A2-030

LTX-109 is Active against CA-MRSA (USA300) and *S. pyogenes* in a Mouse Skin Infection Model

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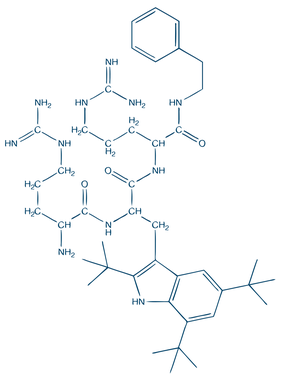
Lytix Biopharma

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 decolonisation 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 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.

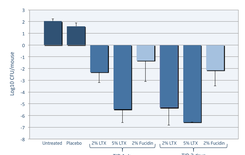
The aim of the present studies was to evaluate the effect of LTX-109 against community-acquired MRSA (CA-MRSA) and *Streptococcus pyogenes* in a mouse skin infection model.

Methods

Superficial skin lesions were made by a tape-stripping and scalpel blade-cut injury method. Infection was established by adding bacterial suspensions of CA-MRSA (USA300) or *S. pyogenes*. Groups of mice were treated with LTX-109 22 hrs from the start of the infection. Skin biopsies were sampled and colony forming units (CFU/ml) were determined.

Results

LTX-109 demonstrates a significant reduction of the CA-MRSA USA300 tissue load



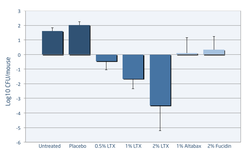
Infection:
Community acquired-MRSA
ATCC BA-1717 (USA300)

Treatment:
TID - one day vs three days

Measure:
Bacterial growth was assessed +9 and +57 hours, respectivly, after first treatment - change in CFU from inoculation load

Result:
Treatment with 1% and 2% LTX-109 was highly effective in reducing bacterial tissue load of CA-MRSA (USA300). A dose-dependent reduction in CFU-counts was observed after one day of treatment. LTX-109 doses of 1% and 2% were significantly better than the comparator Fucidin®

LTX-109 demonstrates a superior effect on CA-MRSA USA300 compared to marketed products



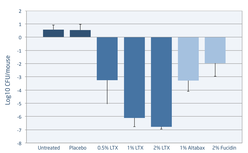
Infection:
Community acquired-MRSA
ATCC BA-1717 (USA300)

Treatment:
TID - one day

Measure:
Bacterial growth was assessed +9 hours after first treatment - change in CFU from inoculation load

Result:
Treatment with 0.5%, 1% and 2% LTX-109 was highly effective in reducing bacterial tissue load of CA-MRSA (USA300). A dose-dependent reduction in CFU-counts was observed after one day of treatment. LTX-109 doses of 1% and 2% were significantly better than the comparators Altabax® and Fucidin®

LTX-109 demonstrates a superior effect upon *S. pyogenes* compared to marketed products



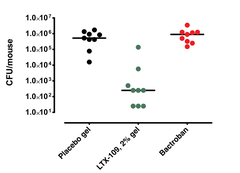
Infection:
Streptococcus pyogenes (SR186)

Treatment:
TID - one day

Measure:
Bacterial growth was assessed +9 hours after first treatment - change in CFU from inoculation load

Result:
Treatment with 0.5%, 1% and 2% LTX-109 was highly effective in reducing bacterial tissue load of *S. pyogenes*. A dose-dependent reduction in CFU-counts was observed after one day of treatment. LTX-109 doses of 1% and 2% were significantly better than the comparators, Altabax® and Fucidin®

LTX-109 demonstrates a superior effect upon *S. pyogenes* compared to Bactroban®



Infection:
Streptococcus pyogenes (CS301)

Treatment:
TID - one day

Measure:
Bacterial growth was assessed +9 hours after first treatment

Result:
Treatment with 2% LTX-109 was highly effective in reducing bacterial tissue load of *S. pyogenes*. LTX-109 treatment was significantly better than the comparator Bactroban®.

(Figure from Svendsen et al, Bactericidal effect of LTX-109 against *Staphylococcus aureus* and *Streptococcus pyogenes* in a murine skin infection model. ICAAC abstract 2008 poster F1-3947)

Conclusions

- LTX-109 demonstrates a significant effect already after a single day of treatment probably due to the bactericidal mode of action of the drug.
- LTX-109 demonstrates a significant effect on communty- acquired MRSA (USA300) and streptococcal tissue loads in a superficial skin infection model after only one day of treatment.
- The effect was superior to Bactroban®, Altabax® and Fucidin®
- LTX-109 appears to be a valuable drug for treatment of Gram (+) skin infections including those caused by CA-MRSA and *S. pyogenes*.
- The drug has been tested in Phase I and two Phase I/IIa trials with good tolerance, minimal systemic bioavailability
- LTX-109 has demonstrated Proof-of-Concept in decolonisation of nasal MRSA / MSSA.
- Further Phase II studies are planned to demonstrate efficacy in larger patient 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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