

2022 European Society for Medical Oncology: Meeting highlights

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Introduction

The European Society for Medical Oncology (ESMO) congress, held in Paris, France, and online from September 9–13, 2022, presented the latest advances in cancer treatment. This year's congress included close to 2000 abstracts with nearly 30 000 participants. Following the congress, on September 15, the Canadian Urological Association (CUA) held an online webinar, where Canadian experts presented the most potentially practice-changing research findings in prostate, bladder, and kidney cancers. This report provides a snapshot of the most ground-breaking advances. The entire webinar can be viewed on UROpedia Canada, and meeting abstracts can be found on ESMO's oncologyPRO site.

Prostate Cancer

Dr. Scott Morgan presented three late-breaking abstracts on biochemical recurrence after radical prostatectomy.

The RADICALS trial focused on two main questions. First, RADICALS-RT addressed the optimal timing of radiotherapy after prostatectomy, adjuvant vs. early-salvage, and results have previously been reported.¹ Second, RADICALS-HD asked whether and for what duration hormonal therapy should be added to postoperative radiotherapy, and initial results were presented at the ESMO meeting.² While it was originally designed as a three-arm study, with patients to be randomized between no androgen deprivation therapy (ADT), short-term ADT (six months), or long-term ADT (24 months), most patients were entered in one of two two-way randomizations: short-term ADT vs. no ADT or short-term vs. long-term ADT. The primary endpoint was metastasis-free survival (MFS), which can be used as a surrogate for overall survival (OS) in localized prostate cancer.³ At a median follow-up of nine years, short-term ADT did not improve MFS

compared to no ADT, and the treatment effect appeared consistent across prespecified subgroups; however, long-term ADT improved MFS compared to short-term ADT, with a 6% absolute improvement in 10-year MFS. Results for OS remain immature. DADSPORT, a systematic review and meta-analysis of randomized trials, including RADICALS-HD, revealed that short-term ADT significantly improves MFS in the postoperative radiotherapy setting compared to no ADT.⁴ Taken together, the results from RADICALS-HD and the DADSPORT meta-analysis demonstrate that short-term ADT confers a modest MFS benefit compared to no ADT, while long-term ADT carries a similarly modest benefit over short-term ADT. The DADSPORT collaborators plan an individual patient data meta-analysis, which may help identify subgroups based on traditional clinical and pathological features, deriving greater or lesser benefit from ADT in this setting. Genomic classifiers and artificial intelligence-based tools using digital histopathology may provide additional guidance.^{5,6}

PRESTO focused on patients that had progressed biochemically despite maximal local therapy to the pelvis, including salvage radiotherapy.⁷ In this setting, intermittent ADT is a standard of care (SoC).⁸ PRESTO investigated the intensification of an intermittent approach to ADT. Patients received 52 weeks of therapy with 1) ADT alone; 2) ADT and apalutamide; or 3) ADT, apalutamide, and abiraterone plus prednisone (AAP). The primary endpoint was prostate-specific antigen (PSA) progression-free survival (PFS). As PSA progression triggers re-initiation of ADT when an intermittent approach is used, the primary endpoint was effectively a measure of the duration of the first off-treatment interval. The addition of apalutamide improved PSA PFS compared to ADT alone by 4.6 months at the median (24.9 vs. 20.3 months). The addition of AAP to apalutamide and ADT did not yield a significant benefit. Given that PSA PFS is not a surrogate for more important oncological endpoints, such as MFS and OS, these results are insufficient to change current practice; however, the data warrant further study of intensified intermittent ADT, especially in those at the highest risk for developing metastases over time.

Dr. Sebastien Hotte presented the latest advances in the treatment of metastatic castration-sensitive prostate cancer (mCSPC). STAMPEDE, a phase 3, multi-arm, multistage, randomized trial evaluated docetaxel vs. AAP in addition to ADT. A post-hoc analysis evaluated the impact of nodal status on OS in men accrued to AAP with subgroups consisting of bone-only or nodal \pm bone.⁹ Of note, the nodal group included a small percentage of patients with visceral metastasis (6–8%), which may confound results, as it is a known negative prognostic factor. In the docetaxel arm, the bone-only group seemed to have the best survival (hazard ratio [HR] 0.62), whereas the nodal group did not benefit from the addition of docetaxel to ADT. In the AAP arm, similar survival benefits were found in both subgroups. Therefore, nodal burden (≥ 5 non-regional lymph nodes) was prognostic for worse outcomes; however, it is difficult to make a definitive statement since more nodes could also be correlated with a higher likelihood of visceral disease.

