# 2015 EUROPEAN CANCER CONGRESS

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Vienna, Austria

## SUMMARY

The European Cancer Congress (ECC 2015) combined the 40th European Society for Medical Oncology (ESMO) congress with the 18th congress of the European CanCer Organisation (ECCO) and was held 25 to 29 September, 2015. The meeting was organised in partnership with the European Society of Radiation and Oncology (ESTRO), the European Society of Surgical Oncology (ESSO), the European Academy for Cancer Research (EACR), the European Oncology Nursing Society (EONS), and International Society of Paediatric Oncology (SIOPE). The efforts of all partner organisations were united to continue advancing multidisciplinarity as the way forward to optimise the prevention, diagnosis, treatment, and care of cancer patients by encouraging participants to leverage knowledge, promote education and build awareness for patient-centred oncology.

## Contents

## GENITOURINARY MALIGNANCIES

# Significantly improved overall survival with nivolumab compared with everolimus in previously treated advanced renal cell carcinoma: Results from CheckMate 025

Padmanee Sharma, MD Anderson Cancer Center, USA presented findings during the Presidential Session from the CheckMate 025 phase III clinical trial showing that nivolumab significantly prolongs overall survival (OS) in patients with advanced kidney cancer, who progressed after their first treatment. CheckMate 025 compared nivolumab with the standard treatment, everolimus, in patients with clear cell renal cell carcinoma. This is the first trial to show improved OS in these patients for any immune checkpoint inhibitor drug; which target molecules playing a role in the immune system's ability to recognise and attack tumours; specifically, nivolumab blocks the interaction between the programmed cell death protein 1 (PD-1) and its ligand PD-L1.

Between October 2012 and March 2014, the trial enrolled 821 patients with advanced clear cell kidney cancer, or metastatic renal cell carcinoma who had received 1 to 2 prior anti-angiogenic therapies and ≤3 systemic therapies, having measurable disease (RECIST v1.1), and a Karnofsky performance status ≥70% that were randomised 1:1 to 3 mg/kg of i.v. nivolumab every two weeks or an oral daily 10 mg tablet of everolimus.

A preplanned interim analysis done after a minimum 15 months follow-up revealed a clear survival advantage with nivolumab over everolimus. Therefore, the trial was terminated early in July 2015 and patients receiving either drug were offered the opportunity to continue with nivolumab. Median OS was 25.0 (95%CI 21.8, NE) with nivolumab versus 19.6 months (95% CI 17.6, 23.1 months) with everolimus, HR 0.73; 95% CI 0.57, 0.93 (p = 0.0018). Progression free-survival was median 4.6 (95% CI 3.7, 5.4) versus 4.4 (95% CI 3.7, 5.5) months with nivolumab and everolimus, respectively, HR 0.88; 95% CI 0.75, 1.03 (p = 0.1135).

Also, tumour shrinkage was greater in response to nivolumab than to everolimus. The objective response rate (ORR) was 25% for patients receiving nivolumab versus 5% for patients on everolimus, odds ratio 6.05; 95% CI 3.69, 9.91 (p < 0.0001). Complete response was achieved by 4 (1%) nivolumab patients versus two (1%) everolimus patients and 98 (24%) versus 20 (5%) nivolumab versus everolimus patients achieved partial response. Stable disease occurred in 139 (34%) nivolumab patients versus 227 (55%) everolimus patients.

The survival benefit with nivolumab was seen in patients regardless of the extent of PD-L1 tumour expression; median OS with nivolumab and everolimus, respectively, was 21.8 versus 18.8 months in patients with PD-L1 expression ≥1% compared with 27.4 versus 21.2 months in patients with expression <1%.

Fewer treatment related adverse events (TRAEs) of any grade occurred with nivolumab than with everolimus; TRAEs were seen in 79% of nivolumab versus 88% of everolimus patients. The most commonly reported with nivolumab were fatigue in 33%, nausea in 14%, and pruritus in 14% of patients compared with fatigue in 13%, 30% stomatitis, and 24% of patients experiencing anaemia with everolimus. Grade 3 or 4 TRAEs occurred in 19% of nivolumab and 37% of everolimus patients. No treatment-related deaths occurred in the nivolumab arm and 2 deaths occurred in the everolimus arm. These results were published simultaneously in the NEJM [N Engl J Med 2015; 373:1803-13]. NCT01668784. Sharma *et al.* Abstract 3LBA.

