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| Platinum Opinions   |    | <p><b>The Platinum Hall of Fame</b> <span style="float: right;">e1</span><br/> <a href="http://dx.doi.org/10.1016/j.eururo.2019.05.008">http://dx.doi.org/10.1016/j.eururo.2019.05.008</a></p>   |
|   |   | <p><b>Development and Prospective Randomized Evaluation of a Decision Aid for Prostate-specific Antigen-based Early Detection of Prostate Cancer in Men Aged Between 55 and 69 Yr: The PSAInForm Trial</b> <span style="float: right;">1</span></p> <p><i>A. Semjonow, H.-W. Hense, K. Schlöbner, A. Simbrich, M. Borowski, C. Bothe, K. Kruse, D. Tiedje, K. Kuss, C.C. Adarkwah, P. Maisel, R. Jendyk, M.-A. Kurosinski, J. Gerß, O. Heidinger, C. Tschuschke, R. Becker, M.J. Roobol, C. Bangma, N. Donner-Banzhoff</i></p> <p>For men interested in early detection of prostate cancer, the potential impact on decisional conflict of a decision aid with or without cost compensation for the prostate-specific antigen test will be investigated.</p> |
|   |   | <p><b>Towards Personalized Neoadjuvant Therapy for Muscle-invasive Bladder Cancer</b> <span style="float: right;">4</span></p> <p><i>R. Li, P.E. Spiess, S.M. Gilbert, A. Necchi</i></p> <p>It has been demonstrated that immune checkpoint blockade has efficacy similar to chemotherapy in the neoadjuvant setting. Biomarkers such as PD-L1 expression levels can be used to rationally design clinical trials aimed at personalizing systemic therapy for patients with muscle-invasive bladder cancer.</p>  |
| <p><b>Anticholinergic Burden in the Elderly Population: An Emerging Concern</b> <span style="float: right;">7</span></p> <p><i>H. Pierce, D. Thomas, T. Asfaw, B. Chughtai</i></p> <p>Antimuscarinics are commonly used to treat overactive bladder, but increase anticholinergic burden, which has been associated with multiple adverse outcomes in older patients. We advocate for standardization of anticholinergic risk assessment and reevaluation of anticholinergic prescribing practices for the elderly.</p> |   |  |
| Brief Correspondence  |  | <p><b>APOBEC-mediated Mutagenesis as a Likely Cause of FGFR3 S249C Mutation Over-representation in Bladder Cancer</b> <span style="float: right;">9</span></p> <p><i>M.-J. Shi, X.-Y. Meng, P. Lamy, A.R. Banday, J. Yang, A. Moreno-Vega, C.-L. Chen, L. Dyrskjøt, I. Bernard-Pierrot, L. Prokunina-Olsson, F. Radvanyi</i></p> <p>We propose that APOBEC-mediated mutagenesis can generate clinically relevant driver mutations, even within suboptimal motifs, such as in the case of FGFR3 S249C, one of the most common mutations in bladder cancer. Knowledge about the etiology of this mutation will improve our understanding of molecular mechanisms of bladder cancer.</p>  |
|   |   | <p><b>Role of Core Number and Location in Targeted Magnetic Resonance Imaging-Ultrasound Fusion Prostate Biopsy</b> <span style="float: right;">14</span></p> <p><i>A.J. Lu, J.S. Syed, K. Ghabili, W.R. Hsiang, K.A. Nguyen, M.S. Leapman, P.C. Sprenkle</i></p> <p>Considerable variability exists in the methodology of targeted fusion prostate biopsy. In this institutional study, we found a two-core biopsy substantially misses high-grade cancers within a lesion while core location is not significant.</p>  |

Platinum Priorities

Original Articles and Brief Correspondence together with the Full Length Editorials

Prostate Cancer

**Molecular Hallmarks of Multiparametric Magnetic Resonance Imaging Visibility in Prostate Cancer** 18

*K.E. Houlahan, A. Salmasi, T.Y. Sadun, A. Pooli, E.R. Felker, J. Livingstone, V. Huang, S.S. Raman, P. Ahuja, A.E. Sisk Jr., P.C. Boutros, R.E. Reiter*

Genome-wide copy number alteration and transcriptomic profiling of tumors invisible and visible on multiparametric magnetic resonance imaging (mpMRI) identified a confluence of aggressive transcriptomic, genomic, and pathological hallmarks correlated with mpMRI visibility. This work provides a molecular basis for the observation that mpMRI-visible tumors are clinically more aggressive.

