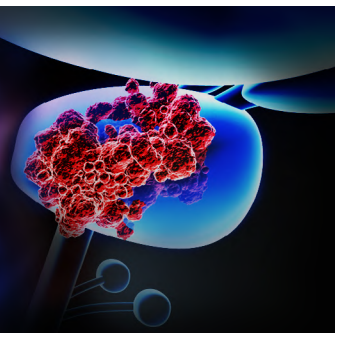
ASCO 2025
Conference Review™
Focus on Prostate Cancer



Making Education Easy

20 May to 3 June, 2025

In this review:

Abbreviations used in this review:

AAP = abiraterone acetate + prednisone; **ADC** = antibody-drug conjugate; **ADT** = androgen deprivation therapy; **ALT** = alanine aminotransferase; **AST** = aspartate aminotransferase; **ARPi** = androgen receptor pathway inhibitor; **CRPC** = castration-resistant prostate cancer; **ECOG PS** = Eastern Cooperative Oncology Group Performance Status; **HR** = hazard ratio; **HRR** = homologous recombination repair; **ICANS** = immune effector cell-associated neurotoxicity syndrome; **NE** = not estimable; **OR** = odds ratio; **ORR** = objective response rate; **OS** = overall survival; **PARP(i)** = poly (ADP-ribose) polymerase inhibitor; **(r)PFS** = (radiographic) progression-free survival; **PSA** = prostate-specific antigen; **PSMA** = prostate-specific membrane antigen; **(TR)AE** = (treatment-related) adverse event.

RESEARCH REVIEW™
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Welcome to our review of the 2025 ASCO Annual Meeting held in Chicago, USA.

This year's meeting featured several important updates in prostate cancer research. We begin with a phase 1/2 trial which described the promising efficacy and safety of a novel B7H3 ADC in patients with heavily pretreated metastatic CRPC. This is followed by an updated 5-year analysis of the ARCHES trial which revealed that enzalutamide plus ADT continued to prolong OS in patients with metastatic hormone-sensitive prostate cancer, including those with high-volume disease. Another fascinating presentation found that PTEN inactivity was associated with significantly improved OS in patients with metastatic prostate cancer receiving docetaxel plus ADT, suggesting the potential utility of PTEN inactivity as a predictive biomarker.

I hope you find these and the other abstracts in this review interesting and informative. I look forward to reading your comments. Detailed abstracts are available online here.

Kind Regards,

Associate Professor Arun Azad
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DB-1311/BNT324 (a novel B7H3 ADC) in patients with heavily pretreated castrate-resistant prostate cancer (CRPC)

Speaker: Andrew Ohyama Parsonson (Macquarie University, Sydney, Australia)

Summary: DB-1311/BNT324 is an investigational B7H3 antibody-drug conjugate (ADC) which has been granted FDA Fast-Track Designation for patients with previously treated castration-resistant prostate cancer (CRPC). This phase 1/2 trial enrolled 393 patients across Australia, East Asia and the US with advanced/metastatic solid tumours, including 65 patients with previously treated CRPC (median age 71 years; range 45–84; 71% ECOG PS 1; 29% bone-only disease; 28% ≥5 prior lines). Patients were randomly assigned to receive DB-1311/BNT324 at doses of either 6mg/kg or 9mg/kg every 3 weeks until progression/toxicity. In the group of 43 evaluable patients, the ORR (primary endpoint) was 27.9% (partial response n=12; stable disease n=29), with a disease control rate of 95.3%, and the median duration of response was not reached. At a median follow-up of 5.7 months, median rPFS was 8.3 months (n=57) and the 6-month rPFS rate was 86.6%. Responses were generally consistent regardless of dosing arm, number of prior lines or type of prior treatment; however, patients with previous PARPi exposure had a lower ORR (16.7%). Andrew Parsonson commented that DB-1311/BNT324 had a manageable safety profile. The rates of discontinuations in the 6mg/kg and 9mg/kg arms were 6.2% and 5.9%, respectively, and haematological TRAEs occurred more frequently in the 9mg/kg dosing arm.

