

Modern chemo better than second targeted hormone therapy against resistant prostate cancer

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A modern chemotherapy drug is more effective for men with advanced prostate cancer than a second targeted hormone therapy in patients who

have stopped responding to treatment, a major clinical trial shows.

Men who had stopped responding to either abiraterone or enzalutamide lived longer before their disease came back when treated with the chemotherapy cabazitaxel than those offered the other targeted treatment.

The results suggest that cancer's lethal ability to develop drug resistance can affect the response not just to one treatment, but across precision medicines that work in a similar way.

Carefully considering the order in which treatments are offered to patients could help manage the impact of drug resistance and could extend the lives of men with [advanced prostate cancer](#).

A team at The Institute of Cancer Research, London, and The Royal Marsden NHS Foundation Trust, led the UK arm of an international trial comparing the benefit of cabazitaxel chemotherapy and targeted [hormone therapy](#) in men with advanced prostate cancer.

The trial looked at 250 men who had previously been treated with another chemotherapy, docetaxel, and with one of the targeted therapies, abiraterone or enzalutamide—and whose disease progressed after less than a year on the targeted treatment.

The study, presented today at the European Society of Medical Oncology conference in Barcelona and published simultaneously in the prestigious *New England Journal of Medicine*, was funded by Sanofi, the manufacturer of cabazitaxel.

The researchers found that on average, men treated with cabazitaxel lived twice as long before their cancer came back than those treated with abiraterone or enzalutamide—eight months compared with four months.

Overall, men treated with cabazitaxel lived for an average of 14 months compared with 11 months for men given abiraterone or enzalutamide.

The researchers believe that when one targeted drug stops working, a patient's cancer also develops resistance to other precision drugs that are aimed at similar weaknesses in the tumour.

Abiraterone—discovered at The Institute of Cancer Research (ICR), and developed with The Royal Marsden—and enzalutamide both exploit prostate cancers' dependence on androgen hormones to grow, by blocking the body's ability to produce or respond to them, respectively.

The study sheds further light on the importance of understanding the mechanisms by which cancers evolve to become resistant to targeted treatments.

Overcoming cancer's lethal ability to evolve in response to treatment will be the main focus of the ICR's new Centre for Cancer Drug Discovery.

The ICR needs to raise £14 million to complete the new Centre, which will bring together evolutionary scientists and drug discovery researchers to carry out a pioneering 'Darwinian' drug discovery programme.

Professor Johann de Bono, Regius Professor of Cancer Research at The Institute of Cancer Research, London, and Consultant Medical Oncologist at The Royal Marsden NHS Foundation Trust, said:

"Our new clinical trial has shown that a modern chemotherapy drug is more effective for men with advanced prostate cancer than giving them a targeted hormone treatment where they have already developed resistance to another.

"Our findings demonstrate the challenge we can face of cross-resistance

between targeted therapies where they have similar mechanisms of action.

"We need to harness our knowledge of which drugs patients have received and of the biology of drug resistance, so we can offer men the sequence of treatments that is likely to benefit them most."

Professor Paul Workman, Chief Executive of The Institute of Cancer Research, London, said:

"Precision medicines such as abiraterone have been revolutionary for men with advanced prostate [cancer](#)—but while targeted treatments like this are often initially very effective, [drug](#) resistance is a major problem.

"In our new Centre for Cancer Drug Discovery, we aim to harness evolutionary science to create exciting new approaches to treatment that can anticipate and overcome [drug resistance](#)."

Provided by Institute of Cancer Research

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