A RANDOMIZED VEHICLE-CONTROLLED TRIAL TO ASSESS THE EFFICACY, SAFETY AND TOLERABILITY OF OZENOXACIN 1% CREAM IN 412 PATIENTS 2 MONTHS AND OLDER WITH IMPETIGO

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ABSTRACT

Introduction
Ozenoxacin is a non-fluorinated quinolone antibiotic with potent activity against gram-positive bacteria that is being developed as a 1% cream for the topical treatment of impetigo.

Objectives
The objectives of this study were to compare the efficacy and evaluate the safety and tolerability of ozenoxacin 1% cream versus vehicle after 5 day BID topical applications (10 applications) in patients with impetigo.

Methods
A Phase 3 multicenter, randomized, vehicle-controlled, parallel, double-blind clinical trial in patients aged 2 months and older with impetigo. Patients were randomized in a 1:1 ratio to ozenoxacin or vehicle. Efficacy was evaluated utilizing a clinical Skin Infection Rating Scale (SIRS) and by microbiological culture. Safety and tolerability were also evaluated.

Results
After 5 days of treatment, ozenoxacin demonstrated clinical superiority to vehicle in clinical response, both for the primary endpoint as well as for the prespecified secondary endpoint of combined criteria of clinical success. Ozenoxacin also demonstrated superior microbiological success compared to vehicle as early as after 2 days of treatment. Ozenoxacin was safe and well tolerated, and these results are consistent with previously published phase 3 results (Gropper 2014).

Conclusions
Ozenoxacin demonstrated superior clinical and microbiological response versus vehicle, and was safe and well tolerated. Ozenoxacin represents a novel topical therapeutic option being developed for the treatment of impetigo.

METHODS

- A total of 412 patients were enrolled into the study globally at 11 sites in the USA, 5 in Puerto Rico, 4 sites in Germany, 4 sites in Romania, 6 sites in Russia, 3 sites in South Africa and 1 site in Spain.
- Eligible patients were randomized to receive ozenoxacin 1% cream (203 patients) or vehicle (199 patients) applied topically BID for 5 days to all impetigo affected areas, with a maximum extension of 100 cm^2. The first application was done under the guidance of the delegated person appointed by the investigator. After randomization, patients returned at: Visit 2 (Day 3-4) and Visit 3 (Day 6-7). Patients returned for a Final Visit (Visit 4, Day 10-13). Additionally, a telephone contact on Day 2 (24-36 hours after baseline visit) was required to assess for any worsening of infection.
- The primary efficacy endpoint was clinical response (success or failure) at end of therapy (Visit 3) analyzed in the intent-to-treat clinical (ITTC) population.
- Success at Visit 3 was defined as a SIRS score of 0 for blistering, exudates/pus, crusting, itching/pain and no more than 1 for erythema/inflammation, tissue edema and itching. It was also required that no additional anti-microbial therapy on the baseline affected area(s) was necessary.
- Main secondary efficacy endpoints were clinical response at all visits in all study populations and microbiological response (success or failure) at all visits in the bacteriological population.
- The evaluation of safety was based on the assessment of adverse events (type, nature, incidence and outcome) and changes in vital signs and physical examination.
- For all efficacy analyses, the primary treatment comparison of interest was ozenoxacin versus vehicle in order to test the superiority of ozenoxacin versus vehicle.

RESULTS

Table 1. Primary Endpoint
Clinical response at end of therapy (Visit 3, Day 6-7) (ITTC population)

P881	Ozenoxacin	Vehicle
N	203	199
Clinical success	112 (55.2%)	78 (39.2%)
Clinical failure	91 (44.8%)	121 (60.8%)
Difference in Success Rates	0.160	
p-value	**0.001**	

Ozenoxacin showed a statistically significant superior clinical response compared to vehicle at end of treatment.

Table 2.
Combined Criteria of Clinical Success at end of therapy (Visit 3, Day 6-7) (ITTC population)

P881	Ozenoxacin	Vehicle
N	203	202
Clinical success	183 (90.1%)	161 (79.7%)
Clinical failure	20 (9.9%)	41 (20.3%)
Difference in Success Rates	0.104	
p-value	**0.003**	

The prespecified secondary endpoint of Combined Criteria of Clinical Success was defined as a total absence of the treated lesions (lesion extension=0) or the treated lesions became dry without crusts compared to baseline (SIRS=0 for exudate and for crusting), or improvement (defined as decline in the size of the affected area, number of lesions or both) such that no further antimicrobial therapy was necessary. This broader definition of clinical success includes improvement, and reflects the same criteria for clinical success as that used in pivotal Phase 3 clinical trials of other topical antibiotics approved for impetigo.

Overall, 3.9% in the ozenoxacin group experienced at least 1 treatment-emergent adverse event (TEAE), and 3.6% in the vehicle group. No severe TEAEs were reported. The incidence of study drug related TEAEs was comparable in the treatment groups, with each group having 2 related TEAEs. No patients experienced an serious adverse event (SAE) during the study. Four patients (1%) had TEAEs leading to discontinuation of study drug or early discontinuation from the study due to the event: 3 patients were in the placebo group and 1 in the ozenoxacin group.

Table 3.
Microbiological response at Visit 2 (day 3-4) and at end of therapy (Visit 3, Day 6-7) (ITTB population)

P881	Ozenoxacin	Vehicle
Visit 2, Day 3-4		
N	125	108
Microbiological Success	109 (87.2%)	76 (70.4%)
Microbiological Failure	16 (12.8%)	32 (29.6%)
Difference in Success Rates	0.168	
p-value	**0.002**	
Visit 3, Day 6-7		
N	123	107
Microbiological Success	115 (93.5%)	87 (81.3%)
Microbiological Failure	8 (6.5%)	20 (18.7%)
Difference in Success Rates	0.122	
p-value	**0.005**	

Ozenoxacin demonstrated a statistically significant superior microbiological response compared to vehicle at Visit 2 (day 3-4) and at end of treatment Visit 3 (day 6-7).

CONCLUSION

In summary, in a randomized controlled trial of 412 patients that included adults and children ages 2 months and older with impetigo, ozenoxacin demonstrated superior clinical and microbiological response versus vehicle after 5 days of therapy, and was safe and well tolerated. Ozenoxacin represents a novel topical therapeutic option being developed for the treatment of impetigo.

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