

FOR IMMEDIATE RELEASE**STREAM CLINICAL TRIAL RESULTS PROVE THAT A NINE-MONTH TREATMENT REGIMEN FOR MDR-TB IS AS EFFECTIVE AS THE 20-MONTH REGIMEN**

(Paris, France) - Final results - released today in the [New England Journal of Medicine](#) and just ahead of World TB Day on 24 March - from Stage 1 of the STREAM randomised clinical trial show that a 9-11-month treatment regimen is as effective in treating multidrug-resistant tuberculosis (MDR-TB), when given under trial conditions, as the 20-24-month treatment regimen recommended in the 2011 World Health Organization (WHO) guidelines.

The STREAM trial is the world's first multi-country randomised phase III clinical trial to test the efficacy, safety and economic impact of shortened MDR-TB treatment regimens. STREAM - funded by the United States Agency for International Development (USAID), initiated by The Union and sponsored by Vital Strategies - is being implemented with key global partners, including the Medical Research Council Clinical Trials Unit at UCL, Liverpool School of Tropical Medicine and Institute of Tropical Medicine Antwerp

Stage 1 of the STREAM trial looked to determine whether a 9-11-month treatment regimen that demonstrated cure rates exceeding 85 percent during a pilot programme in Bangladesh is as effective as the longer regimen under clinical trial conditions. Seven sites in Viet Nam, Mongolia, South Africa, and Ethiopia participated in Stage 1. In June 2015, Stage 1 of the trial enrolled its 424th and final patient. As the 9-11-month regimen provides potential cost savings to patients and health systems compared to the 20-month regimen, an assessment of the costs under each regimen faced by participants and health systems was included in Ethiopia and South Africa.

Worldwide in 2017, an estimated 558,000 people developed TB that was resistant to rifampicin, the most effective first-line drug, and of these, 82 percent had MDR-TB (defined as resistant to at least the two first-line antibiotics isoniazid and rifampicin) (source WHO 2018 Global Tuberculosis Report). MDR-TB has been declared a public health crisis by WHO. The 20-24-month regimen used in many countries globally is costly, has significant side effects and the length of the regimen makes it hard for both patients and the health system. The regimen has an average treatment success rate of approximately 50 percent when used in many real-world treatment settings.

Because of these widely-acknowledged challenges, in 2016 the WHO guidelines were updated to recommend a shorter, 9-12-month regimen for most people with MDR-TB under specific conditions. The guidelines acknowledge that this recommendation is based on very low certainty in the evidence.

THE RESULTS

9-11-month regimen is as effective as the 20-24-month regimen in terms of efficacy

The results showed that the 9-11-month regimen was statistically non-inferior to the 20-24-month regimen, in terms of efficacy (78.8 percent of assessable participants had a favourable outcome, compared to 79.8 percent in the longer regimen).

There was no evidence that efficacy results were worse in HIV-infected participants compared to HIV-negative participants.

I.D. Rusen, Project Director for the STREAM trial said: “Until now there has been a lack of strong supporting evidence to underpin MDR-TB treatment guidelines. The results from STREAM Stage 1 help to fill that gap.

“The final results show that the trial setting meant more patients successfully completed treatment on the 20-24-month regimen than we know is often the case in real life settings. In routine programmes unable to achieve the high STREAM retention rates, the 9-11-month regimen may actually perform better in comparison to the longer regimen.”

Andrew Nunn, STREAM co-Chief Investigator from the MRC Clinical Trials Unit at UCL, said: “We know from programmatic data that the 20-24-month regimen has a number of major drawbacks, including the difficulty of completing such a long treatment, the significant side-effects of the drugs used and poor treatment outcomes. Shorter, more effective and safer regimens are urgently needed.

“The outcomes in patients coinfecting with HIV are particularly important as they suggest that the 9-11-month regimen is no less effective in this patient group than the longer regimen.”

ECG monitoring

The final results show that electrocardiogram (ECG) monitoring was very useful, and required throughout treatment. This was done effectively during the trial, and close monitoring would also be necessary with regimen use in routine programme settings.

Sarah Meredith, clinical co-Chief Investigator for STREAM and Professor of Clinical Trials at the MRC Clinical Trials Unit at UCL, said: “We know that ECG monitoring throughout treatment is likely to be challenging in most routine programme settings, where access to ECG monitoring is limited. We have the opportunity to try to improve the regimen during the remainder of STREAM Stage 2 to see if we can reduce the need for ECG monitoring throughout treatment. This is just one reason why dynamic clinical trials of this nature are so important.”

