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PROSTATE CANCER

Enzalutamide–cabazitaxel interactions

A substantial reduction in cabazitaxel exposure occurs when this drug is given in combination with enzalutamide for metastatic castration-resistant prostate cancer (mCRPC), according to the authors of a new study.

"Preclinical data suggest enhanced efficacy of cabazitaxel when combined with hormonal therapies for mCRPC," says Ron Mathijssen, corresponding author of the paper. "Clinical studies on combining taxanes and androgen-receptor-targeted agents for patients with mCRPC are ongoing. It is important to be aware of any potential drug–drug interactions between these agents, especially as enzalutamide is a known inducer of CYP3A4 and as taxanes are metabolized by this enzyme."

The authors performed a prospective, nonrandomized, nonblinded, crossover pharmacokinetic trial in which 14 patients with mCRPC received three consecutive cycles of cabazitaxel. For the first cycle, patients received cabazitaxel monotherapy and for the second and third they underwent concomitant treatment with enzalutamide. "We were most interested in the pharmacokinetic differences between the first and the third cycles, as we expected the largest influence of enzalutamide in the third cycles when steady-state levels of enzalutamide were reached," says Mathijssen. All patients received androgen-deprivation therapy throughout the study period.

The researchers observed a 22% reduction in cabazitaxel exposure with concomitant enzalutamide use (95% CI 9–34%; $P = 0.005$). No excessive toxic effects were noted.

Mathijssen and co-workers say that as recent study findings support the use of a reduced standard cabazitaxel dose of 20 mg/m^2, researchers should be aware of the interaction with enzalutamide as the addition of this drug could result in subtherapeutic levels of cabazitaxel.

Rebecca Kelsey

ORIGINAL ARTICLE Belderbos, B. P. S. *et al.* Influence of enzalutamide on cabazitaxel pharmacokinetics; a drug–drug interaction study in metastatic castration resistant prostate cancer (mCRPC) patients. *Clin. Cancer Res.* http://dx.doi.org/10.1158/1078-0432.CCR-17-2336 (2017)