9-month, short-course MDR-TB treatment in HIV and non-HIV co-infected patients in Uzbekistan and Swaziland: interim outcomes of two prospective studies

Swaziland Study Team

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Introduction

The WHO-recommended treatment regimen for multidrug resistant tuberculosis (MDR-TB) is lengthy, toxic, and has only a 54% success rate. A success rate of 84% has been reported for a 9-11 month regimen; evidence for this regimen is lacking in high MDR-TB and HIV co-infection settings. MSF, with the respective ministries of health, is using the short-course regimen in Uzbekistan and Swaziland. We present interim outcomes of two prospective, observational studies of the safety and effectiveness of short-course MDR-TB treatment.

Methods

We analysed outcomes from September 2013-December 2014. All consenting MDR-TB patients diagnosed using molecular or culture/drug susceptibility testing were included. Outcomes are defined according to pre-2013 WHO definitions. Toxicity was documented with Division of AIDS (DAIDS) grading. Ethics approval: MSF Ethics Review Board (ERB) and the ERBs of Swaziland and Uzbekistan.

Results

Characteristics of the 105 Uzbekistan patients: median age 30.1 years (IQR 24.0-43.2), 51 (48.6%) male, none HIV-positive, and 74 (70.5%) new cases. Outcomes at analysis: 66 (62.9%) on treatment, 20 (19.0%) cured, 4 (3.8%) treatment complete, 2 (1.9%) died, 3 (2.9%) treatment failure, and 10 (9.5%) lost to follow-up. Culture conversion after 4 months of treatment was 89.3% (95% CI 61.6-84.8). Characteristics of the 57 Swaziland patients: median age 35.0 years (IQR 28.3-43.1), 23 (40.4%) male, 42 (73.7%) HIV-positive (15 [35.7%] male, median age 35 years [IQR 30-38]), and 42 (73.7%) new cases. Outcomes at analysis: 39 (68.4%) on treatment, 10 (17.5%) cured, 6 (10.5%) died, 2 (3.5%) treatment failure, and none lost to follow-up. Outcomes among HIV patients: 29 (69%) on treatment, 6 (14%) cured, 6 (14%) died, and 1 (2.4%) treatment failure. Culture conversion after 4 months of treatment was 90%. Severe adverse events grade 3 and 4 occurred in 5 (9.4%) and 13 (24.5%) patients in Swaziland and in 8 (7.6%) and 2 (1.9%) patients in Uzbekistan, respectively, 3 (5.7%) experienced severe ototoxicity. ECG at 4 weeks: median QTc increase of 16.5 ms (Swaziland) and 21 ms (Uzbekistan); acquired prolonged QT syndrome in one patient resulted in treatment failure (Uzbekistan).

Conclusions

The short-course regimen had satisfactory culture conversion and interim outcomes in high HIV co-infection and drug-resistant populations. Safety, including the first ECG data reported for this regimen was also satisfactory.