

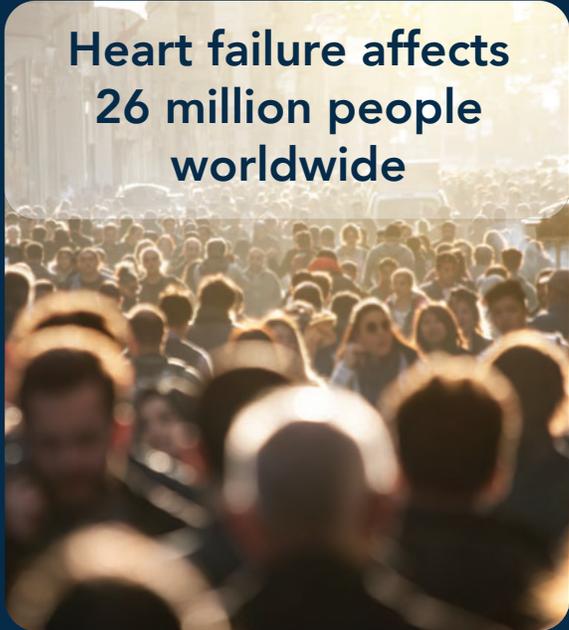
# CASE STUDY HIGHLIGHTS: Bucindolol

How genetic differences may contribute to different efficacies in treatment response

## BACKGROUND

Heart failure, also known as congestive heart failure, occurs when the heart either fails to fill with enough blood (right sided heart failure) and/or is unable to pump enough blood to support other organs in the body (left sided heart failure).

Heart failure affects 26 million people worldwide and, despite significant advances in therapies and preventions, people still suffer from complications and treatment challenges.



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## RESEARCH

A combination of different medications are used in the treatment of heart failure. Bucindolol is a treatment that was tested in clinical trials for heart failure in the BEST (Beta-Blocker Evaluation Survival Trial) clinical trial:

- Bucindolol was given as an additional therapy at the same time as two other drugs to determine if it provided any added benefit.
- The trial specifically recruited selected subgroups (e.g., women, ethnically and racially diverse populations) as it was known that Black patients have a higher death rate from heart failure in the United States.
- Treatment groups were divided by the severity of their heart failure symptoms, sex, and self-reported race.



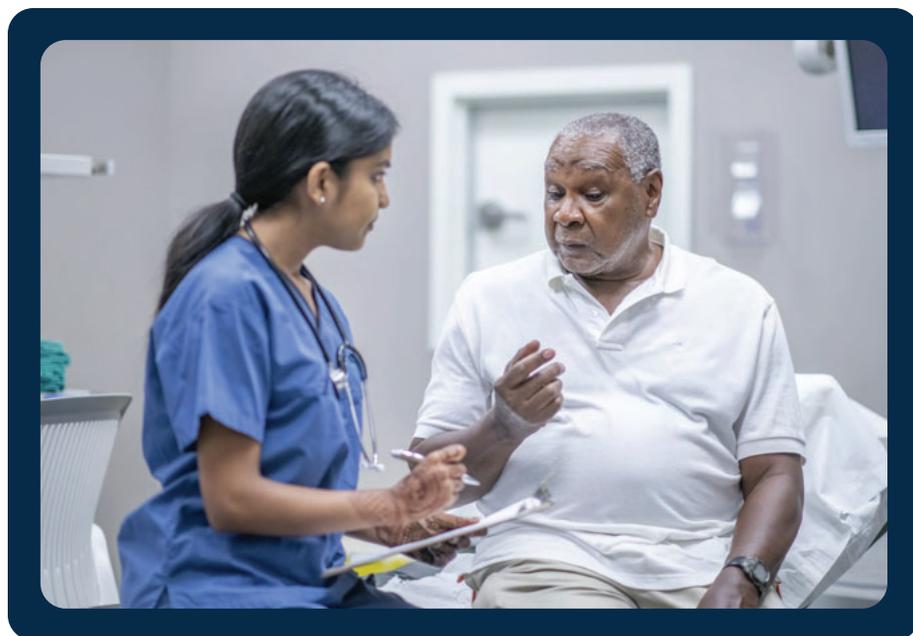
**MULTI-REGIONAL  
CLINICAL TRIALS**

THE MRCT CENTER of  
BRIGHAM AND WOMEN'S HOSPITAL  
and HARVARD

## Findings from trials initially suggested good effect:

- Death from cardiovascular causes was significantly lower in the bucindolol group.
- Bucindolol reduced the average number of hospitalizations and average number of inpatient days per patient.

However, while the addition of bucindolol to standard treatments for heart failure reduced the number of times patients had to go to the hospital, it did not appear to change the risk of death from heart failure.



Careful study and further sub-group analysis, however, showed that “non-Black” patients—those who did not self-identify as Black—did better on bucindolol than without it: the rate of death from heart disease, the number of times that patients had to go back into the hospital for heart problems, and how long they stayed, were all lowered.

Black patients, however, did not experience the same level of survival benefit.

## DISCOVERY

The reason that Black patients did not benefit and that non-black patients did benefit was further studied.

Different forms of one gene change whether or not a person responds to the drug, and one form of that gene is more common (but certainly not always present) in Black patients than non-black patients.

The drug response does not relate to race—it relates to the fact that one form of the gene is more common in one population than another. However, given the lack of impact on overall mortality in the Black population, and the general availability of effective beta-blockers and other therapies, the development of bucindolol in the United States was abandoned. Whether genetic testing would be helpful to drive the choice of therapy has not yet been examined.

## CONCLUSION

Efficacy of beta-blockers, specifically bucindolol, appeared to differ between White and Black patients, a finding that was in part revealed by sufficient representation of both populations to permit post hoc subgroup analyses.

Genetic polymorphisms, and the different background rates of the polymorphism in different race and ethnic populations, may have contributed to different efficacies in response.



The safety profile of a medication may differ among different subpopulations of participants and the possibility of differences in adverse events—and efficacy—is good reason to include participants of diverse backgrounds in clinical trials and post-marketing research studies. Often the biological basis of any difference in safety or efficacy based on demographics is poorly understood.

**For citations and more information on this case, please see the [MRCT Center toolkit](#).**