Highlights in urologic cancer

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In recent years, innovations in renal, bladder and prostate cancer treatments have been introduced at a rapid pace. Every year, oncological societies had to update treatment guidelines according to new insights and results of large phase III trials. This article focuses on practice changing data from the 2019 ESMO congress in Barcelona, Spain.

PROSTATE CANCER

The treatment of prostate cancer (PC) has seen immense changes over the last years, both in early treatment of metastatic disease as in the treatment of (non-)metastatic castration refractory prostate cancer (CRPC) patients.

Two presentations tried to answer the question whether early salvage radiotherapy (RT) is superior to adjuvant RT. Delaying RT after biochemical recurrence (BR) has the potential to lower the total number of instances of RT, omitting RT in non-reoccurring patients. RADICALS-RT is a large multinational randomised trial comparing adjuvant RT (aRT) to salvage RT (sRT) in intermediate or high-risk patients.[1] Salvage RT was triggered when PSA ≥0.1 ng/ml or occurrence of 3 consecutive PSA rises. At this point, follow-up is too short to determine the main primary endpoint (freedom-from-distant metastases). At a median follow-up of 5 years, 62% of patients in the sRT arm still had not received RT and biochemical PFS was not statistically different between groups. When pooling data from three trials in this setting (RADICALS, GETUG-AFU 17 and RAVES), the event-free survival favours early sRT over aRT.[2] This aggregate seems to promote early sRT over aRT after surgery for intermediate and high-risk PC.

In treating metastatic hormone sensitive PC (mHSPC), consensus guidelines all state the addition of either abiraterone or docetaxel (ESMO guidelines 2018). For docetaxel, study results have been mixed as both the CHAARTED and GETUG 7 trial only showed a benefit in high volume (visceral metastases and/or ≥4 bone metastases [≥1 outside vertebral column or pelvis]) disease. A new analysis of the STAMPEDE trial was presented at ESMO 2019.[3] In this analysis, there was no evidence of heterogeneity of the docetaxel effect on OS or PFS between low- and high-volume disease. This means that the addition of docetaxel to ADT in HSPC does improve OS, regardless of metastatic burden. However, metastatic burden is highly prognostic. In practice, the benefit of around 10% in OS at a median follow-up of 6.5 years in the high-volume group and 15% in the low-volume group, should be used to guide patients towards the right treatment. Another analysis of the STAMPEDE data was presented by James *et al.* In M0 HSPC, after RT of the primary tumour, docetaxel did not show an additional benefit in survival. Docetaxel did however improve the failure-free survival (FFS) and PFS.

STOPCAP pooled data from the HORRAD and STAMPEDE trials in a meta-analysis investigating the benefit of local RT in metastatic PC.[4] In the total population, no OS benefit of adding local RT to systemic treatment (ADT) was detected. However, in patients with <5 bone metastases the pooled results showed a 7% improvement in the OS rate at 3-years. RT can be recommended in low volume M1 disease in HSPC. Surgery of the prostate is currently being studied in this setting (LoMP 2 trial, among others).

