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# CLINICAL Genitourinary Prostate, Kidney, & Bladder Cancer

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### Review

- 391 **A Systematic Review and Meta-Analysis of the Role of Immune Checkpoint Inhibitors (ICI) as Adjuvant Treatment for Localized High-Risk Muscle-Invasive Urothelial Carcinoma (MIUC)**

*Fernando Sabino M. Monteiro, Andrey Soares, Vinicius Carrera Souza, Rubens Copia Sperandio, Enrique Grande, Matteo Santoni, Andre Poisl Fay, Andre Deeke Sasse*

### Original Studies

- 399 **Lower Fracture Rates in Patients Treated with Radium-223, Abiraterone or Enzalutamide, When Given Concurrently with Bone Health Agents: A Real-World Analysis**

*Janson Trieu, Mark Chang, Vanessa Rojas, Neilmegh Varada, Yen Cao, Michael Anderson, Nicholas J. Vogelzang*

The phase 3 trial ERA223 demonstrated increased fracture rate with no survival advantage for metastatic castration resistant prostate cancer (mCRPC) patients on combination Radium-223 (Ra-223) and abiraterone compared with abiraterone alone. However, less than half of the study patients received a bone health agent. A retrospective, cohort analysis of electronic health record data of 177 patients receiving Ra-223 by a single provider at a single community center was performed. We observed a 5.7% fracture rate for mCRPC patients who received combination therapy and denosumab or zoledronic acid.

- 404 **A randomized double-blind single center study of testosterone replacement therapy or placebo in testicular cancer survivors with mild Leydig cell insufficiency (Einstein-intervention)**

*Michael Kreiberg, Niels Jørgensen, Anders Juul, Jakob Lauritsen, Peter Oturai, Jørn Wulff Helge, Jesper Frank Christensen, Lise Aksglaede, Tim Schauer, Thomas Wagner, Josephine Rosenvilde, Emma Grunwald, Christian Dehendorff, Gedskede Dagaard, Mikkel Bandak*

The aim was to evaluate if in sixty-nine testicular cancer survivors with mild Leydig cell insufficiency randomly assigned to 12 months of testosterone replacement therapy (TRT) or placebo changed insulin sensitivity and components of metabolic syndrome. No significant changes were observed, and our findings do not support routine use of TRT in these patients.

- 415 **A Phase II, Single-arm Trial of Sunitinib and Erlotinib in Advanced Renal Cell Carcinoma**

*Zizhen Feng, Brendan D. Curti, David I. Quinn, John M. Strother, Zunqiu Chen, Rebecca Agnor, Tomasz M. Beer, Christopher W. Ryan*

Most patients with advanced renal cell carcinoma (RCC) will eventually relapse on tyrosine kinase inhibitor therapy such as sunitinib. The addition of an epidermal growth factor receptor (EGFR) inhibitor may overcome resistance to sunitinib monotherapy. We performed a dose-escalation phase II study of sunitinib plus the EGFR inhibitor erlotinib in 37 patients with advanced RCC. The combination was well tolerated but did not result in an increase in progression-free survival compared to sunitinib monotherapy.