### Practice point and future research opportunities

CheckMate 025 is the first and only study in which an immune checkpoint inhibitor has shown a clear overall survival benefit, when used after prior treatment has failed in patients with advanced kidney cancer. Treatment options are currently limited for patients with renal cell carcinoma, which is the most common type of kidney cancer in adults. Patients with this cancer have a poor prognosis, so effective treatments are desperately needed. These results are significant and clinically meaningful and are likely to change the treatment of patients with advanced kidney cancer, whose disease has progressed on prior treatment. The finding that overall survival was higher among patients treated with nivolumab, irrespective of PD-L1 expression prior to treatment, suggests that nivolumab should be offered regardless of the patient's PD-L1 expression status.

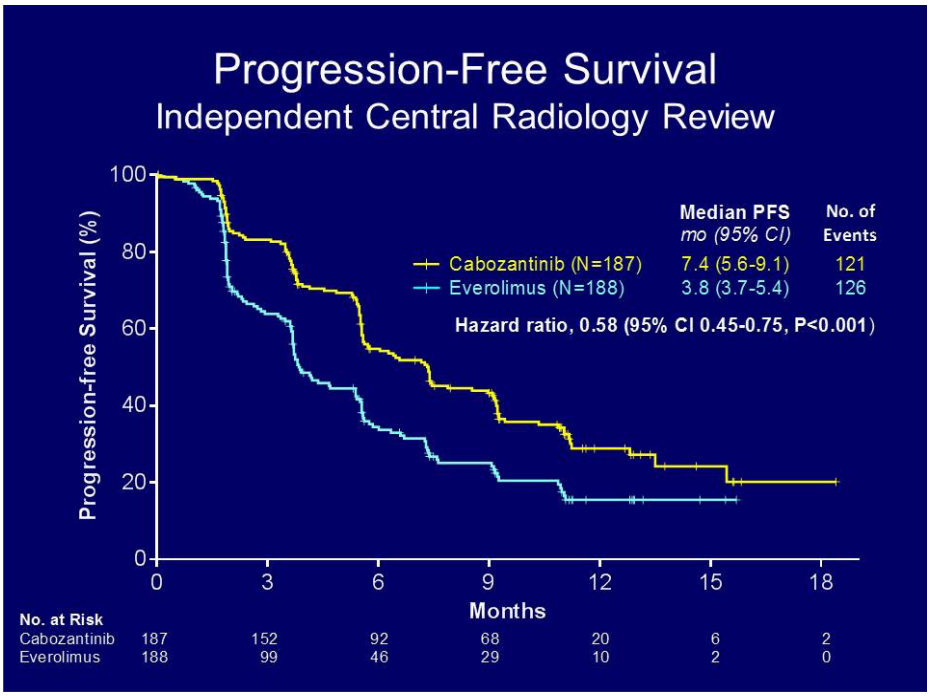
## Cabozantinib out-performs everolimus in patients pretreated for advanced renal cell carcinoma

Results from prespecified subgroup analyses for progression-free survival (PFS) from the open-label phase III METEOR trial were reported by lead investigator Toni Choueiri, from the Dana Farber Cancer Institute in Boston, USA, that showed treatment with cabozantinib reduced the rate of disease progression or death by 42% compared to everolimus in patients with advanced clear-cell renal cell carcinoma (RCC). Cabozantinib inhibits multiple tyrosine kinases (TK), including MET, VEGFR, AXL and RET. Based upon results from the METEOR trial, cabozantinib was granted Breakthrough Therapy Designation by the US FDA on 24 August 2015 for patients with RCC who experienced disease progression following treatment with a TKI; cabozantinib is

currently authourised for treatment of adult patients with progressive, unresectable locally-advanced, or metastatic medullary thyroid cancer.

