Update from the American Society of Oncology (ASCO) 2021 Meeting

By Kalli Spencer

The focus on this year's meeting was on advanced cancer. Two types of cancer were presented: those that would respond to anti-androgen therapy (Castrate sensitive prostate cancer – CSPC) and those who have had anti-androgen therapy and developed resistance to treatment (Castrate resistant prostate cancer- CRPC).

Castrate Sensitive Prostate cancer

The growth and spread of prostate cancer is because of the effects of testosterone and its effect on target receptors within the body. (Androgen signalling). TAK-700 (orteronel), a specific CYP17 lyase inhibitor, interferes with the production of testosterone in the adrenal gland. The SWOG S1216 study evaluated the effects of TAK-700 added to conventional androgen deprivation therapy (ADT) and compared it to ADT plus bicalutamide (control arm)[1]. Similar agents have previously necessitated the addition of prednisone for treatment which is not required with this treatment. It was found that overall survival in the control arm was 70.2 months, compared to 81.1 months in the TAK-700 plus ADT arm. An improvement in progression-free survival [PFS] (the length of time during and after the treatment that a patient lives with the disease but it does not get worse) from 23 months to 47.6 months occurred in the TAK-700/ADT arm. Common side effects were fatigue and hypertension.

The PEACE-1 study, which started recruitment in 2013, looked at the role of abiraterone and the role of radiotherapy in addition to the standard of care[2].
The addition of abiraterone to ADT and docetaxel significantly improved radiographic progression-free survival without adding significant short-term toxicity. Radiological PFS was improved from 2 to 4.5 years with the use of abiraterone. (Defined as length of time where cancer does not get worse, measured using medical imaging). If financially feasible, this triple therapy may become the standard of care in the future.

Castrate Resistant Prostate Cancer (CRPC)

The utility in next generation targeted imaging with therapeutic intervention was highlighted with the emergence of radiopharmaceuticals for prostate cancer treatment. This approach leverages targeting prostate cancer cells using PSMA (prostate specific membrane antigen) targeting radioligands. In other words, specialised drugs are given intravenously, travelling through the blood to reach all the sites in the body harbouring prostate cancer cells, attaching to them and targeting them with a specific type of radiation (ß-particle radiation). PSMA-617 with the beta-

emitter lutetium allows for the targeted delivery to PSMA-expressing cells and the surrounding microenvironment.

Results from the VISION trial were presented, assessing lutetium-177-PSMA-617 in men with PSMA-positive mCRPC who had received previous treatment with next-generation androgen receptor inhibitors (abiraterone and enzalutamide) and one or two prior lines of taxane chemotherapy[3].
Patients were required to have a good performance status and a life expectancy of at least six months. Patients were randomized to receive either 177Lu-PSMA-617 plus standard of care (SOC) or SOC alone. Over a median study follow-up of 20.9 months, 177Lu-PSMA-617 + SOC treatment improved overall survival by a median of 4.0 months compared to SOC alone. In addition, 177Lu-PSMA-617 + SOC significantly improved radiographic progression free survival rPFS by a median 5.3 months.
The treatment also delayed the chance of developing a pathological fracture (a symptomatic skeletal event) by 11.5 months.

Bone protecting agents (BPA) in CRPC

Some men with CRPC and metastatic disease to the bone receive targeted treatment to the bone (Radium-223) in combination with anti-androgen (enzalutamide). This therapy can be toxic to the bone and therefore bone protecting agents may need to be given simultaneously. The PEACEIII Trial investigated the impact of bone protecting agents (BPAs) such as zoledronic acid or denosumab to control the fracture rate during treatment with radium-223 (RAD223) plus enzalutamide for men with asymptomatic or mildly symptomatic metastatic CRPC[4]. In this study, patients were randomised to receive either enzalutamide alone or enzalutamide daily plus radium-223.
At one year the cumulative incidence of fractures was 37.1% in the combination arm (Enzalutmide/RAD223) and 15.6% in the enzalutamide alone arm without BPA. In men who received a BPA, the 1-year incidence of fractures was reduced to 2.7% and 2.6, respectively. At the 18 months timeframe, the cumulative incidence was 45.9% in the combination arm and 21.9% in the enzalutamide alone arm, without a BPA. With the use of a BPA, the incidence was 4.3% and 2.6%.

As a whole, the ASCO 2021 conference (and the Genitourinary Cancers Symposium in particular), covered a host of topics surrounding new research in the field. It has also managed to provide advancement and insight, while remaining undeterred by the challenges posed by the COVID pandemic, whilst presenting new avenues of possibility and hope in the treatment of patients both in the areas of castrate sensitive and castrate resistant disease. There can be little doubt that significant progress has been made that will hopefully result in advantages for all patients worldwide.

References

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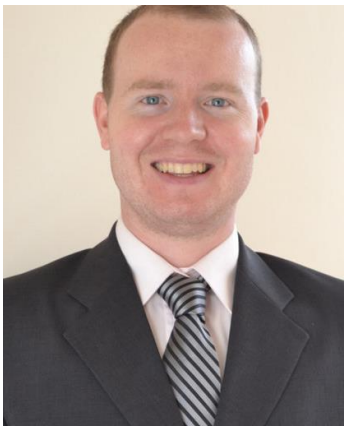

About the Author

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Kalli is an internationally renowned Urological Surgeon, specialising in oncology and robotic surgery. He trained and worked in South Africa, before relocating to Australia where he has worked at Macquarie University Hospital and Westmead Hospital. His passion for what he does extends beyond the operating room, through publichealth advocacy, education and community awareness of men's health, cancer and sexuality.

Kalli has been involved with the Prostate Cancer Foundation of Australia for many years, advocating for improved cancer care and facilitating community prostate cancer support groups.