A meta-analysis of patient data collected from NCI (CHAARTED) and UNICANCER (GETUG) assessed the impact of time to docetaxel on outcome in the mCSPC setting.¹⁰ There was an OS benefit in men with mCSPC treated with ADT and docetaxel who had previous local therapy and a lower volume of disease. After accounting for known major prognostic factors, an earlier start of docetaxel (less than 35 days from the start of ADT vs. 35 days or more) was not associated with improved survival.

PEACE-1, a phase 3 trial, demonstrated improved OS with the addition of AAP to ADT with or without docetaxel in men with de novo mCSPC.¹¹ Moreover, the eight-month PSA was strongly predictive of radiographic (r)PFS and OS outcomes in PEACE-1,¹² with both 0.2 and 4.0 ng/ml cutoffs. Significantly, more men treated with docetaxel and abiraterone had a PSA value of 0.2 or less at eight months. Therefore, early therapeutic intervention in men who do not achieve an adequate PSA decrease early in the treatment course needs to be evaluated in future clinical trials.

Advances in metastatic castration-resistant prostate cancer (mCRPC) treatment with poly (ADP-ribose) polymerase inhibitors (PARPi) were also presented. PROpel is a phase 3 trial of AAP + olaparib (ola) vs. AAP + placebo as first-line therapy for mCRPC patients.¹³ AAP + ola significantly prolonged rPFS, and there was a trend towards an OS benefit vs. AAP + placebo in the intention-to-treat (ITT) population. Biomarker analysis demonstrated meaningful rPFS improvement over eight months in all assessed biomarker subgroups (HRR and BRCA), with patients with BRCA mutations demonstrating the most pronounced rPFS benefit (HR 0.23). Updated results showed a continuing trend towards improved OS in the ITT population but remained immature. Safety and tolerability were generally consistent. These results support superior clinical benefit with AAP + ola vs. AAP + placebo as first-line therapy for patients with mCRPC.

TALAPRO-1 examined the benefits of talazoparib treatment in mCRPC patients according to tumor genetics¹⁴ to try and identify the patients that would benefit most from PARPi therapy. Based on these retrospective, exploratory analyses of TALAPRO-1, patients with BRCA2 copy number loss or homozygous alterations and lack of TP53 alterations exhibited prolonged benefits with PARPi therapy.

Dr. Ricardo Rendon presented abstracts on mCSPC and mCRPC. Two trials from the STAMPEDE study evaluated AAP and the combination of enzalutamide (ENZ) with AAP for mCSPC patients starting ADT.¹⁵ The study had a long median followup but no differences in OS or metastatic PFS were found between the groups. Therefore, AAP and ENZ should not be combined to treat mCSPC or high-risk localized prostate cancer. This further supports previous negative data on the combination of neoadjuvant hormonal therapy for nmCSPC¹⁶ and mCRPC;^{17–19} however, the combination of AAP and ADT demonstrated sustained improvement in OS, with 30% and 48% of patients alive at 84 months in ADT and ADT + AAP arms, respectively.

A post-hoc analysis of the ARCHES trial examined the effect of treatment intensification with ENZ + ADT vs. continuing ADT alone on OS and other efficacy outcomes by post-treatment nadir PSA levels.²⁰ The addition of ENZ to ADT provided benefits for patients in all PSA categories, including those that had a dramatic PSA response to ADT (PSA < 0.2 ng/ml). This supports the addition of androgen receptor-axis-targeted therapies (ARAT) to ADT, even in patients with strong PSA responses.