In METEOR, 658 patients with measurable disease by RECIST 1.1 and Karnofsky performance status ≥70% were stratified by MSKCC prognostic criteria and by the number of prior treatments with vascular endothelial growth factor receptor (VEGFR) TKIs, then randomised 1:1 between August 2013 and November 2014, to receive daily administration of cabozantinib at 60 mg or everolimus at 10 mg. Patients were required to have progressed within 6 months of their prior treatment with VEGFR TKIs; 71% of patients had undergone treatment with one and 29% of patients had received 2 or more prior VEGFR TKIs. According to MSKCC criteria, 46% of patients were favourable, 41% intermediate, and 13% of patients were classified as poor risk.

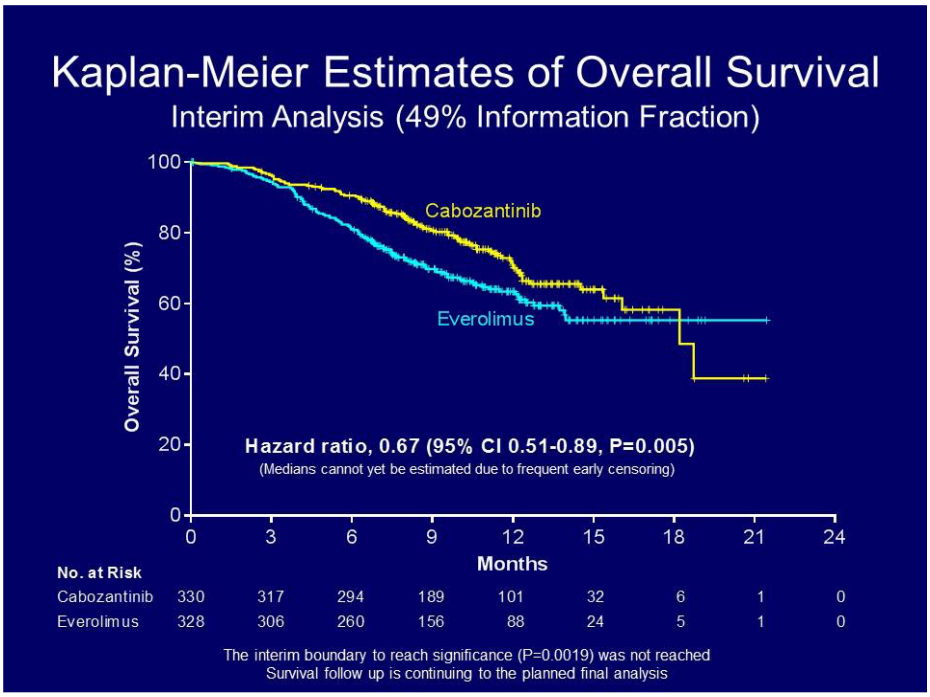
Improved PFS and overall response rate (ORR) were demonstrated with cabozantinib over everolimus in patients with advanced clear-cell RCC who had been pretreated with VEGFR TKIs. The study met the primary endpoint of PFS per independent radiology committee; the estimated median PFS among the first 375 randomised patients was 7.4 months with cabozantinib compared to 3.8 months with everolimus, HR 0.58; 95% CI 0.45, 0.75 ($p < 0.001$).




***Caption:*** *Progression-free survival in the METEOR Phase III trial of cabozantinib vs everolimus in metastatic renal cell carcinoma.*

**Credit:** Toni Choueiri, et al.

Secondary endpoints, including the ORR and overall survival (OS), also favoured cabozantinib; ORR was 21% with cabozantinib compared to 5% with everolimus ($p < 0.001$). At the interim OS analysis (49% information fraction) a trend towards prolonged survival for patients receiving cabozantinib was seen although the median OS could not yet be estimated; the HR was 0.67; 95% CI 0.51, 0.89 ($p = 0.0050$) for the comparison of cabozantinib with everolimus. The criteria for early rejection of the hypothesis were not met at this time point ($p \leq 0.0019$).




