

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).

Treatment of Oligometastasis: Results from the ORIOLE Study

PCF's medical writer Janet Worthington sat down (virtually) with Johns Hopkins radiation oncologist Phuoc Tran, M.D., Ph.D., to discuss his recent trial of radiation therapy.

To the growing list of strategies for attacking prostate cancer, let us add this approach: **Whack-a-Mole**.

That's how Dr. Tran describes it to his patients. The actual scientific name for this highly sophisticated strategy is stereotactic ablative radiotherapy (SABR, highly focused, intense doses of radiation), for men with *oligometastasis* – up to three small bits of cancer that have broken away from the main prostate tumor and started to grow elsewhere.

His strategy was a new one – part of a general rethinking of what represents curable prostate cancer. The boundary used to be very clear: prostate cancer was either confined to the prostate or prostate bed, or it wasn't. A man with only one metastasis was believed to face the same fate, eventually, as a man with widespread metastases. It was just a matter of time.

But Tran believed that the lines of prostate cancer were **not so clear-cut** as scientists had assumed; that instead of two circles – localized and metastatic cancer – that didn't connect, we might be dealing with a **Venn diagram, with oligometastasis as the critical area where the two circles overlap**. "It may be that the window of curability is wider than we thought," he said, and we all hoped that he was right.

Tran and colleagues at Johns Hopkins, Stanford, and Thomas Jefferson University recently published results of the ORIOLE Phase 2 clinical trial in *JAMA Oncology* (<https://jamanetwork.com/journals/jamaoncology/fullarticle/2763312>). The results are promising: 54 men with oligometastasis were randomly assigned either to treatment with SABR or to observation. To detect and keep track of the oligometastases, the study used PSMA-PET scanning, which uses a small molecule linked to PSMA (prostate-specific membrane antigen, found on the surface of prostate cancer cells) as a radioactive tracer. This PSMA-targeting tracer can highlight areas of cancer as small as a BB – much smaller than can be seen on regular PET or CT imaging. "PSMA-PET allows us to treat lesions we otherwise couldn't see," Tran explains. "A CT or bone scan would miss those lesions, and patients would presumably not do as well."

At six months, 61 percent of the men in the observation group progressed – compared to **only 19 percent of the men who received SABR**. "We also saw a **significantly decreased risk of new metastatic lesions** using PSMA PET-CT," says Tran. "The men in the SABR group did considerably better. This is a definite signal that we can perhaps modify metastatic disease."

This was a Phase 2 study, and "we need larger Phase 3 trials," he says. "**But this is very positive, and we hope that in the future, we will be able to change the course of metastatic disease in some men.**"

"**It's like Whack-a-Mole:**" Tran and colleagues have learned from this and other research that men with oligometastasis fall into three basic groups. "Some men do really well after one course of SABR," with no recurrence of cancer. A second group of men have a small recurrence. "Another site pops up; a *microscopic* metastasis that we couldn't see before establishes itself into a *macroscopic* metastasis. It's a limited return of cancer and it responds to another round of SABR." Then some men, after a few months, have multiple new areas of cancer. "For these men, the SABR doesn't control the disease at all."

"**Imagine a green lawn, with one or two dandelions,**" Tran tells his patients: "You can pluck those two or three weeds, and wait and see. Sometimes you get lucky; sometimes another weed or two pops up, and you pluck them. It's like Whack-a-Mole. You can do that for a while," with repeated SABR treatments.

"That probably won't work in every man," Tran says. "Unfortunately, sometimes there will be a whole bunch of seeds all at once, and at that point, you need weed killer all over the lawn," or systemic therapy. However, SABR plus ADT, androgen-blocking drugs, or chemo might one day provide "the multipronged attack required to cure this disease."

More and larger studies are needed but, in the future, Tran envisions men with oligometastasis will require more vigilant monitoring, and ideally, regular follow-up PSMA-PET scanning.

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