In a similar fashion as with docetaxel in STAMPEDE, data on

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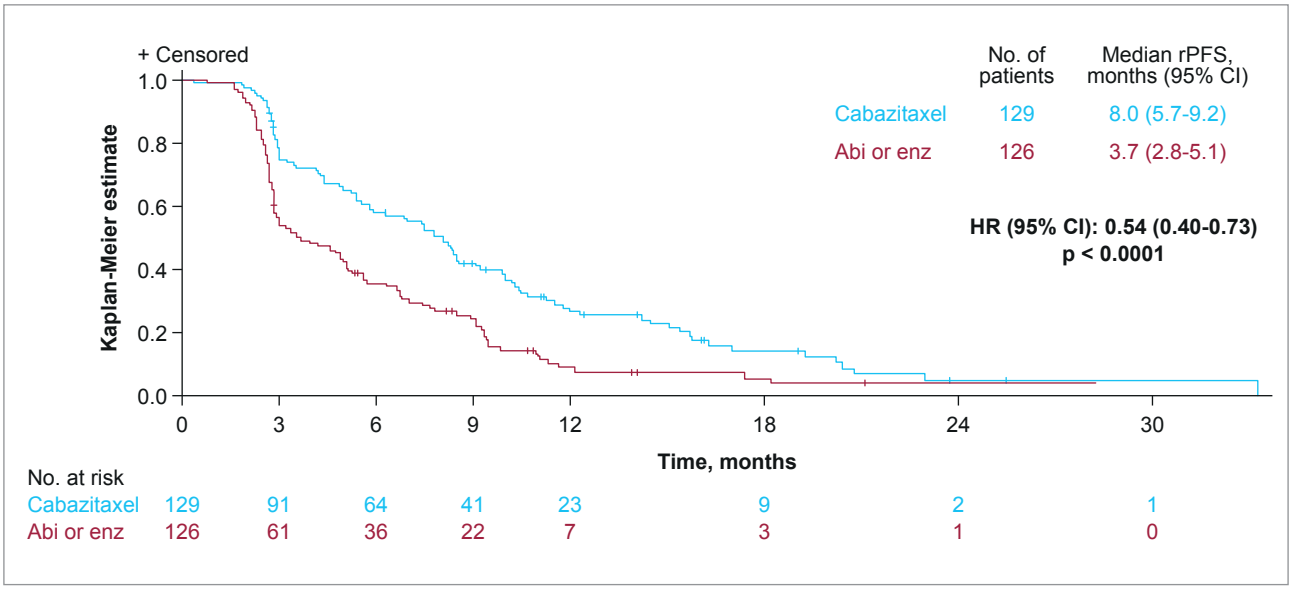

FIGURE 1. Progression-free survival in the CARD trial.[13]

Abi, abiraterone; Enz, enzalutamide; rPFS, radiologic tumour progression (RECIST 1.1) and/or progression of bone lesions (PCWG2) and/or death from any cause.

enzalutamide in HSPC from the recently published ARCHES trial[5] were analysed in function of disease volume. In the overall population, the primary endpoint of radiographic PFS (rPFS) was highly positive (HR[95%CI]: 0.39[0.30-0.50]). This benefit in favour of enzalutamide was seen in patients with both low- and high-volume disease and in patients with low- or high-risk disease. Enzalutamide in combination with ADT demonstrated significant treatment benefit *vs.* placebo plus ADT in men with mHSPC, irrespective of disease volume and risk.

Health related QoL (HRQoL) was analysed from both the ENZAMET and TITAN trial.[6,7] The recently published ENZAMET trial showed a benefit of enzalutamide *vs.* placebo in mHSPC (only in the non-docetaxel treated subgroup).[8] The TITAN trial showed a similar benefit with apalutamide.[9] Treatment exposure in this setting is very long and thus HR QoL data are very important (as are studies looking at the cost and the effect of successive therapies on outcome). Deterioration-free survival (which combined death, clinical progression, cessation of study therapy or worsening of HR QoL) was strongly in favour of enzalutamide for physical function, cognitive function, fatigue, global health and QoL. In TITAN, the addition of apalutamide did not increase the incidence or severity of fatigue and preserved the HRQoL. In conclusion, overall HR QoL was preserved with the addition of both apalutamide and enzalutamide to ADT in patients with mHSPC.

The results of the SPARTAN study, comparing apalutamide to placebo in m0CRPC, were published earlier this year.[10] Apalutamide improved the metastasis-free survival (MFS), but the OS results were immature at the time (only 24% of needed events occurred). Updated results after a median follow-up of 41 months were presented at ESMO 2019.[11] Importantly, patients in the placebo group who did not progress at the time of unblinding, were allowed to cross-over to apalutamide (76 patients). The median OS was not reached in both groups, the 4-year OS is 72.1 % in the apalutamide group (806 patients) as compared to 64.7% in the placebo group (401 patients), resulting in a 7.4% benefit (HR[95%CI]: 0.75[0.59-0.96]), which was not statistically significant. Other efficacy endpoints showed a strong benefit in PFS2 (time from randomisation to disease progression on subsequent anti-cancer therapy or death), while the median time to initiation of chemotherapy was still not reached. As such, this second analysis failed to show a significant OS benefit for apalutamide in the m0 CRPC setting. Moreover, new imaging technologies (especially PSMA PET/CT) are limiting the targeted population of this trial.[12]