- 423 Evolving Trends in the Management of Low-Risk Prostate Cancer**  
*Michael Tzeng, Spyridon P. Basourakos, Meenakshi Davuluri, Himanshu Nagar, Ashwin Ramaswamy, Emily Cheng, Gina DeMeo, Jim C. Hu*  
Deferred treatment is a growing management strategy for low-risk prostate cancer in the United States. However, it is unknown whether changes in practice patterns are influenced by sociodemographic variables. Using the National Cancer Database, we found that black race, low income, and non-private insurance status were associated with smaller increases in deferred treatment.
- 431 Long-term Outcomes of Local and Metastatic Small Cell Carcinoma of the Urinary Bladder and Genomic Analysis of Patients Treated With Neoadjuvant Chemotherapy**  
*Min Yuen Teo, Brendan J. Guercio, Arshi Arora, Xueli Hao, Ashley M. Regazzi, Timothy Donahue, Harry W. Herr, Alvin C. Goh, Eugene K. Cha, Eugene Pietzak, Sherri M. Donat, Guido Dalbagni, Bernard H. Bochner, Semra Olgac, Judy Sarungbam, S. Joseph Sirintrapun, Ying-Bei Chen, Anuradha Gopalan, Samson W. Fine, Satish K. Tickoo, Victor E. Reuter, Britta Weigelt, Anne M. Schultheis, Samuel A. Funt, Dean F. Bajorin, David B. Solit, Gopa Iyer, Irina Ostrovnya, Jonathan E. Rosenberg, Hikmat Al-Ahmadie*  
We evaluated long-term outcomes of small cell carcinoma of the bladder (SCCB), a rare, aggressive disease. Among 199 patients with SCCB treated from 1990 to 2015, those with nonmetastatic disease had excellent long-term survival following neoadjuvant chemotherapy with 5-year disease-free survival rate of 50%. Patients with metastases had poor survival, with median overall survival of 10.3 months. Pathologic downstaging following neoadjuvant chemotherapy was associated with superior survival and ERCC2 mutations conferred increased likelihood of pathologic response.
- 442 RESIRT: A Phase 1 Study of Selective Internal Radiation Therapy Using Yttrium-90 Resin Microspheres in Patients With Primary Renal Cell Carcinoma**  
*Paul L. de Souza, Peter Aslan, William Clark, Ramy Nour, Suresh de Silva*  
Selective internal radiation therapy (SIRT) has a potential role in patients with renal cell carcinoma (RCC) who are unsuitable for conventional treatment. RESIRT is the first prospective trial investigating SIRT for RCC. Intended doses were delivered without any dose-limiting toxicity. SIRT may be a treatment option for RCC unsuitable for conventional therapy and warrants further clinical study.
- 452 Phase 2 Study of Neoadjuvant FGFR Inhibition and Androgen Deprivation Therapy Prior to Prostatectomy**  
*Elizabeth Liow, Nicholas Howard, Chol-Hee Jung, Bernard Pope, Bethany K. Campbell, Anne Nguyen, Michael Kerger, Jonathan B. Ruddle, Angelyn Anton, Benjamin Thomas, Kevin Chu, Philip Dundee, Justin S. Peters, Anthony J. Costello, Andrew S. Ryan, Christopher M. Hovens, Ben Tran, Niall M. Corcoran*  
Disease recurrence is common following prostatectomy in patients with localised prostate cancer with high-risk features. We conducted an open label phase II study of the combination of FGFR inhibition (3 months) and androgen deprivation therapy (4 months) in this patient cohort. Although there was a possible enhanced anti-tumour effect following combination therapy, the poor tolerability in this patient population prohibits the use of this combination in this setting.
- 459 Effect of Positive Surgical Margins in Patients Who Undergo a Partial Nephrectomy Regarding Recurrence, Overall Survival, Recurrence/Progression-Free Survival, and Metastasis-Free Survival. A Systematic Review and Meta-Analysis**  
*Herney Andrés García-Perdomo, Maria Jose, Ribal Caparrós, Antonio, Alcaraz Asensio, Antoni, Vilaseca Cabo*  
We performed a systematic review and meta-analysis to determine the effect of positive surgical margins in patients undergoing a partial nephrectomy regarding survival. We found that positive margin increases the risk of local recurrence, recurrence, and metastasis-free survival.
- 473 A Study of Pazopanib Safety and Efficacy in Patients With Advanced Clear Cell Renal Cell Carcinoma and ECOG Performance Status 2 (Pazo2): An Open label, Multicentre, Single Arm, Phase II Trial**  
*Anjali Zarkar, Sarah Pirrie, Clive Stubbs, Anne-Marie Hodgkins, David Farrugia, Kathryn Fife, Carey MacDonald-Smith, Naveen Vasudev, Emilio Porfiri*  
Patients with advanced kidney cancer and who are unwell are often deemed unsuitable for treatment. Pazo2 was a trial recruiting 75 patients; 70.8% patients did not develop "intolerable" side effects, with 56.9% still alive and cancer-free 6-months after starting pazopanib. Therefore, pazopanib could be a treatment option for patients who cannot receive or tolerate immune checkpoint inhibitors.

