

Advancements in prostate cancer research provide hope for finding a cure and lead to the discovery of new treatments to minimize the impact of a man's prostate cancer and maximize his quality of life. This regular *Hot SHEET* supplement includes some of the latest research from the Prostate Cancer Foundation (www.pcf.org).

The PCF is the world's leading philanthropic organization funding and accelerating prostate cancer research. Founded in 1993, the PCF has raised more than \$745 million and provided funding to more than 2,000 research programs at nearly 200 cancer centers and universities.

No Clinical Benefit with Metformin Added to Docetaxel in mCRPC

At the 2019 ASCO Annual Meeting in early June, Dr. Marc Pujalte Martin presented results of TAXOMET, the first randomized-controlled trial of metformin's impact when given in combination with **docetaxel** treatment (a form of chemotherapy) for metastatic castration-resistant prostate cancer (**mCRPC**).¹ **The results showed that metformin does not have a benefit in non-diabetic patients with mCRPC receiving docetaxel.**

Interest in Metformin

Preclinical data (studies in a lab) and some retrospective studies (looking back at data from patients' medical records) suggest that **metformin**, a drug typically used to treat Type 2 diabetes, may have preventive and therapeutic effects in cancer. Researchers have observed that patients with Type 2 diabetes who are treated with metformin have a lower risk of cancer incidence and mortality. Other studies point to metformin's **antitumor** activity—namely, a link between the drug and the prevention of **tumorigenesis**, or the development of cancer. This has led scientists to further explore the relationship between metformin and prostate cancer. A **randomized-controlled trial** is the “gold standard” study that allows scientists to measure the effect of a particular treatment in a certain type of patient.

The TAXOMET Trial

The study was designed to observe the difference between prostate cancer patients who received metformin with their chemotherapy treatment and those who did not. Participants were **non-diabetic** and had **mCRPC (metastatic prostate cancer that had become resistant to hormone therapy)**. Patients were **randomly assigned to two groups** in which they either: **(A)** received docetaxel treatment with metformin or **(B)** received docetaxel with a placebo. Researchers tracked 99 patients over nearly 3 years, recording information such as their PSA levels, progression-free and overall survival rates, toxicity, and quality of life. *(PSA response rate was defined as 50% [or greater] decrease from baseline PSA level. Progression-free survival is time to disease progression or death from any cause. Overall survival is time to death from any cause).*

The results showed that the **addition of metformin to docetaxel did not improve PSA response rate** (72% in both arms) or median **progression-free survival** (7.3 months in arm A vs. 5.8 months in arm B) or **overall survival** (24.2 months vs. 19.7 months) **compared with docetaxel alone in patients with mCRPC**. (While the duration of survival is longer numerically in Arm A, statistical analysis indicates that those differences could be due to chance alone). More patients who took metformin had diarrhea vs. patients who did not (70% vs. 50%). This study indicates that metformin was not effective in combination with docetaxel treatment in mCRPC patients.

What Does This Mean for Metformin in the Treatment of Prostate Cancer?

It is possible that metformin is simply not effective in men with mCRPC, or that the combination with docetaxel is not efficacious. At ASCO, the results of a small, early phase trial suggested that metformin in combination with enzalutamide was found to be clinically active in men with CRPC.² However, based on the results of TAXOMET, given the lack of clinical benefit, and increased gastrointestinal toxicity, non-diabetic patients with mCRPC should not take metformin in combination with docetaxel for an “anti-cancer” effect.

1. Pujalte Martin M, Borchiellini D, Viotti J, et al. TAXOMET: A French prospective multicenter randomized controlled phase II study comparing docetaxel plus metformin versus docetaxel plus placebo in mCRPC. *J Clin Oncol* 37, 2019 (suppl; abstr 5004)
2. Parikh M, Robles D, Pan C-X, et al. Results from a phase Ib/II study of enzalutamide and metformin in men with castration resistant prostate cancer (CRPC). *J Clin Oncol* 37, 2019 (suppl; abstr 5054)

For more information visit www.pcf.org, email info@pcf.org, or call 1-800-757-2873.