Background and Aims

Streptococcus pneumoniae is a main causative pathogen in CAPB and in acute exacerbations of chronic bronchitis (AECB).

Because of increasing emergence of resistance to first and second line antibiotics commonly recommended in these indications [1], discovery and clinical development of antibiotics active against these resistant strains is essential.

There is no statistically-significant correlation (except for MXF and, to some extent, for PEN, but with a low angular coefficient [negative for PEN]) among the MICs for macrolides, β-lactam-and fluoroquinolone-resistant strains. MICs were determined in cation-adjusted Mueller-Hinton broth supplemented with horse blood using the S. pneumoniae strain ATCC 49619 as control and re-identification of each isolate by the optochin test.

Analyses

Data were first manually analyzed for basic statistics and susceptibility/resistance patterns (EUCAST interpretative criteria).

For NS and R isolates, cross-resistance with SOL was assessed by linear fit, Sivarat normal ellipse analysis (0.95 overlap), and quantile density contour coincidence (QDCC, 0.1 to 0.9) using JMP software (version 10.0.2).

Results

Our aim was to assess the activity of SOL against a large collection of Belgian and German S. pneumoniae isolates enriched in strains with resistance against commonly recommended first and second line antibiotics. Ceftriaxone (CPT) was added as it has been recently approved for CAPB and in acute exacerbations of chronic bronchitis (AECB).

S. pneumoniae isolates (n=425) were selected because of increasing emergence of resistance to first and second line antibiotics commonly recommended in these indications [1], discovery and clinical development of antibiotics active against these resistant strains is essential.

While teltromycin (the first approved ketolide) has represented a step forward in this context, its use has been hampered by the observation of unacceptable toxicities [2].

Solithromycin (SOL) [3] is a new generation of ketolides in which the intrinsic activity of teltromycin against macrolide-resistant isolates has been enhanced. It showed a favourable safety profile vs. levofloxacin in phase 2 trial of CABP [4] and has now entered phase 3 trial in comparison with moxifloxacin.

SOM, a new generation of ketolides in which the intrinsic activity of teltromycin against macrolide-resistant isolates has been enhanced. It showed a favourable safety profile vs. levofloxacin in phase 2 trial of CABP [4] and has now entered phase 3 trial in comparison with moxifloxacin.

Our aim was to assess the activity of SOL against a large collection of Belgian and German S. pneumoniae isolates enriched in strains with resistance against commonly recommended first and second line antibiotics. Ceftriaxone (CPT) was added as it has been recently approved for CAPB and in acute exacerbations of chronic bronchitis (AECB).

Conclusions

SOL maintains low MICs for clinical isolates with NS and R phenotypes to currently used or recently approved antibiotics for treatment of CABP with no statistically-significant correlation (except for MXF and, to some extent, for PEN, but with a low angular coefficient [negative for PEN]). SOL may, therefore, stand as a potentially useful alternative in environments where these antibiotics can no longer be recommended.