The CARD trial, a very interesting study on third-line therapy, was presented at the presidential session of the ESMO 2019 conference and was published simultaneously online.[13] Cabazitaxel was tested against AR-targeted therapies (abiraterone or enzalutamide) in mCRPC patients progressing after docetaxel and the alternative AR-targeting agent (ARTA). Previous treatment with docetaxel or abiraterone was allowed in the hormone sensitive setting. Patients previously treated with ≥3 cycles of docetaxel and progressing within 12 months of first ARTA treatment were included in the tri-

al. The primary endpoint of rPFS was significantly longer in the cabazitaxel group, 8.0 months *vs.* 3.7 months (HR[95%-CI]: 0.54[0.40-0.73]) *(Figure 1)*. This benefit was positive in all sequences (docetaxel first, ARTA second and ARTA first, docetaxel second). Secondary endpoints also favoured cabazitaxel, with an OS benefit of 2.6 months (13.6 *vs.* 11.0) and a PSA response in 36% of patients in the cabazitaxel group *vs.* 14% in the ARTA group. A clinically meaningful reduction in pain (≥30%) was seen in almost half of the cabazitaxel patients (45% *vs.* 19%). One out of three patients in the ARTA group received cabazitaxel subsequently. In total, 20% of patients had to discontinue cabazitaxel due to an adverse event, *vs.* 9% in the ARTA group. These results support the use of cabazitaxel over abiraterone and enzalutamide in mCRPC patients who received prior docetaxel and the alternative ARTA.

Main drivers of resistance to CRPC therapy are the existing (germline) or appearing (somatic) alterations in homologous recombination repair (HRR) genes. The reported prevalence of HRR alterations in CRPC range from 5 to 20%. More than 4,000 patients were screened in the PROfound trial.[14] Out of the 69% of patients with successful sequencing of HRR status, 788 patients were positive (27.9% of sequenced samples, 17% of total screened). Especially *BRCA 2* (8.7%), *ATM* (5.9%) and *CDK12* (6.3%) were prevalent.

The PROfound trial is a phase III study of olaparib *vs.* ARTA (enzalutamide or abiraterone by physician's choice) in mCRPC patients with HRR alterations. Cohort A included *BRCA 1* and *2* and *ATM* alterations, cohort B all the other alterations. About one out of four included patients were metastatic, around 65% received prior taxane therapy and all patients received a form of ARTA (20% received both enzalutamide and abiraterone prior to inclusion). The primary endpoint of rPFS was superior in olaparib treated patients in cohort A (7.4 *vs.* 3.6 months, HR[95%CI]: 0.34 [0.25-0.47]). Also when combining cohort A and B, the rPFS remained in favour of olaparib (5.8 *vs.* 3.5 months). Median OS benefited olaparib in cohort A (19 *vs.* 15 months, HR[95%CI]: 0.64[0.43-0.97]) as well as in cohort A+B (18 *vs.* 14 months, HR[95%CI]: 0.67[0.49-0.93]). In a subgroup analysis, responses differed greatly between different HRR alterations, namely *BRCA2* patients benefited more and *ATM* patients less.

In patients with mCRPC and HRR alterations and prior ARTA treatment, olaparib improves rPFS and ORR compared to the re-introduction of ARTA, with a favourable trend for OS.

BLADDER CANCER

Treatment guidelines state the use of cisplatin based polychemotherapy before local therapy in muscle invasive bladder cancer (MIBC, ≥cT2). However, neo-adjuvant cisplatin polychemotherapy results in only a limited survival benefit (around 10%). Moreover, about half of patients are cisplatin ineligible (mainly due to renal dysfunction) and currently do not receive systemic treatment in the curative setting.