***Caption:*** *Overall survival in the METEOR Phase III trial of cabozantinib vs everolimus in metastatic renal cell carcinoma.*

**Credit:** Toni Choueiri, *et al.*

Cabozantinib was well tolerated by patients in this setting. The most commonly reported serious adverse events (SAEs) with cabozantinib were abdominal pain, pleural effusion, and diarrhoea, which occurred in 3%, 2.7%, and 2.1% of patients, respectively. SAEs with everolimus included anaemia, dyspnoea, and pneumonia, which were each reported in 3.7% of patients. Treatment discontinuation due to adverse events was reported for 9.1% of patients receiving cabozantinib and 10% of patients receiving everolimus.

The authors suggest that these data will impact treatment decisions for patients with advanced clear-cell RCC and may change the treatment landscape altogether. The study was simultaneously published in the NEJM [N Engl J Med 2015; 373:1814-1823]. NCT01865747. Choueiri et al. Abstract 4LBA.Practice point and future research opportunities Enormous progress in the management of renal cell cancer has been recently made with 7 new drugs approved on the basis of progression-free survival. Although METEOR reached its primary endpoint, the overall survival data are not mature; cabozantinib could potentially become the standard in advanced renal cell carcinoma. Cabozantinib may also be relevant in the second or later line treatment option.

## Similar overall survival demonstrated with axitinib and sorafenib as first-line therapy in patients with metastatic renal cell carcinoma

Although approved for treatment of advanced renal cell carcinoma (RCC) in the second line, previous results from this randomised phase III trial in treatment-naive patients demonstrated that axitinib, a selective inhibitor of VEGFR, significantly improved the objective response rate (ORR) compared with sorafenib. At the ECC, lead investigator Thomas E. Hutson, Baylor University Medical Center, Houston, USA, presented results from an analysis of overall survival (OS) from a direct comparison of axitinib with sorafenib as first-line therapy. The trial enrolled 288 treatment-naive patients with measurable (per RECIST v1.0), clear-cell metastatic RCC and ECOG PS 0 or 1 from Eastern Europe (51%), Asia (25%), North America (14%), and South America (10%). Patients were stratified by ECOG PS and randomised 2:1; 192 patients received open-label axitinib at 5 mg twice daily and 96 patients received sorafenib at 400 mg twice daily. The primary endpoint of progression-free survival (PFS) and secondary endpoint of ORR were previously reported.

Median OS in the overall population of patients after long-term follow-up was similar with axitinib and sorafenib; median OS was 21.7 (95%CI 18.0, 31.7) months with axitinib versus 23.3 (95%CI 18.1, 33.2) with sorafenib, stratified HR 0.995; 95%CI 0.731, 1.356 (1-sided p = 0.4883). However, patients with ECOG PS 0, showed numerically improved OS with axitinib of 41.2 (95%CI 29.2, not estimable [NE]) months versus 31.9 (95%CI 18.1, NE) months with sorafenib, HR 0.811; 95%CI 0.522, 1.259 (1-sided p = 0.1748). Patients with ECOG PS 1 showed an OS advantage with sorafenib; median OS was 14.2 (95%CI 9.4, 18.1) months with axitinib versus 19.8 months (95%CI 12.3, 25.8) with sorafenib, HR 1.203; 95%CI 0.778, 1.859 (1-sided p = 0.7973). The incidence and severity of common adverse events were consistent with previous reports of each agent. The authors suggest that the noteworthy difference in median OS in patients with axitinib by ECOG PS (PS 0 compared with PS 1), which was 41.2 versus 14.2 months, respectively, may have been

influenced by practice standards in resource-limited regions, where most patients were enrolled, and by subjectivity in classifying patients to ECOG PS categories. NCT00920816. Hutson *et al.* Abstract 2509.

### Practice point and future research opportunities

Axitinib, is approved to treat advanced RCC after 1 prior systemic therapy, but has demonstrated an improved objective response rate, as well as, progression-free and overall survival comparable to sorafenib in previously untreated patients with metastatic RCC. The authors noted the large difference between median overall survival with axitinib according to ECOG performance status and suggest possible confounding factors. Further investigation of first-line axitinib is warranted, as is, clarification of this issue.

