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INTRODUCTION OF NEW DRUGS AND SHORTENED REGIMENS FOR MDR-TB TREATMENT

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The approaches currently used for MDR-TB management are not validated in clinical trials, require a very lengthy treatment period (at least 20 months) as well as great financial and human resources and are therefore difficult to implement. Despite the latest developments in rapid diagnostic tests for DR-TB (e.g., Xpert MTB/RIF assay from Cepheid and Genotype®MTBDRsl from Hain) and the availability of new bactericidal drugs, MDR-TB treatment success rates remain unacceptably low.

Recent international experience demonstrates that for MDR-TB patients without additional resistance or intolerance to key second-line drugs (SLDs)—i.e., fluoroquinolones (FQs) and second-line injectables (SLIs), the treatment duration can be substantially shortened, thus reducing the burden for patients and national TB programs. More than 1000 MDR-TB patients have been enrolled in shortened treatment regimens in 9 piloting countries with more than 84% treatment success rate based on interim outcome analysis. One of the main requirements for successful introduction of shortened MDR-TB treatment regimens is an ability to rule out resistance to key SLDs, given the dependence of the shortened regimen on these drugs. Yet drug-susceptibility tests (DSTs) for pre-XDR (MDR with additional resistance to either FQs or SLIs) and XDR (MDR with additional resistance to both FQs and SLIs) are infrequently offered and/or are limited to MDR-TB patients who do not respond well to standard MDR-TB treatment. Available tests are not always properly utilized (e.g., delayed or not well targeted to test the most appropriate population) and test results may not influence treatment decisions due to delayed results or lack of confidence in the test.

In recent years, bedaquiline and delamanid received conditional approval by stringent regulatory authorities (United States Food and Drug Administration [FDA], European Medicines Agency [EMA], and Pharmaceuticals and Medical Devices Agency, Japan) and the World Health Organization (WHO) issued interim policy guidance on their use in MDR-TB treatment. Although several observational studies and clinical trials have shown more rapid culture conversion rates and more favorable outcomes using bedaquiline and delamanid, evidence on the effectiveness and safety of their use in programmatic settings is urgently needed before they can be recommended for routine use in MDR-TB treatment, or at least for patients who cannot be accurately treated with shortened or standard MDR-TB regimens.

The Challenge TB (implemented by PATH and KNCV in Ukraine) approach is to implement diagnostic and treatment algorithms that allow allocation of tailored MDR-TB treatment regimen groups to rifampicin-resistant TB patients, depending on the additional resistance to SLDs detected or suspected (e.g., based on previous treatment with a specific drug). This will allow for shorter and/or more-effective regimens for eligible patients. Patients without or with limited resistance to SLDs will be allocated to shortened MDR-TB treatment regimens. Patients with more extensive resistance to SLDs will be allocated to standard-length treatment (20 to 24 months) with the addition of WHO Group 5 drugs, including new drugs (bedaquiline or delamanid), to the regimen.