The VISION trial compared SoC vs. SoC with ¹⁷⁷Lu-PSMA-617 in patients with progressive prostate-specific membrane antigen (PSMA)-positive mCRPC. There was a significant improvement in defined rPFS and OS with the addition of lutetium. Lutetium treatment also delayed the time to the first skeletal symptomatic event or death. Patients treated with ¹⁷⁷Lu-PSMA-617 plus SoC also experienced a greater decline in PSA from baseline compared to those receiving SoC alone. An exploratory post-hoc analysis demonstrated that the magnitude of PSA decline from baseline was strongly associated with prolonged rPFS and OS in this setting.²¹ Therefore, PSA decline is important for clinical outcomes during radioligand therapy with ¹⁷⁷Lu-PSMA-617 and can be used as a prognostic indicator in this patient population.

Another post-hoc analysis from the VISION trial examined the correlation between several endpoints and the eventual survival endpoint.²² There was a moderate-to-strong correlation between rPFS and OS, suggesting that rPFS may be relevant as an early endpoint for regulatory approval and clinical trial design in mCRPC patients undergoing radioligand therapy. The RALU study demonstrated that ¹⁷⁷Lu-PSMA therapy in patients previously treated with radium-223 (Ra223) had an acceptable safety profile and effectiveness in terms of OS and rPFS, and was similar to other findings

with ^{177}Lu -PSMA, indicating no cross-resistance.²³ Therefore, patients who have received Ra223 are still good candidates for ^{177}Lu -PSMA.

Bladder cancer

Dr. Peter Black presented abstracts on localized bladder cancer, where several new concepts could lead to major paradigm shifts in the future. BladderPath, a randomized trial, compared magnetic resonance imaging (MRI) vs. cystoscopic staging for newly diagnosed bladder cancer.²⁴ This trial investigated the feasibility of replacing complete transurethral resection of bladder tumor (TURBT) with a cystoscopic biopsy combined with a staging MRI in patients with bladder cancer. Transurethral piecemeal resection of an aggressive bladder tumor does not conform to basic oncological principles. Complications are also common after TURBT and the TURBT delays the initiation of definitive therapy.

Patients (n=143) in BladderPath were randomized to the SoC vs. an image-directed strategy. The time to correct treatment for all patients was 31 days in the SoC arm and 37 days in the image-directed arm. The time to correct treatment for patients with muscle-invasive bladder cancer (MIBC), which was the primary endpoint of the trial, was 53 days in the MRI group (n=14) compared to 98 days in the conventional TURBT group (n=12; HR 3.4, 95% confidence interval [CI] 1.4, 8.3, p=0.0046). Although this novel diagnostic pathway accelerated the delivery of definitive treatment to patients with MIBC, the small sample size limits the conclusions that can be drawn. Moreover, complete TURBT provides additional pathological risk parameters, including the presence of variant histology and lymphovascular invasion, which could be lost without TURBT; however, the impact of this on patient outcomes is uncertain. A key limitation of this study's image-directed strategy is the poor specificity of MRI,²⁵ which puts non-muscle-invasive bladder cancer (NMIBC) patients at risk of being treated as MIBC. Moreover, MRI is not routinely performed for bladder cancer staging in Canada and would present a significant learning curve for radiologists. The study's premise that conventional TURBT is harmful remains unproven, and the delay incurred by TURBT is specific to the U.K. healthcare system, although we are likely faced with similar delays in Canada.

Preliminary results were presented from the phase 2 RACE IT trial, which sought to test an alternative neoadjuvant therapy before radical cystectomy in patients (n=33) with locally advanced (cT3/T4 or cN+) bladder cancer who were cisplatin-ineligible or refusing cisplatin.²⁶ The neoadjuvant therapy consisted of 50.4 Gy radiation plus four cycles of immunotherapy (nivolumab every two weeks) but no chemotherapy. The primary endpoint (completion of treatment, including surgery, by week 15) was achieved by 87% of patients, which surpassed the prespecified completion rate of 70%.

A complete pathological response was observed in 38.7% of patients, and downstaging to NMIBC or less (ypT \leq 1N0) was observed in 58.1%. The disease-free survival (DFS) at 12 months was 90.6%. Most of the toxicity was anticipated toxicity from nivolumab. This trial demonstrated the feasibility and safety of this treatment paradigm. The response rates were encouraging, and it could be an attractive neoadjuvant option for patients otherwise not offered neoadjuvant therapy. The main concern is the uncertainty regarding the need to combine radiation with surgery, as definitive radiation with immunotherapy may achieve an equivalent outcome without the need for cystectomy.

