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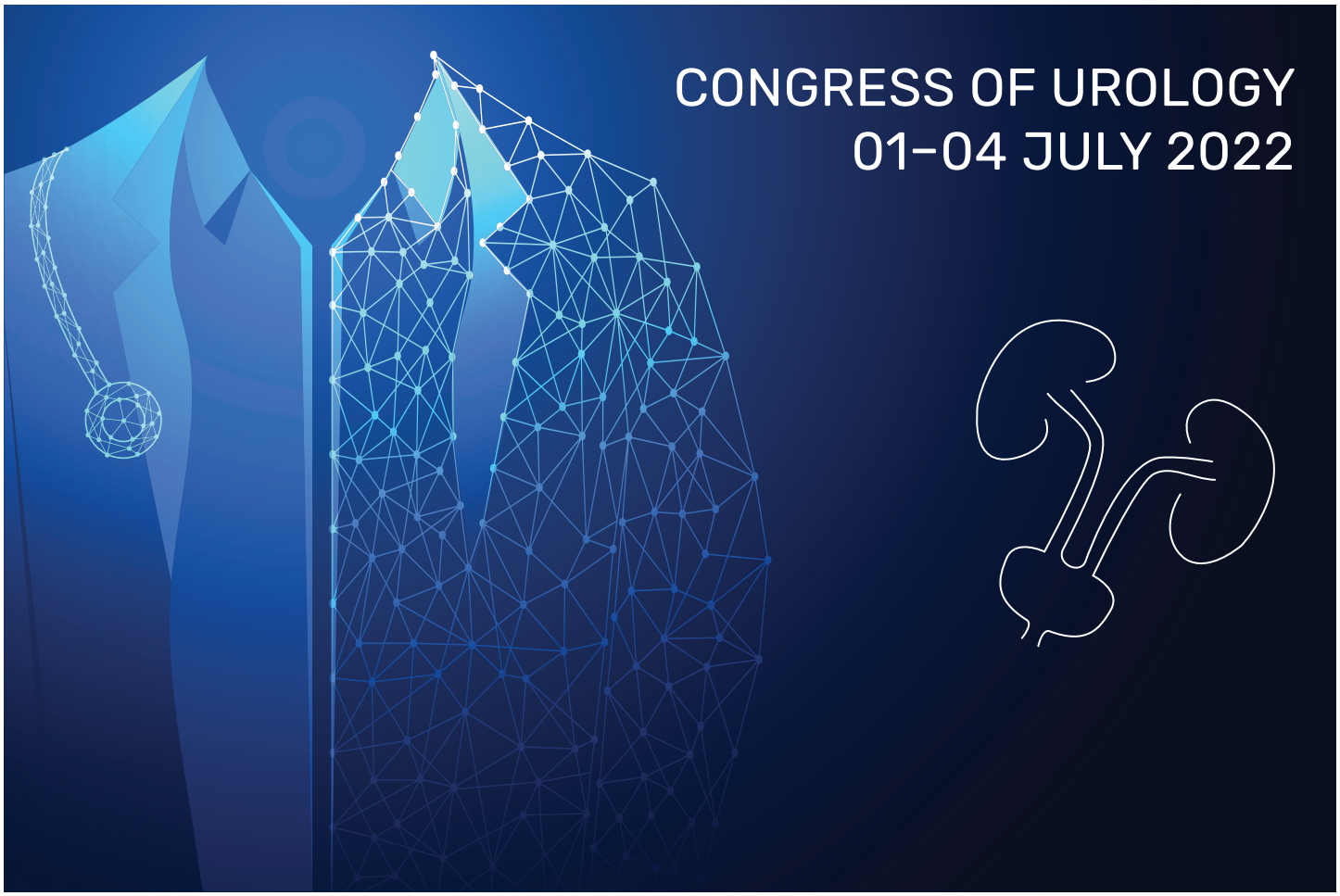