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*L. Marconi, T. Stonier, R. Tourinho-Barbosa, C. Moore, H.U. Ahmed, X. Cathelineau, M. Emberton, R. Sanchez-Salas, P. Cathcart*

Robotic radical prostatectomy (RALP) after focal therapy is safe and urinary continence outcomes are similar to those for primary RALP. Men identified as having infield recurrence after focal therapy have a higher chance of recurrence after surgery and should be counselled regarding the potential need for multimodal therapy.

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*C.H. Pearn, E.M. Ebot, A. Pettersson, R.E. Graff, F. Giunchi, T.U. Ahearn, A.G. Gonzalez-Feliciano, S.C. Markt, K.M. Wilson, K.H. Stopsack, E. Gazeeva, R.T. Lis, G. Parmigiani, E.B. Rimm, S.P. Finn, E.L. Giovannucci, M. Fiorentino, L.A. Mucci*

In this prospective study of physical activity and prostate cancer among 49 160 men, vigorous activity was associated with lower risk of lethal and *TMPRSS2:ERG*-positive disease. Long-term vigorous activity may be beneficial in prevention of lethal prostate cancer and may involve pathways specific to *TMPRSS2:ERG*-positive disease.

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This European Randomized study of Screening for Prostate Cancer trial follow-up reports that repeated screening reduces the risk of dying from prostate cancer for up to 16 yr.

**Solid Science for the Upside but Lack of Solid Science for the Downside—Towards Cutting-edge Prostate-cancer Screening** 52

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Bladder Cancer

**Diagnostic Accuracy and Interobserver Agreement for the Vesical Imaging-Reporting and Data System for Muscle-invasive Bladder Cancer: A Multireader Validation Study** 54

*Y. Ueno, M. Takeuchi, T. Tamada, K. Sofue, S. Takahashi, Y. Kamishima, N. Hinata, K. Harada, M. Fujisawa, T. Murakami*

Multiparametric magnetic resonance imaging is useful for the diagnosis of muscle-invasive bladder cancers. With further efforts to refine its application and standardization, the Vesical Imaging-Reporting and Data System may become an important comprehensive tool for appropriate treatment planning for patients with bladder cancers.