Comment: ADCs are standard of care drugs for several malignancies. B7H3 is uniformly expressed in prostate cancer and therefore is an excellent target for ADCs. In this phase 1/2 trial in heavily pre-treated metastatic CRPC patients, DB-1311/BNT324 (a B7H3 ADC with a topoisomerase-I payload) had encouraging efficacy with an ORR of 28% and median rPFS of 8.3 months. Treatment was well-tolerated with discontinuations from treatment occurring in only 6% of patients. With several other B7H3 ADCs in clinical development for prostate cancer, these data are promising and may herald a new class of treatments for patients.

Abstract #5015
Abstract

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Independent commentary by Associate Professor Arun Azad

Associate Professor Arun Azad is a medical oncologist and translational researcher based at Peter MacCallum Cancer Centre and University of Melbourne with a subspecialist interest in urological malignancies.

ARCHES: 5-year follow-up overall survival (OS) analysis of enzalutamide (ENZA) plus androgen-deprivation therapy (ADT) in patients (pts) with metastatic hormone-sensitive prostate cancer (mHSPC)

Speaker: Andrew J Armstrong (Duke University School of Medicine, North Carolina, US)

Summary: Previous data from the final OS analysis of the phase 3 ARCHES trial (median follow-up 44.6 months) demonstrated significant improvements in OS with enzalutamide plus androgen-deprivation therapy (ADT) versus ADT in patients with metastatic hormone-sensitive prostate cancer (HR 0.66; 95% CI 0.53–0.81; p<0.0001). In this session, Andrew Armstrong presented the updated analysis of long-term OS from >5 years of follow-up (cut-off July 31, 2024). At a median follow-up of 61.4 months, patients who received enzalutamide plus ADT continued to show prolonged median OS versus ADT (not reached vs. not reached; HR 0.70; 95% CI 0.58–0.85; p=0.0003). The benefit in OS was observed across all clinically relevant subgroups, including those stratified by age, low-/high-volume disease and prior use of docetaxel. It was highlighted that patients with high-volume disease experienced a 36-month improvement in OS with enzalutamide plus ADT (83.1 vs. 47.6 moths; HR 0.70; 95% CI 0.56–0.88).

Comment: The treatment paradigm for metastatic hormone-sensitive prostate cancer has rapidly changed in the last decade, with ADT + androgen receptor pathway inhibitors (ARPis) now standard of care. This 5-year follow up from the ARCHES trial showed that the combination of ADT + enzalutamide led to excellent long-term outcomes in metastatic hormone-sensitive prostate cancer patients. The benefit from ADT + enzalutamide over ADT alone was seen in all subgroups. Of note, median OS in patients with high-volume disease treated with ADT + enzalutamide was 7 years, which is quite remarkable. These results reinforce enzalutamide as an excellent treatment option for patients with metastatic hormone-sensitive prostate cancer, irrespective of disease volume or metastatic status at diagnosis.

Abstract #5005
Abstract

Transcriptome classification of PTEN inactivation to predict survival benefit from docetaxel at start of androgen deprivation therapy (ADT) for metastatic prostate cancer (PC): An ancillary study of the STAMPEDE trials

Speaker: Emily Grist (University College London Cancer Institute, London, UK)