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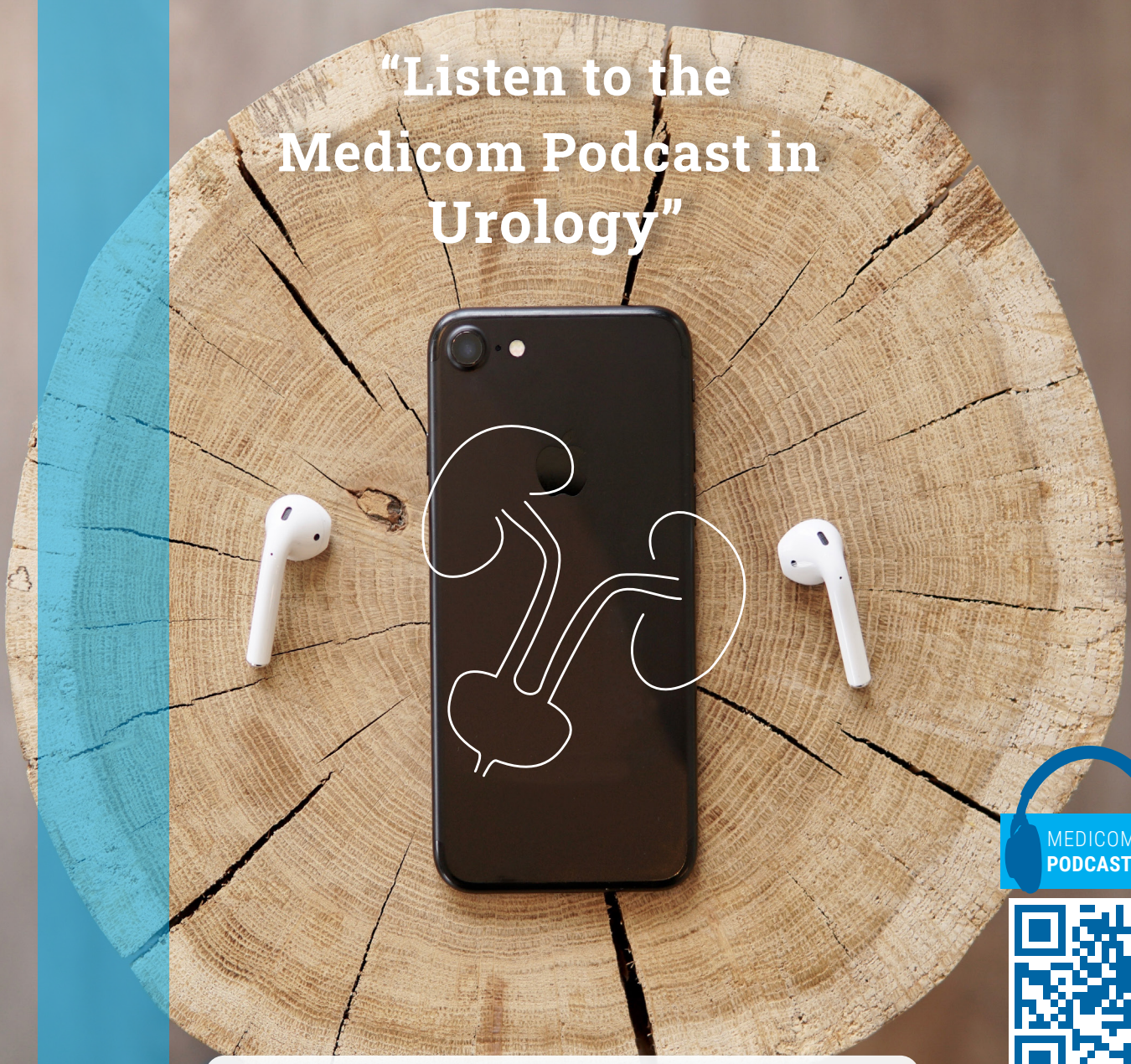

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Ruijterlaan 1-A
3742 AE Baarn
The Netherlands

Postal address
Medicom Medical Publishers
PO Box 90
3740 AB Baarn
The Netherlands

Telephone +31 85 4012 560
E-mail publishers@medicom-publishers.com
www.medicom-publishers.com

COLOPHON
Editor Dr Rachel Giles
Medical writer Robert van den Heuvel
Publishing Director Paul Willers
Medical Project Manager Anne van Ham
Editorial Coordinator Dr Joery Goossens
Graphic Design MOOZ grafisch ontwerp

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1. Does systematic biopsy add value to the detection rate of prostate cancer?

In patients with suspected prostate cancer and positive multiparametric (mp) MRI, targeted biopsy plus systematic biopsy did not perform significantly better than targeted biopsy alone in the detection of prostate cancer. Nonetheless, a substantial proportion of clinically significant prostate cancers was only detected through systematic biopsy [1].

mpMRI, followed by targeted biopsy and systematic biopsy, is the standard protocol to identify disease in individuals with suspected prostate cancer. "Whether systematic biopsy adds real value to the detection of prostate cancer is a topic of debate," explained Dr Enrico Checcucci (University of Turin, Italy). To address this issue, Dr Checcucci and co-investigators developed a clinical trial in which participants with suspected prostate cancer and positive mpMRI were randomised to targeted biopsy plus systematic biopsy (n=190) or to targeted biopsy alone (n=201). The detection rates of prostate cancer and clinically significant prostate cancer were the endpoints of this trial.

The double biopsy protocol did not result in a significantly higher detection rate of prostate cancer than targeted biopsy alone (71.1% vs 64.7%; P=0.17). The corresponding detection rates of clinically significant prostate cancer displayed a similar pattern (63.2% vs 60.7%; P=0.61). However, Dr Checcucci pointed out that a non-negligible rate of clinically significant prostate cancers (7.9%) was detected with a positive systematic biopsy and a negative targeted biopsy. A multivariate analysis demonstrated that systematic biopsy was an independent predictive variable of prostate cancer in lesions with diameters below 10 mm (OR 3.84; P=0.04).