## IMA901 multipeptide cancer vaccine added to sunitinib fails to show survival advantage over sole sunitinib as first-line therapy for patients with advanced/metastatic renal cell carcinoma

There was no improvement in overall survival (OS) from adding IMA901 to first-line sunitinib in patients with advanced renal cell cancer (RCC); OS was comparable in both arms in favourable risk patients and longer OS was observed in intermediate-risk patients with sole sunitinib. Therefore, methods to improve immune responses would need to be identified before further development of IMA901 in metastatic RCC (mRCC) is indicated, according to lead author Brian Rini, Case Western Reserve University, Cleveland, USA. He presented findings from a phase III trial designed to demonstrate the OS benefit of the cancer vaccine, IMA901, in combination with standard first-line sunitinib therapy in patients with mRCC compared to sunitinib monotherapy. IMA901 is based on naturally presented tumour-associated peptides (9 HLA-A*02- and 1 HLA-DR-binding peptides) that has shown promise in a phase II trial. This trial enrolled 339 previously untreated HLA-A*02-positive patients with mRCC who were randomised 3:2 to receive up to 10 intradermal vaccinations of IMA901 plus 75 µg GM-CSF and standard sunitinib versus sunitinib alone. Patients in the vaccine arm were given a single infusion of cyclophosphamide 3 days before the first vaccination to reduce regulatory T cells. Patients were stratified according to risk group (Heng), nephrectomy, and region.

The primary analysis showed no significant difference in OS between the treatment arms; median OS for sunitinib monotherapy was not reached [NR] compared with 33.1 months with IMA901/sunitinib, HR 1.34

(p = 0.08). The OS according to stratified subgroups showed favourable-risk patients had median OS of 33.7 months versus NR with sunitinib and IMA901/sunitinib, respectively, HR 0.82 (p = 0.59); however, longer OS was observed for sole sunitinib in intermediate-risk patients; median OS was NR versus 27.8 months, respectively, HR 1.52 (p < 0.05). The independent central review also showed comparable outcomes among patients in both arms; PFS was 15.1 versus 15.1 months, HR 1.05 (p = 0.62). However, PFS by investigator assessment showed a trend for longer PFS that favoured the sunitinib monotherapy; median PFS was 17.9 versus 15.1 months, respectively, HR 1.18 (p = 0.19) possibly due to the higher sunitinib exposure occurring in the monotherapy arm of median 13.7 with sunitinib arm versus 11.2 grams with IMA901/sunitinib.

IMA901 was well-tolerated and similar rates of adverse events (AEs) observed in both arms. Transient injection-site reactions were the most frequently reported AEs with IMA901. Immune data showed that sunitinib led to a significant decrease in monocytes after the first injection. There was no clear or significant association between T-cell responses and clinical outcome. Rini *et al.* Abstract 17LBA.

### Practice point and future research opportunities

The IMA901 vaccine added to sunitinib failed to improve outcomes over sunitinib as first-line therapy for patients with advanced/metastatic RCC. Although phase II results showed a survival difference with the vaccine in patients with RCC premedicated with cyclophosphamide who developed immune responses, these data were not replicated in this phase III trial and further development of IMA901 is not supported at this time.

## STAMPEDE shows adding docetaxel to hormone therapy improves survival in patients with hormone-naive prostate cancer

Nicholas D. James, University of Warwick, Coventry, UK presented findings on behalf of colleagues from the STAMPEDE trial, which is the largest randomised clinical trial of treatment for men with prostate cancer ever conducted. STAMPEDE is an ongoing randomised clinical trial in men with high-risk locally advanced or metastatic prostate cancer starting long-term hormone therapy for the first time that uses a multi-arm multi-stage (MAMS) design, allowing several treatments to be assessed against a single control arm. Updated survival data were presented at the ECC from 2,962 men who were assigned to 4 cohorts: Standard of care (SOC; at least two years of hormone therapy), SOC plus docetaxel (75 mg/m$^2$ for six 3-weekly cycles with prednisolone at 10 mg daily), SOC plus zoledronic acid (4 mg for six 3-weekly cycles then 4-

weekly up to 2 years), or SOC plus both docetaxel and zoledronic acid. The primary endpoint was overall survival (OS). Patients were followed up for a median of 43 months.

