

PRESS RELEASE - CONFIDENTIAL

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STREAM CLINICAL TRIAL RESULTS PROVIDE VITAL INSIGHT INTO NINE-MONTH TREATMENT REGIMEN FOR MULTIDRUG-RESISTANT TUBERCULOSIS

(Guadalajara, Mexico) -- Preliminary results - released today at the 48th Union Conference on Lung Health - from Stage 1 of the STREAM randomised clinical trial show that the nine-month treatment regimen being tested achieved favourable outcomes in almost 80 percent of those treated.

The results suggest the nine-month regimen is very close to the effectiveness of the 20-24 month regimen recommended in the 2011 WHO guidelines, when both regimens are given under trial conditions.

The STREAM trial - initiated by The Union in 2012 with its main partner, the Medical Research Council Clinical Trials Unit at UCL, is the world's first multi-country randomised clinical trial to test the efficacy, safety and economic impact of shortened multidrug-resistant tuberculosis (MDR-TB) treatment regimens.

Stage 1 of the STREAM trial seeks to determine whether a nine-month treatment regimen that demonstrated cure rates exceeding 80 percent during a pilot programme in Bangladesh is as effective as the longer regimen under clinical trial conditions. Seven sites in Vietnam, Mongolia, South Africa, and Ethiopia are participating in Stage 1. In June 2015, Stage 1 of the trial enrolled its 424th and final patient.

Multidrug-resistant TB (MDR-TB), defined as forms of TB that are resistant to at least the two first-line antibiotics isoniazid and rifampicin affected an estimated 480,000 people in 2015 (source WHO 2016 Global Tuberculosis report) and has been declared a public health crisis by the World Health Organization (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, nine-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

Nine-month and 20-month regimen very close in terms of efficacy

The results suggest the efficacy of the nine-month regimen in the trial will be very close to the longer regimen currently also recommended by WHO, but, statistically,

we are not currently able to say the nine-month regimen is equivalent to the longer regimen (78.1 percent of patients receiving the nine-month regimen achieved a favourable outcome, compared to 80.6 percent of patients receiving the 20-24 month regimen)

I.D. Rusen, Union lead for the STREAM trial said: “The nine-month regimen did as well or even better than we expected given the rigorous standards of the clinical trial, but the 20-24 month regimen did much better than routinely reported outcomes from programme settings.

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

Andrew Nunn, statistician at the MRC Clinical Trials Unit at UCL and STREAM co-chief investigator, said: “STREAM provides a robust comparative estimate of what can be achieved by both regimens under rigorous trial conditions and in diverse settings. The outcomes in patients coinfecting with HIV are particularly important as they suggest that the nine-month regimen is no less effective in this patient group than the 20-24 month regimen.”

ECG monitoring

The preliminary 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 Medical Research Council Clinical Trials Unit at UCL, said: “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, and why we felt it important to release these preliminary results as soon as they became available.”

Health economics

In terms of the economic burden of MDR-TB, **health economics analysis conducted by the Liverpool School of Tropical Medicine** show the nine-month regimen reduces costs to both the health system and patients, compared to the 20-24 month regimen. In both Ethiopia and South Africa where these costs were measured the nine-month regimen reduced the cost to the health system for each patient by a least a third. Patients’ direct costs were also reduced due to fewer visits to health facilities, reduced spending on supplementary food and the fact that the patient was able to return to work sooner than if on the 20-24 month regimen.

Pill burden

The nine-month regimen also has a reduction in pill burden by approximately two-thirds compared to the 20-24 month regimen.

Follow-up of Stage 1 is on going, and full results will be published next year, which will include data from the final follow-up visits. These additional data are unlikely to materially change the results.

The STREAM trial is currently implemented by The Union, the Medical Research Council Clinical Trials Unit at UCL and several key partners. Vital Strategies, based in New York, is supporting several important areas of the trial including pharmaceutical management and community engagement. Other collaborating partners include Institute of Tropical Medicine and Liverpool School of Tropical Medicine.

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 U.S. Agency for International Development (USAID) with additional funding from the UK Medical Research Council and the UK Department for International Development (DFID).

WHAT THE UNION SAYS

In a response to the preliminary results released today Dr Paula I Fujiwara, Scientific Director, The Union, said:

“The Union is pleased with the performance of the nine-month regimen in the STREAM trial. We believe that this regimen has been shown to be feasible to implement in the field and should continue to result in good treatment outcomes for patients.

“We believe that the results support the current WHO recommendation to change to a shortened regimen for many patients, and that close monitoring remains an important feature of the regimen.

“The nine-month regimen performed in the STREAM trial in a way that was consistent with its use to date within programme settings, such as in the Bangladesh, West Africa and MSF cohort studies. These outcomes were observed despite the high standards of the clinical trial, including stringent definitions of unfavourable outcomes and very long follow-up periods after treatment was completed.

“Observations over many years of supporting programmes in MDR-TB management tells us that the high retention of patients on a 20-24 month regimen in the STREAM trial is very difficult to achieve in the field, and such good treatment outcomes have not to-date and likely will not be replicated in ‘real world’ settings. Nor can patients be expected to tolerate an eight-month period of injections and the huge burden of pills that the 20-24 month regimen requires.

“The STREAM trial demonstrates the importance of evaluating treatment regimens in clinical trials to fully understand their potential. Further research is required to explore ways to make the nine-month regimen even more effective and as safe as possible so its potential can be maximised. STREAM Stage 2 is an important step forward in this process.

“The Union’s Expanded MDR-TB Programme team looks forward to working with our technical partner agencies, including WHO, to fully support programmes as they transition to this shortened treatment regimen.”

From WHO:

“Scientific data form the premise for WHO public health policy recommendations,” said Dr Mario Raviglione, Director of the WHO Global Tuberculosis Programme

(GTB). “It is heartening to see the rapid evolution of scientific evidence on MDR-TB treatment over the past 10 years”. Dr Karin Weyer, GTB Coordinator for Drug resistance, added: “At WHO we are ready to update or refine current policy recommendations on the shorter MDR-TB regimen based on new and quality data, so as to rapidly transfer benefits to people and programmes who struggle with MDR-TB daily.”

From USAID

USAID's Acting Assistant Administrator for Global Health, Irene Koek, said:

“USAID is committed to helping develop new tools and better approaches to combatting TB that can be used effectively at the country level. As the major donor, USAID welcomes the interim results of the first world’s first randomised STREAM clinical trial on MDR-TB regimens. We are committed to a patient-centered approach and support the development of better, shorter, more affordable TB treatment regimens. USAID thanks the Union for their leadership in this effort.”

ENDS

About The Union

The Union is a global scientific organisation with the mission to improve health among people living in poverty. We do that by conducting scientific research, working with governments and other agencies to translate research into better health for people around the world, and delivering projects directly in the field. The Union is made up of a membership body of people around the world who help to advance our mission, and a scientific institute that implements public health projects within countries. For close to 100 years, we have been leaders in the fight against some of the world’s biggest killers, including tuberculosis, lung diseases and tobacco use. Theunion.org

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 Vital Strategies

Vital Strategies is a global health organization that believes every person should be protected by a strong public health system. 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.

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