Health economics

The analysis of the economic burden of MDR-TB, led by the Liverpool School of Tropical Medicine in collaboration with University of Warwick and investigators in South Africa and Ethiopia, will be published in due course. For South Africa and Ethiopia, this analysis presents a breakdown of health system data for each regimen from including costs of in-patient stay, laboratory tests, cardiac safety monitoring, medication, staff time, social support, and consumables. More detailed data are presented from Ethiopia on costs of management of Serious Adverse Events (SAEs) and costs incurred by trial participants, which also give an insight into the financial and social well-being of

participants on each regimen.

Bertie Squire, co-Investigator for STREAM and lead for the Health Economic Analysis said: “This is the first phase III trial of TB treatment that includes a within-trial economic evaluation. The results will be useful for countries and programmes as they decide on whether and how to introduce shorter regimens for treatment of MDR-TB”.

Stage 1 of the Standardised Treatment Regimen of Anti-TB Drugs for Patients with MDR-TB (STREAM) trial was funded through the TREAT TB cooperative agreement with the United States Agency for International Development (USAID) with additional funding from the UK Medical Research Council and the UK Department for International Development (DFID).

WHAT USAID SAYS

Irene Koek, Deputy Assistant Administrator in USAID's Global Health Bureau, said:

“USAID is proud to have supported the STREAM study, the first randomised clinical trial for MDR-TB. This study has already served as a benchmark for other MDR-TB clinical trials and as a result, there are now more MDR-TB treatment regimens being studied than ever. In addition, data from this study, combined with data from observational studies, have demonstrated that shorter, less toxic, effective, and well-tolerated treatment regimens are now feasible.”

WHAT THE UNION SAYS

Dr Paula I Fujiwara, Scientific Director, The Union, said:

“The results from STREAM Stage 1 support the programmatic evidence that the STREAM Stage 1 9-11 month shorter regimen is as good as the longer 20-24-month regimen, recommended in the 2011 WHO guidelines, in terms of efficacy. Observational studies and individual patient data show that the regimen performs similarly in the Randomised Clinical Trial (RCT) as in programmatic conditions. This cannot be said for the previous longer regimen.

“The shorter duration of the shorter regimen is a clear advantage to the patient and increases the likelihood that the treatment is completed, with an earlier return of the patient to work and social activity.

“The STREAM Stage 1 results come at a time when TB science is progressing quickly; we are very keen to keep this momentum going. There is still a very real and urgent need to improve the efficacy and safety of MDR-TB treatment and trials like STREAM and STREAM Stage 2, as well as other ongoing trials are a vital part of this work.”

[Read Union response in full here](#)

ENDS

About The Union

The Union was founded in 1920 and is the world's first global health organisation. We are a global leader in ending TB, we fight the tobacco industry, and we solve key problems in treating major diseases. We use science to design the best treatments and policies for the most pressing public health challenges affecting people living in poverty around the world. The Unions members, staff

and consultants operate in more than 150 countries and embody our core values of accountability, independence, quality and solidarity.

theunion.org

About Vital Strategies

Vital Strategies is a global health organization that believes every person should be protected by a strong public health system. Our programs reach into 73 countries and help prevent death and illness from noncommunicable disease, reduce harm caused by environmental factors, and support cities as engines for public health. We consult with governments on issues including restricting junk food marketing to kids, promoting smoke-free laws, improving indoor and outdoor air quality, and strengthening road safety. These are protections that can add up to millions of lives saved. Our team combines evidence-based strategies with innovation to help develop and implement sound public health policies, manage programs efficiently, strengthen data systems, conduct research and design strategic communication campaigns for policy and behavior change.

To find out more, please visit www.vitalstrategies.org or Twitter @VitalStrat.

About the Medical Research Council Clinical Trials Unit at UCL

The Medical Research Council Clinical Trials Unit (MRC CTU) at UCL has a strong track record of resolving internationally important questions in infectious diseases and cancer, and delivering swifter and more effective translation of scientific research into patient benefits. Our research helps to improve healthcare in the UK and around the world. We are part of the Institute of Clinical Trials and Methodology in the UCL School of Life and Medical Sciences. We receive core funding from the UK Medical Research Council. The Medical Research Council is at the forefront of scientific discovery to improve human health. Founded in 1913 to tackle tuberculosis, the MRC now invests taxpayers' money in some of the best medical research in the world across every area of health.

www.mrc.ac.uk

About LSTM

Liverpool School of Tropical Medicine (LSTM) is the world's oldest centre of excellence in tropical medicine and international public health. It has been engaged in the fight against infectious, debilitating and disabling diseases since 1898 and continues that today with a research portfolio over £320 million and an expanding teaching programme attracting students from over 65 countries. For more info see www.lstmed.ac.uk

About The Institute of Tropical Medicine (ITM) in Antwerp

The Institute of Tropical Medicine (ITM) in Antwerp, Belgium is the central microbiology laboratory for the STREAM clinical trial. ITM is one of the world's leading institutes for training, research and service delivery in tropical medicine and health care in developing countries. For more info see www.itg.be

www.treattb.org

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