Patients receiving docetaxel/SOC (HR 0.78; p = 0.006) or combined docetaxel and zoledronic acid/SOC (HR 0.82; p = 0.022) showed a survival advantage compared to SOC that was not observed in patients receiving zoledronic acid/SOC (HR 0.94; p = 0.45). Docetaxel improved survival by 10 months over SOC; median survival was 77 months with docetaxel versus 67 months with SOC. Adding zoledronic acid to docetaxel did not seem to increase the benefit observed with sole docetaxel (HR 1.06; p = 0.592).

The time to first reported symptomatic skeletal event (SSE) was prolonged compared to SOC in both docetaxel arms; docetaxel (HR 0.60; p < 0.0001), and docetaxel/zoledronic acid (HR 0.55; p < 0.0001) but not with sole zoledronic acid (HR 0.88; p = 0.213). In the docetaxel, combination, and zoledronic acid arms, respectively, 112, 108, and 153 SSEs occurred. In men presenting with newly diagnosed bony metastasis, zoledronic acid did not prolong the time to first reported SSE (HR 0.94; p = 0.556). Osteonecrosis of the jaw was reported in 11 patients receiving zoledronic acid and in 19 patients receiving docetaxel plus zoledronic acid, but not in the other arms. In the docetaxel, docetaxel/zoledronic acid, and zoledronic acid groups 175, 187 and 201 deaths occurred compared to 415 deaths in the SOC only cohort. Of these, 3 deaths in the docetaxel arm and 8 deaths in the docetaxel/zoledronic acid arms were determined to be treatment-related. James *et al.* Abstract 19LBA.

### Practice point and future research opportunities

STAMPEDE shows that survival is clinically and statistically significantly improved by adding docetaxel to long-term hormone therapy in treatment naive patients beginning treatment. Docetaxel also prolonged the time to first symptomatic skeletal event, whereas zoledronic acid, either alone or in combination, did not.

## Orteronel shows promising anti-tumour activity in metastatic castration resistant prostate cancer

Lead investigators Silke Gillessen, of the Kantonsspital St. Gallen, and Richard Cathomas, of the Kantonsspital Graubünden in Chur, Switzerland presented results showing that orteronel used as switch maintenance therapy had clinical benefit in patients with metastatic castration-resistant prostate cancer (mCRPC). Orteronel is an investigational oral, non-steroidal, selective inhibitor of 17,20-lyase, a key enzyme in the production of steroidal hormones, including androgens. This

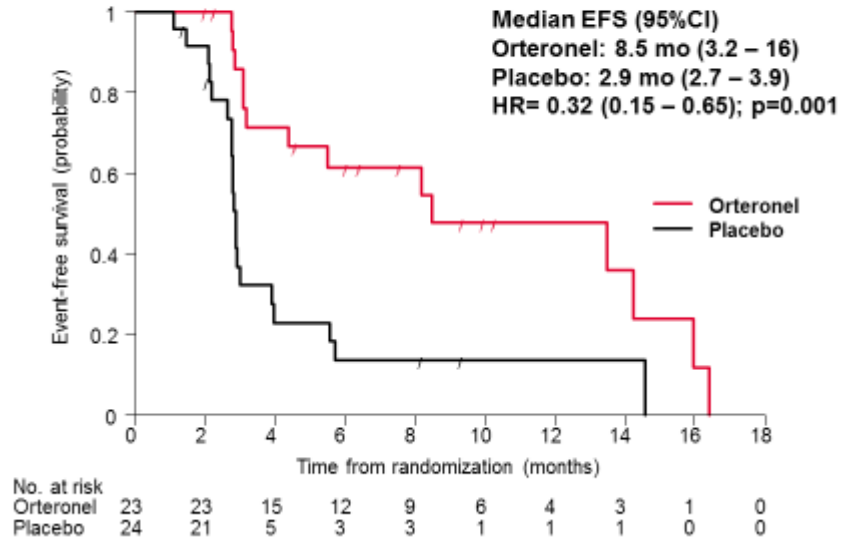
multicentre randomised double-blind placebo-controlled phase III study was designed to enroll 96 patients; however just 47 patients were enrolled between November 2012 and June, 2014; 23 patients were randomised to orteronel at 300 mg twice daily plus best supportive care (BSC) and 24 to placebo plus BSC. The median patient age was 70 years (range: 51 to 85 years) and all patients had non-progressive disease after receiving a cumulative dose of ≥ 300 mg/m2 of first line docetaxel. Orteronel plus BSC was initiated at 3 to 6 weeks after the final administration of docetaxel. The trial's primary endpoint was median event-free survival (EFS), which was defined as the time from randomisation to death, or a combination of at least two outcomes that included radiographic, clinical or prostate specific antigen (PSA) progression. Secondary endpoints included PSA decline >50%, time to PSA progression, radiographic PFS (rPFS), toxicity, quality of life (QoL) and overall survival (OS).