NABUCCO is a Dutch phase Ib single arm study which accrued cisplatin ineligible patients (or patients who refused cisplatin) with a good performance status and cT3-4 and/or N1-3 M0 and resectable urothelial cancer.[15] Patients were given a short course of combination immunotherapy (cycle I: ipilimumab (3mg/kg); cycle II: ipilimumab (3mg/kg) and nivolumab (1mg/kg); cycle III: nivolumab (1mg/kg)) before surgery. The primary endpoint was feasibility of surgery within 12 weeks after completion of neo-adjuvant treatment. Twenty-four patients were included, of which 42% had nodal involvement. Surgical resection within 12 weeks of neo-adjuvant treatment completion was achieved in 96%. Overall, 75% of patients received all three cycles of immunotherapy. The pathological complete response rate (pCR) was 46%, but only 17% in patients who received only 2 cycles of neo-adjuvant treatment. No radiological progression was observed during treatment, one patient died on study due to development of metastatic disease after surgery. This study shows the feasibility of immune therapy in the neo-adjuvant setting. Currently, various studies are recruiting patients: Aurora is a Belgian trial studying a combination of IO and chemotherapy in a similar patient population.[16] Response rates in NABUCCO are high and similar to cisplatin polychemotherapy[15], toxicity profiles are different but in cisplatin ineligible patients neo-adjuvant immunotherapy seems to be a good alternative.

In the PURE-01 study (NCT02736266), neo-adjuvant pembrolizumab resulted in 42% of pCR in MIBC.[17] Biomarker analyses suggest that immunological markers and a high tumour mutational burden (TMB) may predict higher response rates. In a new analysis presented at ESMO, genomic *FGFR-3* mutations were analysed in the, still recruiting, PURE-01 expanded cohort (405 patients) and an addition of 415 patients from the GRID registry (NCT02609269). About 20% of patients harboured *FGFR-3* mutations (in concordance with earlier studies), but the genomic signature did not predict pathological response. In contrast, tumours with active *FGFR3* signalling did show a lower immune signature (Immune190 score) and could be predictive for IO resistance.

In metastatic and locally advanced bladder cancer, IO therapy is reimbursed in first line (cisplatin ineligible patients with a high immune score) and in second line (after platinum-based chemotherapy). IMVIGOR 130 studied the possible benefit of combining atezolizumab to chemotherapy *vs.* chemotherapy alone in first line mUCC patients.[18] In a mandated amendment, an option of atezolizumab in monotherapy was added. Results after a follow-up of about one year