1. Checcucci E, et al. Target vs. Target plus Standard biopsy in naïve patients: Results of a prospective randomized controlled trial. Abstract 0455, EAU 2022, 01–04 July.

2. PSMA PET/CT cannot replace mpMRI for diagnosis of prostate cancer

^{18}F-DCFPyL PSMA PET/CT imaging did not demonstrate better accuracy than multiparametric (mp)MRI in diagnosing prostate cancer, the results of a phase 3 trial showed. Therefore, mpMRI remains the standard option for detecting prostate cancer [1].

"Diagnosing prostate cancer with mpMRI remains imperfect," stated Prof. Lih-Ming Wong (University of Melbourne, Australia), explaining the rationale of a phase 3 trial that compared PSMA-PET/CT to mpMRI, hypothesising that the first would be superior to the latter. A total of 235 participants with elevated PSA levels (>3.0, or >2.0 in case of positive family history), an abnormal digital rectal exam (DRE), and a low free/total PSA ratio (<25%) underwent both mpMRI and ^{18}F-DCFPyL PSMA PET with chest/abdomen/pelvis CT to assess the diagnostic accuracy of both options. Participants with positive or equivocal findings were scheduled to undergo a biopsy to verify the results.

mpMRI displayed a better diagnostic accuracy for detecting prostate cancer than PSMA-PET/CT, as indicated by AUROC values (0.77 vs 0.62; P=0.0131). The corresponding sensitivity, specificity, and negative predictive values were 77.2%, 75.9%, and 61.2% for mpMRI and 68.4%, 55.6%, and 45.5% for PSMA-PET/CT. Prof. Wong added that clinically significant cancers were missed with both imaging techniques.

Although mpMRI outperformed PSMA-PET/CT in this trial, Prof. Wong argued that there may be a role for PSMA-PET/CT in the future. "PSMA-PET/CT needs finetuning. For example, we will not only be using SUVmax in the future, as was the case in this trial. Also, PSMA-PET/CT may be applied in patients with contraindications to MRI or in patients with equivocal MRI results who are reluctant to undergo biopsy."

1. Wong L-M, et al. Phase III study comparing diagnostic accuracy of mpMRI prostate to 18F-DCFPyL PSMA PET/CT. Game-changing session 6, EAU 2022, 01–04 July.

3. Prostate cancer treatments reduce quality of life

In the EUPROMS 2.0 study, all therapies for patients with prostate cancer, other than active surveillance, were associated with a reduced quality of life. Therefore, active surveillance should be the first treatment option if it is applicable, argued the authors [1].

The EUPROMS 2.0 study measured the effect of prostate cancer treatments on quality of life through a 20-minute online survey, including 4 QoL questionnaires: EQ-5D-5L, EORTC-QLQ-C30, EPIC-26, and SDM-Q-9. Mainly, the study aimed to confirm and complement the results of the EUPROMS 1.0 study, which showed that prostate cancer treatments, except active surveillance, are related to a decreased quality of life. Mr André Deschamps (Europa Uomo, Belgium) presented the findings of the study, which reported on a total of 3,571 patients who completed the online survey.

In general, the results of EUPROMS 1.0 were confirmed. Prostate cancer therapies were associated with a reduced quality of life. An

issue that was unresolved with the EUPROMS 1.0 study was the potential influence of co-morbidities on quality of life. The current study demonstrated that high blood pressure was the only common comorbidity among patients (26.7%) and that 55.2% of the patients had no comorbidities, suggesting that the influence of comorbidities on quality of life is limited. EUPROMS 2.0 also showed that shared-decision making is fairly well integrated in clinical practice, with a median score of 34 out of 45 on the SDM-Q-9 questionnaire.

Additionally, EPIC incontinence scores were similar to those of the EUPROMS 1.0, with lower scores for radical prostatectomy (71), and higher scores for radiotherapy (94) and chemotherapy (94). No difference between treatment type and EPIC sexual score was displayed, with similar reductions for all therapies, except for active surveillance.

Mr Deschamps concluded that all therapies besides active surveillance reduced the quality of life of patients with prostate cancer, confirming the results of EUPROMS 1.0. "Active surveillance should be the first treatment if it can be applied safely, and healthcare professionals should use the results of EUPROMS 2.0 to discuss treatment options for their patients."

1. Deschamps A, et al. The real effect of prostate cancer treatment: EUPROMS 2.0 study patient-driven quality of life study follow-up in order to answer questions following EUPROMS 1.0. Game-changing session 2, EAU 2022, 01–04 July.

4. PROpel: Good results for abiraterone plus olaparib in mCRPC

Exploratory endpoints of the phase 3 PROpel trial favoured first-line abiraterone plus olaparib over abiraterone plus placebo in patients with metastatic castration-resistant prostate cancer (mCRPC). The safety profile of the combination regimen was manageable and consistent with the known safety profiles of the individual agents [1].