Summary: These researchers explored the predictive utility of PTEN activity signatures as biomarkers for OS in patients receiving treatment for metastatic hormone-sensitive prostate cancer. Prostate tumour samples were analysed from patients in the STAMPEDE trials randomised to ADT versus ADT plus docetaxel ± zoledronic acid, or ADT versus ADT plus abiraterone acetate plus prednisone. Transcriptome-wide profiles revealed that 50% of tumours (n=419) were PTEN-inactive, and the PTEN mRNA score distribution was relatively comparable across patients with high- and low-volume disease (p=0.310). Among patients who received ADT plus abiraterone acetate plus prednisone, PTEN inactivity was associated with significantly shorter OS (HR 1.56; 95% CI 1.06–2.31). There was a strong association between PTEN inactivation and sensitivity to docetaxel (p=0.002). Docetaxel was associated with improved OS in PTEN-inactive patients (HR 0.57; 95% CI 0.42–0.76), and this benefit was observed in PTEN-inactive patients with low-volume disease (HR 0.53; 95% CI 0.33–0.86) and high-volume disease (HR 0.59; 95% CI 0.39–0.88); no benefits were seen in PTEN-active patients. Researchers estimated that patients with PTEN-inactive and high Decipher tumours derived a 45% reduction in the risk of death with the addition of docetaxel to ADT (HR 0.55; 99% CI 0.34–0.89).

Comment: Predictive biomarkers to help treatment choice between ARPi drugs like abiraterone and docetaxel chemotherapy in metastatic hormone-sensitive prostate cancer could be highly useful in the clinic. In this study, gene expression profiling was performed on samples from the STAMPEDE trials. A PTEN inactivation signature was associated with less benefit from abiraterone. However, this same signature was linked to improved outcomes with docetaxel. These intriguing results are perhaps the most useful data regarding predictive biomarkers in metastatic hormone-sensitive prostate cancer. Independent validation in other large metastatic hormone-sensitive prostate cancer cohorts is planned, and may have clear implications for the use of triplet versus doublet therapy.

Abstract #5003
Abstract

Phase 1 study results of JNJ-78278343 (pasritamig) in metastatic castration resistant prostate cancer (mCRPC)

Speaker: Capucine Baldini (Drug Development Department [DITEP], Institut Gustave Roussy, Villejuif, France)

Summary: This was a first-in-human, phase 1 study of pasritamig (first-in-class T-cell-redirecting bispecific antibody) in patients with metastatic CRPC. At the time of data cut-off, 174 eligible patients (median age 69 years; range 36–89; median 4 prior therapies) had received ≥1 dose of pasritamig. Overall, pasritamig was very well tolerated. Although 82.2% of patients experienced ≥1 TRAE, these were predominantly mild, and 9.2% of patients experienced a grade ≥3 TRAE. There was one dose-limiting toxicity after 50mg step-up subcutaneous pasritamig (transient grade 3 ALT/AST elevation). In the recommended phase 2 dose safety population (n=45), the most frequent TRAEs were infusion-related reactions (22.2%; all grade 1–2), followed by fatigue (15.6%; all grade 1–2) and cytokine release syndrome (8.9%; all grade 1). There were no pasritamig-related deaths or TRAE-related discontinuations and no cases of ICANS. In the recommended phase 2 dose efficacy population (n=33), 42.4% of patients achieved PSA50, the median rPFS was 6.77 months (95% CI 2.89 to NE), and 39.4% of patients showed ongoing responses at the time of reporting. Among the 85 patients with measurable disease, those with lymph node (± bone) disease had an ORR of 16.1% (5/31), and those with visceral disease had an ORR of 3.7% (2/54); the median duration of response was 11.27 months (95% CI 3.59 to NE).

Comment: Pasritamig is a bispecific antibody that binds the CD3 receptor on T cells and KLK2, a protein expressed on prostate cancer cells, with limited normal tissue expression. In this first-in-human study in heavily pre-treated metastatic CRPC patients, pasritamig had promising activity with a PSA50 response rate of 42% and median rPFS of 6.8 months. Most importantly, treatment was very well tolerated in comparison with some other bispecific antibodies, with cytokine release syndrome only occurring in 8.9% of patients and all cases being grade 1 (mild). These data set the scene for several phase 3 trials of pasritamig.

