New tuberculosis treatment could save millions of lives

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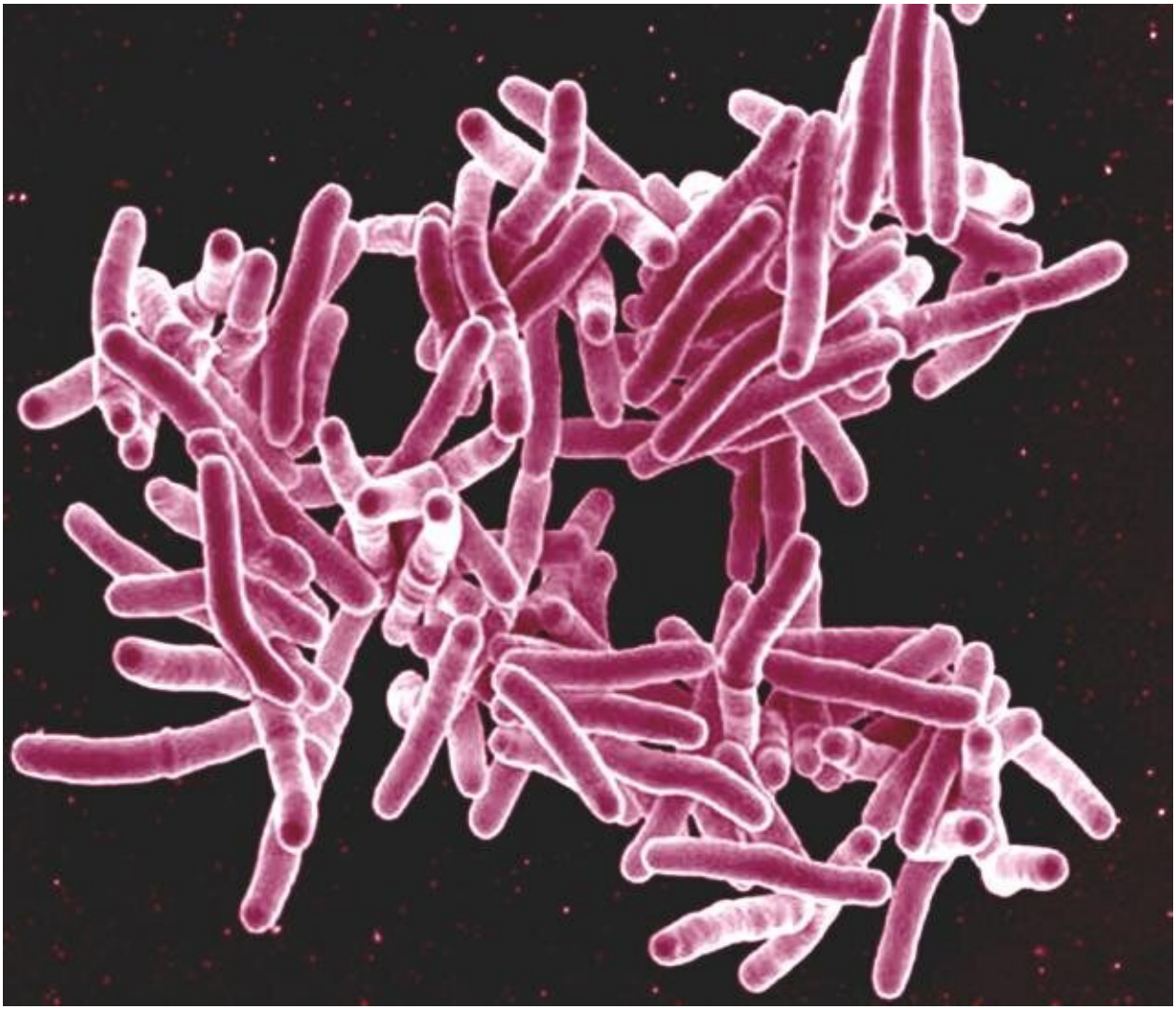

Scanning electron micrograph of *Mycobacterium tuberculosis* bacteria, which cause TB. Credit: NIAID

Scientists from the University of St Andrews reveal a new tuberculosis (TB) therapeutics that could shorten the treatment of the disease by up to two months, potentially saving millions of lives.

