LINEZOLID-RESISTANCE IN *M. TUBERCULOSIS*-ISOLATES

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The ongoing global burden of tuberculosis and the increasing problem of multidrug-resistant TB have led to the increased application of second-line anti-TB drugs. Linezolid is a recently approved antituberculosis drug, belonging to a new class of antibiotics, the oxazolidinones. Early studies have shown that linezolid is a protein synthesis inhibitor that interacts with 23S rRNA. The lack of cross-resistance between oxazolidinones and other antibiotics supports evidence for a novel mechanism of action.

To date, linezolid-resistant *M. tuberculosis* strains seemed to be rare. In the German National Reference Center for Mycobacteria 210 MDR *M. tuberculosis* strains were examined for linezolid resistance. Out of these, four exhibited linezolid resistance. At that time these 4 strains were already resistant to at least Isoniazid, Rifampicin, Streptomycin, and Ethambutol. Linezolid MIC-value determinations of all resistant strains and their respective susceptible predators revealed 4 µg/ml (patient 3) and 8 µg/ml (patients 1, 2, and 4) for the resistant strains, and 0.5 µg/ml (patients 1, 2, and 4), and 1 µg/ml (patient 3) for the respective susceptible strains.

To investigate if these strains are restricted to certain genotypes, a real- time assay for discrimination of Beijing and non-Beijing genotype was performed, identifying two isolates as Beijing genotypes (patients 1 and 3) and the other two as non-Beijing genotype *M. tuberculosis* strains.

To discover the mechanism of resistance, DNA sequencing of putative target genes (23S rRNA gene, the *rplV* and *rplD* genes, the *erm37* gene, and *whiB7*) was performed for all linezolid-resistant strains. The alignment of all sequences revealed no alterations between susceptible or resistant strains nor with the *M. tuberculosis* H37 wild type. Thus, the resistance mechanism remains unexplained.

Mechanisms of resistance are described for linezolid resistant *M. smegmatis* strains by Sander and co-workers. It will be discussed if similar mechanisms can be assumed for the isolated *M. tuberculosis* strains.