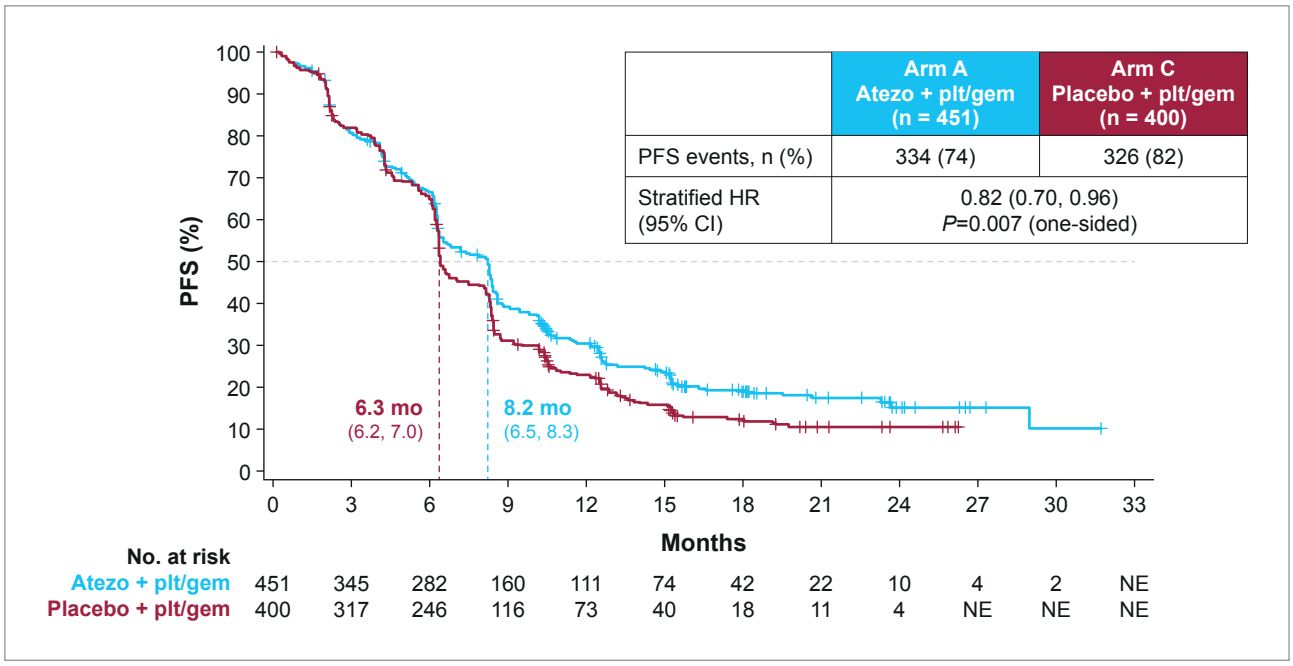

FIGURE 2. Final PFS analysis in the phase III IMvigor130 trial.[18]

were presented at ESMO. The co-primary endpoint of PFS was higher in the combination group *vs.* chemotherapy alone (HR[95%CI] 0.82[0.70-0.96]) (*Figure 2*) but OS failed to reach a significant benefit (HR[95%CI]: 0.83[0.69-1.00]). Surprisingly, only half of the patients initially considered to be cisplatin eligible, received cisplatin polychemotherapy. When comparing atezolizumab monotherapy to chemotherapy, no OS benefit was reached (HR[95%CI]: 1.02[0.83-1.24]). The ORR was 47% in the combination group, 23% with atezolizumab monotherapy and 44% in the chemotherapy group. A CR was observed in 13, 6 and 7% of patients, respectively. In conclusion, a short course of chemotherapy at the start of first-line chemotherapy can prolong response to atezolizumab but does not benefit OS after one year of follow-up. Only longer follow-up can determine if the combination strategy is superior to sequential therapy, as is currently reimbursed. The use of IO in patients with auto-immune (AI) disease is a common concern. The SAUL trial is a phase IIIb trial in patients who are mostly excluded from earlier IO trials.[19] Of the more than 1,000 patients included in this trial, only 35 were AI patients. Efficacy of IO in these patients seemed similar to other patients. Safety evaluation showed a higher rate of colitis which was manageable and rarely led to treatment discontinuation.

Enfortumab vedotin (EV) is an investigational antibody-drug conjugate targeting nectin-4, which is highly expressed in UCC. Phase II trials have shown activity in second- and third-line mUCC and several phase III trials are currently recruiting patients. At ESMO 2019, results were presented of expansion cohorts of EV-103, a phase IB study of EV in combination with pembrolizumab in first-line cisplatin ineligible patients with locally advanced and metastatic UCC.[20] EV was given in a 3-week schedule (day 1 and 8, 1.25mg/kg) with pembrolizumab on day 1 (200 mg fixed dose). A total of 45 patients were included. Response rates are very encouraging (ORR of 71% and CR 13%). Half of the patients experienced peripheral neuropathy and rash while about 10% experienced hyperglycaemia.