Dr. Muge Cevik, a clinical academic in infectious diseases and medical virology based in the Infections and Global Health Research Division of the School of Medicine at St Andrews, delivered the results of the worldwide TB Alliance's SimpliciTB clinical trial at the 30th annual Conference on Retroviruses and Opportunistic Infections (CROI) in Seattle on Monday, February 20.

Tuberculosis causes about 1 million deaths every year. To change this and save lives, new tools and new treatments are required. Active TB must be treated with a combination of drugs; the most drug-sensitive forms of TB require at least four months of treatment using four anti-TB drugs. According to the World Health Organization (WHO) an estimated 1.6 million people died of TB in 2021, although the precise numbers are not known, and recent research suggests that TB could have killed many more people.

The international SimpliciTB trial was conducted to evaluate the BPaMZ regimen, consisting of bedaquiline (B), pretomanid (Pa), moxifloxacin (M), and pyrazinamide (Z). This combination previously showed high efficacy and treatment shortening potential in both preclinical evaluations and an early-stage clinical study in drug resistant patients.

SimpliciTB enrolled 455 patients with drug-susceptible (DS) or drug-resistant (DR) tuberculosis (TB) at 26 sites across eight countries: South Africa, Tanzania, Georgia, Brazil, Russia, the Philippines, Uganda, and Malaysia. The clinical trial was designed to evaluate the safety and efficacy of BPaMZ in patients with either DS-TB or DR-TB.

As presented at CROI, the results of the trial showed that the BPaMZ

regimen was highly potent against the TB bacteria, meeting its primary endpoint with DS-TB participants 2.93 times more likely to culture convert by week eight. However, the four-month experimental BPaMZ regimen did not meet the secondary endpoint of noninferiority in percent favorable outcomes compared to six months of HRZE in DS-TB. This was due to adherence challenges, with approximately 10% of patients on the BPaMZ arms discontinuing treatment due to side effects.

"Recent progress in tuberculosis therapeutics has been limited, with few new drug classes emerging in the last 50 years," said Dr. Muge Cevik. "Innovative clinical trials like SimpliciTB help us better understand how novel drug regimens work against both drug-sensitive and drug-resistant TB, lighting the way to better treatment options for all TB patients."

In 2021, 10 million people were infected with TB and about 1.6 million people died. It is estimated that about 500,000 people every year are infected by a drug-resistant form of the disease, and in some regions as many as 40% of all cases are drug resistant. Novel drug regimens are urgently needed to help bring the TB pandemic under control.

Drug-resistant TB develops when the long, complex, decades-old TB drug regimen is improperly administered, or when people contract TB from others who have drug-resistant disease—highlighting the urgent need to develop better and shorter treatment regimens. Only an estimated one third of people with drug-resistant TB infections received treatment in 2021.

The Infection and Global Health Research Division at the University of St Andrews works in a wide range of fields that includes clinical trials, genetics, anti-microbial resistance, diagnostic tools, education, and global health policy. Professor Stephen Gillespie, leader of the infection group at St Andrews, said, "This study shows the value of St Andrews world-leading partnership working with international collaborators and

the TB Alliance. Together, we have a sustained commitment to develop new and better treatments for tuberculosis which remains a threat to human health globally."

Dr. Derek Sloan, senior lecturer in the School of Medicine involved in the global trial added, "The trial suggests that new antibiotic combinations can kill all types of TB bacteria faster than traditional approaches, which is exciting. However, as we find new options to improve TB treatment, we still need to work out which therapies are most suitable for each individual patient.

"Future work will include more detailed investigation of which anti-TB antibiotics work best together. Future considerations will include patient safety and the complex logistics of how to implement new treatment strategies across the diverse range of settings where TB is a major threat to health, worldwide."

The TB Alliance plans to submit data from SimpliciTB to a peer-reviewed publication. The TB Alliance is a not-for-profit organization dedicated to the discovery, development and delivery of better, faster-acting and affordable tuberculosis drugs that are available to those who need them.

Provided by University of St Andrews