P1335
Paper Poster Session
New agents in clinical development against gram-positive bacteria

In-vitro activity of solithromycin against anaerobic bacteria in the normal intestinal microbiota

Andrej Weintraub*[1], Mamun Ur Rashid[2], Carl Erik Nord[1]

[1]*Karolinska Institutet, Karolinska University Hospital, Department of Laboratory Medicine, Stockholm, Sweden*

[2]*Karolinska Institutet, Karolinska University Hospital, Department of Laboratory Medicine, Department of Laboratory Medicine, Stockholm, Sweden*

Background: The normal microbiota acts as a barrier against colonization by potentially pathogenic microorganisms and against overgrowth of already present opportunistic microorganisms. Administration of antimicrobial agents, therapeutically or as prophylaxis, causes disturbances in the ecological balance between the host and the normal microbiota. Solithromycin is a new fluoroketolide. It is being developed as intravenous and oral formulations for the treatment of patients with community-acquired bacterial pneumonia (CABP). Solithromycin inhibits bacterial protein synthesis via a unique ribosomal binding pattern to domains II and V, as well as to the peptide tunnel, of the 23S component of the 50S ribosomal subunit. The objective was to determine the *in-vitro* activity of solithromycin in comparison to amoxicillin/clavulanic acid, azithromycin, ceftriaxone, metronidazole and levofloxacin by determining the minimum inhibitory concentration (MIC) against the normal anaerobic intestinal microbiota.

Material/methods: 1024 anaerobic strains including bifidobacteria, lactobacilli, clostridia, bacteroides, prevotella and veillonella were isolated from the faecal samples of healthy volunteers (22) having no history of systemic antibiotics within the past 3 months and no medical conditions that can alter their health or microbiota. Faecal samples were diluted from tenfold to 10^7 and inoculated on non-selective and selective agars. The agar plates were incubated for 2-7 days at 37°C in anaerobic jars. After incubation, different colony types were analysed according to Gram-reaction and colony morphology, and identified by MALDI-TOF. The MICs of solithromycin, amoxicillin/clavulanic acid, azithromycin, ceftriaxone, metronidazole and levofloxacin were determined by the agar dilution method. The final inoculum was 10^5 colony forming units (CFU) per spot. Inoculated plates were incubated for 48 h at 37°C in anaerobic jars. Reference strains were *Bacteroides fragilis* ATCC 25285, *Clostridium difficile* ATCC 700057 and *Eubacterium lentum* ATCC 43055.

Results: The MICs for solithromycin against bifidobacteria (254) were: MIC_{50}, 0.008 mg/l; MIC_{90}, 0.008 mg/l; MIC range, 0.008-0.5 mg/l; lactobacilli (257): MIC_{50}, 0.008 mg/l; MIC_{90}, 0.016 mg/l; MIC range, 0.008-0.5 mg/l; clostridia (225): MIC_{50}, 0.5 mg/l; MIC_{90}, 8.0 mg/l; MIC range, 0.008-8.0 mg/l; bacteroides (255): MIC_{50}, 0.5 mg/l; MIC_{90}, 4.0 mg/l; MIC range, 0.016-4.0 mg/l; prevotella (26): MIC_{50}, 2.0 mg/l; MIC_{90}, 2.0 mg/l; MIC range, 0.032-256 mg/l; veillonella (7): MIC_{50}, 0.016 mg/l; MIC_{90}, 1.0 mg/l; MIC range, 0.016-4.0 mg/l. Most of the Gram-positive anaerobic bacteria were sensitive to amoxicillin-clavulanic acid but less sensitive to azithromycin, ceftriaxone and levofloxacin. Bifidobacteria and lactobacilli were resistant to metronidazole. Bacteroides strains showed high MIC-

values for amoxicillin-clavulanic acid, azithromycin, ceftriaxone and levofloxacin and low MIC-values for metronidazole. Similar MIC-patterns were observed in *Prevotella* and *Veillonella* strains.

Conclusions: The study showed that solithromycin is active against bifidobacteria, lactobacilli and most clostridia isolated from the normal intestinal microbiota. Solithromycin is less active against bacteroides strains which may explain the protective role in developing *C. difficile* infections.