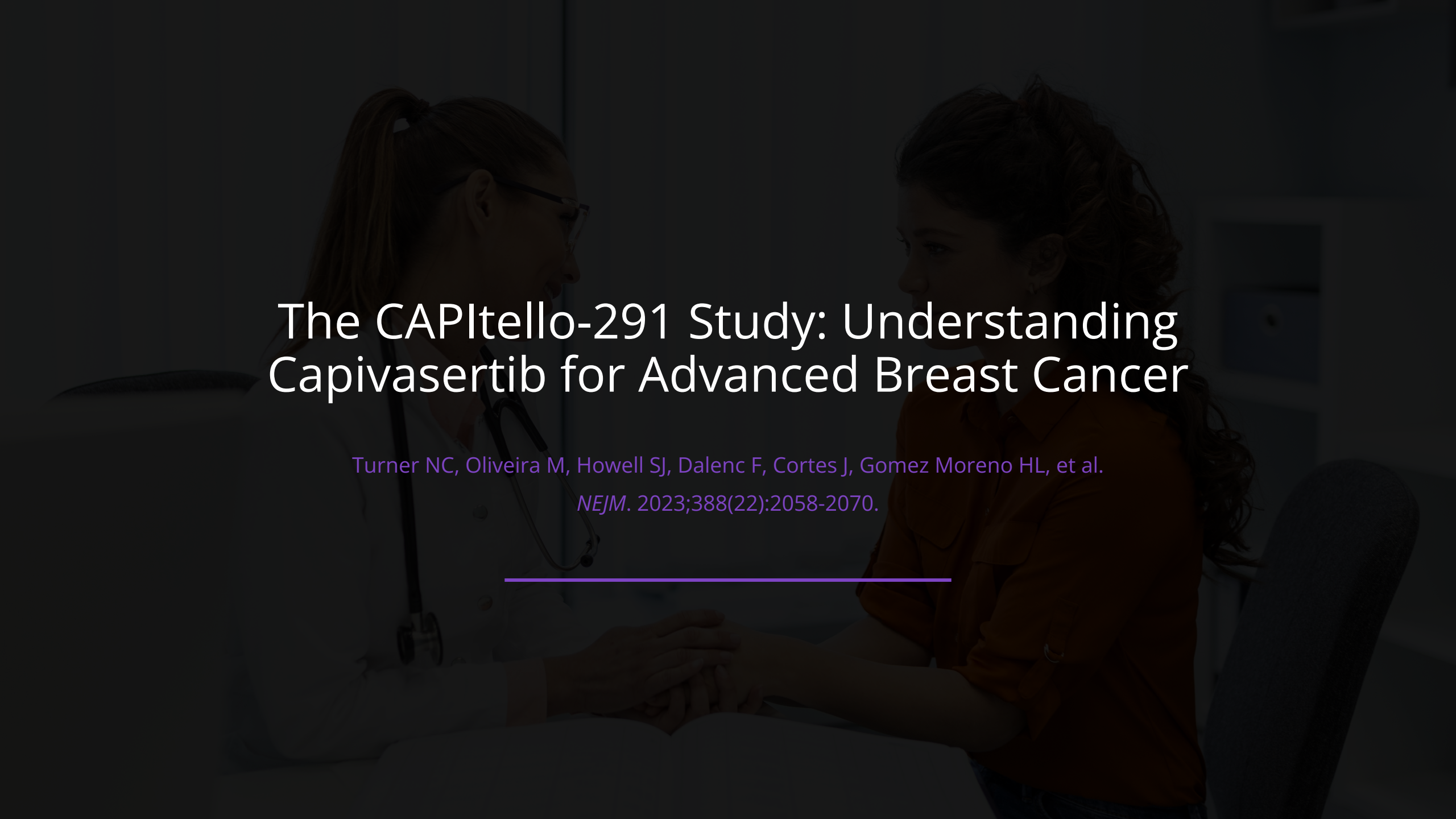

The CAPItello-291 Study: Understanding Capivasertib for Advanced Breast Cancer

Turner NC, Oliveira M, Howell SJ, Dalenc F, Cortes J, Gomez Moreno HL, et al.

