

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.

A New Standard of Care for Low-Volume Metastatic Prostate Cancer

Men diagnosed with metastatic prostate cancer will often not undergo local treatments, such as surgery or radiation, of the primary prostate tumor. Primary hormone therapy (also known as androgen deprivation therapy or ADT) has long been the standard of care, although recently the addition of docetaxel or abiraterone to ADT has become a standard of care option. In March, the National Comprehensive Cancer Network (NCCN) released its 1.2019 version of guidelines for prostate cancer. For men with **low-volume metastatic disease** who have not previously been treated with hormone therapy, there is an important update: the option of **radiation therapy (RT) to the prostate in addition to ADT** (unless medically contraindicated).

Digging Deeper Into Trial Results

This update is based on results of a large **randomized controlled trial** called STAMPEDE. But before STAMPEDE, there was another trial called HORRAD, the first study adding RT to ADT in patients with metastatic prostate cancer. In the analysis of all 400+ patients in the HORRAD trial, there was **no difference in overall survival**. Taken at face value, adding RT "didn't work." Case closed?

Not so fast ... because, when researchers looked at a small **subset of patients** who had a **low number of metastatic disease sites**, they saw a suggestion of a survival **benefit**.

A Large European Trial

STAMPEDE is a very large multi-arm, multi-stage trial conducted in Europe that is comparing the efficacy of several different treatment regimens in men with prostate cancer who are starting long-term ADT. Within the overall trial, one "arm" looked specifically at the benefit of adding RT to ADT in patients with metastatic disease. **There were two treatment groups (ADT, and ADT + RT), each with more than 1000 patients.** Eighteen percent of the patients in each group also took docetaxel and, prior to the trial, the groups were similar to each other in other important ways.

Randomized Trials: High Quality Evidence

A randomized controlled trial is the "gold standard" of medical evidence, a study in which patients are assigned at random to one treatment vs. another. The "random" piece is key – it means that, ideally, **the only difference between the two groups is the treatment itself**. This means that scientists, physicians, and patients can have confidence that **any difference in effects are, in fact, likely due to the treatment** rather than due to one group being, for example, older or sicker.

Once again, as in the HORRAD trial, when looking at the entire patient cohort, no benefit was seen with RT to the prostate added to ADT. However, **when analyzing only the patients with a low metastatic disease burden, the researchers saw a 32% reduction in the risk of death**. More patients in the RT group (81%) were alive after 3 years, compared to the group that received only ADT (73%).

This is why the "random" assignment of patients to treatment groups is so important: We know that it's very likely that **the RT group survived longer than the no-RT group because of the addition of RT**, not because the RT group had less severe disease or was otherwise in better shape.

But wait ... what about side effects of radiation? The study also assessed toxicity, and found **no difference in rates of severe events** between the two treatment arms.

Based on this large, well-designed trial, the National Comprehensive Cancer Network (NCCN) guidelines were updated in March 2019 to recommend RT to the prostate in combination with ADT as the new standard of care for men with low-volume metastatic prostate cancer who have no contraindications to RT. **Talk to your doctor about whether this approach is right for you.**

References: Choudhury A, Chen RC, Henry A, et al. *Int J Radiation Oncol Biol Phys* 2019; 104(1):33-35 and Parker CC, James ND, Brawley CD, et al. *Lancet* 2018;392:2353-66.

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