- 482 **Clinicopathological Features of *FGFR3* - Mutated Upper Tract Urothelial Carcinoma: A Genomic Database Analysis**  
*Alessandro Rizzo, Veronica Mollica, Matteo Santoni, Francesco Massari*  
This large-scale database analysis suggested that *FGFR3* mutations may represent a prognostic factor in this disease, with a statistically longer overall survival compared to wild-type patients. This study may support the design of appropriate prospective clinical trials and preclinical models to develop novel pharmacologic approaches for UTUC patients. Genomic characterization of UTUC is destined to become increasingly important, and more efforts aimed at implementing UTUC genomics analysis are warranted.
- 488 **Efficacy and Safety of Concomitant Proton Pump Inhibitor and Nivolumab in Renal Cell Carcinoma: Results of the GETUG-AFU 26 NIVOREN Multicenter Phase II Study**  
*Elie Rassy, Cécile Dalban, Emeline Colomba, Lisa Derosa, Carolina, Alves Costa Silva, Sylvie Negrier, Christine Chevreau, Gwenaelle Gravis, Stephane Oudard, Brigitte Laguerre, Philippe Barthelemy, Marine Gross Goupil, Lionnel Geoffrois, Frederic Rolland, Antoine Thiery-Vuillemin, Florence Joly, Sylvain Ladoire, Florence Tantot, Bernard Escudier, Laurence Albiges*  
As proton pump inhibitors (PPI) were shown to impact the effectiveness of immune checkpoint inhibitors (ICI) in lung and bladder cancers, we sought to evaluate the effect of PPIs on the outcomes patients with metastatic renal cell carcinoma (mRCC) treated with ICI.

## Editor's highlight

- 495 **Impact of Novel Hormonal Agents (Abiraterone, Enzalutamide) on the Development of Visceral and/or Brain Metastases in Patients With Bone-metastatic Castration-resistant Prostate Cancer**  
*Cédric Pobel, Emeline Laurent, Aline-Marie Florence, Gaëlle Fromont, Gilles Calais, Bérengère Narciso, Claude Linassier, Mathilde Cancel*  
We aimed to study whether the use of novel hormonal agents (NHAs) increases the risk of developing visceral or brain metastases (VBM) in bone metastatic castration-resistant prostate cancer (bmCRPC). Among the 187 bmCRPC patients included, VBM incidence increased after 2011 ( $P = .04$ ). Yet, the longer was the treatment with NHAs, the lower was the risk of VBM.
- 496 **Real-World Cabazitaxel Use and Outcomes in Metastatic Castrate-Resistant Prostate Cancer: The Impact of Response to First ARPI**  
*Alexander S Watson, Richard Gagnon, Eugene Batuyong, Nimira Alimohamed, Richard Lee-Ying*  
In metastatic prostate cancer, optimal sequence of therapies is uncertain. We retrospectively analyzed the treatments and responses of 592 such patients, finding poor response to a first androgen receptor pathway inhibitor helped identify those who appear to derive more benefit from cabazitaxel chemotherapy. Clinicians under-utilized cabazitaxel over the study period. These real-world results can support clinician therapeutic decision making.
- 497 **Association of Surgical Approach With Treatment Burden, Oncological Effectiveness, and Perioperative Morbidity in Adrenocortical Carcinoma**  
*Kevin B. Ginsburg, Akhil A. Chandra, Elizabeth A. Handorf, Jared P. Schober, Ali Mahmoud, Marc C. Smaldone, Rosalia Viterbo, Robert G. Uzzo, Richard E. Greenberg, David Y.T. Chen, Alexander Kutikov, Andres F. Correa*  
In the National Cancer Database (NCDB), patients treated with minimally invasive adrenalectomy (MIA) for adrenocortical carcinoma (ACC) had similar oncological outcomes and cumulative treatment burden with less morbidity compared with open adrenalectomy (OA). Although OA remains the standard of care for adrenal lesions concerning for malignancy, MIA in appropriately selected patients may offer equivalent oncological outcomes.

