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**Abstract****Full text links**

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**Anti-androgens inhibit ABCB1 efflux and ATPase activity and reverse docetaxel resistance in advanced prostate cancer.**Zhu Y<sup>1</sup>, Liu C<sup>1</sup>, Armstrong C<sup>1</sup>, Lou W<sup>1</sup>, Sandher A<sup>1</sup>, Gao AC<sup>2</sup>.**Author information****Abstract**

**PURPOSE:** Previous studies show that inhibition of ABCB1 expression overcomes acquired docetaxel resistance in C4-2B-TaxR cells. . In this study, we examined if anti-androgens, such as bicalutamide and enzalutamide, could inhibit ABCB1 activity and overcome resistance to docetaxel.

**EXPERIMENTAL DESIGN:** ABCB1 efflux activity was determined using a rhodamine efflux assay. ABCB1 ATPase activity was determined by Pgp-Glo™ assay systems. The effects of the anti-androgens bicalutamide and enzalutamide on docetaxel sensitivity were determined by cell growth assays and tumor growth in vivo.

**RESULTS:** We found that bicalutamide and enzalutamide inhibit ABCB1 ATP-binding cassette transporter activity through blocking ABCB1 efflux activity. Bicalutamide inhibited ABCB1 efflux activity by 40%, while enzalutamide inhibited ABCB1 efflux activity by ~60%. Both bicalutamide and enzalutamide inhibit ABCB1 ATPase activity. In addition, bicalutamide and enzalutamide inhibit ABCB1 efflux activity and desensitize docetaxel resistant and androgen receptor (AR)-negative DU145 cells. Combination of bicalutamide with docetaxel had a significant anti-tumor effect in both AR-positive and AR-negative docetaxel resistant xenograft models, suggesting that bicalutamide desensitizes docetaxel resistant cells to docetaxel treatment independent of AR status.

**CONCLUSIONS:** We identified a novel mechanism of action for anti-androgens such as bicalutamide and enzalutamide as inhibitors of ABCB1 efflux and ATPase activity. Bicalutamide and enzalutamide desensitize docetaxel resistant prostate cancer cells to docetaxel treatment independent of AR status. These studies may lead to the development of combinational therapies with bicalutamide/enzalutamide and docetaxel as an effective regiment to treat advanced castration resistant prostate cancer (CRPC) independent of AR status.

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