Introduction and Purpose:
Solithromycin is a fourth generation macrolide and the first fluoroketolide. It is being developed as intravenous and oral formulations for the treatment of patients with community-acquired bacterial pneumonia (CABP) (1). Solithromycin exhibits potent in vitro activity against the bacterial pathogens associated with CABP, including macrolide-resistant strains and atypical bacteria (2). 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 (3). Consequently, the risk of development of resistant strains and transfer of resistance elements between microorganisms is increased. The objective was to assess the impact of solithromycin on the intestinal microbiota during and after oral administration of solithromycin.

Methods:
Twelve healthy volunteers received oral capsules of solithromycin 800 mg on Day 1 followed by 400 mg once-daily on Days 2-7. Faecal samples were collected at baseline and on Days 2, 5, 7, 9, 14 and 21 for pharmacokinetic and microbiological analyses.

Faecal concentrations of solithromycin were assayed by the agar well diffusion method using antibiotic Medium No. 1 (Difco, Sparks, MD, USA) and Micrococcus luteus ATCC 9341 as the indicator strain. The lower limit of sensitivity was 0.064 mg/kg faeces.

Results:
The number of Escherichia coli strains decreased during the study and was normalized on Day 14. The number of other enterobacteria also decreased during the study and the number of enterococci decreased from Day 2 to Day 9 and was normalized on Day 14. The number of Candida strains was not changed (Figure 1). The number of lactobacilli decreased from Day 2 to Day 14 and was normalized on Day 21.

The number of bifidobacteria decreased on Day 2 and was normalized on Day 21. There was a decrease of Clostridium strains on Day 2 and Days 7-14. On Day 21, clostridia were normalized. No Clostridium difficile strains or toxins were detected. The number of Bacteroides strains was not significantly changed (Figure 2). The solithromycin concentrations in faeces on Days -1, 2, 5, 7, 9, 14 and 21 were 0 mg/kg, 15.8-65.4 mg/kg, 24.5-82.7 mg/kg, 21.4-82.7 mg/kg, 12.1-72.4 mg/kg, 0.2-25.6 mg/kg and 0.0-0.5 mg/kg, respectively.

Conclusions:
The ecological effect of solithromycin on the intestinal microbiota was similar as reported for other macrolides. E. coli, other enterobacteria, enterococci, bifidobacteria, lactobacilli and clostridia decreased while bacteroides and candida were unchanged. No C. difficile strains or toxins were detected. The protective role of bacteroides against C. difficile in the intestinal microbiota is known and explains this finding.

References: