Progress on Prostate Cancer Research March 2020

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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).

Focus on STAMPEDE: A Uniquely Designed Clinical Trial is Delivering Practice-Changing Findings to Patients (Part 2)

Last month, we discussed the design of the STAMPEDE phase 3 clinical trial, which uses a multi-arm, multi-stage approach to simultaneously test multiple interventions against a single control arm. Patients in this trial have node-positive or metastatic prostate cancer, are newly diagnosed or relapsing after previous primary treatment with surgery or radiation, and are starting ADT. Here, we describe results in three key areas.

Addition of Docetaxel to ADT

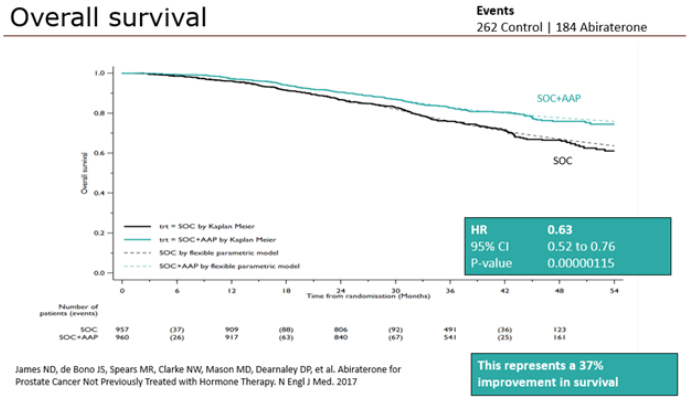
STAMPEDE demonstrated that the addition of docetaxel in men with hormone-naïve prostate cancer who are starting ADT improves overall survival, with a reduction in risk of death representing 22%. Docetaxel also improved failure-free survival by 39% and reduced the risk of skeletal events by 40%. While the phase 3 CHAARTED trial found that the addition of docetaxel in this setting only benefitted men with high-burden metastatic disease, STAMPEDE found that adding docetaxel to the standard of care (ADT +/- radiotherapy) improves overall and failure-free survival in newly diagnosed metastatic hormone-naïve prostate cancer regardless of metastatic burden. In STAMPEDE, docetaxel reduced the risk of death by 34% in patients with low-burden metastatic disease and by 19% in patients with high-burden metastatic disease. **These results have contributed to recommendations that docetaxel should now be considered as an option for patients newly diagnosed with metastatic hormone-naïve prostate cancer who are starting ADT**.

Abiraterone

The STAMPEDE trial found that the addition of abiraterone in men with hormone-naïve prostate cancer who are starting ADT improves overall survival, **with a reduction in risk of death representing 37%** (see Figure). **Abiraterone was beneficial in patients with both high-risk and low-risk disease (reduction in risk of death representing 46% and 34%)**. Abiraterone also improved failure-free survival by 71% and reduced the risk of skeletal events in patients with metastatic disease by 64%. A head-to-head comparison performed using 566 patients who were treated contemporaneously on the abiraterone and docetaxel arms found no significant difference in overall survival between the two regimens. However, slightly more men in the abiraterone arm died from non-prostate cancer causes such as cardiovascular disease and fractures, suggesting that overtreatment with abiraterone may have increased the risk of death in some men. Based on the results from STAMPEDE and a second phase 3 trial, LATITUDE, **abiraterone is now FDA-approved for the treatment of men with hormone-sensitive metastatic prostate cancer who are starting ADT**.

Radiation Therapy

The STAMPEDE trial found that the addition of radiotherapy to the primary tumor improves survival in men with newly-diagnosed low burden metastatic prostate cancer who are starting ADT +/- docetaxel (reduction in risk of death representing 32%; reduction in failure-free survival of 41%). No statistical benefit was seen for the addition of radiotherapy in patients with high-burden metastatic disease. **Based on the results from STAMPEDE, NCCN guidelines now include radiation therapy to the prostate as an option in patients with low-volume hormone-naïve metastatic prostate cancer**.



Approximately 4,000 men have already experienced a gain in survival on the completed arms in this trial. Correlative studies are being conducted using samples from patients on the trial to evaluate questions such as whether patients with certain hereditary cancer risk genes or tumor mutations have different treatment responses, and to evaluate the relationships between tumor biology, pathology, and molecular imaging. **Altogether, STAMPEDE has demonstrated that a trial of this design can rapidly test numerous treatment regimens in a multi-center phase 3 randomized setting, and has resulted in several new standard-of-care regimens for men with advanced prostate cancer**.

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