The primary analysis of the global, randomised, double-blind, phase 3 PROpel trial (NCT03732820; n=797) demonstrated a significant benefit of first-line abiraterone plus olaparib over abiraterone plus placebo in terms of radiographic progression or death (rPFS) in patients with mCRPC [2]. Prof. Noel Clarke (University of Manchester, UK) presented exploratory endpoints of this trial during a game-changing session.

First, Prof. Clarke emphasised that the effect of the combination regimen on rPFS was consistent in patients with homologous recombination repair gene mutations (HRRm; HR 0.50; 95% CI 0.34–0.73) and patients without mutations (HR 0.76; 95% CI 0.60–0.97). Second, a positive trend could be observed in the overall survival data in favour of the combination regimen (HR 0.86; P=0.29), but the results were only 28.6% mature at the time of the analysis. Other secondary endpoints displayed a significant benefit for patients who received abiraterone and olaparib, such as 'time to first subsequent therapy or death' (HR 0.74; P=0.004) and 'time to second progression or death' (PFS2; HR 0.69; P=0.0184). Similarly, in patients with measurable disease (n=321), the overall response rate was higher in patients receiving the combination therapy (58.4% vs 48.1%; P=0.0409). PSA response rates showed a clinical benefit of the combination regimen as well (HR 0.55; 95% CI 0.45–0.68).

Prof. Clarke added that the toxicity of abiraterone plus olaparib was elevated compared with abiraterone alone, but that the safety profile of the combination therapy was nevertheless manageable. Anaemia (46.0%), fatigue (37.2%), and nausea (28.1%) were the most prevalent any-grade adverse events in the experimental group.

1. Clarke N, et al. Exploratory endpoints from PROpel: A Phase III trial of abiraterone + olaparib vs. abiraterone + placebo in 1st line metastatic castration-resistant prostate cancer. Game-changing session 5, EAU 2022, 01–04 July.
2. Clarke N, et al. NEJM Evidence. 2022;EVIDoa2200043.

5. Neoadjuvant hormonal therapy promising in high-risk prostate cancer

Neoadjuvant degarelix plus apalutamide outperformed degarelix alone in patients with high-risk prostate cancer who were planned to receive a radical prostatectomy. The results of the phase 2 ARNEO trial encourage the development of phase 3 trials to further explore degarelix plus apalutamide in this population [1].

"Even with the current therapies, there is a huge unmet need for patients with high-risk prostate cancer," said Prof. Steven Joniau (UZ Leuven, Belgium). A retrospective analysis suggested a survival benefit of neoadjuvant hormonal therapy prior to radical prostatectomy in patients with high-risk disease [2]. To confirm the results of this study prospectively, the phase 2 ARNEO trial (NCT03080116) was designed, which randomised 89 patients with high-risk prostate cancer to 3 months of neoadjuvant degarelix plus apalutamide therapy or to degarelix alone, prior to their radical prostatectomy.

The primary endpoint, the proportion of patients with minimal residual disease (<0.25 mL) after neoadjuvant treatment, was met. In the experimental arm, 38% of the patients displayed minimal residual disease after treatment compared with 9% in the placebo arm (RR 4.2; P=0.002). Correspondingly, the median residual cancer burden was 1.7 mL in the placebo arm and 0.48 mL in the experimental arm. Furthermore, downstaging to pT2-disease occurred more often in the apalutamide arm than in the placebo arm (51% vs 27%;

P=0.03). The authors found that PSMA levels and residual cancer volume were correlated, suggesting that PSMA has a monitoring role in future neoadjuvant trials. Finally, *PTEN* gene loss was associated with poor response to therapy (11% vs 43%; P=0.002).

Prof. Joniau concluded that the results of this phase 2 trial justify the development of phase 3 trials assessing neoadjuvant hormonal therapy in patients with high-risk prostate cancer.

1. Devos G, et al. Randomized phase II trial of neoadjuvant degarelix with or without apalutamide prior to radical prostatectomy for unfavorable intermediate- and high-risk prostate cancer. Game-changing session 3, EAU 2022, 01–04 July.
2. Tosco L, et al. Prostate Cancer Prostatic Dis. 2017;20:407-412.

6. Darolutamide performs well across subgroups in mHSPC

Darolutamide added to androgen-deprivation therapy (ADT) and docetaxel improved the overall survival (OS) of patients with metastatic hormone-sensitive prostate cancer (mHSPC) compared with a regimen of ADT, docetaxel, and placebo in the ARASENS trial. This result was consistent across 'extent of disease' and alkaline phosphatase (ALP) level subgroups [1].

The primary analysis of the phase 3 ARASENS trial (NCT02799602; n=1,305) showed that darolutamide added to ADT and docetaxel resulted in an OS benefit for patients with mHSPC compared with ADT, docetaxel, and placebo [2]. Now, Prof. Bertrand Tombal (Université Catholique de Louvain, Belgium) presented the OS results of this trial according to the extent of metastatic disease and ALP levels of the patients, which are known prognostic factors in this population [3].

