

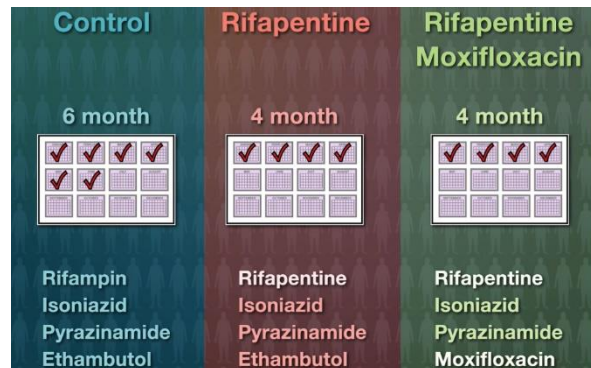
Is a 4-Month Regimen to Treat Drug-Susceptible TB on the Horizon?

One of the core strategies for eliminating TB is to develop better diagnostics and treatment regimens. A very significant improvement would be to shorten the duration of treatment, potentially improving patient treatment adherence and completion while also reducing case management time for public health personnel.

In May 2021, the results of a large international study of two 4-month regimens to treat drug-susceptible TB were published in the New England Journal of Medicine¹. The study – also referred to as “Study 31” – was funded by the Centers for Disease Control and Prevention (CDC) and conducted by the Tuberculosis Trials Consortium (TBTC), “a unique collaboration of researchers from (the) CDC, domestic and international public health departments and academic medical centers, and selected Veterans Administration medical centers”.



As illustrated below, Study 31 compared two 4-month rifapentine (RPT) based regimens to the standard 6-month regimen of rifampin (RIF), isoniazid (INH), pyrazinamide (PZA) and ethambutol (EMB), or RIPE. In one 4-month regimen, RIF was replaced with RPT; in the other, RIF was replaced with RPT and EMB was replaced with moxifloxacin (MXF).



The study results indicate that the 4-month regimen of RPT, INH, PZA, and MXF was noninferior to the standard 6-month regimen of RIPE to treat drug-susceptible TB. However, the 4-month regimen of RPT, INH, PZA, EMB did not meet the criteria for noninferiority to the 6-month RIPE regimen.

It's important to note that while the results for the 4-month regimen of RPT, INH, PZA and MXF are promising, the regimen is not yet recommended for use in the U.S. The Pennsylvania TB Program will not support use of the regimen until it is included in U.S. treatment guidelines for drug-susceptible TB.

Discussion of the study findings and guidance for use of the 4-month regimen were on the agenda for the December 14, 2021 meeting of the U.S. Advisory Council for the Elimination of Tuberculosis² (ACET). The ACET provides “advice and recommendations regarding the elimination of tuberculosis to the Secretary, Department of Health and Human Services; the Assistant Secretary for Health; and the Director, CDC. Meeting minutes will be posted to the [ACET webpage](#) on the CDC website in early 2022.

¹ To review the full article, go to <https://www.nejm.org/doi/full/10.1056/NEJMoa2033400>

² For more information about the ACET, visit <https://www.cdc.gov/tb/topic/research/tbtc/>

Some of the topics likely discussed during the ACET meeting include:

- All study participants had newly diagnosed pulmonary TB.
 - Would this limit initial use of the regimen to patients with pulmonary TB?
- All study participants were “confirmed on culture to be susceptible to isoniazid, rifampin, and fluoroquinolones”.
 - Rapid molecular tests for drug-susceptibility to fluoroquinolones and isoniazid are currently available via the CDC and some private laboratories but are not widely available.
- Overall, the study participants were sicker than the average U.S. patient:
 - Seventy-three percent (73%) had cavitation on chest radiography; and
 - The median body weight of study participants was 53.1 kgs, or 108.7 lbs.
- In this study, “no evidence was found of a difference in the percentage of participants who had an adverse event of grade 3 or higher (the primary safety outcome)... between the rifapentine–moxifloxacin group and the control (RIPE) group”.
- However, “given the theoretical increase in the risk of hepatotoxicity with increased exposure to a rifamycin”, the study authors state “careful monitoring for hepatotoxicity should be performed during the course of the 4-month rifapentine regimens.”
- The authors also noted “there was no clinical evidence of (an) increased risk of cardiotoxicity, although electrocardiographic monitoring was not a required component of the study”.

Potential challenges to initiating use of the RPT/INH/PZA/MXF 4-month regimen include rifapentine supply and the higher cost of the 4-month regimen compared to that of the 6-month standard regimen (RIPE), though the latter may be offset by the decrease in case management time with a 4-month regimen.

The TB Program will provide more information as appropriate.