#### Abstract Highlights

The following highlights spotlight abstracts presented at the 39<sup>th</sup> Annual European Association of Urology (EAU) Congress. Selected abstracts reflect the evolving landscape of clinical and surgical practice in urology, including timely topics such as advances in prostate cancer detection, robotic surgery for management of urinary tract complications, and analysis of oncological outcomes in kidney transplant recipients.

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# Award-Winning Abstract: PSMA-PET-Guided Intensification of Salvage Radiotherapy After Radical Prostatectomy

PROSTATE-specific membrane antigen (PSMA)-PET imaging can influence decision-making in prostate cancer, improving survival outcomes. The research, presented by Colin Belliveau, Centre Hospitalier de l'Université de Montréal, Québec, Canada, was awarded best abstract in oncology at the 39<sup>th</sup> EAU Annual Congress.

The team conducted a Phase II, multicentre randomised controlled trial to determine if PSMA-PET-guided intensification of salvage radiotherapy (PSMAiSRT) after radical prostatectomy (RP) improves failure-free survival (FFS). A total of 128 patients with biochemical failure (prostate specific antigen >0.1 ng/mL) following RP, and planned for salvage radiotherapy (SRT), were enrolled between May 2018–February 2021.

Patients were randomised 1:1 to standard-of-care SRT or <sup>18</sup>F-DCFPγL PSMA-PET/CT prior to treatment, and SRT was subsequently intensified targeting newly identified disease sites detected on PSMA-PET/CT. Analysis of the primary FFS endpoint was based on the number of failure events reported. FFS was measured from the last day of RT to the date of biochemical recurrence (nadir+0.2 ng/mL), locoregional failure, distant metastasis, initiation of the next line of therapy, or death from any cause, whichever occurred first.

Intensified SRT was delivered in 33/64 patients who underwent PSMA-PET/CT (28% addition of pelvic SRT, 3% addition of metastases-directed RT, 30% lymph node boost, and 23% prostate bed boost). The use of adjuvant hormonal therapy (6-24 months) was equally high in both arms (86% control; 84% PSMAiSRT). The authors found that, at median follow-up of 37 months, PSMAiSRT significantly improved FFS outcomes (control: 20 failure events; PSMAiSRT: 10 failure events; P=0.04; hazard ratio: 0.46; 95% confidence interval: 0.21-0.98). To date, the study reports no differences in metastasis-free survival based on conventional imaging (control: 4 events; PSMAiSRT: 5 events), and in overall survival (one death in each arm).

"At median follow-up of 37 months, PSMAiSRT significantly improved FFS outcomes."

This study demonstrates improved prostate cancer control outcomes with PSMAiSRT after RP. The authors emphasised that, considering a variable worldwide access to PSMA-PET imaging, patients planned for SRT after RP should be prioritised access, given its positive impact on outcomes. A Phase III randomised controlled trial is currently completing accrual, and will shed further light on those patients who benefit most from PSMAiSRT.

### Award-Winning Abstract: Optimal Clinical and Cost-Effective Ways to Manage Kidney Stones

RENAL tract stones are prevalent, and the European Association of Urology (EAU) usually recommends extracorporeal shock wave lithotripsy (ESWL) and flexible ureteroscopic stone treatment (FURS) as first-line treatment. PUrE, a randomised controlled trial, investigated the best clinical and cost-effective approach for lower pole kidney stones, and was awarded best abstract in a non-oncology specialty at the 39th EAU Annual Congress.

Oliver Wiseman, Department of Urology, Cambridge University Hospitals National Health Service (NHS) Trust, UK, and colleagues, conducted a pragmatic multicentre, open-label, superiority randomised controlled trial to determine whether ESWL or FURS offers the best outcomes. They assessed which treatment option provided a better quality of life, clinical effectiveness, and cost-effectiveness for individuals with lower pole kidney stones ≤10 mm.

The trial received ethics approval from the North of Scotland NHS Research Ethics Committee, and randomised 461 patients (230 to ESWL and 231 to FURS) across participating NHS urology departments. The health status area under the curve was measured weekly with the EuroQol 5-Dimension 5-level questionnaire until 12 weeks post-intervention, to determine the primary outcome.

