

P1986 *In vitro* intracellular activity of levonadifloxacin against *Legionella pneumophila*Jacques Dubois*¹, Maitée Dubois¹¹ M360 Inc., Sherbrooke, Canada

Background: Levonadifloxacin (WCK 771) is a broad spectrum, bactericidal antibiotic belonging to benzoquinolizine sub-class of quinolones. The absence of conventional amine at C-8 position and presence of tricyclic chiral benzoquinolizine core imparts WCK 771, a differentiated mechanism of action involving high-affinity targeting towards Staphylococcal DNA gyrase. Moreover, the anionic nature of WCK 771 helps potentiates its activity in acidic environment. **Levonadifloxacin** is undergoing Phase 3 evaluation in India. To determine if this compound could be used as monotherapy for the treatment of CABP involving atypical RTI pathogens, *in vitro* intracellular activity against a variety of *L. pneumophila* was investigated.

Materials/methods: Intracellular activity of **levonadifloxacin** was compared with levofloxacin (LE), moxifloxacin (MO) and erythromycin (ER) against 1 ER-resistant and 1 ER-susceptible strains of *L. pneumophila*. Intracellular activity was determined by exposing human monocytes U937 cell line infected with intracellular *Legionella* at 1 or 2XMIC of antibiotic for each strain during 6 days exposure. After 2 days of antibiotic exposure, infected cell line was split into two groups; one group was kept drug-free and the other was treated with the same antibiotic as before till further 5 days. Viable CFU/mL were enumerated at time 0, 24h, 48h, 72h, and every day till next 4 days, by plating on Buffer-Charcoal-Yeast-Extract agar in duplicate.

Results: Significant reduction ($> 3 \log_{10}$ CFU/mL or 99.9%) of both tested *L. pneumophila* grown in monocytes was observed after 2 days of antibiotic exposure until day 7 by **levonadifloxacin** (1 or 2XMIC) and MO. Regrowth of *L. pneumophila* in monocytes was observed after 1 day of ER exposure and after 4 days of LE exposure. Such regrowth was not observed with **levonadifloxacin** and MO. After drug wash-out at day 3, rapid regrowth of *L. pneumophila* was observed with ER, LE and MO in contrast to substantially delayed regrowth observed with **levonadifloxacin** and that too at only 1XMIC. However **levonadifloxacin** concentration at 2XMIC completely prevented regrowth. Significant decrease of *L. pneumophila* count in monocytes was observed with **levonadifloxacin** until day 7 at 2XMIC.

Conclusions: Levonadifloxacin shows good human monocytes penetration features and demonstrates potent bactericidal effect for intracellular *L. pneumophila*.