Abstract #5017
Abstract

First-in-human results of terbium-161[^{161}Tb]Tb-PSMA-I&T radioligand treatment in patients with metastatic castration-resistant prostate cancer (VIOLET)

Speaker: James Patrick Buteau (Peter MacCallum Cancer Centre, University of Melbourne, Australia)

Summary: The aims of the single-centre, single-arm, phase 1/2 VIOLET study were to examine the safety and efficacy of [^{161}Tb]Tb-PSMA-I&T in patients with previously-treated metastatic CRPC. The study enrolled eligible patients (n=30; median age 69.0 years; range 66.0–74.8; median baseline PSA 26.9ng/mL) with progressive metastatic CRPC which had been previously treated with an ARPi, with or without taxane chemotherapy. No dose-limiting toxicities were observed, and 7.4GBq was identified as the maximum tolerated dose and the recommended phase 2 dose. Low rates of grade ≥3 TRAEs were reported (lymphopenia and pain flare only), and no treatment-related deaths occurred. Overall, 70% and 40% of patients achieved PSA50 and PSA90, respectively. The median PSA-PFS rate was 9.0 months (95% CI 5.7–15.1) and median rPFS was 11.1 months (95% CI 6.6–11.7).

Comment: Terbium-161 (^{161}Tb) is a new radionuclide that emits beta-radiation, but unlike lutetium-177 (^{177}Lu), it also emits high-energy, ultra-short, path-length Auger electrons. This may lead to better targeting of micrometastases, and in pre-clinical models, ^{161}Tb exhibited greater anti-tumour activity than ^{177}Lu. In this first-in-human study of metastatic CRPC patients treated with an ARPi ± a taxane, treatment with [^{161}Tb]Tb-PSMA-I&T was safe with no treatment-related deaths and no dose-limiting toxicities. Grade 3–4 AEs were uncommon. Importantly, there was impressive efficacy with a PSA50 response rate of 70%, median PSA-PFS of 9.0 months and median rPFS of 11.1 months. These data provide a platform for ongoing clinical development of this exciting agent.

Abstract #5010
Abstract

PBS information: Authority required for various advanced prostate cancer indications. Refer to www.pbs.gov.au and search 'XTANDI' for full authority information.

Please review full Product Information before prescribing, available from https://rss.medsinfo.com.au/ax/pi.cfm?product=axpxtand or by scanning the QR code.

SCAN QR CODE to see full XTANDI Product Information.

ADT=androgen deprivation therapy; ARPI = androgen receptor pathway inhibitor; BCR=biochemical recurrence; HSPC=hormone-sensitive prostate cancer; mHSPC=metastatic hormone-sensitive prostate cancer; nmHSPC=nonmetastatic hormone-sensitive prostate cancer.

References:

1. XTANDI (enzalutamide) Approved Product Information.
2. Zytiga (abiraterone) Approved Product Information.
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Phase 3 AMPLITUDE trial: niraparib (NIRA) and abiraterone acetate plus prednisone (AAP) for metastatic castration-sensitive prostate cancer (mCSPC) patients (pts) with alterations in homologous recombination repair (HRR) genes

Speaker: Gerhardt Attard (Cancer Institute, University College London, UK)

