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## How to Get More Men in Breast Cancer Trials?

— New draft recommendations from the FDA designed to step up inclusion of more men in breast cancer research

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### Expert Critique

FROM THE ASCO READING ROOM



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As described here, a study by Narijst Duma, et al. found that 65% of breast cancer trials in the past 19 years have

[Full Critique](#)



The FDA recently drafted new recommendations encouraging the inclusion of more men in breast cancer clinical trials.

The [industry draft guidance](#) urges that eligibility for breast cancer drugs should include both men and women, and that there should be a scientific rationale included in a trial protocol when men are excluded from trials.

In addition, the FDA suggests that in cases when men are excluded from, or their inclusion is limited in clinical trials, it "may be possible to extrapolate findings to include male patients in the FDA-approved indication for the drug where no difference in efficacy or safety is anticipated between males and females based on the mechanism of action of a drug." And when there is a concern about the differential efficacy or safety between males and females, additional data should be sought, the FDA said.

"When finalized, the recommendations in the draft guidance will provide clarity for industry regarding how additional data to support efficacy and safety for male patients with breast cancer can be generated through a variety of trial designs using different data sources, including studies using real-world data," said Richard Pazdur, MD, director of the FDA's Oncology Center of Excellence and acting director of the Office of Hematology and Oncology Products in the FDA's



breast cancer and ultimately, provide additional FDA-approved treatment options for patients.

This isn't the first time it has been suggested that there should be greater access to clinical trials for men with breast cancer. For example, in 2013, Oliver Bogler, PhD, currently at the ECHO Institute at the University of New Mexico, and a breast cancer survivor, [presented a study at the San Antonio Breast Cancer Symposium](#) in which he reported that an analysis of 5,000 clinical trials showed that just about one-third recruited both men and women.

And those numbers don't appear to have changed.

In a study published last year in *JNCI Cancer Spectrum*, researchers led by Narjust Duma, MD, then of the Mayo Clinic in Rochester, Minnesota, and now at the University of Wisconsin Carbone Cancer Center in Madison, reported that 65% of 426 breast cancer trials that took place from January 1, 2000 through April 31, 2017, excluded male breast cancer patients in the enrollment criteria.

Overall, 0.42% of trial participants were men, with the lowest enrollment rates in hormonal and targeted therapy trials (both 0.1%). In addition, no men were included in the 70 trials studying neoadjuvant therapies.

"When a female breast cancer patient comes to us, we make our treatment recommendations based on data," said Duma. "But what can we tell men, when we don't have the data? 'We think it will work, but we really don't have the evidence.' It's fundamentally unfair."

Since few prospective studies of treatment in men have been performed, management of male breast cancer is based largely on extrapolation from results in postmenopausal women.

However, Duma pointed out, despite the fact that breast cancers in men and women have similar characteristics, "they are different," -- as demonstrated in the case of aromatase inhibitors, for example.

"When aromatase inhibitors came out we believed they would be very effective in male patients," said Duma. The reason for this is that these inhibitors stop estrogen production by blocking aromatase in fat tissue that converts male hormones from the adrenal glands into estrogen.

However, the data seems to suggest that aromatase inhibitors aren't as effective in suppressing estrogen in men as they are in women. Larissa Korde, MD, MPH, writing in *The Oncologist*, said that "although aromatase inhibitors are the treatment of choice for postmenopausal female breast cancer, it is generally not considered the standard for [male breast cancer]."

However, as Korde pointed out later in the article, oncologists "continue to extrapolate from data from female patients to make clinical treatment decisions, despite growing evidence of biological differences between male and female breast cancer. The use of aromatase inhibitors in the



## Funding Issues

Funding continues to be a major barrier to including more men in clinical trials. In his 2013 paper, Bogler, using the SciVal Funding database, found that about \$7.5 million over 10 years of funded projects even consider male breast cancer.

"This works out to an average of \$750,000 a year -- well below 1% of the \$620 million annually committed by NCI to breast cancer overall," he wrote. "It works out to be less than \$330 per newly diagnosed man vs \$2,600 per newly diagnosed woman. Funding male breast cancer research at 1% would commit \$6.2 million a year, or sufficient to support 15 RO1 grants, providing significant opportunity for discovery."

According to the American Cancer Society, 2,670 new cases of invasive breast cancer will be diagnosed in men in 2019. Finding and recruiting these men into clinical trials will also require more funding, Duma noted.

However, even the relatively small number of male breast cancers is not a completely reasonable explanation for the inability to include these men in trials, she continued. "It's true it's not a lot of men, but 2,500 cases are more than for many sarcomas for which we do have clinical trials."

She also pointed to the International Male Breast Cancer Program as a model that demonstrates that it is possible to recruit enough patients to run a clinical trial for such a small population. Through this program, investigators created a prospective registry for male breast cancer with the twin goals of evaluating the clinical and biological features of male breast cancer, as well as the feasibility of carrying out a prospective clinical trial.

The investigators were able to [prospectively accrue 557 patients to the registry](#), demonstrating the "feasibility of pursuing a therapeutic clinical trial in men with breast cancer."

**Duma and co-authors reported having no conflicts of interest.**

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- **Primary Source**

*JNCI Cancer Spectrum*

Source Reference: [Duma N, et al "Exclusion of Male Patients in Breast Cancer Clinical Trials" \*JNCI Cancer Spectrum\* 2018;](#)

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