As radiation-based therapy for bladder cancer increases in Canada and elsewhere, biomarkers to guide this treatment are gaining importance. A retrospective biomarker analysis of two randomized trials (BC2001 and BCON) tested the ability of a 24-gene hypoxia signature derived from RNA expression profiling to predict two critical outcomes: 1) the benefit of concurrent chemotherapy in BC2001; and 2) the benefit from accelerated, hypofractionated delivery of the radiation in both trials.²⁷ This hypoxia signature has been previously demonstrated to predict benefit from the hypoxia-modifying combination of carbogen and nicotinamide,²⁸ which improved outcomes after radiation therapy in the BCON trial.²⁹ Combined analysis of BCON and BC2001 also demonstrated that moderate hypofractionation (55 Gy in 20 fractions) improves locoregional disease control with no adverse toxicity compared to conventional fractionation (64 Gy in 32 fractions).³⁰ The hypoxia signature was prognostic for OS but not locoregional disease control in the BC2001 trial;³¹ however, the signature was not predictive of benefits from the addition of concurrent chemotherapy. The benefit of hypofractionation compared to conventional fractionation was limited to patients with non-hypoxic tumors, as determined by the 24-gene hypoxia signature; however, this does not necessarily mean that these patients have worse outcomes with hypofractionation compared to conventional fractionation, and hypofractionation may still have benefits with respect to patient convenience and other secondary parameters. The authors conclude that hypoxic tumors should be treated with hypoxia modification, which they previously demonstrated.

Dr. Maria Jiang presented part II of the latest advances in urothelial cancer. Checkmate 274, a phase 3 trial, examined whether patients with resected high-risk, muscle-invasive urothelial cancer treated with adjuvant nivolumab for up to one year had a DFS advantage over placebo. The median DFS was 21.0 vs. 10.9 months (HR 0.70) in the ITT population, with median DFS not reached vs. 10.8 months (HR 0.53) in the PD-L1+ patient population;³² however, biomarkers remain an unmet need in this setting. Therefore, this update focused on tumor and immune features associated with DFS with adjuvant nivolumab.

Higher expression of pro-inflammatory genes (interferon γ and CD4), as determined by RNAseq, was associated with improved DFS in the nivolumab arm. Higher tumor mutation burden also showed a trend towards DFS benefit, while CD8 infiltration, as determined by immunohistochemistry, was prognostic but did not correlate with treatment outcomes. Despite these promising findings, validated, predictive biomarkers remain lacking for this setting.³³

In France, adjuvant nivolumab was approved by the European Medicines Agency (EMA) for PD-L1+ high-risk, resected, muscle-invasive urothelial cancer. A health economics study suggested that compared to surveillance, adjuvant nivolumab had an incremental cost-effectiveness ratio (ICER) of €17 413/life-year gained, and an incremental cost-utility ratio (ICUR) of €26 691/quality-adjusted life-year (QALY) gained.³⁴ This represented a cost-effective strategy, assuming a willingness to pay (WTP) threshold of €32 000/QALY; however, in Canada, where the approved indication is based on the ITT population, the ICER was much higher, at \$112 386 CAD/QALY (Canada's Drug and Health Technology Agency, CADTH). A drug price reduction of at least 56% would be required to achieve the WTP threshold compared to observation. Adjuvant chemotherapy remains the more cost-effective treatment option for patients who are eligible.³⁵