**498 Primary Tumor Shrinkage and the Effect on Metastatic Disease and Outcomes in Patients With Advanced Kidney Cancer With Intermediate or Poor Prognosis Treated With Nivolumab Plus Ipilimumab or Cabozantinib**

*Roberto Iacovelli, Chiara Ciccarese, Marco Maruzzo, Francesco Atzori, Luca Galli, Sarah Scagliarini, Francesco Massari, Elena Verzoni, Antonella Cannella, Maria Grazia Maratta, Claudia Caserta, Davide Bimbatti, Filippo Maria Deppieri, Mariele Dessi, Federico Paolieri, Ferdinando Riccardi, Sergio Bracarda, Ugo De Giorgi, Umberto Basso, Giampaolo Tortora, Giuseppe Procopio*

Activity of immune checkpoint inhibitor-based combinations on the primary tumor is still one of the most debated issues. We reported as the extension of the primary tumor did not affect patient survival, while its response was significantly related to the response on metastatic disease and survival. No significant differences in tumor shrinkage were identified between nivolumab+ipilimumab or cabozantinib.

**499 Efficacy of Pembrolizumab in Patients With Variant Urothelial Carcinoma: A Multicenter Retrospective Study**

*Akinori Minato, Nobuki Furubayashi, Mirii Harada, Takahito Negishi, Naotaka Sakamoto, Yoohyun Song, Yoshifumi Hori, Toshihisa Tomoda, Shingo Tamura, Kentaro Kuroiwa, Narihito Seki, Ikko Tomisaki, Kenichi Harada, Motonobu Nakamura, Naohiro Fujimoto*

Urothelial carcinoma with histological variants is a clinically aggressive disease. We compared the clinical outcomes of urothelial carcinoma with histological variants to pure urothelial carcinoma in patients with advanced-stage bladder and upper urinary tract cancer receiving pembrolizumab after failure of platinum-based chemotherapy. The response of histological variants to pembrolizumab was not inferior to that of pure urothelial carcinoma.

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**e353 Cost Effectiveness Analysis of Radiofrequency Ablation (RFA) Versus Stereotactic Body Radiotherapy (SBRT) for Early Stage Renal Cell Carcinoma (RCC)**

*Elysia K. Donovan, Feng Xie, Alexander V Louie, William Chu, Shankar Siva, Anil Kapoor, Anand Swaminath*

Stereotactic body radiotherapy (SBRT) and radiofrequency ablation (RFA) are treatment options for early-stage renal cell carcinoma (RCC), with acceptable oncologic outcomes. This analysis aims to assess cost effectiveness of these treatments. SBRT appears more cost effective than RFA for larger tumors, while RFA is more cost-effective for smaller tumors, though incremental cost-effectiveness ratios are highly dependent on probabilities and utilities. Treatment decision should consider a number of factors and further research is required.

**e362 Preexisting Autoantibodies and Immune Related Adverse Events in Metastatic Urothelial Carcinoma Patients Treated by Pembrolizumab**

*Zahra Castel-Ajgal, Claire Gouvestre, Sonia Zaibet, Jennifer Arrondeau, Marie Bretagne, Michael Peyromaure, Frédéric Batteux, Jerome Alexandre, Francois Goldwasser, Olivier Huillard*

Stereotactic body radiotherapy (SBRT) and radiofrequency ablation (RFA) are treatment options for early-stage renal cell carcinoma (RCC), with acceptable oncologic outcomes. This analysis aims to assess cost effectiveness of these treatments. SBRT appears more cost effective than RFA for larger tumors, while RFA is more cost-effective for smaller tumors, though incremental cost-effectiveness ratios are highly dependent on probabilities and utilities. Treatment decision should consider a number of factors and further research is required.

**e369 Physical Activity in Patients With Kidney Cancer: A Scoping Review**

*Fernanda Z. Arthuso, Kerry S. Courneya*

We provide the first scoping review on physical activity (PA) in patients with kidney cancer (KC). We identified only 17 published articles from nine independent studies, resulting in no firm conclusions. Evidence on the safety, feasibility, and efficacy (benefits and harms) of PA in patients with KC is lacking. Systematic research on this topic is warranted.