NEJM. 2023;388(22):2058-2070.

Why Was This Study Important?

Goal of the Study

- This study wanted to see how well a new treatment regimen worked in men and women with HR+, HER2- advanced breast cancer

Study Background

- The usual first-line treatment used for these patients includes a hormone therapy (which blocks or reduces certain hormones that help cancer grow) plus another type of targeted cancer therapy called a CDK inhibitor
- However, many patients still get worse after getting this treatment
- This might be because they have tumors that have AKT pathway alteration, which means they cannot respond to hormone therapy

Possible Benefit for Patients

- Some new drugs have shown that they can stop AKT pathway alteration to help those tumors respond to hormone therapy and help patients live longer without their cancer getting worse
- This study looked at capivasertib, which is one of these drugs that can stop AKT pathway alteration
- This study helped to provide more proof that using a drug that can stop AKT pathway alteration in addition to hormone therapy can be helpful for patients with HR+, HER2- advanced breast cancer

HER2, human epidermal growth factor receptor 2; **HR**, hormone receptor.

1. Turner NC, et al. *NEJM*. 2023;388(22):2058-2070.

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What Was This Study About?

The study looked to see how well capivasertib worked for women and men with HR+, HER2- advanced breast cancer

The cancer had to have already progressed during or after treatment with an aromatase inhibitor (an older type of hormone therapy), with or without treatment with a CDK4/6 inhibitor

The goal was to see if adding capivasertib to fulvestrant (a type of hormone therapy) could help people live longer without their cancer getting worse

HER2, human epidermal growth factor receptor 2; **HR**, hormone receptor.

1. Turner NC, et al. *NEJM*. 2023;388(22):2058-2070.

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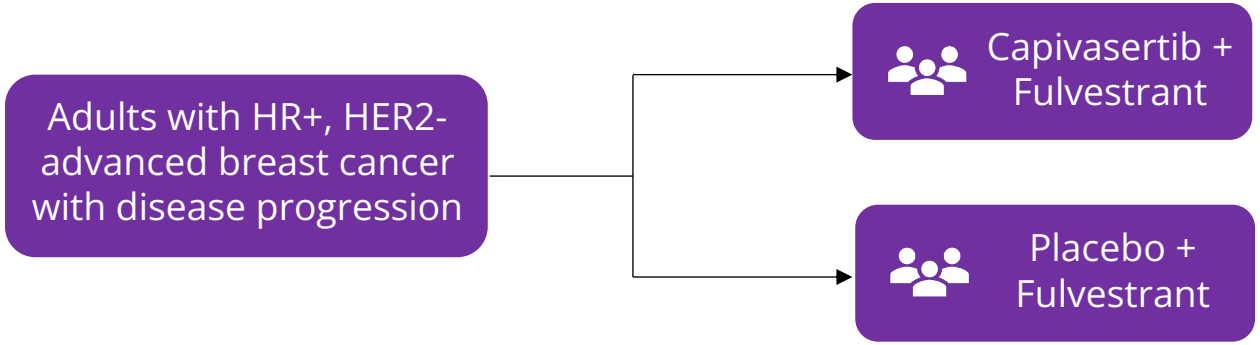
How Did the Study Work?

- The study randomly assigned people to one of two groups, where they either were treated with the drug (capivasertib) or a placebo (sugar pill) in combination with fulvestrant:[1]



- It was called a “double-blind” study, which means that neither the patients nor the doctors knew who was getting the real medicine[1,2]
- The primary endpoint (the main result that was measured) was PFS (how long a patient lives without the cancer getting worse)[1,3,4]
- People took the medicine (or placebo) until their cancer got worse, they had too many side effects, they chose to stop taking the medicine, or they died[1]

HER2, human epidermal growth factor receptor 2; **HR**, hormone receptor; **PFS**, progression-free survival.