Summary: Previous data from the MAGNITUDE trial revealed significant improvements in rPFS with niraparib plus abiraterone acetate plus prednisone (AAP) in patients with HRR-altered metastatic CRPC. The double-blind, phase 3 AMPLITUDE trial examined the efficacy and safety of niraparib plus AAP in patients with HRR-altered metastatic castration-sensitive prostate cancer. Eligible patients (n=696; median age 68 years; 78% high-volume disease) with germline or somatic HRR gene alterations (*BRCA1*, *BRCA2*, *BRIP1*, *CDK12*, *CHEK2*, *FANCA*, *PALB2*, *RAD51B*, *RAD54L*) were randomly assigned 1:1 to niraparib plus AAP (n=348) or placebo plus AAP (n=348). At a median follow-up of 30.8 months (first interim analysis), patients in the niraparib plus AAP arm achieved significantly longer rPFS versus AAP alone (not reached vs. 29.5 months, respectively; HR, 0.63; 95% CI 0.49–0.80; p=0.0001). The prespecified subgroup of patients with *BRCA1/2* alterations (55.6%) experienced a particularly pronounced benefit in rPFS with niraparib plus AAP (HR 0.52; 95% CI 0.37–0.72; p<0.0001). Patients administered niraparib plus AAP also showed improvements in time to symptomatic progression (HR 0.50; 95% CI 0.36–0.69; p<0.0001; *BRCA1/2* HR 0.44; 95% CI 0.29–0.68; p=0.0001), and a trend towards improved OS (HR 0.79; 95% CI 0.59–1.04; p=0.10; *BRCA1/2* HR 0.75; 95% CI 0.51–1.11; p=0.15). The rates of grade ≥3 AEs in the niraparib plus AAP and AAP arms were 75.2% and 58.9%, respectively; the most common grade ≥3 AEs were hypertension (26.5% vs. 18.4%) and anaemia (29.1% vs. 4.6%). AE-related discontinuations occurred in 11.0% of patients in the niraparib plus AAP arm and in 6.9% of those in the AAP arm.

Comment: AMPLITUDE is the first trial to evaluate PARP inhibition in metastatic hormone-sensitive prostate cancer with alterations in HRR genes. The primary endpoint was reached with significantly longer rPFS favouring AAP + niraparib versus AAP. OS also favoured AAP + niraparib, but was not statistically significant. Grade 3–4 AEs were common in the AAP + niraparib arm, in particular anaemia and hypertension. These data establish the efficacy of niraparib in metastatic hormone-sensitive prostate cancer with HRR gene alterations, but whether this will lead to regulatory approval without an OS benefit is unclear. Toxicity management will also be vital in the real-world setting, as will monitoring for acute myeloid leukaemia/myelodysplastic syndromes with long-term PARPi use.

Abstract #LBA5006
Abstract

Exploratory analyses of homologous recombination repair (HRR) gene subgroups and potential associations with secondary efficacy endpoints in the HRR-deficient population from TALAPRO-2

Speaker: Stefanie Zschaebitz (National Center for Tumor Disease, Heidelberg University Hospital, Germany)

Summary: The TALAPRO-2 trial demonstrated a significant rPFS benefit with first-line talazoparib plus enzalutamide versus placebo plus enzalutamide in metastatic CRPC. These investigators conducted an exploratory analysis to determine whether efficacy differed between HRR gene subgroups in patients with HRR-altered tumours. Patients harbouring *BRCA2* alterations experienced significantly improved outcomes with talazoparib plus enzalutamide ([ORR 78.9% vs. 33.3%; OR 0.13]; [PFS2 not reached vs. 26.1 months; HR 0.44]; [PSA50 87.0% vs. 58.3%]; [time to PSA progression not reached vs. 9.2 months; HR 0.20]; [time to initiation of cytotoxic chemotherapy not reached vs. 17.0 months; HR 0.27]). These benefits were comparable across the *BRCA* cluster and *BRCA1* single gene groups, whereas the *PALB2* single gene and cluster groups derived slightly smaller benefits. The *CDK12* single gene group also showed improved outcomes with talazoparib plus enzalutamide ([ORR 70.0% vs. 28.6%; OR 0.17]; [PFS2 36.4 vs. 18.8 months; HR 0.29]; [PSA50 85.7% vs. 53.3%]; [time to PSA progression 13.8 vs. 11.1 months]), and similar results were seen in the *CDK12* cluster. Patients in the *ATM* single gene group only experienced numerical benefits in ORR (81.8% vs. 20.0%; OR 0.06), time to PSA progression (26.8 vs. 15.9 months; HR 0.61) and time to initiation of cytotoxic chemotherapy (not reached vs. not reached; HR 0.60). Patients in the *CHEK2* single gene group only experienced numerical benefits in PSA and time to initiation of cytotoxic chemotherapy.

