

転移性前立腺がんの新たな治療選択 (Abstract LBA2)

ENZAMET: 標準治療にエンザルタミドを併用することにより転移性ホルモン感受性前立腺がん男性の生存率が改善する

ENZAMET: Adding enzalutamide to standard treatment improves survival for men with metastatic hormone-sensitive prostate cancer

標準治療にアンドロゲン受容体阻害薬であるエンザルタミドを併用した場合、従来の非ステロイド性抗アンドロゲン薬 (NSAA) 併用に比べ、転移性ホルモン感受性前立腺がん男性に対する有効性は高い、と2019 ASCO Annual Meeting で発表され、同時に *New England Journal of Medicine* に掲載された。第III相 ENZAMET 試験の中間解析の結果、エンザルタミドを投与された患者においてはその他のNSAAを投与された患者に比べ、死亡リスクが33% 低下したことが示された。重篤な有害事象の発現は、エンザルタミド群の42% に対し、NSAA群では34% であった。

Full Text

An interim analysis of the international randomized, phase III ENZAMET trial found that 80% of men with metastatic hormone-sensitive prostate cancer (mHSPC) who received the non-steroidal anti-androgen (NSAA) medicine enzalutamide along with the standard of care treatment were alive after 3 years compared with 72% of men who received other NSAAs along with standard treatment ($p=0.0016$). The study was led by the Australian and New Zealand Urogenital and Prostate (ANZUP) Cancer Trials Group.

The findings from this late breaking clinical trial were presented in the Plenary Session at the 2019 American Society of Clinical Oncology (ASCO) Annual Meeting and simultaneously published in the *New England Journal of Medicine*.

"Physicians and patients with prostate cancer now have a new treatment option with enzalutamide, and this is especially relevant for men who cannot tolerate chemotherapy and have a lower burden of disease seen on scans," said study co-chair Christopher Sweeney, MBBS, a medical oncologist at the Lank Center for Genitourinary Oncology, Dana-Farber Cancer Institute, Boston, MA.

"In men with metastatic prostate cancer starting testosterone suppression, enzalutamide and docetaxel are both active and are reasonable alternatives but have different side effects, costs, risks, and benefits," said study co-chair Ian D. Davis, PhD, Monash University Eastern Health Clinical School in Melbourne, Australia.

Metastatic HSPC is initially treated with surgical removal of the testes or injection with a hormone analogue to reduce the blood levels of androgens. Depending on the situation, other treatments can be added as well, including abiraterone, another hormone treatment that decreases non-testicular male hormones, or docetaxel chemotherapy. If the cancer continues to progress, additional hormone treatments and chemotherapy are used, and these can also improve longevity.

The study found that enzalutamide is a more effective inhibitor of the androgen receptor than bicalutamide, nilutamide, or flutamide, the comparison standard NSAAs used in the trial, but it can lead to different side effects.

Men with mHSPC were randomly assigned between March 2014 and March 2017 to receive an injection of a testosterone-suppressing medicine (such as goserelin, leuprolide, or degarelix) with either a 160-milligram enzalutamide pill daily or one of three standard NSAAs: bicalutamide, nilutamide, or flutamide. Of the 1,125 men enrolled in the trial, 503 men received early doses of docetaxel and 602 did not. Men were followed for a median of 34 months.

After 3 years, 80% of men with metastatic hormone-sensitive prostate cancer who received enzalutamide along with testosterone suppression, with or without early docetaxel, were alive compared with 72% of men who received one of the other three NSAAs in the trial. Overall, there was a 33% decrease in the risk of death in men receiving enzalutamide compared to those who took an NSAA.

Researchers further analyzed the data to identify the impact of enzalutamide in key groups at the 3-year mark:

- Of 596 men with a higher amount of disease on imaging scans, 71% taking enzalutamide were alive compared with 64% taking another NSAA.
- Of 529 men with a low amount of disease on imaging scans, 90% taking enzalutamide were alive compared with 82% taking another NSAA.
- The increase in survival with enzalutamide was most obvious in men who did not receive docetaxel: among patients who received enzalutamide without docetaxel, 83% were alive compared with 70% taking another NSAA.
- 64% of men were still taking enzalutamide compared with 36% of men taking another NSAA at the time of the first analysis of the data.
- Serious adverse events occurred in 42% of men taking enzalutamide compared with 34% of the men taking one of the other NSAAs.

Dr. Sweeney noted that a survival benefit is not seen with docetaxel in men with a low volume of disease, but that enzalutamide does improve survival in these men. Enzalutamide is a new option for men with metastatic hormone-sensitive prostate cancer and is superior to current standard therapy.

"We see here that giving enzalutamide early can offer worthwhile benefits, especially for certain groups of men. In addition to helping men live longer overall, this approach means they can also likely go longer without having to take steroids or receive chemotherapy," said ASCO Expert Neeraj Agarwal, MD.

The results from this trial are being compiled with results from other similar trials so that researchers have a dataset that includes over 10,000 men. With that large dataset at hand, researchers hope to be able to make extensive comparisons between medicines and determine which might benefit specific groups of men the most, according to Dr. Sweeney.

ENZAMET is a global collaborative investigator-initiated trial led by ANZUP Cancer Trials Group and sponsored by the University of Sydney, in collaboration with Canadian Cancer Trials Group, Dana-Farber Cancer Institute, and Cancer Trials Ireland (enrolling patients from Ireland and the United Kingdom).

Astellas Pharma provided drug and financial support but was not involved in study conduct or data analysis. ANZUP receives infrastructure funding from the Australian Government through Cancer Australia.

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