In metastatic urothelial cancer (mUC), the current standard first-line treatment for cisplatin-ineligible patients is 4–6 cycles of carboplatin-based chemotherapy (overall response rate [ORR] ~40%³⁶), followed by maintenance avelumab if there is no disease progression post-chemotherapy (median OS 21.4 months³⁷). EV103, a phase 1/2 trial, evaluated the combination of enfortumab vedotin plus pembrolizumab (EV + PEMBRO) and EV alone in the cisplatin-ineligible first-line setting. Cohort K presented at ESMO 2022 reported an ORR of 64.5% with EV + P and 45.2% with EV alone. Preliminary PFS at 12 months was 55.1% in the EV + PEMBRO group and 35.8% in the EV group. Followup for OS was immature. Grade ≥ 3 treatment-related adverse effects (TRAEs) were more common in the EV + PEMBRO group (63.2% vs. 47.9%), including rash (17.1% vs. 1.4%), most likely due to the overlapping skin toxicity of both agents. Overall, the combination of EV + PEMBRO represents a very promising first-line combination treatment. EV 302 is an ongoing phase 3 trial that will definitively test EV + PEMBRO against the current SoC. Further data is needed to define the optimal number of cycles of upfront EV, sequencing strategy and the true synergistic potential of this combination approach. Careful toxicity management and patient education will be critical to ensure safety in the real-world setting.

In mUC, PD-L1 expression varied depending on the assay used, based on data from the IMvigor 130 trial.³⁸ SP142, which uses a threshold of $\geq 5\%$ PD-L1 expression on immune cells, selected different patient populations than the 22C3 assay, which scores both immune and tumor cells using

a cutoff of $\geq 10\%$. The SP142 had better prognostic utility for patients with mUC who received first-line atezolizumab than 22C3. Overall, the definition of PD-L1 positivity varied depending on the assay used, and its predictive ability was inconsistent across studies.

Kidney cancer

Dr. Melissa Huynh presented updates on adjuvant trials in locoregional and completely resected oligometastatic (M1 NED) renal cell carcinoma (RCC). The PROSPER, ECOG-ACRIN EA8143 trial was the first phase 3 randomized trial of neoadjuvant immunotherapy in RCC. This trial investigated the efficacy of neoadjuvant and adjuvant nivolumab prior to surgery in clear cell and non-clear cell RCC patients with a high risk of recurrence.³⁹ At a median followup of 16 months, an interim efficacy analysis demonstrated no benefit of neoadjuvant and adjuvant nivolumab in the primary endpoint of RFS, and the study was terminated early for futility. This study may have had negative results for several reasons. Approximately 50% of patients had clinical T1 or T2, given that enrolment was based on a clinical or radiological diagnosis. Moreover, about 10% of patients ultimately did not undergo surgery, and 3% of the patients who did undergo surgery were not rendered disease-free, which automatically counted as an event on Day 1, favoring the null hypothesis.

IMmotion-010, a double-blind, randomized, placebo-controlled trial, examined adjuvant atezolizumab treatment in clear cell RCC (ccRCC) or RCC with a sarcomatoid component.⁴⁰ This population was similar, though not entirely identical, to the KEYNOTE-564 trial with adjuvant PEMBRO, which demonstrated a DFS benefit.⁴¹ The primary endpoint of IMmotion-010 was DFS in the ITT population.⁴² Median followup was 44 months, and the 24-month DFS was 67.3% in the adjuvant atezolizumab arm compared to 65% in the placebo arm. The median DFS by investigator was 57.2 months in the treatment arm vs. 49.5 months in the placebo arm, translating to a HR of 0.93. Similarly, there was no observed OS benefit, thus yielding another negative trial. The safety profile was consistent with other studies involving atezolizumab monotherapy.

Arm A of CHECKMATE-914, another double-blind, randomized, placebo-controlled trial, investigated the role of adjuvant nivolumab and ipilimumab in RCC with clear cell histology or sarcomatoid features.⁴³ Unlike the other two trials, the investigators did not include any M1 NED patients. While this combination immunotherapy was successful in the intermediate and poor-risk advanced RCC population,⁴⁴ it did not translate to a benefit in the high-risk localized RCC population. At a median followup of 37.0 months, the HR for DFS was 0.92, and the 24-month DFS rate was 76.4% for adjuvant nivolumab and ipilimumab compared to 74% for placebo. A formal OS analysis was not performed, given

the lack of DFS benefit. A subgroup analysis suggested some benefits for RCC patients with sarcomatoid features, although this comprised less than 5% of the total study population. Therefore, results should be interpreted with caution, and further study is warranted. There was a significant discontinuation rate of 43%, with 33% being secondary to study drug toxicity. The results from arm B of CHECKMATE-914, with adjuvant nivolumab monotherapy, are pending.