The previously reported OS benefit of additional darolutamide over placebo appeared to be consistent in patients with M1b disease (HR 0.66; 95% CI 0.54–0.80) and in patients with M1c disease (HR 0.76; 95% CI 0.53–1.10). Subgroups of patients with ALP levels <upper limit of normal (ULN; HR 0.65; 95% CI 0.47–0.89) and those with ALP levels ≥ULN (HR 0.69; 95% CI 0.56–0.85) experienced comparable OS benefits with darolutamide. Also, the time to castration-resistant prostate cancer was increased with darolutamide therapy in all subgroups. Importantly, darolutamide did not add toxicity to the regimen of ADT and docetaxel. Again, this result was consistent across subgroups.

Prof. Tombal concluded that darolutamide in combination with ADT and docetaxel should become a new standard-of-care therapy in patients with mHSPC.

1. Tombal B, et al. Overall Survival With Darolutamide Versus Placebo in Combination With Androgen-deprivation Therapy and Docetaxel by Stratification Factors in the Phase 3 ARASENS Trial. Game-changing session 5, EAU 2022, 01–04 July.
2. Smith MR, et al. N Engl J Med 2022;386:1132-1142.
3. Gravis G, et al. Eur Urol. 2015;68:196-204.

7. Shorter hospital stay with robotic surgery versus open surgery in bladder cancer

The time in hospital after surgery was significantly shorter for patients with bladder cancer who underwent complete robotic radical cystectomy than for those who received open surgery. In addition, both the length of stay and the readmission rates were lower in the robotic surgery arm [1].

The randomised phase 3 iROC trial (NCT03049410) was designed to compare robotically assisted radical cystectomy with open radical cystectomy in patients with urothelial cell carcinoma (n=338; mean age 69 years). During the opening session of EAU 2022, Prof. James Catto (University of Sheffield, UK) presented the results of the trial. The number of days alive and out of hospital within 90 days of surgery (DAOH90) was the primary outcome of this study, including both the length of stay and readmissions.

The DAOH90 was significantly higher in the robotic surgery arm than in the open surgery arm (median 82 vs 80 days; P=0.01). Prof. Catto added that both the length of stay (median 7 vs 8 days; P=0.045) and the readmission rates (21.8% vs 32.2%; P=0.04) contributed to the favourable DAOH90 outcomes for patients in the robotic surgery arm.

Several quality-of-life measures indicated an improved quality of life 5 to 12 days after surgery for patients in the robotic surgery arm. However, 26 days after surgery, the quality-of-life outcomes were comparable for those who underwent robotic surgery and those who received open surgery.

Wound infections (5.6% vs 17.3%) and thromboembolic events (1.9% vs 8.3%) were more common in patients who underwent open surgery. There were no substantial differences in mortality rates (14.3% vs 14.7%; P=0.8) or cancer recurrence rates (18% vs 16%) between the 2 study arms.

Prof. Catto concluded that the iROC trial showed that robotic surgery may offer benefits over open surgery in patients with urothelial carcinoma, but that the clinical importance of the observed differences remains uncertain.

1. Catto J, et al. Effect of robot-assisted radical cystectomy with intracorporeal urinary diversion vs. open radical cystectomy on 90-day morbidity and mortality among patients with bladder cancer: a randomized clinical trial. Game-Changing Session 1, EAU 2022, 01–04 July.

8. Improved risk stratification for high-risk NMIBC

The response to intravesical Bacillus Calmette-Guérin (BCG) treatment in patients with high-risk non-muscle invasive bladder cancer (NMIBC) could be predicted by molecular subtyping of the tumours. According to the authors, this approach has the potential to be applied in the clinic, to select patients for early radical cystectomy [1].

"Intravesical BCG therapy is the standard-of-care for patients with high-risk NMIBC, but only delivers clinical benefits in 50% of the patients undergoing this treatment," clarified Mr Florus de Jong (Erasmus University Medical Center, the Netherlands). The current study aimed to improve risk stratification of high-risk NMIBC and to identify molecular subtypes related to BCG treatment response. RNA sequencing was performed on the tumour tissue of 2 patient groups (cohort A, n=132; cohort B, n=151). The primary outcome of the study was progression-free survival (PFS).

Three molecular subtypes were related to BCG response in cohort A, named BCG-response subtype (BRS)1, 2, and 3. Patients with BRS3 displayed a reduced PFS compared with patients with BRS1 (P=0.003) or BRS2 (P=0.017). These findings were confirmed in cohort B. BRS3 tumours were characterised by high levels of EMT-basal markers and displayed an immunosuppressive profile, added Mr de Jong. BRS3 tumours could be identified with high accuracy (AUROC 0.87) using a commercially approved qPCR-based assay, providing options to use this improved risk stratification method in clinical practice and thus select patients who may benefit from early radical cystectomy. The authors also found that recurring BRS3 tumours after BCG treatment were highly enriched. In these patients, several druggable regulators (TGFβ, DDR2) were upregulated after BCG treatment.

