Androgen Deprivation Therapy Potentiates the Efficacy of Vascular Targeted Photodynamic Therapy of Prostate Cancer Xenografts

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Résumé en anglais	WST11 vascular targeted photodynamic therapy (VTP) is a local ablation approach relying upon rapid, free radical-mediated destruction of tumor vasculature. A phase III trial showed that VTP significantly reduced disease progression when compared with active surveillance in patients with low-risk prostate cancer. The aim of this study was to identify a druggable pathway that could be combined with VTP to improve its efficacy and applicability to higher risk prostate cancer tumors. Transcriptome analysis of VTP-treated tumors (LNCaP-AR xenografts) was used to identify a candidate pathway for combination therapy. The efficacy of the combination therapy was assessed in mice bearing LNCaP-AR or VCaP tumors. Gene set enrichment analysis identifies the enrichment of androgen-responsive gene sets within hours after VTP treatment, suggesting that the androgen receptor (AR) may be a viable target in combination with VTP. We tested this hypothesis in mice bearing LNCaP-AR xenograft tumors by using androgen deprivation therapy (ADT), degarelix, in combination with VTP. Compared with either ADT or VTP alone, a single dose of degarelix in concert with VTP significantly inhibited tumor growth. A sharp decline in serum prostate-specific antigen (PSA) confirmed AR inhibition in this group. Tumors treated by VTP and degarelix displayed intense terminal deoxynucleotidyl transferase-mediated dUTP nick end labeling staining 7 days after treatment, supporting an increased apoptotic frequency underlying the effect on tumor inhibition. Improvement of local tumor control following androgen deprivation combined with VTP provides the rationale and preliminary protocol parameters for clinical trials in patients presented with locally advanced prostate cancer. .

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