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P1547 Optimizing empiric treatment for MDR-TB patients from Georgia

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Background: Current treatment recommendations in Georgia suggest the use of a standardized empiric treatment regimen for multidrug-resistant tuberculosis (MDR-TB): capreomycin (Cm), moxifloxacin (Mfx), cycloserine (Cs), PAS, ethionamide (Eto), and pyrazinamide (Z). However, this regimen may not be adapted to high levels of drug resistance in the country. Hence, we sought to assess the validity of the current policy, and of an alternative regimen where drugs with high (>50%) frequency of resistance were replaced by new/re-purposed drugs, on isolates of Georgian patients who came to France, stratifying the findings according to results of molecular resistance testing for second-line drugs.

Materials/methods: We searched the database of the French National Reference Center for Mycobacteria, including all culture-proven MDR-TB cases from 01/01/2010 to 31/12/2016, for patients with: 1) Georgian nationality; 2) Phenotypic drug susceptibility testing (DST) results available for Cm, a fluoroquinolone, PAS, Eto, and Cs; 3) DST or pncA sequencing results for Z; 4) gyrA/rrs molecular testing results (GenoType MTBDRsl). A sensitivity analysis was performed excluding patients with previous tuberculosis treatment.

Results: Overall, 229 isolates from Georgian MDR-TB patients were included in the study. Following resistance rates were detected: Eto (81%), Z (56%), fluoroquinolone (38%), Cs (33%), Cm (27%), and PAS (25%). The number of effective drugs in current and alternative empiric regimen are shown in the Table. The results did not differ significantly when excluding patients with previous tuberculosis treatment.

Conclusions: Current empiric regimen is not effective for the majority of patients, and is effective in less than 80% of cases even among patients with no *gyrA*/*rrs* mutation. Conversely, an alternative empiric regimen would be effective in 85% of patients. However, the presence of any *gyrA*/*rrs* mutation should lead to individualizing the treatment.

Table:

	Current empiric regimen (Cm+Mfx+Cs+PAS+Eto+Z)		Alternative empiric regimen (Cm+Mfx+Cs+PAS+2 new/re-purposed drugs)	
	Effective drugs, median (IQR)	Patients with ≥4 effective drugs, n (%)	Effective drugs, median (IQR)	Patients with ≥4 effective drugs, n (%)

All (n=229)	3 (2-5)	112 (49%)	5 (4-6)	194 (85%)
Non-mutated *gyrA* and *rrs* (n=110)	4 (4-5)	87 (79%)	6 (5-6)	110 (100%)
Mutated *gyrA* and/or *rrs* (n=119)	3 (2-3)	25 (21%)	4 (3-5)	84 (71%)