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Fluoroquinolones and isoniazid-resistant tuberculosis: implications for the 2018 WHO guidance

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WHO has assessed regimen recommendations for isoniazid-resistant TB to be of very low certainty. The addition of fluoroquinolones to a 12-month (isoniazid, rifamycin, ethambutol, short-duration pyrazinamide) regimen may be unnecessary in certain settings. http://bit.ly/2XoTgNL

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ABSTRACT

Introduction: 2018 World Health Organization (WHO) guidelines for the treatment of isoniazid (H)-resistant (Hr) tuberculosis recommend a four-drug regimen: rifampicin (R), ethambutol (E), pyrazinamide (Z) and levofloxacin (Lfx), with or without H ([H]RZE-Lfx). This is used once Hr is known, such that patients complete 6 months of Lfx (≥6[H]RZE-6Lfx). This cohort study assessed the impact of

fluoroquinolones (Fq) on treatment effectiveness, accounting for Hr mutations and degree of phenotypic resistance.

Methods: This was a retrospective cohort study of 626 Hr tuberculosis patients notified in London, 2009–2013. Regimens were described and logistic regression undertaken of the association between regimen and negative regimen-specific outcomes (broadly, death due to tuberculosis, treatment failure or disease recurrence).

Results: Of 594 individuals with regimen information, 330 (55.6%) were treated with (H)RfZE (Rf=rifamycins) and 211 (35.5%) with (H)RfZE-Fq. The median overall treatment period was 11.9 months and median Z duration 2.1 months. In a univariable logistic regression model comparing (H)RfZE with and without Fqs, there was no difference in the odds of a negative regimen-specific outcome (baseline (H)RfZE, cluster-specific odds ratio 1.05 (95% CI 0.60–1.82), p=0.87; cluster NHS trust). Results varied minimally in a multivariable model. This odds ratio dropped (0.57, 95% CI 0.14–2.28) when Hr genotype was included, but this analysis lacked power (p=0.42).

Conclusions: In a high-income setting, we found a 12-month (H)RfZE regimen with a short Z duration to be similarly effective for Hr tuberculosis with or without a Fq. This regimen may result in fewer adverse events than the WHO recommendations.