The study was halted prior to completing enrollment when Takeda Pharmaceutical announced on June 19, 2014 that it was ending the development of orteronel in prostate cancer after 2 phase III clinical trials found that orteronel plus prednisone extended time to disease progression but not OS in patients with mCRPC.

At the time of the impromptu termination, the median patient follow-up was 17 months. Patients on orteronel maintenance achieved EFS that was nearly three times longer than similar patients receiving placebo. EFS

was 8.5 (95% CI 3.2, 16.0) months with orteronel versus 2.9 (95% CI 2.7, 3.9) months with placebo, HR 0.32 (95% CI 0.15, 0.65; p = 0.001). PSA decline >50% was observed in 57% of orteronel patients compared to just 4% of placebo patients. The time to PSA progression was also significantly increased to 6.5 months with orteronel compared to 1.8 months with placebo (HR 0.37; 95% CI 0.18, 0.75; p = 0.004), and rPFS was 8.5 versus 2.8 months with orteronel and placebo, respectively, (HR 0.42; 95% CI 0.20, 0.91; p = 0.02).

**Maintenance orteronel after prior disease stabilisation with docetaxel significantly prolongs event-free survival in mCRCP patients**




***Caption:*** *Maintenance orteronel after prior disease stabilisation with docetaxel significantly prolongs event-free survival in mCRPC patients.*

**Credit**: Richard Cathomas

Adverse events were reported in 61% of orteronel versus 83% of placebo patients during treatment. Higher, but manageable, toxicity occurred in the orteronel arm. Grade 2 toxicity events with orteronel included fatigue in 17%, nausea in 26%, hypertension in 17%, and hypokalaemia in 17% of patients, whereas grade 2 fatigue, nausea, and hypertension each occurred in 4% and hypokalaemia was reported in 13% of patients receiving placebo. Grade 3 fatigue, hypertension, and hypokalaemia were reported in 9%, 9%, and 4%, respectively, of orteronel patients, whereas 4% of placebo patients reported grade 3 AEs of nausea, and 8% hypertension. Grades 2/3 elevation of liver enzymes occurred in 17% and 4% of patients receiving orteronel versus 17% and 8% in the placebo arm, respectively. With orteronel, one (4%) patient experienced transient adrenal insufficiency grade 3, and one (4%) patient developed grade 4 pneumonitis, both responded to treatment.

The investigators stated that this was the first trial, to their knowledge, using an active pharmaceutical ingredient as switch maintenance in mCRPC and that the concept of maintenance therapy after disease stabilisation with chemotherapy warrants further research in mCRPC. Gillessen *et al.* Abstract 2500.

### Practice point and future research opportunities

Orteronel showed important anti-tumour activity as a switch maintenance therapy in patients with metastatic castration resistant prostate cancer and non-progressive disease following docetaxel. Maintenance therapy after disease stabilisation with orteronel or another agent warrants further investigation.

