Can RA-223 improve Enzalutamide efficacy for early castration resistant prostate cancer?

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Globally, prostate cancer is the second most common type of cancer and the fifth leading cause of cancer-related death in men.

Prof. Bertrand Tombal of the Cliniques Universitaires Saint-Luc in Brussels, Belgium, and Coordinator of this study says, "For men with advanced disease, the objective is to control the disease while maintaining quality of life. Here, androgen deprivation therapy is generally administered initially, but often patients become resistant to this treatment."

The new standards of care for these so called "castration resistant" patients are the new androgen receptor pathways inhibitors enzalutamide (Xtandi) and abiraterone. Administrated in asymptomatic or moderately symptomatic patients, they delay treatment with chemotherapy, onset of significant pain, and deterioration of quality of life while improving overall survival.

RA-223 (Xofigo) is a drug that specifically targets bone metastases, the predominant metastatic site in early castration resistant prostate cancer patients. RA-223 has been used at a later stage of the disease when patients were symptomatic.

EORTC trial 1333 has now opened to investigate whether an upfront combination of enzalutamide and RA-223 would improve radiological progression-free survival compared to enzalutamide alone in patients with castration resistant prostate cancer metastatic to bone.

Prof. Silke Gillessen (photo) of the Kantonsspital St Gallen in Switzerland and Co-Coordinator of this study says, "The combination of enzalutamide and RA-223 could attack two important features of metastatic castration resistant prostate cancer. One of these is an adaptation by cancer cells so that they continue to stimulate the androgen receptor pathway, thus simulating cancer (re)growth. The other is their ability to grow in places where bone remodeling has been disrupted."

"Enzalutamide prevents androgens from binding to their receptor, and RA-223, by mimicking calcium, targets areas of bone metastases," adds Prof. Gillessen. "The fact that the safety profiles of both drugs for the most part do not overlap and both treatments are generally well tolerated makes them interesting combination partners. Furthermore RA-223 offers an additional mechanism of action when combined with enzalutamide that is approved for this indication, which makes them a potentially effective combination, too."

The men in the experimental arm will receive the combination of enzalutamide and RA-223 treatment, and the men in the standard arm will receive enzalutamide alone.

The intergroup EORTC trial 1333 is coordinated by the EORTC Genito-Urinary Cancers Group in collaboration with the Academic and Community Cancer Research United and the Ireland Cooperative Oncology Research Group. It plans to accrue 560 patients at 59 institutions located in ten countries: Belgium, Denmark, France, Germany, Republic of Ireland, Italy, Poland, Spain, Switzerland, the United Kingdom, and the United States of America.

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