, Emanuele Montanari, Ottavio de Cobelli, Gwenaelle Gravis, Jochen Walz

Micro-ultrasound (Micro-US) is a new prostate cancer (PCa) imaging technology. We compared data from patients who underwent Micro-US and MRI before surgery. The sensitivity of Micro-US in the index lesion detection was 76.5%, specificity 76.6%, negative predictive value 85.6%, positive predictive value 64.1% and 76.6% of accuracy. Micro-US is reliable and comparable to MRI in identifying PCa index lesions.

e346 Evidence or Prejudice? Critical Re-Analysis of Randomized Controlled Trials Comparing Overall Survival After Cisplatin Versus Carboplatin-Based Regimens in Advanced Urothelial Carcinoma

Anke Richters, Lambertus A.L.M. Kiemeney, Niven Mehra, Hans M. Westgeest, Alison Birtle, Richard T. Bryan, Katja K.H. Aben

Guidelines recommend cisplatin over carboplatin for treatment of advanced urothelial carcinoma since 2008. This recommendation is based on (a meta-analysis of) two small RCTs, one with a questionable censoring approach. Secondary analysis of individual patient data from these RCTs did not demonstrate overall survival benefit from cisplatin over carboplatin. Considering lower toxicity and larger population eligibility for carboplatin, guideline recommendations should be reconsidered.