Finally, BISCAY, an adaptive, biomarker driven, study in mUCC of durvalumab in combination with various targeted therapies did not show positive results.[21] Biomarkers included *FGFR3* mutations and *HRR* gene alterations among others. Patients harbouring *FGFR 1-3* alterations received FGF-R inhibitor therapy or a combination of an FGFR inhibitor and durvalumab. *ATM*, *BRCA1/2* and other *HRR* genes received a PARP inhibitor and durvalumab. *RICTOR*, *TSC1*, *TSC2* received a TORC1-2 inhibitor in combination with durvalumab and patients with an absence of biomarkers were treated with durvalumab monotherapy. The predicted ORR was estimated to be >55%. However, the observed response rates were much lower (20 to 36%) and dose reduction and interruptions were very frequent. Presence of biomarkers could be more prognostic than predictive in this setting.

RENAL CELL CANCER

Localised renal cell cancer (RCC) is treated primarily with surgical resection while conservative techniques such as stereotactic radiotherapy, radiofrequent ablation or cryo-abla-

tion are used to a lesser extent. Recurrence rates in high risk (Fuhrman grade >III, pT3a-4, node positive disease) RCC are high and multiple studies have investigated adjuvant treatment strategies. Unfortunately, none of them have been able to show a benefit in OS.

The SORCE trial studied adjuvant sorafenib in intermediate or high risk RCC.[22] This randomised double-blind phase III trial, recruited 1,711 patients who received three years of placebo, one year of sorafenib and two years placebo or three years of sorafenib treatment. Around 15% of included patients had non-clear cell RCC histology and less than 5% had nodal involvement at pathological staging. The primary endpoint of DFS was similar in all groups (67% at five years). Active surveillance remains the standard in intermediate and high risk of recurrence following nephrectomy.

In metastatic RCC (mRCC) the treatment landscape has changed dramatically over the last years. Four combination trials have shown benefit over sunitinib in first-line, and these combinations will be included in new treatment guidelines (IMmotion151, JAVELIN Renal 101, KEYNOTE-426 and CheckMate 214). However, the question remains how to better tailor these combinations to patients. In Belgium, the combination of nivolumab and ipilimumab has become available in first-line intermediate and poor prognosis patients. However, side effects of this combination are feared, and its use varies from centre to centre. TITAN-RCC is a multicentre European study that enrolled 258 first- and second-line mRCC patients (intermediate and poor risk).[23] Patients were started on nivolumab (240mg, fixed dose) for eight or sixteen weeks (four or eight cycles). When early (week 8) PD or either SD or PD at sixteen weeks was observed, patients were given two to four cycles of nivolumab plus ipilimumab, followed by nivolumab monotherapy in maintenance. In total, 108 first-line patients were included, as well as 99 second-line patients. At 36 weeks, the ORR of this tailored approach was 29% (nivolumab only) and 37% (nivolumab with ipilimumab boost if non-responding) in first-line and 18% and 28% in second-line, respectively. In patients progressing under initial nivolumab, boost therapy did not show CR in first-line and only in five patients in second-line (of total of 57 patients). In conclusion, the use of ipilimumab as add-on or boost therapy during nivolumab increased ORR by 10%, both in first- and second-line setting. However, CR rates are lower in this approach when compared to initial combination therapy (CheckMate 214).

A subgroup analysis of the JAVELIN Renal 101 trial of first-line avelumab and axitinib looked at the response of the primary renal tumour in mRCC.[24] The ORR of the primary tumour was seen in 33% in the combination group compared to only 11% in the sunitinib arm. The combination of avelumab and axitinib also resulted in a longer duration of response.

Another subgroup analysis of the JAVELIN Renal 101 trial looked at the efficacy in patients with sarcomatoid histology.[25] In total, 108 patients were randomised to combination therapy or sunitinib. PFS was strongly in favour of avelumab and axitinib (HR[95%CI]: 0.57[0.33-1.00]), and the 1-year OS was 83% in the combination group *vs.* 67% in sunitinib group. The ORR was more than double in the combination arm *vs.* the control arm (47% *vs.* 21%).

The phase II KEYNOTE-427 trial looked at pembrolizumab monotherapy in the first-line treatment of ccRCC (cohort A) and non-cc RCC (cohort B).[26] ORR differed highly between different groups in cohort B, ranging from 10% in chromophobe RCC and 42% in RCC with sarcomatoid features. In the whole of cohort B, PD-L1 status was highly predictive (ORR of 10% in CPS <1 and 35% in CPS ≥1). Response duration of ≥12 months was seen in 57% of patients. These promising results of pembrolizumab in first-line non-cc RCC, should be confirmed in a larger phase III trial.