During the 12-week period, the average health status for the FURS group (n=164) was 0.807 (standard deviation: 0.205), and for the ESWL group (n=188) was 0.826 (standard deviation: 0.207); with a slight difference of 0.024 (95% confidence interval: -0.004, 0.053) favouring FURS after accounting for an initial baseline imbalance. FURS achieved a higher rate of complete stone clearance (72%) compared to ESWL (36%). The incremental cost-effectiveness ratio for FURS was 65,163 GBP per quality-adjusted life year gained. At a threshold of 20,000 GBP per quality-adjusted life year gained, there was a 99.9% probability that ESWL was cost-effective. The study's limitations include the inability to conceal the identity of the participants and healthcare providers. Additionally, there were variations in waiting times between interventions, although adjusting for this yielded similar treatment effect estimates.

The PUrE investigation revealed that for lower pole stones measuring ≤10 mm, ESWL proved to be a more economical option compared to FURS. Although FURS had higher rates of complete stone clearance, there was no significant discrepancy in patient health status between the two methods. ●

"The trial received ethics approval from the North of Scotland NHS Research Ethics Committee, and randomised 461 patients."





## Impact of Systematic Sampling on Prostate Biopsy Results

THE BENEFIT of adding systematic sampling to a targeted MRI/transrectal ultrasound (TRUS) fusion biopsy for prostate cancer (PCa) is unclear. New research presented at the 39<sup>th</sup> EAU Congress, held from 5<sup>th</sup>–8<sup>th</sup> of April 2024, aimed to identify patients who could benefit from systematic sampling in terms of newly diagnosed PCa, and clinically significant prostate cancer (csPCa). It did this by comparing the observed cancer detection rate.

The team recruited patients submitted to both systematic sampling and MRI/TRUS fusion biopsy at Araba University Hospital, Vitoria-Gasteiz, Spain, from 2018–2021 (n=188). For each patient, the McNemar test was used to compare the global result of the biopsy considering only the targeted sampling, with the combination of the targeted and the systematic ones. Subgroup analyses were performed according to the Prostate Imaging-Reporting and Data System (PIRADS) score of the index lesion on MRI, prostate-specific antigen (PSA) density, and

the personal history of previous systematic biopsies. The team defined csPCa as International Society of Urological Pathology (ISUP) Grade ≥2.

Overall, addition of systematic sampling to targeted sampling led to an increased cancer detection rate of PCa and csPCa. Results from the subgroup analyses further showed that biopsy-naïve patients, and those with a PIRADS score ≤3, did not show any benefit from the addition of the systematic sampling. Patients with a PSA density ≤0.15 only benefitted in terms of PCa detection.

The study concluded that patients might benefit from the addition of systematic sampling while being submitted to an MRI/TRUS fusion biopsy for newly diagnosed PCa and csPCa. Patients with lesions scored as PIRADS 4–5, a PSA density  $\geq 0.15$ , and a history of previous biopsies, seemed to benefit the most from the addition of systematic sampling to targeted sampling.  $\blacksquare$ 

"Addition of systematic sampling to targeted sampling led to an increased cancer detection rate of PCa and csPCa."

### **Liquid Biomarkers for Clinically Significant Prostate Cancer Detection**

LIQUID biomarkers may enhance detection of clinically significant prostate cancer (csPCa), helping to avoid unnecessary prostate biopsies. A recent study presented at the 39<sup>th</sup> EAU Congress, held in Paris, France, from 5<sup>th</sup>–8<sup>th</sup> April 2024, aimed to assess the diagnostic accuracy of multi-analyte biomarkers for csPCa detection.

In March 2023, the researchers conducted a comprehensive literature search through PubMed, Web of Science, and Scopus for prospective and retrospective studies that reported the diagnostic performance of liquid biomarkers for csPCa detection. They included all studies that explored patients with suspected PCa, and those that compared patients positive for liquid biomarker to those with negative liquid biomarker. Outcomes of interest were the diagnostic performance of liquid biomarkers for csPCa detection, and identification of optimal thresholds for each biomarker. A total of 49 studies were eligible for this meta-analysis.

"Outcomes of interest were the diagnostic performance of liquid biomarkers for csPCa detection."

Using each representative threshold based on the Youden index, the team found that the pooled sensitivity and specificity for detecting csPCa were 0.85 and 0.37 for prostate cancer antigen 3 (PCA3), 0.85 and 0.52 for prostate health index (PHI), 0.87 and 0.58 for 4K, 0.82 and 0.56 for SelectMDx, 0.85 and 0.54 for ExoDx, and 0.82 and 0.59 for MyProstateScore, respectively. Diagnostic odds ratio was highest for 4K (8.84), followed by MyProstateScore (7.00), and PHI (6.28). According to the meta-analysis incorporating multiple thresholds, the corresponding sensitivity was 0.77 for 4K, 0.69 for PHI, and 0.63 for PCA3; and specificity was 0.72 for PHI, 0.70 for 4K, and 0.69 for PCA3.