1. Turner NC, et al. *NEJM*. 2023;388(22):2058-2070. 2. NCI Dictionary of Cancer Terms. Double-blind study. Available at: https://www.cancer.gov/publications/dictionaries/cancer-terms/def/double-blind-study. Accessed April 28, 2025. 3. NCI Dictionary of Cancer Terms. Primary endpoint. Available at: https://www.cancer.gov/publications/dictionaries/cancer-terms/def/primary-endpoint . Accessed April 28, 2025. 4. NCI Dictionary of Cancer Terms. Progression-free survival. Available at: https://www.cancer.gov/publications/dictionaries/cancer-terms/def/progression-free-survival. Accessed April 28, 2025.

Who Could Participate in the Study?

Patients were included if they were/had...

- Premenopausal, perimenopausal (approaching menopause), or postmenopausal women or men age ≥18 years (≥20 years in Japan)[1,2]
- HR+, HER2- locally advanced or metastatic breast cancer[1]
- Worsening disease after being treated with a specific type of breast cancer treatment[1]
- Cancer that could be measured on scans like CT or MRI[1]
- Performance level of 0 (fully active) or 1 (limited with difficult physical activity but able to do light physical activity)[1,3]

Patients were excluded if they were/had...

- Treated before with hormone therapy, fulvestrant, or another therapy that works similarly to it[1]
- Treated before with drugs that work similarly to capivasertib[1]
- Diabetes requiring insulin, or HbA1c level (a diabetes blood measurement) ≥8.0%[1]

CT, computed tomography; **ECOG**, Eastern Cooperative Oncology Group; **HbA1c**, hemoglobin A1c; **HER2**, human epidermal growth factor receptor 2; **HR**, hormone receptor; **MRI**, magnetic resonance imaging.

1. Turner NC, et al. *NEJM*. 2023;388(22):2058-2070. 2. NCI Dictionary of Cancer Terms. Perimenopausal. Available at: https://www.cancer.gov/publications/dictionaries/cancer-terms/def/perimenopausal. Accessed April 28, 2025. 3. Oken MM, et al. *Am J Clin Oncol*. 1982;5(6):649-655.

What Did the Study Find?

Treatment with capivasertib + fulvestrant caused longer PFS compared to placebo + fulvestrant in:

Overall population

	# Patients	# Events	PFS (Months)
Capivasertib + Fulvestrant	335	258	7.2
Placebo + Fulvestrant	353	293	3.6

Patients with tumors that had AKT pathway alteration

	# Patients	# Events	PFS (Months)
Capivasertib + Fulvestrant	155	121	7.3
Placebo + Fulvestrant	134	115	3.1

Adding capivasertib to fulvestrant helped people live longer without their cancer getting worse

PFS, progression-free survival.

1. Turner NC, et al. *NEJM*. 2023;388(22):2058-2070.

SP MEDICAL WRITING

What Were the Side Effects?

The most common side effects after treatment with capivasertib were diarrhea and rash:

	Capivasertib + Fulvestrant	Placebo + Fulvestrant
Diarrhea	72.4%	20.0%
Rash	38.0%	7.1%

Side effects also caused patients to miss doses, require a decrease in dose, and/or leave the study all together:

	Capivasertib + Fulvestrant	Placebo + Fulvestrant
Side Effects Causing Patients to Miss Doses	34.9%	10.3%
Side Effects Causing a Decrease in Dose	19.7%	1.7%
Side Effects Causing Patients to Leave the Study	13.0%	2.3%

- The data shown here is what was seen in the overall population
- Side effects were similar in patients with tumors that had AKT pathway alteration

1. Turner NC, et al. *NEJM*. 2023;388(22):2058-2070.

Key Takeaways

- Capivasertib is a new treatment option for advanced breast cancer that has stopped responding to other hormone therapies

- Adding capivasertib to fulvestrant helped patients with advanced breast cancer who had disease progression live longer without their cancer getting worse

- The side effects caused by capivasertib found in the study were similar to other drugs that work the same way (stopping AKT pathway alteration)

- The number of patients who had to leave the study because of side effects was low (13%)

1. Turner NC, et al. *NEJM*. 2023;388(22):2058-2070.