PROMISING NEW ANTIANDROGENS

Novel therapies being developed for castrate-resistant prostate cancer have yielded positive results in early clinical trials. Tran *et al.* found that two diarylthiohydantoins lowered levels of serum PSA and shrank tumors in mice and humans.

The two compounds, RD162 and MDV3100, are second-generation antiandrogens designed to prevent androgen from stimulating the proliferation of prostate cancer cells. Both compounds are readily absorbed into the blood when taken orally. The investigators tested the efficacy of these drugs against bicalutamide—an antiandrogen currently used to treat prostate cancer—in mouse models of castrate-resistant prostate cancer.

"To our delight, we found that these compounds caused very dramatic shrinkage of tumors in the mice," said co-investigator Charles Sawyers of the Memorial Sloan–Kettering Cancer Center, NY. "While treating these animals with bicalutamide produced a modest effect on their tumors, the new drugs caused the tumors to shrink dramatically, and in some animals almost completely," he added. RD162 and MDV3100 bind to the androgen receptor with a 5–8-fold greater affinity than bicalutamide. The compounds work well in cells with a heightened sensitivity to hormones, a characteristic that leads to antiandrogen therapy resistance.

Low-dose MDV3100 (30 mg per day or 60 mg per day) was selected for clinical testing in 30 men with castrate-resistant prostate cancer; 22 responded favorably to the drug, displaying a decline in serum PSA levels for at least 12 weeks. Decreases in serum PSA levels of more than 50% were observed in 13 men. The drug was well tolerated, with 11 patients continuing on the study for over 25 weeks.

The trial continues, with a further 110 patients being treated with higher doses of the drug.

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Original article Tran, C. *et al.* Development of a second-generation antiandrogen for treatment of advanced prostate cancer. *Science* **324**, 787–790 (2009).