Drug shown to significantly improve survival in men with metastatic prostate cancer

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The final survival analysis of an international study of a new drug for prostate cancer has found an even greater median survival benefit than previously reported, and has established a new class of treatment for men with metastatic prostate cancer. In addition, researchers are exploring a potential biomarker of response to treatment in general. The results were presented today by Howard I. Scher, MD, Chief of the Genitourinary Oncology Service at Memorial Sloan-Kettering Cancer Center at the 2011 Annual Meeting of the American Society of Clinical Oncology. The drug, abiraterone acetate (trade name Zytiga) was recently approved by the FDA.

"In addition to demonstrating that abiraterone acetate prolongs lives, this treatment also offers men with metastatic castration resistant disease after docetaxel chemotherapy a new treatment option at a point in the illness where hormonal agents are typically not considered. The survival benefit demonstrated that these tumors are not uniformly resistant to hormonal therapy. Of additional interest is that we have a potential new biomarker for measuring a drug's effectiveness in prostate cancer," said Dr. Scher.

Interest in the clinical relevance of circulating tumor cells (CTC) is longstanding, but has increased significantly with the availability of assays and devices to detect, count and characterize these cells. Circulating tumor cells (CTC) represent approximately one cell in a billion of those found in the blood stream. According to Dr. Scher, "a critical unmet need in patient management and drug development in

prostate cancer is for reliable indicators of clinical benefit. This is because there are no standards to assess disease in bone, the most common site of spread, and while PSA levels are used to guide patient management, there are situations in which the patient may be benefitting from treatment when levels are going up, and not benefitting when they are going down."

In this study, the demonstrated survival benefit of abiraterone acetate enabled Dr. Scher and his team to begin the process of examining the question of a surrogate endpoint in clinical trials. Surrogate endpoints are biomarkers that can be "substituted" or used in place of a clinical endpoint. "A critical goal of our research is to identify an early biomarker endpoint that can be used as a surrogate for survival in a clinical trial," said Dr. Scher. "A surrogate endpoint for survival that has been qualified by the FDA, can be used in New Drug Applications and enable the accelerated approval of drugs," he added.

The randomized, double blind, placebo controlled trial included 1195 men with metastatic prostate cancer whose disease had progressed after docetaxel-based chemotherapy. Patients were randomized 2:1 to receive prednisone with either the experimental drug called abiraterone acetate or placebo. In this final analysis, after following up with patients after 20.2 months on treatment, overall survival for the abiraterone acetate group was 15.8 months versus 11.2 months for the placebo group. In September 2010, the data monitoring committee recommended unblinding the study to allow the placebo group to switch to abiraterone acetate. Interim results of the trial were published on May 26, 2011 in The New England Journal of Medicine and found that in patients followed for a little more than 12 months, overall survival for the abiraterone acetate group was 14.8 months versus 10.9 months for the placebo plus prednisone group. In this final analysis, presented at ASCO, the difference in median overall survival between the two groups improved from 3.9 to 4.6 months. In April 2011, abiraterone acetate was

approved by the FDA for use in men with metastatic prostate cancer who have failed on chemotherapy.

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