1. De Jong FC, et al. Non-muscle invasive bladder cancer subtypes with differential response to intravesical bacillus Calmette-Guerin treatment. Abstract 0068, EAU 2022, 01–04 July.

9. Adjuvant atezolizumab may benefit ctDNA-positive patients with post-op muscle-invasive urothelial carcinoma

An exploratory analysis of the phase 3 IMvigor010 trial revealed that adjuvant atezolizumab improved the overall survival (OS) of patients with post-operative muscle-invasive urothelial carcinoma who had levels of circulating tumour DNA (ctDNA) exceeding a predetermined threshhold. To validate this result prospectively, the phase 3 IMvigor011 trial has been launched [1].

The IMvigor010 study (NCT02450331) compared adjuvant atezolizumab with observation in patients with post-operative muscle-invasive urothelial carcinoma (n=809). No significant difference in disease-free survival was reported between participants in the atezolizumab group and those in the observation group. However, an exploratory analysis did indicate that ctDNA-positive patients benefitted from atezolizumab (HR 0.59; 95% CI 0.41–0.86). The updated results of this trial were presented by Prof. Jürgen Gschwend (Technical University Munich, Germany).

After a median follow-up of 36.4 months, the OS of the total study population was still not increased with atezolizumab treatment instead of observation (HR 0.91; 95% CI 0.73–1.13). However, patients with a known ctDNA-positive status (n=214) displayed a significant OS benefit if they had been randomised to the atezolizumab arm (HR 0.59; 95% CI 0.42–0.83), with corresponding median OS results of 29.8 months and 14.1 months for ctDNA-positive patients in the atezolizumab and observation arm, respectively. Prof. Gschwend added that ctDNA-positivity was associated with a worse prognosis than ctDNA-negativity (HR 6.30; 95% CI 4.30–9.30).

Furthermore, the effect of atezolizumab on the OS of ctDNA-positive patients appeared to be somewhat more pronounced in patients whose tumours had PD-L1 expression levels ≥5% (HR 0.51; 95% CI 0.30–0.85) than in those with PD-L1 levels <5% (HR 0.75; 95% CI 0.49–1.16).

Prof. Gschwend emphasised that these results are hypothesis-generating only and that adjuvant atezolizumab is currently being assessed prospectively in ctDNA-positive patients with muscle-invasive urothelial carcinoma in the IMvigor011 trial (NCT04660344).

1. Gschwend JE, et al. Overall survival (OS) by circulating tumor DNA (ctDNA) status in patients with post-operative muscle-invasive urothelial carcinoma (MIUC) treated with atezolizumab (atezo): update from IMvigor010. Game-changing session 5, EAU 2022, 01–04 July.
2. Bellmunt J, et al. Lancet Oncol. 2021;22:525–537.

10. New prognostication in N3 penile cancer

Patients with N3 penile squamous cell cancer had a worse overall survival (OS) if they displayed either extra-nodal extension in inguinal lymph node metastasis or pelvic lymphadenopathy. Patients with extra-nodal inguinal lymph node extension also appeared to have a better prognosis than those with pelvic lymphadenopathy. Further analysis of larger datasets is needed to verify the observed stratification of the TNM N3 group [1].

"Currently, TNM staging for penile squamous cell cancer distinguishes between 'clinical N3', with fixed inguinal lymph node metastasis or pelvic lymphadenopathy, and 'pathologic N3', with pelvic lymph node metastasis and/or extra-nodal extension in any lymph node," outlined Dr James Churchill (St George Hospital, Australia). The current study evaluated whether N3 staging can be further stratified based on pelvic lymphadenopathy and extra-nodal extension, to allow more accurate prognostication for patients and guide treatment decisions based on logical stage groupings. It was hypothesised that patients with pelvic lymphadenopathy had a worse prognosis than patients with extra-nodal extension in inguinal lymph node metastasis. In total, 213 patients were analysed retrospectively with OS being the primary outcome.

Patients without pelvic lymphadenopathy and extra-nodal inguinal lymph node extension had an improved OS compared with patients with either pelvic lymphadenopathy (HR 3.67 P<0.001) or inguinal lymph node extra-nodal extension (HR 1.99; P=0.006). Also, a numerical difference was observed between patients with extra-nodal extension (median OS of 25.4 months) and patients with pelvic lymphadenopathy (median OS of 19.6 months; P=0.19). In a corresponding multivariate analysis, patients with pelvic lymphadenopathy displayed 62% increased risk of death, which did not reach statistical significance, compared with patients with inguinal lymph node extra-nodal extension (P=0.072).

1. Churchill J, et al. Survival in N3 penile cancer: Does pelvic lymphadenopathy predict a worse prognosis than inguinal extra-nodal extension? Abstract 0691, EAU 2022, 01–04 July.