## Atezolizumab benefit with increased PD-L1 expression in metastatic urothelial carcinoma

Atezolizumab demonstrated clinical benefit in patients with metastatic urothelial carcinoma (mUC) who had a poor prognosis after progressing on platinum-based chemotherapy, according to phase II trial results reported by Jonathan Rosenberg, Memorial Sloan Kettering Cancer Centre, New York, USA, lead investigator of the IMvigor study. Atezolizumab is a monoclonal antibody that blocks PD-L1 activity and restores the patient's immune response. It has demonstrated activity in mUC, where there is currently a high, unmet need for viable treatments, leading to the granting of breakthrough designation for atezolizumab by the US FDA in 2014 for patients with mUC whose tumour expressed PD-L1.

IMvigor 210 was an international multicentre phase II trial of atezolizumab in patients with locally-advanced or metastatic mUC that enrolled 316 patients who had progressed during or following platinum-based chemotherapy. Atezolizumab was administered at 1200 mg i.v. on the first day of each 21-day cycle until no further clinical benefit was demonstrated; the median treatment duration was 12 (range: 0 to 46) weeks. The co-primary endpoints were overall response rate (ORR), as assessed by central review (RECIST v1.1) and ORR assessed by the investigators using modified RECIST v1.1. Secondary endpoints included duration of response (DoR), progression-free survival (PFS), overall survival (OS) and safety. By May 5, 2015, data from 311 patients were evaluable for efficacy and safety. Baseline characteristics showed that the median patient age was 66 years, 78% were male, 62% of patients had ECOG PS 1, and 31% of patients had metastasis to the liver. The patients had been heavily pre-treated; 40% of patients had undergone ≥2 prior systemic regimens in the metastatic setting and 74% of patients had received cisplatin-based chemotherapy.

PD-L1 expression was prospectively assessed using the SP142 antibody-based IHC assay on tumour cells/TC) and immune cells (IC); however, both the patients and investigators were blinded as to PD-L1 status. The results were evaluated according to the degree of PD-L1 expression. The ORR after atezolizumab significantly improved with higher PD-L1 expression; ORR by RECIST 1.1 was 15% ($p = 0.0058$) in all comers, 18% ($p = 0.0004$) in the IC1/2/3 group (PD-L1 expression

≥1%) and ORR 27% (p = 0.0001) in the IC2/3 group (PD-L1 expression ≥5%). The median DoR had not been reached at the time of data cut-off, however, at a minimum follow-up of 24 weeks, 92% of responding patients maintained response. Overall, 12 patients achieved complete response (CR), and 35 achieved partial response (PR). In addition, 15 additional unconfirmed RECIST v1.1 CR/PRs were seen. The median PFS at a median follow-up of 24 weeks was 2.1 months across all groups. The OS data are not yet mature but prolonged OS has been noted in patients with higher PD-L1 expression.

Treatment-related adverse events (AEs) of any grade occurred in 66% of patients, with 15% of patients experiencing grades 3/4 AEs including fatigue in 6 (2%) patients. Treatment discontinuation due to an AE was reported in 3% of patients. Studies of atezolizumab as first-line in treatment naive, platinum ineligible patients are ongoing, as is a phase III trial of atezolizumab versus chemotherapy. Rosenberg *et al.* 21LBA.

## Practice point and future research opportunities

IMvigor 210 is the first phase II study of an agent targeting PD-L1/PD-1 in mUC. Classical chemotherapy, with docetaxel as used in the US or vinflunine in Europe, is not very effective in second-line treatment of metastatic bladder cancer. The study data are promising, but it is necessary to await the results of phase III studies (IMvigor and Keynote trials amongst others) before reviewing the current standard of care. It is also important to identify patients with immune cells and /or tumour cells that express PD-L1, since higher PD-L1 expression on immune cells associated with higher overall response rates. Prospective agents currently under evaluation as second-line therapies are atezolizumab that targets PD-L1, pembrolizumab that targets PD-1, and docetaxel/ramucirumab that targets VEGFR-2.

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## AFFILIATION AND DISCLOSURE

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### Disclosure

No conflicts of interest to disclose.

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