With three negative adjuvant immunotherapy RCC trials presented at ESMO 2022, KEYNOTE-564 remains the only positive study, with a 32% reduction in risk of disease recurrence or death, though OS data is not yet mature.⁴¹ It is unclear why adjuvant PEMBRO was met with success, whereas the other three did not have significant activity despite having similar mechanisms of action. Results from arm B of the CHECKMATE-914 trial, with adjuvant nivolumab monotherapy, and the RAMPART trial,⁴⁵ with adjuvant durvalumab and combination durvalumab with tremelimumab, are eagerly awaited.

Biomarker analyses are being conducted to help inform future adjuvant and neoadjuvant immunotherapy trials in the RCC with a high risk of recurrence setting. This is particularly important, given that many patients may be cured by surgery alone. Consequently, giving adjuvant therapy to all high-risk patients under the current risk stratification systems would unnecessarily expose many of them to the risks of drug toxicity. Therefore, there is an unmet need for improved biomarkers to identify patients who will benefit from adjuvant immunotherapy.

Dr. Lori Wood presented the latest findings in ccRCC. COSMIC-313 investigated the combination of ipilimumab and nivolumab plus either cabozantinib 40 mg a day or placebo in the first-line setting in advanced ccRCC.⁴⁶ Intermediate- and poor-risk International Metastatic RCC Database Consortium (IMDC) patients were included in the study, with PFS as the primary endpoint. The trial met its primary endpoint, where median PFS was not reached in the initial ITT population compared to 11.3 months in the control arm. Significance was seen in the intermediate-risk patients but not in the poor-risk patients. The response rates were 43% in the triplet therapy arm compared to 36% in the control arm. The primary progression rate was lower with triplet therapy, at 8%, compared to 20% in the placebo arm; however, toxicity was higher in the triplet arm (especially liver toxicity), which resulted in treatment cessation (of at least one of the drugs) in 45% of patients on triplet therapy. Although this was the first positive triplet phase 3 study where the primary endpoint was met, implications for current and future clinical practice remain unclear without OS data, which remains immature. Significant toxicity and a high percentage of steroid use, both of which impact quality of life, remain concerning. If OS data is not favorable, triplet therapy may not necessarily become the new SoC.

CLEAR, a phase 3 trial, compared PEMBRO and lenvatinib (PEMBRO + LEN) vs. sunitinib (SUN) in the first-line ccRCC advanced disease setting.⁴⁷ The updated primary endpoint, PFS, was 23.3 months with PEMBRO + LEN compared to 9.2 months with SUN (HR 0.42). This benefit was seen in all IMDC risk groups. The OS was not yet reached in either arm, but the HR was 0.72 in intermediate- and poor-risk patients. The response rate was 71% and complete response (CR) was 17.2% with PEMBRO + LEN compared to 36.1% and 4.2%, respectively, with SUN. These are clinically meaningful results, with the highest CR rates reported to date. This combination is now Health Canada-approved, and in July 2022, CADTH and the Expert Review Committee recommended reimbursement; however, LEN has a long half-life, which can become an issue given the overlapping toxicities of LEN and PEMBRO. Therefore, more real-life data within the clinical setting is required.

LITESPARK-004 was a phase 2 study in patients with a germline von Hippel-Lindau (VHL) alteration. Patients had to have at least one measurable RCC tumor of less than 3 cm not requiring immediate surgery.⁴⁸ All patients were given belzutifan (an inhibitor of hypoxia-inducible factor 2 alpha), and the primary endpoint was response rate. Results were positive, with 92% of patients experiencing a reduction in the target lesion size. The overall objective response rate by RECIST 1.1 criteria was 64%, with 7% having a CR, 57% having a partial response, and 34% having stable disease. Belzutifan treatment also resulted in a marked decrease in the number of surgical procedures patients required, not only for their kidney cancers but also for pancreatic tumors, central nervous system disease, adrenal lesions, retinal lesions, and epididymal cysts. This is a very promising drug for patients with VHL. Health Canada approval was granted in July 2022; however, it is important to note that this drug does have real toxicities, including hypoxia, as well as the most common toxicity, anemia (because HIF-2 α is involved in erythropoietin regulation) and thus will require expertise and close clinical followup.

