Nature Reviews Urology | Published online 21 Feb 2017; doi:10.1038/nrurol.2017.28

PROSTATE CANCER

TARGETING LIPID METABOLISM

Untargeted chemotherapies, such as docetaxel, remain a standard-of-care treatment of patients with metastatic castration-resistant prostate cancer, despite the high risk of adverse events. Now, promising early data indicate the clinical potential of targeting altered lipid metabolism, an established hallmark of cancer, as a treatment for prostate cancer.

Researchers found that the lipid precursor ethanolamine is toxic to two different prostate cancer cell lines (PC3 and DU145), and that this toxicity is the result of the choline-kinase-catalysed conversion of ethanolamine to the cytotoxic lipid precursor phosphoethanolamine. The specificity of this approach was demonstrated by the finding that the nonmalignant RWPE-1 prostate cell line is insensitive to ethanolamine, and that choline kinase knockdown confers resistance to ethanolamine in PC3 cells. After confirming the oral stability and tolerability of ethanolamine using *in silico* and *in vivo* approaches, researchers investigated the *in vivo* effectiveness of ethanolamine using mouse prostate cancer xenograft models: a 67% reduction in tumour volume, with a 55% reduction in tumour weight was observed in PC3-luc xenograft mice after 4 weeks of treatment with ethanolamine. Furthermore, no changes in body weight were observed in non-tumour-bearing mice treated with ethanolamine, thus confirming the safety of this approach. Further investigations revealed increased pro-apoptotic marker expression (such as c-Parp and Bim), and decreased expression of the antiapoptotic protein Bcl-2, suggesting that ethanolamine-induced cell death is mediated by mitochondria.

These findings reveal the potential of ethanolamine as a novel treatment of prostate cancer.

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ORIGINAL ARTICLE Saxena, R. *et al.* Preclinical development of a non-toxic oral formulation of monoethanolamine lipid precursor, for prostate cancer treatment. *Clin. Cancer Res.* http://dx.doi.org/10.1158/1078-0432.CCR-16-1716 (2017)