

# CASE STUDY HIGHLIGHTS:

## Omapatrilat

How diverse participation in clinical trials can reveal differing safety profiles of a treatment

### BACKGROUND

High blood pressure, also known as hypertension, is a common condition that occurs when the blood that flows through veins or arteries is at a higher than normal pressure.

High blood pressure increases risk for heart disease and stroke. In 2017, nearly 500,000 deaths in the U.S. listed hypertension as a primary or contributing cause. Rates of high blood pressure vary by sex, race, ethnicity, and geography, which further complicates treatment and medication management.

Treatment for high blood pressure involves a combination of therapies, lifestyle changes, and medications. A common medication used to treat hypertension is angiotensin-converting enzyme (ACE) inhibitors, which work by blocking the hormone responsible for narrowing blood vessels.

### RESEARCH

Omapatrilat, a drug developed by Bristol-Myers Squibb, was initially viewed as a more effective anti-hypertensive treatment because it lowered blood pressure in different ways.

Clinical trials with omapatrilat were promising. They showed that omapatrilat was more effective in lowering blood pressure than another, common marketed drug.

An estimated 1.13 billion people worldwide have hypertension, the majority of which live in low and middle income countries.



**MULTI-REGIONAL  
CLINICAL TRIALS**

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However, these studies also showed an increase in a side effect called **angioedema** – a **condition where there is localized swelling of the skin particularly on the face, lips, mouth, and throat.**

Additional studies again showed that omapatrilat significantly reduced blood pressure as compared to another drug and those who received omapatrilat did not require as much antihypertensive therapy overall.


This was true for all subgroups analyzed (e.g., age, sex, ethnicity, race, type of and severity of hypertension, comorbidity).

## DISCOVERY

Despite the reduction in blood pressure seen across all subgroups, the rate of angioedema was approximated 3x higher in Black patients, and was also higher among smokers.

- Given the risk of serious cardiovascular disease, the reduction in potential cardiovascular events by treatment with omapatrilat **would outweigh the risk of clinically significant angioedema when considering all patient groups.**
- The increased risk in Black patients and smokers would need to be considered prior to prescribing the drug.





Bristol-Myers Squibb initially decided to stop developing omapatrilat in the United States, even for patients with severe disease and with careful follow-up. Then, after a non-approval vote by a U.S. FDA advisory committee, clinical development was stopped completely.

To date, the biological cause of angioedema remains unexplained and the pathophysiological explanation for the increased risk in Black patients remains unknown.

## CONCLUSION

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.

Safety of a drug must be measured with regard to benefit, both which may vary by subpopulation. 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**.