

Introduction

LTX-109 is a first-in-class chemically synthesized, stable antimicrobial peptidomimmetic being developed for topical infections and nasal decolonisation^{1,2}. The drug is a novel mimetic of a membrane-active host defence peptide having a rapid lysing mode of action^{3,4}.



IN NON-CLINICAL AND CLINICAL STUDIES LTX-109 HAS DEMONSTRATED THE FOLLOWING KEY FEATURES:

- Novel mode of action⁴
- Rapid bactericidal effect^{5,6}
- Broad spectrum of activity^{7,8}
- Low propensity for resistance development^{9,10}
- Effective against antibiotic-resistant species¹¹
- Safe and well tolerated¹²

Impetigo is a highly contagious bacterial skin infection, commonly affecting infants and children (2-5 year olds) worldwide. There are two types; bullous impetigo (large blisters) and non-bullous impetigo (crusted). Impetigo is mainly caused by Staphylococcus aureus and/or Streptococcus pyogenes.

Objective

There is an unmet medical need for new topical antimicrobials with activity against resistant bacterial strains such as MRSA. The present study was designed to investigate the efficacy and safety of two dose levels of LTX-109 (1% and 2%) given 3 times daily (TID) for 5 days in patients with impetigo.

Methods

Randomised, double-blind, placebo-controlled study to evaluate the efficacy and safety of two doses of LTX-109 (1% and 2%) versus vehicle (placebo) in impetigo.

Patient selection

- \geq 2 years

- Nonfebrile

Primary endpoint:

• Proportion of patients with clinical success at one or more of the visits

Secondary endpoints:

- termination

Treatment TID 5 days	
	Baseline Day 1
Clinical and bacteriological evaluations	1

Skin Infection Rating Scale (SIRS)

- Success: Resolution of signs and symptoms of infection of the target lesion. No additional antimicrobial therapy required to treat the impetigo. SIRS score of 0 each for exudate/pus, crusting and pain, and 0 or 1 each for erythema/ inflammation and itching
- Improvement: SIRS score of 0 for exudate/pus but does not meet all the criteria for clinical success
- Clinical Failure: SIRS score of 1 or greater for exudate/pus and requires further antibiotic treatment (oral or topical)
- Unevaluable: Valid clinical assessment could not be made

Bacteriological response defined as:

- Success: The causative pathogen isolated from the target lesion at Baseline (Day 1) (*S. aureus* and/or *S. pyogenes*) is eliminated on culture, or no exudate/pus was available for culture and therefore is evidence of pathogen eradication
- Failure: Non-eradication of the *S. aureus* and/or *S. pyogenes* Unevaluable: Bacteriological evaluation could not be made due to a reason other than no exudate/pus being available for culture

LTX-109 - A Novel Antimicrobial Drug in the Treatment of Impetigo

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- Positive Gram-stain
- Total lesions $\leq 40 \text{ cm}^2$, target lesion max 3 cm²
- Total SIRS \geq 4, and 1 or more for exudate and pus
- Clinical and bacteriological response assessed at all visits and at early
- Safety evaluated by adverse events and clinical signs and symptoms



- 5 parameters assessed to evaluate the clinical response: exudate/pus, crusting, erythema/inflammation, itching, pain. Score scale 0 – 3:
 - 0 = absent 1 = mild 2 = moderate 3 = severe

Clinical response defined as:

Results

	Study Population	
ITT	Randomised patients who has recieved at least one dose and have at least one post-baseline evaluation	n=206
mITT	ITT population excluded patients who did not have pathogens (<i>S.aureus, S.pyogenes</i>) in the baseline culture (<i>def.</i> not impetigo)	n=197
PP	mITT population excluded patients that used a prohibited medication before entry to the study and that came on study visit(s) outside a pre- defined window or missed a full visit or non-compliant	n=182

EXAMPLES OF IMPETIGO LESIONS TREATED WITH LTX-109





Baseline (Day 1)



