New Combination of Old Drugs Improves Survival in Patients With Prostate Cancer

Adding Zytiga plus prednisolone to standard therapy lengthened survival.

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A novel combination of well-known drugs prolongs survival in patients with hormone/castration-sensitive prostate cancer, according to late breaking research presented at the European Society for Medical Oncology annual meeting (ESMO Congress 2021).

The PEACE-1 and STAMPEDE studies found that the addition of abiraterone acetate [Zytiga] plus prednisolone (AAP) to standard therapy lengthened survival compared to standard therapy alone.

Commenting on the findings, Dr. Maria De Santis, Chair of Interdisciplinary Urological Oncology, Department of Urology, Charité Universitätsmedizin, Berlin, Germany said: “The findings have the potential to be implemented in our daily practice right away as we do not have to wait for the approval of a new drug. The clearly positive results are reassuring and should convince patients and physicians to intensify the treatment of patients with metastatic and high-risk locally advanced hormone/castration-sensitive prostate cancer early on. I expect this kind of treatment intensification to be implemented as a standard of care.”

For men with metastatic prostate cancer, androgen deprivation therapy (ADT) was the standard of care for decades. In 2015, docetaxel (a chemotherapy agent) was shown to improve survival when added to ADT and in 2017, abiraterone (a next generation hormonal agent) was also shown to improve survival when added to ADT. Until now, though, it was unknown whether one or both agents should be added to ADT to achieve the best outcomes.

PEACE-1 found that using three drugs upfront is better than just two in men with metastatic prostate cancer, not only to postpone cancer progression, but also to prolong life. When AAP was added to ADT and docetaxel, men experienced an additional 25% reduction in the risk of death compared to ADT and docetaxel alone.

Study author Prof. Karim Fizazi, Medical Oncologist at Institute Gustave Roussy and Professor in Oncology at the University of Paris-Saclay, Villejuif, France said: “PEACE-1 is the first trial to establish that triplet treatment should be offered to these men, especially those with the most

aggressive cancers (those with multiple metastases). Moreover, additional side effects with the triplet combination were mostly mild, with very few severe side-effects."

Fizazi pointed out that for men with high-burden metastatic prostate cancer, the triplet treatment used in PEACE-1 provided 2.5 additional years without cancer progression and approximately 18 additional months of life. "For the first time these men can expect to live more than five years whereas before 2015 their median survival was less than three years. By 2022 all three treatments will be generic drugs which should improve access for patients worldwide."

Fizazi noted that more follow-up is required in men with low-burden metastatic prostate cancer to accurately assess survival. "Triplet systemic treatment clearly postponed cancer progression in these patients but we need more time to determine whether it improves survival. This also applies to the role of local radiotherapy directed to the primary prostate cancer where we need longer follow-up to establish whether and how to best combine it with systemic treatments."

STAMPEDE focused on non-metastatic (no spread visible on conventional scans) but high-risk (of spread) prostate cancer. Approximately 20% of localised prostate cancers are high-risk at diagnosis but [these] account for the majority of relapses and consequently deaths in this population. Androgen deprivation is given for two or three years and combining it with local radiotherapy to the prostate and pelvis improves life expectancy. Adding treatments such as docetaxel chemotherapy has been tested and shown to prolong time to relapse but did not prolong life expectancy.

The trial found that at six years, men who had received standard treatment plus AAP for two years had an improvement in metastasis-free survival from 69% to 82%, an improvement in overall survival from 77% to 86% and an improvement in prostate cancer specific survival from 85% to 93%—compared to standard treatment alone.

Study author Prof. Gerhardt Attard, John Black Charitable Foundation Endowed Chair in Urological Cancer Research at University College London, UK said: "Based on these results, all men with high-risk non-metastatic prostate cancer should be considered for two years of abiraterone. This will involve more hospital visits during this period to manage administration of the drug but by reducing subsequent relapse, may reduce the overall burden for both patients and health services."

Attard noted that more information is needed on the optimal length of AAP therapy. "We did not study different durations of treatment so administering AAP for a shorter time may be equivalent and longer may be even more effective."

Comparing these results with the current treatment options, De Santis said: "The survival benefit in PEACE-1 is a clear improvement and adds to the advances recently made for patients with metastatic hormone/castration-sensitive prostate cancer. With regards to the non-metastatic patients in STAMPEDE, this is a completely new patient group that has not been included in other published trials. The addition of systemic treatment with AAP for at least two years in this population will change our former treatment strategy which has been only ADT plus or minus

radiotherapy to the prostate for many years.”

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