11. KEYNOTE-564: Updated results of adjuvant pembrolizumab in RCC

Patients with intermediate-high- or high-risk renal cell carcinoma (RCC) continued to benefit from adjuvant pembrolizumab compared with placebo, updated results of the KEYNOTE-564 trial showed. These findings support adjuvant pembrolizumab as a potential standard-of-care in patients with RCC and risk factors for recurrence [1].

The phase 3 KEYNOTE-564 trial (NCT03142334) enrolled patients with intermediate-high- or high-risk RCC, a group in whom until recently no standard-of-care existed after surgery, explained Prof. Thomas Powles (Barts Cancer Institute, UK). Participants were randomised to adjuvant pembrolizumab (n=496) or placebo (n=498). The primary analysis, published in the New England Journal of Medicine, displayed a significant disease-free survival (DFS) benefit for patients who were treated with pembrolizumab over those who received placebo [2].

After 30.1 months of follow-up, the trial update indicated that DFS was still significantly higher in the pembrolizumab arm than in the placebo arm (HR 0.63; P<0.0001), with corresponding 24-month DFS rates of 78.3% and 67.3%. This result was consistent across subgroups, including disease risk category and PD-L1 status. Importantly, an exploratory analysis indicated that the rate of distant recurrences was higher in the placebo arm than in the pembrolizumab arm (HR 0.63), both in patients with M0-disease (n=936; 29.0% vs 20.8%) and in patients with M1-disease (n=58; 55.2% vs 20.7%). Prof. Powles added that the overall survival results were not yet mature, with 66 of the 200 needed events registered to date, but that a promising trend could be observed (HR 0.52; 95% CI 0.31–0.86).

The updated safety analysis did not reveal a substantial increase in adverse events (AEs). Fatigue (20.3%), pruritis (18.6%), hypothyroidism (17.4%), diarrhoea (15.8%), and rash (15.0%) were the most common any-grade AEs in the pembrolizumab arm.

1. Powles T, et al. Pembrolizumab (pembro) as adjuvant therapy for patients (pts) with renal cell carcinoma (RCC): Updated results from the 30-month follow-up of KEYNOTE-564. Game-changing session 2, EAU 2022, 01–04 July.
2. Chouieri TK, et al. N Engl J Med 2021;385:683–694.

12. Fewer complications with robotic surgery in renal cancer

Numerically lower complication rates were observed with robotic surgery versus open surgery in patients with intermediate or high complexity renal tumours. In addition, shorter hospital stays were reported in patients who underwent robotic surgery [1].

The phase 3 OpeRa trial (NCT03849820) was designed to show the superiority of robot-assisted partial nephrectomy (RAPN) to open partial nephrectomy (OPN) in patients with

intermediate or high complexity kidney tumours. Prof. Marc-Oliver Grimm (Universitätsklinikum Jena, Germany) presented the results. Due to slow enrolment, only 240 patients instead of the indicated 606 patients were randomised 1:1 to RAPN or OPN. In total, 95% of patients in the RAPN group and 77% of patients in the OPN group received the anticipated treatment. The 30-day post-operative complication rate was the primary endpoint of the trial.

A trend towards a reduced 30-day complication rate was observed in favour of the RAPN arm (36.6% vs 46.1%; P=0.175). This effect was mostly driven by a decreased rate of grade 1 (OPN 19.1% vs RAPN 11.6%) and grade 2 (19.1% vs 13.4%) adverse events (AEs) in the RAPN arm. The corresponding grade 3-a, grade 3-b, and grade 4-a AE rates were comparable between the 2 arms, with 3.4%, 3.4%, and 1.1% in the OPN arm and 5.4%, 4.5%, and 1.8% in the RAPN arm, respectively. A substantial difference between AEs 'possibly or definitely' related to treatment was observed to the benefit of those who received RAPN (37.1% vs 23.2%; P=0.032). Also, the number of post-operative hospital days to discharge was lower in patients who received RAPN (7 vs 6; P<0.001). In contrast, the median operating time was significantly longer in the RAPN arm (167 vs 122 minutes; P<0.001).

Prof. Grimm concluded that, although underpowered, the trial showed a clear trend for fewer complications with robotic surgery compared with open surgery in patients with intermediate or high complexity renal tumours. Analyses of postoperative pain medication, patient-reported outcomes, and quality of life are ongoing.

1. Grimm M-O, et al. Complications with open versus robotic-assisted partial nephrectomy (OpeRa) in patients with intermediate/high-complexity kidney tumours. Game-changing session 1, EAU 2022, 01–04 July.

13. Novel therapeutic targets for benign prostatic hyperplasia

A large genome-wide association study revealed novel therapeutic targets for patients with benign prostatic hyperplasia (BPH) requiring surgery. Moreover, ethnic-specific targets were detected. This study made a first important step towards personalised medicine for patients with clinically significant BPH [1].