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|                   | <p><b>Should We Perform Multiparametric Magnetic Resonance Imaging of the Bladder Before Transurethral Resection of Bladder? Time to Reconsider the Rules</b> 57</p> <p><i>V. Panebianco, Y. Narumi, G. Barchetti, R. Montironi, J.W.F. Catto</i></p>   |
|                   | <p><b>Impact of Immune and Stromal Infiltration on Outcomes Following Bladder-Sparing Trimodality Therapy for Muscle-Invasive Bladder Cancer</b> 59</p> <p><i>J.A. Efstathiou, K.W. Mouw, E.A. Gibb, Y. Liu, C.-L. Wu, M.R. Drumm, J.B. da Costa, M. du Plessis, N.Q. Wang, E. Davicioni, F.Y. Feng, R. Seiler, P.C. Black, W.U. Shipley, D.T. Miyamoto</i></p> <p>Gene expression profiling of muscle-invasive bladder cancer reveals that immune infiltration is associated with improved disease-specific survival after bladder-sparing trimodality therapy, but not after radical cystectomy. Conversely, stromal infiltration is associated with worse outcomes after cystectomy, but not after trimodality therapy.</p> <p><b>Predictive Biomarkers for Muscle-invasive Bladder Cancer: The Search for the Holy Grail Continues</b> 69</p> <p><i>A. Choudhury, P.J. Hoskin</i></p> <p><b>Reply from Authors re: Ananya Choudhury, Peter J. Hoskin. Predictive Biomarkers for Muscle-invasive Bladder Cancer: The Search for the Holy Grail Continues. Eur Urol 2019;76:69–70.</b> 71</p> <p><i>K.W. Mouw, D.T. Miyamoto, J.A. Efstathiou</i></p> |
| Urothelial Cancer | <p><b>Primary Results from SAUL, a Multinational Single-arm Safety Study of Atezolizumab Therapy for Locally Advanced or Metastatic Urothelial or Nonurothelial Carcinoma of the Urinary Tract</b> 73</p> <p><i>C.N. Sternberg, Y. Loriot, N. James, E. Choy, D. Castellano, F. Lopez-Rios, G.L. Banna, U. De Giorgi, C. Masini, A. Bamias, X.G. del Muro, I. Duran, T. Powles, M. Gamulin, F. Zengerling, L. Geczi, C. Gedy, S. de Ducla, S. Fear, A.S. Merseburger</i></p> <p>SAUL confirms the tolerability of atezolizumab in real-world patients with urinary tract carcinoma. Efficacy in the IMvigora211-like subgroup and the broader unselected population was consistent with previous anti-PD-L1/PD-1 pivotal trials, supporting the use of atezolizumab in these patients.</p> <p><b>Atezolizumab in “Real World” Patients: Do Phase 3b Trials Help Bridge the Gap Between Efficacy and Effectiveness?</b> 82</p> <p><i>V.G. Patel, M.D. Galsky</i></p>   |
| Surgery in Motion | <p><b>Transvaginal Repair of Apical Vesicovaginal Fistula: A Modified Latzko Technique—Outcomes at a High-volume Referral Center</b> 84</p> <p><i>D.-Y. Luo, H. Shen</i></p> <p>We studied an alternative surgical technique for the treatment of apical vesicovaginal fistula. We conclude that this technique is simple, safe, and effective with no apparent complications.</p>  |
| Original Articles | <p><b>Compound Genomic Alterations of TP53, PTEN, and RB1 Tumor Suppressors in Localized and Metastatic Prostate Cancer</b> 89</p> <p><i>A.A. Hamid, K.P. Gray, G. Shaw, L.E. MacConaill, C. Evan, B. Bernard, M. Loda, N.M. Corcoran, E.M. Van Allen, A.D. Choudhury, C.J. Sweeney</i></p>   |
| Prostate Cancer   | <p><b>Alterations of TP53, PTEN, and RB1 tumor suppressor genes are present across the clinical spectrum of prostate cancer and are particularly frequent in metastatic and castration-resistant disease. Alterations are associated with poorer outcomes, with incremental risk seen with compound loss, thereby identifying at-risk patient subgroups in the early and advanced disease settings.</b></p> <p><b>Early-Medium-Term Outcomes of Primary Focal Cryotherapy to Treat Nonmetastatic Clinically Significant Prostate Cancer from a Prospective Multicentre Registry</b> 98</p> <p><i>T.T. Shah, M. Peters, D. Eldred-Evans, S. Miah, T. Yap, N.A. Faure-Walker, F. Hosking-Jervis, B. Thomas, T. Dudderidge, R.G. Hindley, S. McCracken, D. Greene, R. Nigam, M. Valerio, S. Minhas, M. Winkler, M. Arya, H.U. Ahmed</i></p> <p>Focal cryotherapy used primarily for anterior intermediate and high-risk prostate cancer results in good rates of cancer control and low rates of treatment-related side effects in the medium term.</p>  |

Words of Wisdom

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*F. Preisser, F.K.H. Chun, R.S. Pompe, A. Heinze, G. Salomon, M. Graefen, H. Huland, D. Tilki*

Persistent prostate-specific antigen (PSA;  $\geq 0.1$  ng/ml) at 6 wk after radical prostatectomy represents an independent predictor for worse long-term oncological outcome after radical prostatectomy in patients with nonmetastatic prostate cancer. Specifically, persistent PSA is associated with death and development of metastasis. In selected patients, salvage radiotherapy may lead to a survival benefit in patients with persistent PSA.