**e380 Contemporary Pathological Stage Distribution After Radical Prostatectomy in North American High-Risk Prostate Cancer Patients**

*Francesco Chierigo, Marco Borghesi, Christoph Würnschimmel, Rocco Simone Flammia, Gabriele Sorce, Benedikt Hoeh, Lukas Hohenhorst, Zhe Tian, Fred Saad, Derya Tilki, Michele Gallucci, Alberto Briganti, Francesco Montorsi, Felix K.H. Chun, Shahrokh F. Shariat, Guglielmo Mantica, Nazareno Suardi, Carlo Terrone, Pierre I. Karakiewicz*

Our study aimed to illustrate the relationship between clinical characteristics and pathological stage after radical prostatectomy in NCCN high-risk patients, which represent 17% to 31% of newly diagnosed prostate cancers. Our results show increasingly higher rates of non-organ-confined disease with increasingly less favorable clinical characteristics. These lookup tables may be used in the preoperative counselling of high-risk prostate cancer patients.

**e390 The Accuracy of Sequential Urethral Frozen Section and its Impact on Urethral Recurrence After Radical Cystectomy**

*Georgios Gakis, Manuel Alexander Schmid, Fahmy Hassan, Arnulf Stenzl, Markus Renninger*

We assessed the accuracy of frozen section analysis (FSA) for detecting malignant urethral margins during radical cystectomy for bladder cancer. FSA for detecting malignant urethral margins is high on initial examination but drops considerably in case of re-resection. A positive urethral FSA was the only independent risk for a positive final margin. Conversion of a positive FSA finding to a negative final margin was associated with a lower risk of urethral recurrence.

**e396 Patient- And Provider-Level Predictors of Survival Among Patients With Metastatic Renal Cell Carcinoma Initiating Oral Anticancer Agents**

*Lisa P. Spees, Michaela A. Dinan, Bradford E. Jackson, Christopher D. Baggett, Lauren E. Wilson, Melissa A. Greiner, Deborah R. Kaye, Tian Zhang, Daniel J. George, Charles D. Scales, Jessica E. Pritchard, Michael Leapman, Cary P. Gross, Stephanie B. Wheeler*

Oral anticancer agents (OAAs) could improve survival and reduce disparities for medically underserved patients. We evaluated characteristics associated with mortality among a population-based multi-payer cohort of metastatic renal cell carcinoma (mRCC) patients who initiated OAAs. Frailty, de novo metastatic diagnosis, and Medicare were associated with mortality. These real-world data underscore the importance of access to high-quality care for resource-limited patients.

**e406 A Combinatorial Neural Network Analysis Reveals a Synergistic Behaviour of Multiparametric Magnetic Resonance and Prostate Health Index in the Identification of Clinically Significant Prostate Cancer**

*Francesco Gentile, Evelina La Civita, Bartolomeo Della Ventura, Matteo Ferro, Michele Cennamo, Dario Bruzzese, Felice Crocetto, Raffaele Velotta, Daniela Terracciano*

This study evaluated the combination of phi and multiparametric magnetic resonance in the identification of aggressive prostate cancer to ameliorate the choice of the therapy for each patient. We analysed 177 patients who underwent radical prostatectomy. Combining phi and multiparametric magnetic resonance help to better estimate the risk category of prostate cancer at initial diagnosis, allowing a personalized treatment.

**e411 Long-Term Oncological Efficacy of Retroperitoneoscopic Radical Nephrectomy of Localized Renal Cell Cancer pT1-3 ( $\leq 12$  cm)**

*Florian A Schmid, Kathrin Bausch, Marian S Wettstein, Antje Feicke, Boris Weltzien, Daniel M Schmid, R to T Strebelt, Cedric Poyet, Niels J Rupp, Tullio Sulser, Hans Helge Seifert, Thomas Hermanns*

Investigation of oncological efficacy in retroperitoneoscopic radical nephrectomy (RRN) of patients with localized renal cell carcinoma (RCC). Consecutive patients undergoing RRN for localized stage pT1-3 RCC in 2 tertiary care centers in Switzerland were evaluated. Excellent long-term oncological efficacy was found. Our long-term follow-up validates the survival outcome from comparable literature after conventional open or laparoscopic radical nephrectomy.