REFERENCES

1. Parker C, Clarke NW, Cook A, et al. Timing of radiotherapy (RT) after radical prostatectomy (RP): First results from the RADICALS RT randomised controlled trial (RCT) [NCT00541047]. Ann Oncol. 2019;30(Suppl 5):LBA49_PR.

2. Vale CL, Brihoum M, Chabaud S, et al. Adjuvant or salvage radiotherapy for the treatment of localised prostate cancer? A prospectively planned aggregate data meta-analysis. Ann Oncol. 2019;30(Suppl 5):LBA48_PR.

3. James ND, Ingleby FC, Clarke NW, et al. Docetaxel for hormone-naïve prostate cancer (PCa): Results from long-term follow-up of non-metastatic (M0) patients in the STAMPEDE randomised trial. Ann Oncol. 2019;30(Suppl 5):855PD.

4. Burdett S, Boevé LM, Ingleby FC, et al. Prostate Radiotherapy for Metastatic Hormone-sensitive Prostate Cancer: A STOPCAP Systematic Review and Meta-analysis. Eur Urol. 2019;76:115-24.

5. Armstrong AJ, Szmulewitz RZ, Petrylak DP, et al. ARCHES: A Randomized, Phase III Study of Androgen Deprivation Therapy With Enzalutamide or Placebo in Men With Metastatic Hormone-Sensitive Prostate Cancer. J Clin Oncol. 2019;doi:10.1200/JCO.19.00799 [Epub ahead of print].

6. Stockler MR, Martin AJ, Dhillon H, et al. Health-related quality of life (HRQL) in a randomized phase III trial of enzalutamide with standard first-line therapy for metastatic, hormone-sensitive prostate cancer (mHSPC): ENZAMET (ANZUP 1304), an ANZUP-led, international, co-operative group trial. Ann Oncol. 2019;30(Suppl 5):LBA53.

7. Agarwal N, McQuarrie K, Bjartell A, et al. Patient-reported outcomes (PROs) from TITAN: A phase III, randomized, double-blind study of apalutamide (APA) versus placebo (PBO) added to androgen deprivation therapy (ADT) in patients (pts) with metastatic castration-sensitive prostate cancer (mCSPC). Ann Oncol. 2019;30(Suppl5):851PD.

8. Davis ID, Martin AJ, Stockler MR, et al. Enzalutamide with Standard First-Line Therapy in Metastatic Prostate Cancer. N Engl J Med. 2019;381:121-31.

9. Chi KN, Agarwal N, Bjartell A, et al. Apalutamide for Metastatic, Castration-Sensitive Prostate Cancer. N Engl J Med. 2019;381:13-24.

10. Small EJ, Saad F, Chowdhury S, et al. Apalutamide and overall survival in non-metastatic castration-resistant prostate cancer. Ann Oncol. 2019;doi:10.1093/annonc/mdz397 [Epub ahead of print].

11. Smith MR, Saad F, Chowdhury S, et al. Apalutamide (APA) and overall survival (OS) in patients (pts) with nonmetastatic castration-resistant prostate cancer (nmCRPC): Updated results from the phase III SPARTAN study. Ann Oncol. 2019;30(Suppl 5):843O.

12. Rowe SP, Macura KJ, Ciarallo A, et al. Comparison of Prostate-Specific Membrane Antigen-Based 18F-DCFBC PET/CT to Conventional Imaging Modalities for Detection of Hormone-Naïve and Castration-Resistant Metastatic Prostate Cancer. J Nucl Med. 2016;57(1):46–53.

13. de Wit R, de Bono J, Sternberg CN, et al. Cabazitaxel versus Abiraterone or Enzalutamide in Metastatic Prostate Cancer. N Engl J Med. 2019;doi:10.1056/NEJMoa1911206 [Epub ahead of print].

