

LTX-109 – A Position Paper

“Bacterial resistance to antibiotics is a major healthcare problem”

The discovery of penicillin in the 1930s was an important breakthrough for medical science. Prior to this, infections were a frequent cause of death, but with the help of penicillin it was possible to save lives – never before had the power of modern medical science been more evident. Penicillin and a host of other antibiotics are still invaluable tools in the treatment of infections. However, soon after the introduction of antibiotics to medical practice, treatment failures were observed, and it was noted that bacteria could quickly develop resistance against the antibiotic. Today, the spread of antibiotic-resistant bacteria is alarming in the hospital environment where “superbugs” such as MRSA (methicillin-resistant *Staphylococcus aureus*), are leading causes of mortality. Conservative estimates suggest that in the US alone, more than 2 million patients acquire infections when hospitalized and as many as 90 000 of those patients die each year – three times the number as from HIV/AIDS (“Bad Bugs, No Drugs White Paper - IDSA report 2004). To make the problem worse few new antibiotics have become available to fight such infections in the recent years.

“More than three times as many die each year from hospital-acquired infections such as MRSA than from HIV/AIDS...”

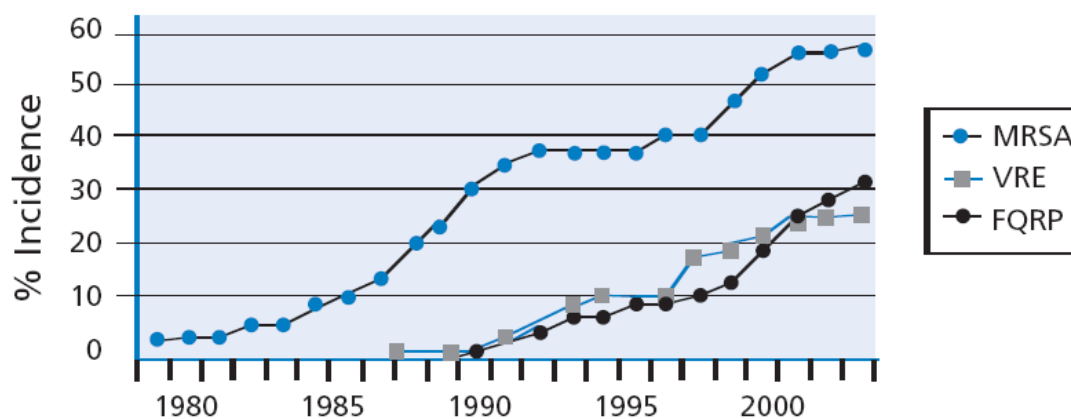


Figure – The rapid spread of antibiotic-resistant bacteria in the US – Surveillance data from CDC (Centre for Disease Control, USA) – MRSA, methicillin-resistant *Staphylococcus aureus*; VRE, vancomycin-resistant *Enterococcus*; FQRP, fluoroquinolone-resistant *Pseudomonas aeruginosa* (“Bad Bugs, No Drugs Whitepaper”, IDSA 2004).

Superbug skin infections are difficult and costly to treat

Hospital-acquired infections can directly cost over \$30,000 per incident and accounts for \$4.5 billion annually in total extended care and treatment in the USA (U.S. Centre for Disease Control, CDC). The emergence of aggressive types of resistant bacteria in the community is considered particularly worrisome. Infections typically originate on the skin – in most cases classed as uncomplicated infections such as impetigo, secondarily infected traumatic lesions (SITL) and infected eczemas. These uncomplicated infections can in many instances progress into complicated, and in many cases life-threatening situations. Although these initial infections are in many cases managed by existing gold standard topical agents such as fusidic acid (Fucidin) or mupirocin (Bactroban), increased resistance is being reported. Rates of resistance to fusidic acid were for example reported to be as high as 50% in patients attending a dermatology clinic (Shah & Mohanraj, 2002, British J. Dermatol. 148: 1018-1020).

LTX-109 is a novel, topical antimicrobial agent

Lytix is developing a novel antimicrobial agent with a rapid membrane-lysing mode of action for topical treatment of skin infections and nasal decolonisation of MRSA. The drug preferentially binds to negatively charged membrane components on microorganisms via electrostatic interactions, subsequently inducing lysis and cell death. (Haug, BE; Strøm, MB.; Svendsen, JS, 2007; Current Medicinal Chemistry 14: 1-18). LTX-109 has demonstrated antimicrobial activity *in vitro* against a broad range of bacteria including Gram (+) and Gram (-) strains such as methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococci* (VRE) and multi-resistant *Pseudomonas* isolates. In addition, the drug displays good efficacy against filamentous fungi and yeasts. The membrane-lysing mode of action may be associated with a lower propensity to the development of resistance and to date LTX-109 demonstrates no *in vitro* target-specific cross-resistance with other classes of antibiotics.

Key differentiators – Unique Selling Points

- **Broad spectrum of activity.** *The activity of the drug spans Gram(+) and Gram (-) bacteria, fungi and yeasts indicating usefulness in several important markets*
- **Ultra-rapid efficacy.** *The rapid mechanism of bacterial kill potentially translates into a convenient dosing regimen of significantly shorter dosing time compared to marketed products*
- **Activity against resistant organisms.** *The drug is equally effective against resistant “superbug” microorganisms such as MRSA, providing a real treatment option, independent of pathogen resistance-status*
- **Low chance of resistance development.** *The difficulty for bacteria to become resistant to the drug should provide longer term clinical usefulness*
- **Efficacy against biofilm infections.** *The ability to eradicate bacterial and fungal biofilms is important when treating complicated infections*