- e419 Evaluation of a Novel Multimodal Opioid-Free Postoperative Pain Management Pathway Following Robotic-Assisted Radical Prostatectomy: A Pilot Series in the Veteran Population**  
*Caleb Bercu, Ashok Hemal, Gopal Badlani, Rahul Dutta, Ram Pathak*  
MicroAbstract This study evaluates an opioid-free regiment consisting of ketorolac, gabapentin, and IV acetaminophen for postoperative pain control following robotic-assisted radical prostatectomy at a Veterans Affairs Medical Center. No significant differences of average postoperative pain scores were observed in the opioid (n=33) and opioid-free (n=24) cohorts. The opioid-free treatment may be utilized for postoperative recovery for Veterans undergoing robotic-assisted radical prostatectomy.
- e424 Complications in the Early Recovery Period After Radical Cystectomy—Real Data From Impartial Inpatient Rehabilitation**  
*Mayumi Götte, Henning Bahlburg, Marius Cristian Butea-Bocu, Nicolas von Landenberg, Karl Tully, Florian Roghmann, Joachim Noldus, Guido Müller*  
To obtain a better basis for patient counseling, we evaluated postoperative complications after radical cystectomy and creation of ileum conduit or neobladder in a contemporary series of bladder cancer patients. Our multi-institution approach (135 different hospitals in Germany) with prospective documentation at inpatient rehabilitation revealed a significantly higher complication rate than previously published. Risk factors for severe complications were creation of a neobladder and higher comorbidity.
- e432 Systemic Immunological Determinants of Oncological Outcomes After Surgery for Localized Renal Cell Carcinoma**  
*Andrew W. Silagy, Amy L. Tin, Phillip Rappold, Emily A. Vertosick, Roy Mano, Kyrollis Attalla, Angela Yoo, Stanley Weng, Renzo G. DiNatale, Andrew J. Vickers, Daniel D. Sjoberg, Jonathan A. Coleman, Paul Russo, Abraham Ari Hakimi*  
Evaluating the postoperative neutrophil-to-lymphocyte (NLR) ratio following nephrectomy for localized renal cell carcinoma and oncological outcomes. A prospectively managed database of 996 patients operated between 2005 and 2020. There was no association between NLR dynamics and disease recurrence. Therefore, there is no clinical role for monitoring the NLR in patients after renal surgery.
- e440 Association Between Sites of Metastasis and Outcomes With Immune Checkpoint Inhibitors in Advanced Urothelial Carcinoma**  
*Dimitrios Makrakis, Rafee Talukder, Genevieve Ihsiu Lin, Leonidas N. Diamantopoulos, Scott Dawsey, Shilpa Gupta, Lucia Carril-Ajuria, Daniel Castellano, Ivan de Kouchkovsky, Vadim S. Koshkin, Joseph J. Park, Ajjai Alva, Mehmet A. Bilen, Tyler F. Stewart, Rana R. McKay, Nishita Tripathi, Neeraj Agarwal, Naomi Vather-Wu, Yousef Zakharia, Rafael Morales-Barrera, Michael E. Devitt, Alessio Cortellini, Claudia Angela Maria Fulgenzi, David J. Pinato, Ariel Nelson, Christopher J. Hoimes, Kavita Gupta, Benjamin A. Gartrell, Alex Sankin, Abhishek Tripathi, Roubini Zakopoulou, Aristotelis Bamias, Jure Murgic, Ana Fröbe, Alejo Rodriguez-Vida, Alexandra Drakaki, Sandy Liu, Eric Lu, Vivek Kumar, Giuseppe Di Lorenzo, Monika Joshi, Pedro Isaacsson-Velho, Lucia Alonso Buznego, Ignacio Duran, Marcus Moses, Albert Jang, Pedro Barata, Guru Sonpavde, Evan Y. Yu, Robert Bruce Montgomery, Petros Grivas, Ali Raza Khaki*  
Immune checkpoint inhibitors are a well-established treatment option for advanced urothelial carcinoma, and biomarkers of response are needed for better patient selection. We show that metastatic disease confined to lymph nodes is associated with better outcomes, while metastases to liver, bone or both are associated with poor outcomes with immune checkpoint inhibitor therapy. Results are hypothesis-generating but relevant to practice.