14. De Bono JS, Fizazi K, Saad F, et al. Central, prospective detection of homologous recombination repair gene mutations (HRRm) in tumour tissue from >4000 men with metastatic castration-resistant prostate cancer (mCRPC) screened for the PROfound study. Ann Oncol. 2019;30(Suppl 5):847PD.

15. Van der Heijden MS, van Dijk N, Smit L, et al. Pre-operative ipilimumab and nivolumab in locoregionally advanced, stage III, urothelial cancer (NABUCCO). Ann Oncol. 2019;30(Suppl 5):904PD.

16. www.clinicaltrials.gov

17. Necchi A, Anichini A, Raggi D, et al. Pembrolizumab as Neoadjuvant Therapy Before Radical Cystectomy in Patients With Muscle-Invasive Urothelial Bladder Carcinoma (PURE-01): An Open-Label, Single-Arm, Phase II Study. J Clin Oncol. 2018;doi: 10.1200/JCO.18.01148 [Epub ahead of print].

18. Grande E, Galsky M, Arranz Arija JA, et al. IMvigor130: Efficacy and safety from a phase III study of atezolizumab (atezo) as monotherapy or combined with platinum-based chemotherapy (PBC) vs placebo + PBC in previously untreated locally advanced or metastatic urothelial carcinoma (mUC). Ann Oncol. 2019;30(Suppl 5):LBA14_PR.

19. Loriot Y, Sternberg CN, Castellano Gauna D, et al. Safety and efficacy of atezolizumab (atezo) in patients (pts) with autoimmune disease (AID): Subgroup analysis of the SAUL study in locally advanced/metastatic urinary tract carcinoma. Ann Oncol. 2019;30(Suppl 5):922P.

20. Hoimes CJ, Rosenberg JE, Srinivas S, et al. EV-103: Initial results of enfortumab vedotin plus pembrolizumab for locally advanced or metastatic urothelial carcinoma. Ann Oncol. 2019;30(Suppl 5):901O.

21. Powles T, Balar A, Gravis G, et al. An adaptive, biomarker directed platform study in metastatic urothelial cancer (BISCAY) with durvalumab in combination with targeted therapies. Ann Oncol. 2019;30(Suppl 5):902O.

22. Eisen TQ, Frangou E, Smith B, et al. Primary efficacy analysis results from the SORCE trial (RE05): Adjuvant sorafenib for renal cell carcinoma at intermediate or high risk of relapse: An international, randomised double-blind phase III trial led by the MRC CTU at UCL. Ann Oncol. 2019;30(Suppl 5):LBA56.

23. Grimm MO, Schmidinger M, Duran Martinez I, et al. Tailored immunotherapy approach with nivolumab in advanced renal cell carcinoma (TITAN-RCC). Ann Oncol. 2019;30(Suppl 5):LBA57.

24. Albiges L, Rini BI, Haanen JBAG, et al. Primary renal tumour shrinkage in patients (pts) who did not undergo upfront cytoreductive nephrectomy (uCN): Subgroup analysis from the phase III JAVELIN Renal 101 trial of first-line avelumab + axitinib (A + Ax) vs sunitinib (S) for advanced renal cell carcinoma (aRCC). Ann Oncol. 2019;30(Suppl 5):908PD.

25. Choueiri K, Larkin JMG, Pal SK, et al. Efficacy and biomarker analysis of patients (pts) with advanced renal cell carcinoma (aRCC) with sarcomatoid histology (sRCC): Subgroup analysis from the phase III JAVELIN renal 101 trial of first-line avelumab plus axitinib (A + Ax) vs sunitinib (S). Ann Oncol. 2019;30(Suppl 5):910PD.

26. Suárez C, Lee JL, Ziobro M, et al. First-line pembrolizumab (pembro) monotherapy for advanced non-clear cell renal cell carcinoma (nccRCC): Updated follow-up for KEYNOTE-427 cohort B. Ann Oncol. 2019;30(Suppl 5):948P.