Shorter tuberculosis treatment not a successful alternative

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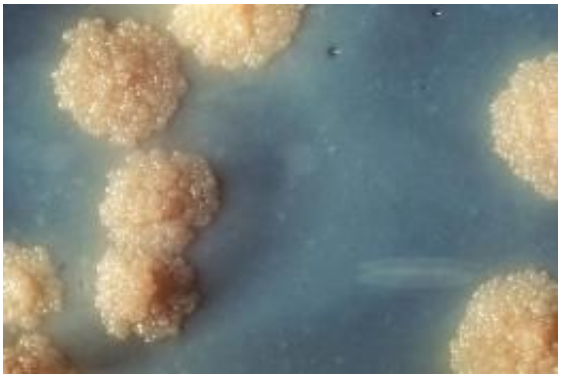

M. tuberculosis bacterial colonies. Credit: Centers for Disease Control and Prevention.

A clinical drug trial conducted in five Sub-Sahara African countries shows that a shortened (four month) treatment for tuberculosis (TB) is well tolerated and may work well in subsets of TB patients, but overall could not be considered as an alternative to the current six month standard treatment. The results of the study were published in the *New England Journal of Medicine*.

TB remains a significant public health problem worldwide. There were an estimated 8.6 million people who developed TB and 1.3 million died from the disease in 2012. The study was designed to verify whether replacing one of the four drugs of the standard regimen with gatifloxacin could shorten the overall treatment duration of TB from six to four

months.

The new treatment was found to be safe and cleared the lungs from TB bacteria rapidly, but a proportion of patients relapsed within months after treatment ended. The shortened treatment appeared beneficial to patients with no TB cavitation in their lungs, undernourished patients, and people living with HIV, but it was less effective among other groups. Therefore, this shortened regimen could not be recommended to replace the current treatment, though the difference in effectiveness between the two treatments varied considerably across the different countries where the study took place.

"The standard treatment is very effective if taken for the full six months," says Dr Christian Lienhardt, who initiated the study while at the Institut de Recherche pour le Développement (IRD) and who now works at the World Health Organization. "But in reality, many do not do this. Poor patient adherence to treatment may increase the risk of TB becoming drug resistant and thus potentially fatal. Shortening treatment duration remains, therefore, a global priority, as it would lead to more patients following the complete treatment."

The study enrolled over 1,800 patients in five African countries (Benin, Guinea Conakry, Kenya, Senegal and South Africa). Half of the patients received the standard six month treatment (rifampicin, isoniazid, pyrazinamide and ethambutol); the other half received the shortened four month treatment with gatifloxacin replacing ethambutol.

"While, unfortunately, the results do not support a much-needed shortened TB regimen," says Dr Piero Olliaro, an author and head of TDR's intervention and implementation research, "this study will teach us a lot about TB treatment response. For example, three of the African partners were TB national programmes, showing that high-level clinical research can be embedded in national control programmes, which is one

of our goals."

The trial is the result of broad collaboration between two sponsors, three national African TB programmes (Benin, Guinea Conakry and Senegal), two African research institutes (Kenyan Medical Research Institute in Nairobi, Kenya and Medical Research Council in Durban, South Africa) and four European institutions: Assistance Publique - Hôpitaux de Paris (France), St Georges Hospital Medical School (UK), the Institute of Tropical Medicine in Antwerp (Belgium), and the London School of Hygiene & Tropical Medicine (UK).

"The study will help improve the way future studies of TB will be conducted, due to the investments made in strengthening capacities for quality clinical trials in highly endemic TB countries," said Dr Corinne Merle, the study coordinator from the London School of Hygiene & Tropical Medicine. "Given the variety of TB drugs that are currently in the development pipeline, these skills will continue to be needed."

This was a large study with 1,356 patients from five countries, noted the trial statistician Dr Katherine Fielding from the London School of Hygiene & Tropical Medicine. "Additional analyses of our data and combining data from other trials will be essential to continue the search for new and improved TB treatments."

"We have ethical, scientific and economic obligations to make the best out of this and other recent TB trials," says Olliaro. "Sharing data will help shorten the journey to the next TB regimen." TDR is organising consultations with stakeholders on the establishment of a TB clinical data sharing platform and community of practice.

More information: Corinne Merle, Katherine Fielding, Piero Olliaro, Christian Lienhardt et al. A Four-Month Gatifloxacin-Containing Regimen for Treating Tuberculosis. *New England Journal of Medicine*.

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