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This prospectively designed systematic review showed that prostate radiotherapy did not improve survival in unselected men. A difference in effect by metastatic burden was evident across included trials and outcomes; 3-yr survival increased by 7% in men with fewer than five bone metastases.

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*D.A. Castillo-Jimenez, H.A. García-Perdomo*

**Reply to Diana A. Castillo-Jimenez and Herney A. García-Perdomo's Letter to the Editor re: Niranjana J. Sathianathan, Badrinath R. Konety, Fernando Alarid-Escudero, Nathan Lawrentschuk, Damien M. Bolton, Karen M. Kuntz. Cost-effectiveness Analysis of Active Surveillance Strategies for Men with Low-risk Prostate Cancer. Eur Urol 2019;75: 910-917 Standardized Reporting for Economic Analyses Should be Mandatory** e10

*N.J. Sathianathan, B.R. Konety*

**Re: Paul C.M.S. Verhagen, Egbert R. Boevé. The European Association of Urology Guideline on Renal Cell Carcinoma (RCC) is Not Concise in its Recommendation to Perform Partial Nephrectomy in T1b RCC. Eur Urol. In press. 2019:76:136-7** e12

*L. Marconi, K. Bensalah, A. Bex*

**Reply to Lorenzo Marconi, Karim Bensalah, and Axel Bex's Letter to the Editor re: Paul C.M.S. Verhagen, Egbert R. Boevé. The European Association of Urology Guideline on Renal Cell Carcinoma (RCC) is Not Concise in its Recommendation to Perform Partial Nephrectomy in T1b RCC. Eur Urol 2019:76:136-7** e14

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**Re: Thomas Van den Broeck, Roderick C.N. van den Bergh, Nicolas Arfi, et al. Prognostic Value of Biochemical Recurrence Following Treatment with Curative Intent for Prostate Cancer: A Systematic Review. Eur Urol 2019; 75: 967-987** e15

*X. Zhou, X. Han*

**Reply to Xueliang Zhou and Xinwei Han's Letter to the Editor re: Thomas Van den Broeck, Roderick C.N. van den Bergh, Nicolas Arfi, et al. Prognostic Value of Biochemical Recurrence Following Treatment with Curative Intent for Prostate Cancer: A Systematic Review. Eur Urol 2019; 75: 967-987** e16

*T. Van den Broeck, N. Mottet, T. Lam*

**Reply to Steven C. Campbell, Chalairat Suk-Ouichai, and Yun-Lin Ye's Words of Wisdom re: Below Safety Limits, Every Unit of Glomerular Filtration Rate Counts: Assessing the Relationship between Renal Function and Cancer-specific Mortality in Renal Cell Carcinoma. Antonelli A, Minervini A, Sandri M, et al. Eur Urol 2018;74:661-7 and 2019;75:198** e17

*A. Antonelli, A. Minervini, U. Capitanio*

**Reply to Joe O'Sullivan, Daniel Heinrich, Nicholas D. James, et al's Letter to the Editor re: The Case Against the European Medicines Agency's Change to the Label for Radium-223 for the Treatment of Metastatic Castration-resistant Prostate Cancer. Eur Urol 2019; 75: e53** e19

*R. Leibowitz-Amit*

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The illustration on the cover of this issue is taken from the article by Ming-Jun Shi, Xiang-Yu Meng, Philippe Lamy, A. Rouf Banday, Jie Yang, Aura Moreno-Vega, Chun-Long Chen, Lars Dyrskjøt, Isabelle Bernard-Pierrot, Ludmila Prokunina-Olsson, François Radvanyi, APOBEC-mediated Mutagenesis as a Likely Cause of FGFR3 S249C Mutation Over-representation in Bladder Cancer, which is published on pp. 9-13 of this issue.