Visit 2 (Day 4)



Visit 3 (Day 8)

PATHOGEN IDENTIFICATION AT BASELINE

Placebo	1% LTX-109	2% LTX-109	Total
n (%)	n (%)	n (%)	n (%)
44 (66%)	37 (56%)	41 (64%)	122 (62%)
2 (3%)	4 (6%)	5 (8%)	11 (6%)
21 (31%)	25 (35%)	18 (28%)	64 (32%)
	Placebo n (%) 44 (66%) 2 (3%) 21 (31%)	Placebo 1% LTX-109 n (%) n (%) 44 (66%) 37 (56%) 2 (3%) 4 (6%) 21 (31%) 25 (35%)	Placebo 1% LTX-109 2% LTX-109 n (%) n (%) n (%) 44 (66%) 37 (56%) 41 (64%) 2 (3%) 4 (6%) 5 (8%) 21 (31%) 25 (35%) 18 (28%)

In 23% of the *S. aureus* MRSA was detected





TOTAL CLINICAL AND BACTERIOLOGICAL SUCCESS RATES



CLINICAL RESPONSE PER TREATMENT GROUP AND VISIT

Time	Clinical response	Placebo	1% LTX-109	2% LTX-109
Micit 2 (Day 4)	Clinical Success	22%	23%	24%
VISIT 2 (Day 4)	Clinical Improvement	58%	53%	60%
	Clinical Failure	19%	24%	16%
Visit 3 (Day 6)	Clinical Success	52%	61%	62%
	Clinical Improvement	36%	27%	29%
	Clinical Failure	12%	12%	9%
Visit 4 (Day 12)	Clinical Success	82%	92%	91%
	Clinical Improvement	14%	6%	7%
	Clinical Failure	4%	2%	2%

SAFETY

Adverse Events reported (ITT population)	Placebo (n)	1% LTX-109 (n)	2% LTX-109 (n)	Total (n)
No. of patients with any adverse event	З	З	4	10
No. of patients with 1 adverse event	З	З	4	10
No. of patients with 2 adverse events	0	0	0	0
No. of patients with >= 3 adverse events	0	0	0	0
No. of patients with any possibly related adverse event	0	0	1	1
No. of patients with serious adverse events	0	0	0	0

• Of the 206 patients in the study, only 10 patients (5%) reported a total of 10 adverse events (AE) • The majority of the AEs were considered to be mild in intensity, and only one AE was of moderate

One AE (Pyrexia) was considered as possibly related to the study medication

No serious AEs or deaths occurred in the study

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Discussion

This study describes for the first time the clinical outcome in patients with impetigo after treatment with LTX-109.

- All efficacy variables demonstrated a consistent trend of improvement for both 1 % LTX-109 and in particular 2 % LTX-109 over placebo:
- The total SIRS-score range for the 1% and 2% LTX-109 dose groups was half that of the placebo group at study completion
- For the individual SIRS symptoms the LTX-109 dose groups showed consistent improvement in overall symptom scores over placebo; symptoms were also resolved quicker with LTX-109 treatment versus placebo
- The study results show that clinical effect is associated with bacteriological response, i.e. bacterial eradication by LTX-109 correlated with clinical success
- Both doses of LTX-109 were found to be well-tolerated when applied to impetigo lesions
- In the study population of 206 patients a total of 10 AEs were reported and only one considered as possibly related to the study drug

LTX-109 kills bacteria, regardless of resistance, has a different mechanism of action than existing antibiotics. Due to the increasing incidence of resistant bacteria there is an unmet medical need for new and effective alternatives for topical treatment of skin infections.

Conclusions

- Treatment of impetigo with LTX-109 was safe and well tolerated
- The clinical success rate of LTX-109 was higher than placebo in both treatment groups at visit 3 and 4, demonstrating a dose response relationship
- The bacteriological response was higher in the 2% LTX-109 group than in the placebo group

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