Comment: TALAPRO-2 led to FDA approval of enzalutamide + talazoparib in metastatic CRPC with HRR gene alterations. In this exploratory biomarker analysis, the benefit of this combination was evaluated in individual HRR genes. As expected, benefit was seen in patients with alterations in *BRCA1*, *BRCA2* and *PALB2*. In keeping with prior reports, alterations in *CDK12* but not *CHEK2* also conferred benefit from enzalutamide + talazoparib. Perhaps surprisingly, *ATM* alterations were also associated with benefit. Of course, all of these individual gene analyses were underpowered and therefore hypothesis-generating only, and in my opinion, the clear PFS and OS benefits seen with enzalutamide + talazoparib in HRR-altered metastatic CRPC means that the combination should be used irrespective of any specific gene alteration.

Abstract #5019
Abstract

Lutetium-177-PSMA-617 in oligo-metastatic hormone sensitive prostate cancer (BULLSEYE trial)

Speaker: Bastiaan M Privé (Radboudumc, Nijmegen, The Netherlands)

Summary: BULLSEYE was an international, open-label phase 2 trial which randomly assigned 58 eligible patients with PSMA-expressing, recurrent, oligometastatic hormone-sensitive prostate cancer (median age 72 years; median baseline PSA 3.6) to [^{177}Lu]Lu-PSMA-617 (n=29) or standard of care deferred ADT (n=29). At a median follow-up of 7 months, patients who received [^{177}Lu]Lu-PSMA-617 achieved significantly longer median PFS (primary outcome) versus standard of care (not reached vs. 5 months; HR 0.07; 95% CI 0.02–0.19; p<0.001). There was a lower rate of progressive disease in the [^{177}Lu]Lu-PSMA-617 arm (38% vs. 93%), and 21% of [^{177}Lu]Lu-PSMA-617-treated patients achieved complete remission. The most frequent TRAEs were dry mouth (59%), fatigue (55%), nausea (48%) and bone marrow toxicity (24%–30%), all of which were grade 1 and resolved over time. Grade ≥2 AEs occurred in <15% of patients and were not considered to be clinically significant.

Comment: This small but important randomised phase 2 trial evaluated [^{177}Lu]Lu-PSMA-617 versus standard of care (i.e. deferred ADT) in PSMA-positive oligometastatic hormone-sensitive prostate cancer. The trial was clearly positive, with median PFS being not reached in the [^{177}Lu]Lu-PSMA-617 arm versus 5 months in the standard of care arm. Treatment was also well tolerated. These results indicate that [^{177}Lu]Lu-PSMA-617 may be a useful tool in delaying ADT, at least in some patients, but is the approach better than stereotactic ablative radiotherapy? Ongoing trials will address this question. Furthermore, many would argue that the standard of care in these patients is ADT + an ARPi rather than deferred ADT. Nevertheless, for patients wanting to defer ADT, [^{177}Lu]Lu-PSMA-617 or stereotactic ablative radiotherapy may be important and useful options.

Abstract #5009
Abstract

A multicenter, randomized, phase 2, investigator-initiated ETCTN trial of olaparib + radium-223 vs. radium-223 in men with castration-resistant prostate cancer (CRPC) with bone metastases (BM) (COMRADE)

Speaker: Rana R McKay (University of California San Diego, California, US)

Summary: In the phase 2 COMRADE trial, 120 patients with CRPC and bone metastases were randomly assigned to olaparib plus radium-223 (α-emitting radioisotope; n=61) or radium-223 alone (n=59). Overall, 96% of patients had prior ARPi exposure, 53% had previous use of docetaxel, 32% had nodal disease and 46% had more than 20 bone metastases. There was a significant improvement in median rPFS (primary endpoint) with olaparib plus radium-223 versus radium-233 (8.6 vs. 4.0 months; HR 0.51; 80% CI 0.37–0.70; p=0.005), and this rPFS benefit was observed among patients with HRR-positive tumours (HR 0.52; 80% CI 0.26–1.04) and HRR-negative tumours (HR 0.54; 80% CI 0.38–0.77). Grade ≥3 TEAEs occurred in 56% of patients administered olaparib plus radium-223 versus 35% of those in the radium-233 arm; the most frequent TEAEs were anaemia (22.0% vs. 18.0%), lymphocyte reductions (30.5% vs. 9.1%), platelet reductions (6.8% vs. 3.6%) and neutrophil reductions (5.1% vs. 7.3%).

