L1-275

LTX-109 is an Effective, Novel Agent for Nasal Decolonization of MRSA/MSSA – Results from a Phase I/IIa Study

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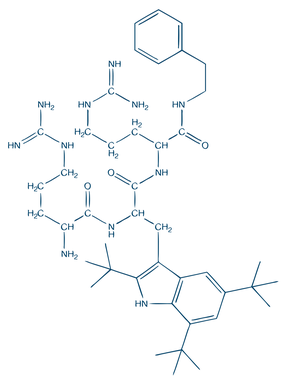
Lytix Biopharma

LTX-109

- A synthetic protein fragment - a peptidomimetic
- High stability against degradation
- Prooduced synthetically in large scale
- Low cost of synthesis



Chemical structure of LTX-109.

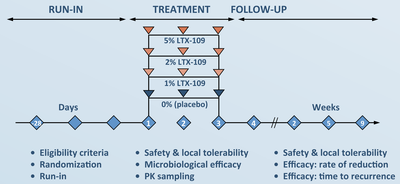
Background

LTX-109 is a novel antimicrobial drug in clinical development for skin infections and nasal decolonization of MRSA. The drug mimics the effects of natural antimicrobial peptides in a synthetic small molecule. LTX-109 has demonstrated a broad activity against several Gram (+) and Gram (-) bacteria *in vitro*, as well as activity against a range of yeast and fungal species. The compound is equally effective against antibiotic-resistant species such as methicillin resistant *Staphylococcus aureus* (MRSA), vancomycin resistant *Enterococci* (VRE) and multi-resistant *Pseudomonas* isolates. The ultra-rapid membrane lysing mode of action may result in a lower propensity to resistant development and a rapid bactericidal mechanism of action, as shown in *in vitro* studies. To date LTX-109 demonstrates no *in vitro* cross-resistance with other classes of antibiotics.

The present Phase I/IIa clinical study investigated the safety, tolerability and efficacy of LTX-109 as an agent for nasal decolonization of MRSA/MSSA.

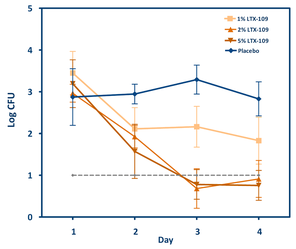
Methods

Subjects were included in the study after being confirmed on three separate occasions as persistent carriers of either MRSA or MSSA. Groups of subjects were randomized and treated in a double-blind manner with increasing doses of LTX-109 or placebo, TID for three days.



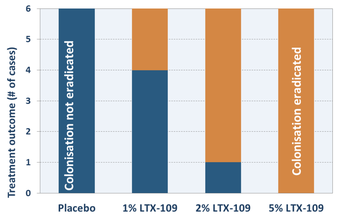
Results

LTX-109 rapidly clears MRSA/MSSA colonization



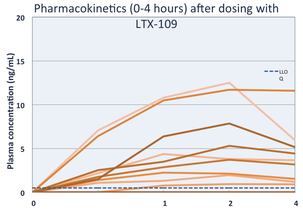
The Nasal Log CFU (MRSA/MSSA) analyses for the period Day 1 (Baseline) - Day 4 showed a statistically significant treatment effect (p = 0.0014). At Day 3 and Day 4 there was a statistically significant difference of Nasal Log CFU (MRSA/MSSA) between placebo and 2% LTX-109 and between placebo and 5% LTX-109.

LTX-109 rapidly clears MRSA/MSSA colonization



Nasal eradication for the time period Day 2 (inclusive) - Day 4 was observed in 13 of the 18 subjects treated with LTX-109. The majority of subjects treated with 2% and 5% LTX-109 were eradicated at Day 3. (BLUE – Not eradicated; ORANGE – Eradicated)

Dosing in anterior nares leads to negligible systemic uptake



Plasma samples were analyzed for presence of LTX-109 using a previously validated methodology. Overall, the plasma concentration/systemic uptake was low. The highest plasma concentration measured during the initial 4 h was 12.5 ng/mL in a subject receiving 1% LTX-109 (detection limit 0.5 ng/mL). C_{max} was reached approximately 2 h after the initial dosing. Negligible levels of LTX-109 were observed in plasma at 48h and 72h after the initial dosing (not shown). At Follow-up (Day 8) there was no measurable plasma concentrations of LTX-109 (not shown).

Conclusions

- The present study is the first time LTX-109 has been tested for nasal decolonization
- LTX-109 has been shown to be safe, tolerated when applied in the anterior nares
- LTX-109 has been demonstrated to clearly effective at eradicating nasal carriage of MRSA/MSSA
- The systemic uptake of LTX-109 from the nose is negligible
- Further Phase II studies are planned to demonstrate efficacy in larger populations

LTX-109

- Novel mechanism of action
- Broad spectrum of activity
- Low propensity for resistance development and active against drug-resistant strains
- Effective against fungal and bacterial biofilms
- Superior efficacy compared to market leaders (Bactroban®, Fucidin®, Altabax®/Altargo®)

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