Progress on Prostate Cancer Research July 2020

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Advancements in prostate cancer research provide hope for finding a cure and lead to the discovery of new treatments to minimize the impact of a man's prostate cancer and maximize his quality of life. This regular *Hot SHEET* supplement includes some of the latest research from the Prostate Cancer Foundation (www.pcf.org).

ASCO 2020: Spotlight on PSMA Therapy Trial Results

The 2020 ASCO Virtual Scientific Program Annual Meeting was held the last weekend of May. While this year's conference took place on the web, there was no shortage of talks, discussions, and programming to share breaking news of developments in the fight against cancer.

One exciting new area in prostate cancer that continues to be in the spotlight is PSMA-targeted treatment. PCF-funded researcher Professor Michael Hofman, MBBS, of the Peter MacCallum Cancer Centre in Australia has been a leader in this field and serves as the principal investigator of a Phase 2 clinical trial called TheraP. His team's presentation at ASCO revealed how a **PSMA-targeting treatment may represent a potential new class of effective, safe therapy for men with metastatic castration-resistant prostate cancer (mCRPC)**.

PSMA, short for Prostate-Specific Membrane Antigen, is a protein that is found in relatively larger amounts on the surface of prostate cancer cells. The strategy is to **target the cancer cells** by creating a small molecule that will bind to the PSMA on their surface. Attached to this molecule is a radioactive element (Lutetium-177, or Lu-177 for short) that **delivers radiation directly to the cancer cells, killing them**. Thus, the treatment is called Lu-PSMA.

One important aspect of the TheraP trial is that it compares this new PSMA treatment to cabazitaxel - a known active, FDA-approved treatment for prostate cancer – **not a placebo**! Patients in the trial had resistant disease: they had progressed on docetaxel, and over 90% had been treated with enzalutamide or abiraterone. To be eligible, men also had to have prostate cancer with "high PSMA expression," the cancer cells had to make enough PSMA to be visible on scans.

The study divided 200 men into groups, where they received either Lu-PSMA or cabazitaxel. The TheraP study team looked to understand the activity and safety of Lu-PSMA vs. cabazitaxel by **measuring PSA response**, defined as a reduction of PSA of at least 50% from baseline. They also observed **PSA-progression free survival (PFS) and adverse events**.

In all, there was **a large difference in outcomes between the two groups**. 66% of participants who underwent Lu-PSMA therapy showed a PSA response, compared to the 37% of participants treated with cabazitaxel. This **significant 29% percent difference** was also accompanied by a **lower frequency of Grade 3-4 (more severe) adverse events** in the Lu-PSMA group: 35% of patients vs. 54% in the cabazitaxel group. These results suggest that **Lu-PSMA may be a viable, safe option** for men with mCRPC progressing after docetaxel.

TheraP is the first-in-field randomized trial of Lu-PSMA to be completed. The study provided an active control arm, **and the substantial difference in PSA response points to a potential novel approach to treating aggressive mCRPC, for which new treatments are urgently needed**. The team is continuing to follow other outcomes including quality of life and overall survival.

For more on the TheraP trial, visit **https://bit.ly/2CBim7x**.