"There is a need to detect genomic drivers of BPH and find new targets for the treatment of this condition," explained Prof. Richard Bryant (University of Oxford, UK) at the start of his presentation. "Although a recent genome-wide association study reported 23 genome-wide significant variants at 14 loci, this data did not include surgically-treated BPH [2]." The current study aimed to identify genomic drivers of BPH requiring surgery for the purpose of finding new potential treatment targets. In total, 109,627 patients with BPH and 805,054 control participants were analysed through single-cell RNA sequencing.

The analysis detected 17 genetic variants that were significantly associated with surgically-treated BPH. Of these 17 variants, 8 had not been associated with BPH in prior studies, added Prof. Bryant. Furthermore, 3 genetic variants were only observed in certain ethnic groups. Prof. Bryant mentioned that the results of this large genome-wide association study provide a proof-of-principle that genetic risk scores are related to BPH severity and the need for surgery. "Several promising candidates for therapeutic development have been discovered and a first step towards personalised medicine for clinically significant BPH has been made."

1. Ng M, et al. Trans-ethnic genome-wide association study reveals new therapeutic targets for benign prostatic hyperplasia. Abstract 0590, EAU 2022, 01–04 July.
2. Gudmondsson J, et al. Nat Commun. 2018;9:4568.

14. Mini-slings non-inferior to standard mid-urethral slings in SUI

Single-incision mini-slings were non-inferior to standard mid-urethral slings in women with stress urinary incontinence (SUI). Also, the hospital stay was shorter in patients receiving mini-slings compared with those who received mid-urethral slings. These results could help patients and clinicians make an informed shared decision regarding the surgical treatment of SUI [1,2].

Robust evidence regarding the effectiveness of mini-slings compared with the effectiveness of mid-urethral slings is lacking, said Prof. Mohamed Abdel-fattah (University of Aberdeen, UK). Therefore, his group conducted the pragmatic multicentre, non-inferiority, randomised-controlled SIMS trial, including 600 adult women with SUI who failed or declined conservative treatment, and received an adjustable anchored mini-sling or a tension-free standard mid-urethral sling. The patient global impression of improvement (PGI-I) questionnaire at 15 months was the primary measure of treatment success.

According to the PGI-I results at 15 months, the success rate of mini-slings (79.1%) was non-inferior to that of standard mid-urethral slings (75.6%). The 3-year results displayed a similar result, with success rates of 72.0% and 66.8% in the experimental arm and control arm, respectively. The post-operative hospital stay was shorter in the experimental arm than in the control arm (7.2 hr vs 9.7 hr). However, no substantial difference was reported in the percentage of patients that had returned to normal activities within 28 days after surgery (75.2% vs 70.8%). Prof. Abdel-fattah added that the rates of 'any degree' groin or thigh pain were similar for both arms, with 14% of the patients experiencing these complaints at 36 months,

but that the 36-month dyspareunia rate was higher in the experimental arm than in the control arm (11.7% vs 4.8%).

1. Abdel-fattah M, et al. Single-Incision Mini-Slings for Stress Urinary Incontinence in Women. Game-changing session 4, EAU 2022, 01–04 July.
2. Abdel-fattah M, et al. N Engl J Med 2022;386:1230-1243.

15. Non-inferiority of methenamine hippurate to antibiotics in recurrent UTIs

The non-antibiotic preventive treatment methenamine hippurate displayed non-inferiority to daily low-dose prophylactic antibiotics in women with recurrent urinary tract infections (UTIs). The authors of the ALTAR trial concluded that methenamine hippurate could therefore be considered a novel standard first-line option in women with recurrent UTIs [1].

The multicentre, randomised, non-inferiority ALTAR trial (ISRCTN70219762) included 240 women with recurrent UTIs to compare the effectiveness of antibiotic prophylaxis (n=120) with that of methenamine hippurate (n=120). The primary outcome was the incidence of self-reported symptomatic antibiotic-treated UTIs during the 12-month treatment period, with a non-inferiority margin of 1 UTI episode per year.

Methenamine hippurate demonstrated non-inferiority to antibiotic prophylaxis, with incidence rates of 1.38 (95% CI 1.05–1.72) and 0.89 (95% CI 0.65–1.12), respectively. Prof. Christopher Harding (Newcastle University, UK) added that only 52% of the antibiotic-treated UTIs were confirmed by a positive culture, indicating that relying on microbiological cultures only would result in missing almost half of the UTIs. Next, patients in the antibiotic prophylaxis arm displayed a trend towards a higher resistance to at least one antibiotic in *E. coli* during the 12-month treatment period compared with the patients in the non-antibiotic treatment arm (P=0.052).

Prof. Harding concluded that the results of the ALTAR trial show that methenamine hippurate is an effective alternative to antibiotic preventative treatments in women with recurrent UTIs and that this agent should be considered a novel first-line standard of care.

1. Harding C, et al. Alternative to prophylactic antibiotics for the treatment of recurrent urinary tract infections in women: multicentre, open label, randomised, non-inferiority trial. Game-changing session 4, EAU 2022, 01–04 July.