Comment: Radium-223 has had somewhat of a resurgence in metastatic CRPC based on the PEACE-3 trial results. This randomised phase 2 trial showed that olaparib + radium-223 had significantly longer rPFS than radium-223 alone, and interestingly, the benefit was seen irrespective of HRR gene alteration status. There were more toxicities in the olaparib + radium-223 arm, but these were mainly asymptomatic laboratory abnormalities. Although I am not sure how this combination will proceed in clinical development given the very crowded therapeutic space in advanced prostate cancer, the results are nevertheless interesting, and provide further evidence that PARPis can have activity in HRR-negative prostate cancer.

Abstract #5007
Abstract

^{177}Lu-PSMA-617 with ipilimumab (ipi) and nivolumab (nivo) in metastatic castration-resistant prostate cancer (mCRPC): An investigator-initiated phase 2 trial (EVOLUTION; ANZUP2001)

Speaker: Shahneen Sandhu (Peter MacCallum Cancer Centre, University of Melbourne, Australia)

Summary: The objective of the phase 2 EVOLUTION trial was to evaluate the activity and safety of ipilimumab plus nivolumab plus [^{177}Lu]Lu-PSMA-617 in patients with metastatic CRPC. Eligible patients (n=93; median age 70 years; range 45–83; 100% prior ARPi; 80% prior docetaxel) were randomly assigned 1:2 to [^{177}Lu]Lu-PSMA-617 alone (n=30), or [^{177}Lu]Lu-PSMA-617 plus induction ipilumab and nivolumab, followed by maintenance nivolumab (n=57). Following four cases of treatment-related myocarditis in the [^{177}Lu]Lu-PSMA-617 plus ipilimumab/nivolumab arm (including one death due to myocarditis), recruitment was ceased early. Patients who received [^{177}Lu]Lu-PSMA-617 plus ipilimumab/nivolumab achieved significantly higher 12-month PSA-PFS versus [^{177}Lu]Lu-PSMA-617 alone (33% vs. 17%, respectively), although there was no between-group difference in median PSA-PFS (7.6 vs. 7.1 months; HR 0.70; 0.43–1.13). There was a substantially higher rate of grade 3–4 AEs in the [^{177}Lu]Lu-PSMA-617 plus ipilimumab/nivolumab arm (75% vs. 29%).

Comment: There is an urgent need to develop strategies that improve the durability of benefit seen with [^{177}Lu]Lu-PSMA-617. The EVOLUTION trial, sponsored by the ANZUP Cancer Trials Group, evaluated [^{177}Lu]Lu-PSMA-617 + ipilimumab and nivolumab versus [^{177}Lu]Lu-PSMA-617 in metastatic CRPC patients treated with a prior ARPi. [^{177}Lu]Lu-PSMA-617 + ipilimumab/nivolumab significantly improved PSA-PFS at 12 months, but no significant benefit was observed for other efficacy endpoints. Treatment with [^{177}Lu]Lu-PSMA-617 + ipilimumab/nivolumab was also associated with high rates (75%) of grade 3–4 AEs, which included four cases of myocarditis that led to early cessation of the trial. It is hard to see the combination of [^{177}Lu]Lu-PSMA-617 + ipilimumab/nivolumab moving forward in metastatic CRPC, given the modest efficacy benefit but clearly greater toxicity over [^{177}Lu]Lu-PSMA-617 alone.

Abstract #5016
Abstract