To conclude, the study found that 4K had the highest diagnostic performance for detecting csPCa among all commercial liquid biomarkers. Based on calculations of optimal thresholds in the meta-analysis, 4K was also found to have the highest sensitivity for csPCa detection, and PHI the highest specificity. Nevertheless, the team emphasised the importance of combination strategies between liquid and imaging biomarkers during clinical decision-making.





### **Insights Into Non-muscle Invasive Bladder Cancer Outcomes**

RECIPIENTS of kidney transplants are at greater risk of bladder cancer compared to the general population. With limited existing research on the outcomes and characteristics of *de novo* bladder cancer in kidney transplant recipients, Simone Livoti, University of Turin School of Medicine, Italy, and colleagues, conducted a large international cohort study. Results of this study were presented at the 39<sup>th</sup> Congress of the EAU, held in Paris, France from the 5<sup>th</sup>–8<sup>th</sup> April 2024.

Subjects included in the study were kidney transplant recipients who had received a *de novo* bladder cancer diagnosis between 2000–2022. It was a multicentre retrospective collaboration across eight international referral centres, with 89 patients in total (mean age: 64 years; interquartile range: 56–68). The measured outcomes were recurrence-free survival, progression-free survival, cystectomy-free survival, and overall survival.

Results revealed that the median time from kidney transplantation to bladder cancer diagnosis was 98 months. The clinical stage of the tumour at diagnosis was cTa, cT1, cT2, cT3, and cT4 in 25 (29%), nine (10%), 27 (31%), 25 (29%), and one (1%) patient, respectively. Regarding the primary outcomes, 37% underwent a radical cystectomy, 38% had experienced disease recurrence, and 9% progression. Furthermore, the overall survival rate at 1, 3, and 5 years was 78%, 53%, and 47%, respectively.

Overall, this study has made important steps in identifying the oncological outcomes in kidney transplant recipients with *de novo* bladder cancer. It is the largest series reporting oncological outcomes in this patient population type, and highlights the tailored management they specifically require.

"Results revealed that the median time from kidney transplantation to bladder cancer diagnosis was 98 months."

#### Robotic Surgery in Managing Urinary Complications Post-kidney Transplant

URINARY tract (UT) complications following kidney transplantation occur in approximately 5–10% of cases and can lead to significant morbidity. Surgical repair is often the treatment of choice, with a high success rate. Robotic surgery offers the advantages of minimally invasive procedures, especially in complex cases. Presented at the EAU 2024 congress, held from 5<sup>th</sup>–8<sup>th</sup> April 2024, this study aims to evaluate the efficacy and safety of robotic surgery in the management of UT complications in kidney transplant recipients.

The protocol for robotic surgery is as follows: prior to surgery, a nephrostomy (NP) tube is placed, and a pyelography and CT scan are performed. A modified robotic pelvic surgery protocol is employed for the surgical technique, with robotic ultrasound (US) being a crucial tool, and a double J stent is always placed. Postoperatively, all tubes remain open for 24 hours, after which the NP tube is closed and removed between Days 5-7 if no complications arise. In cases of reimplantation, a bladder catheter remains in place for between 5-7 days. The double J stent is removed at Week 4. Follow-up includes US after double J stent removal, control at 3, 6, and 12 months, and subsequently annually.

This cohort study included kidney transplant recipients who underwent robotic surgery for UT complications between January 2018–September 2023. A total of 28 patients were included in the study, the largest series reported.

Among the 28 patients, there were 26 cases of stenosis, and two ureteral fistulas. For distal stenosis, a robotic uretero-vesical reimplantation was performed in 12 cases, while upper and long UT stenosis cases underwent robotic anastomosis to the native ureter (16 cases). One case required conversion to open surgery due to adhesions. The median surgical time was 150 minutes (interquartile range [IQR]: 113-170), and the median hospital stay was 3 days (IQR: 2-6). In 26 out of 28 patients, all urinary drainage was successfully removed, representing a 93% success rate, with a median follow-up of 13 months (IQR: 6-20). As for complications, there were eight cases of graft pyelonephritis, and two cases of haematuria. There were two stricture recurrences, considered a failure of the surgical technique.

"Robotic uretero-vesical reimplantation was performed in 12 cases."