Conclusions

The ESMO 2022 congress showcased the latest advances in cancer research and treatment, with innovations in genitourinary cancers highlighted by the CUA webinar. A consistent theme that emerged across GU cancers is the urgent need for prognostic and predictive biomarkers and early measures. Early biomarkers are vital for identifying patients who benefit most from therapy and can act as early indicators of treatment outcomes.

In prostate cancer, PSA levels and nodal status emerged as prognostic and predictive of outcomes in mCSPC. While in mCRPC, tumor genetics, such as BRCA and TP53 mutation status, were predictive of PARPi benefits. In patients under-

going radioligand therapy, rPFS has shown promise as an early endpoint indicator. Moreover, ADT was found to confer modest MFS benefits in the biochemical recurrence after radical prostatectomy setting in a treatment duration-dependant manner, while the addition of an ARAT to ADT improved outcomes in mCSPC. Lutetium continued to show promise in the treatment of mCRPC, as did PARPi, with patients with BRCA mutations demonstrating the most benefit.

In bladder cancer, a hypoxia gene signature showed some prognostic promise for OS but not locoregional disease control in patients treated with radiotherapy; however, it failed to predict chemotherapy outcomes. PD-L1 positivity was shown to be affected by the assay used, while validated, readily available predictive biomarkers remain lacking for adjuvant nivolumab. In the first-line metastatic setting, the combination of EV + PEMBRO represents a very promising treatment strategy warranting further investigation.

In kidney cancer, biomarkers are needed to help inform future adjuvant and neoadjuvant immunotherapy trials in the setting of RCC with a high risk of recurrence, as well as help identify patients who will benefit from adjuvant immunotherapy. Moreover, the three trials presented on adjuvant immunotherapy at ESMO 2022 had negative results, therefore KEYNOTE-564, with adjuvant PEMBRO, remains the only study positive for DFS.

Strong, reproducible, and reliable biomarkers remain a common unmet need in GU cancers.

Competing interests: Dr. Rendon has been an advisory board member for AbbVie, Amgen, Astellas, AstraZeneca, Bayer, Ferring, Janssen, and Sanofi; a speakers' bureau member for Astellas, Amgen, Bayer, Ferring, Janssen, and McKesson; and has participated in clinical trials supported by AAA, AbbVie, Amgen, Astellas, AstraZeneca, Ferring, Janssen, Myovant, Pfizer, Point, and Sanofi. Dr. Hotte has received grants (institutional) from Bayer, BMS, and Janssen; has been a consultant/advisory board member for and received honoraria from Astellas, AstraZeneca, Bayer, BMS, Eisai, Ipsen, Janssen, Merck, Pfizer, Roche, and SeaGen; and has participated in clinical trials supported by Astellas, AstraZeneca, Ayala, Bayer, BMS, Eisai, Exelixis, Janssen, Ipsen, Merck, Roche, Sanofi, SeaGen, and SignalChem. Dr. Morgan has been a consultant/advisory board member for Astellas, Bayer, Janssen, and TerSera. Dr. Black has been a consultant for AbbVie, Astellas, AstraZeneca, Bayer, BMS, EMD Serono, Ferring, Janssen, MDxHealth, Merck, Minogue, Nonagen, Nanology, Protara, QED, Roche, Sanofi, Sesen, STIMIT, Therelase, UroGen, and Verity; a speaker for Bayer, BioSynt, Pfizer, Sanofi, and TerSera; has participated in clinical trials supported by Roche; and holds a patent from Veracyte. Dr. Jiang has received consulting fees from EMD Serono, McKesson, and Pfizer; and has received honoraria from Janssen. Dr. Huynh has received honoraria from Knight Therapeutics Inc.; and has been an advisory board member for Astellas. Dr. Wood has been an advisory board member (with no personal financial compensation) for AstraZeneca, BMS, Ipsen, Merck, and Pfizer; and has received research funding (institutional) from AstraZeneca, BMS, Merck, Pfizer, and Roche.

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