Robotic surgery for managing UT complications following kidney transplantation is effective and safe in both the short and long term. It offers the advantages of minimally invasive surgery with enhanced surgical precision, particularly in complex cases. Notably, this study represents the largest reported series of such cases, adding knowledge in the field of kidney transplantation and robotic surgery.





#### Robot-Assisted Radical Cystectomy and Peritoneal Metastasis

CONCERNS about robot-assisted radical cystectomy (RARC) leading to a higher incidence of peritoneal metastasis than open radical cystectomy (RC) are frequent among urologists. Despite RARC being the standard of care for patients with muscle-invasive bladder cancer, the procedure needs to be validated in real-world clinical practice, as the frequency of peritoneal metastasis has only been analysed in clinical trials.

"Frequency of peritoneal metastasis has only been analysed in clinical trials."

In order to analyse the results of RARC, a research team from the Hirosaki University Graduate School of Medicine, Japan, retrospectively looked at 415 cases of radical cystectomy (open RC versus RARC), taking place from 2011–2023. The frequency of peritoneal metastasis was examined, risk factors identified, and oncological outcomes assessed. In total, the open RC group was made up of 271 patients

(median age: 71 years), and the RARC group consisted of 144 individuals (median age: 69 years).

The team found that incidence of peritoneal metastasis was similar between the open RC (n=13; 4.8%) and RARC (n=6; 4.2%). Multivariate logistic regression analysis showed that the robotic approach was not significantly associated with peritoneal metastasis (odds ratio: 0.99; P=0.98). Pre-operative high risk factor (cT3-4 or N+) was significantly associated with peritoneal metastasis. Additionally, they found that neoadjuvant chemotherapy was significantly associated with reduction of peritoneal metastasis (odds ratio: 0.25; P=0.01).

This analysis, presented at the 2024 EAU Congress, held in Paris on 5<sup>th</sup>–8<sup>th</sup> April, demonstrated that RARC is not a significant factor for recurrence-free survival and overall survival, but post-operative pathological high risk was identified as a significant factor for recurrence-free survival and overall survival.

#### **Empower Pathway for Testicular Cancer Follow-Up**

A NEW pathway for encouraging patients with testicular cancer to self-manage has proven to be promising, according to research presented at the EAU Congress 2024, held in Paris, France from 5<sup>th</sup>–8<sup>th</sup> April. The so-called Empower Pathway aims to combat the inconsistent management of treatment and encouragement of self-management often found in consultant-led clinics, by holistically managing patients in follow-up, and, at the same time, educating them on long-term physical, psychological, and social sequelae of treatment.

The Empower Pathway was trialled in a 15-month long pilot study of 120 patients, with the aim of providing a personalised stratified follow-up. Post-treatment patients who had completed 6 months of consultant-led surveillance were invited to participate in the programme, and no patients in clinical trials, who have cancer, or with treatment complexity in follow-up care, were included. An advanced nurse practitioner model was used to facilitate holistic care. Finally, patients were only re-referred to a consultant-led clinic when disease recurrence was confirmed.

An integrated pathway was created, focusing on physical, mental, and social health. Each consultation included a shared care plan, and induction included a video seminar pack, a patient leaflet, and information on the scope of practice. Initially, 100 patients (mean age: 39.6 years) were surveyed in October 2022, and again in October 2023. Of this initial group, 1% of consultations requested onward GP referral, and 12% required internal referral. The majority (87.5%) of patients felt that lifestyle and exercise were adequately addressed by the Empower Pathway, and all patients felt that mental health was addressed, as well as efforts made to understand and listen to health concerns. Every patient also reported feeling that effort was made to involve them in what mattered to them as individuals in their care.

"An integrated pathway was created, focusing on physical, mental, and social health."

The researchers concluded that the Empower Pathway follow-up model resulted in improved patient outcomes when run alongside traditional, consultant-led clinics. Patients generally responded well to the more personalised approach, and, as a result, this pathway may have the potential to change the approach to follow-up not only in patients with testicular cancer, but in other tumour groups.





#### Study Identifies Optimal Treatment Regimens for Metastatic Prostate Cancer

TRIPLET therapy regimens have shown promising results for patients with metastatic hormonesensitive prostate cancer (mHSPC). Presented at the EAU 2024 congress, held from the 5th–8th of April, this research focuses on the novel guideline-recommended treatment combination of androgen receptor signalling inhibitors (ARSI) plus docetaxel plus androgen-deprivation therapy (ADT). Which patients stand to benefit the most from this innovative approach remains unclear.

To address this gap, researchers conducted a systematic review, meta-analysis, and network meta-analysis to evaluate the efficacy of triplet therapy compared to doublet treatment regimens in patients with mHSPC, stratified by disease volume. The study analysed data from eight randomised controlled trials, that were retrieved from three databases and meeting abstracts. The primary measure of interest was overall survival (OS), following the guidelines outlined by the PRISMA guideline and AMSTAR2 checklist.

The findings revealed that triplet therapy, consisting of ARSIs plus docetaxel plus ADT, significantly improved OS compared to docetaxel plus ADT, in patients with both high- and low-volume mHSPC. Specifically, the pooled hazard ratios for OS were 0.73 (95% confidence interval [CI]: 0.64–0.84) for high-volume

disease, and 0.71 (95% CI: 0.52–0.97) for low-volume disease.

When comparing ARSI with docetaxel added to ADT, no statistically significant difference in OS was observed across disease volumes. However, through analysis of treatment rankings, darolutamide plus docetaxel plus ADT emerged as the preferred regimen for patients with high-volume disease, with an improved OS of 90%. Enzalutamide plus ADT showed the highest likelihood of improved OS in those with low-volume disease, with an improvement of 84%.

Triplet therapy demonstrates an improvement in OS for patients with mHSPC compared to docetaxel-based doublet therapy, regardless of disease volume. However, the study suggests that the optimal treatment approach may vary depending on disease volume, with triplet therapy being more favourable for high-volume cases, and ARSI plus ADT potentially sufficient for low-volume disease management. These findings provide crucial insights for clinicians in tailoring treatment strategies for patients with mHSPC, ultimately leading to improved outcomes, and better patient care.

"Triplet therapy demonstrates an improvement in OS for patients with mHSPC compared to docetaxel-based doublet therapy."

#### **Bladder Cancer: Challenging the Treatment Paradigm**

BACILLUS Calmette–Guérin (BCG) is the gold standard treatment in intermediate and high-risk non-muscle invasive bladder cancer (NMIBC). However, a substantial proportion of patients are unresponsive to BCG therapy, posing a significant clinical challenge. Although current treatment paradigms recommend against administration of additional BCG in BCG-unresponsive patients, a recent study presented at the 39<sup>th</sup> Annual EAU Congress, held from 5<sup>th</sup>–8<sup>th</sup> of April 2024, reports that additional rescue BCG demonstrates efficacy in this patient population.

The team performed a review of consecutive patients diagnosed with NMIBC between January 2000–September 2021, approved by the Institutional Review Board (IRB), to identify those who met BCG-unresponsive criteria. They analysed the outcomes of patients who received rescue BCG as primary therapy; the primary outcome was event-free survival (EFS), defined as any high-grade recurrence, progression, or death. The Kaplan–Meier method was used to estimate EFS, cystectomy-free survival, progression to muscle-invasive or metastatic-free survival, and overall survival.

The study identified 163 patients with BCG-unresponsive disease, of whom 35 received rescue BCG as primary treatment.

Twenty-six (74%) patients showed no disease after rescue BCG; of these, 25 (96%) received maintenance. Median follow-up was 5.9 years. Kaplan-Meier estimates of EFS after rescue BCG were 68% at 12 months, 62% at 24 months, and 48% at 36 months. In the 2 years following rescue BCG, 21 patients still had no evidence of disease, four progressed to muscle-invasive bladder cancer, and nine recurred without progression. Of these, two had cystectomy, and seven had further bladder-sparing therapies. This resulted in cystectomy-free survival at 12, 24, and 36 months of 88% (95% confidence interval [CI]: 72-95), 79% (95% CI: 61-90), and 79% (95% CI: 61-90), respectively. Progressionfree survival at 12, 24, and 36 months was 91% (95% CI: 82-100), 88% (95% CI: 77-100), and 76% (95% CI: 61–94), respectively. Overall survival at 12, 24, and 36 months was 94% (95% CI: 86-100), 91% (95% CI: 82-100), and 85% (95% CI: 73-98), respectively.

Results from this study challenge the current treatment paradigms for patients with BCG-refractory NMIBC. The authors emphasise the need for further randomised clinical trials to evaluate the potential of rescue BCG as a suitable therapy for BCG-unresponsive NMIBC.

"The study identified 163 patients with BCG-unresponsive disease, of whom 35 received rescue BCG as primary treatment."

