

# Ozenoxacin, a novel, topical antibacterial agent for treatment of adult and pediatric patients with impetigo: phase III clinical trials pooled analysis results

Nuria Albareda BS<sup>1</sup>, Noah Rosenberg MD<sup>2</sup>, Sandra Roth PharmD<sup>2</sup>, Ilonka Zsolt, MD PhD<sup>1</sup>, Theodore Rosen MD<sup>3</sup>, Adelaide A. Hebert MD<sup>4</sup>

<sup>1</sup>Ferrer Internacional SA, Barcelona, Spain, <sup>2</sup>Medimetrics Pharmaceuticals Inc., Fairfield, NJ, USA, <sup>3</sup>Baylor College of Medicine, Houston, TX, USA,

<sup>4</sup>UTHealth McGovern Medical School, Houston, TX USA

## INTRODUCTION

**Background:** Ozenoxacin is a novel topical antibacterial agent with potent bactericidal activity against Gram-positive bacteria that has been developed as a 1% cream for treatment of impetigo. This dataset represents a pooled analysis of the two pivotal clinical trials of Ozenoxacin.

**Objectives:** To evaluate the efficacy, safety, and tolerability of ozenoxacin 1% cream after twice-daily topical treatment for 5 days in patients with impetigo.

**Methods:** Data from two multicenter, randomized, double-blind, vehicle-controlled studies in patients with impetigo and results were pooled and analyzed.

877 Subjects were enrolled in 53 centers in 7 countries (USA, South Africa, Germany, Romania, Russia, Ukraine, and Spain).

For both studies patients were deemed eligible if they had a clinical diagnosis of impetigo with a total affected area at baseline not exceeding 100 cm<sup>2</sup>. For patients <12 years old, the total area could not exceed 2% of the body surface area (BSA). Eligible subjects were randomized to receive ozenoxacin 1% cream, placebo cream or retapamulin 1% ointment (Study 1 only). In both studies the severity of impetigo at baseline was assessed using the Skin Infection Rating Scale (SIRS).

During the 5-day treatment period, patients were instructed to apply a thin layer of study drug to the baseline affected area(s) twice daily. Assessments were conducted at four visits: pre-therapy (baseline, visit 1), on therapy (visit 2, day 3-4), end of therapy (visit 3, day 6-7), and post-therapy (visit 4, day 10-13). In addition, a telephone call was arranged 24 to 36 hours after the start of study medication for early evaluation of whether the patient's lesions were progressing.

Efficacy was measured using SIRS and microbiological culture. Safety and tolerability were evaluated.

### Primary efficacy endpoint:

- Clinical response (clinical success or clinical failure) at end of therapy (Visit 3) in the intent-to-treat clinical (ITTC) population.

### Key secondary efficacy endpoints:

- Clinical response at Visit 3 incorporating combined criteria of clinical success (reflecting previously accepted methodology for other topical antibiotics approved for impetigo) and Microbiological response at visits 2 and 3. Evaluation of safety was based on adverse events, vital signs and physical examination.

## DEMOGRAPHICS AND BASELINE CHARACTERISTICS IN THE ITTC POPULATION

	Ozenoxacin 1% cream (N = 361)	Placebo cream (N = 362)	Retapamulin 1% ointment (N = 154)	Overall (N = 877)
Mean (SD) age (years)	17.6 (18.0)	17.9 (18.0)	15.1 (15.0)	17.3 (17.5)
≥ 2 months to < 12 years old	207 (57.3)	207 (57.2)	95 (61.7)	509 (58.0)
≥ 12 years to < 18 years old	43 (11.9)	40 (11.0)	15 (9.7)	98 (11.2)
≥ 18 years	111 (30.7)	115 (31.8)	44 (28.6)	270 (30.8)
Male gender, n (%)	211 (58.4)	194 (53.6)	92 (59.7)	497 (56.7)
Caucasian	180 (49.9)	202 (55.8)	50 (32.5)	432 (49.3)
Black or African-American	130 (36.0)	115 (31.8)	79 (51.3)	324 (36.9)

## CLINICAL RESULTS

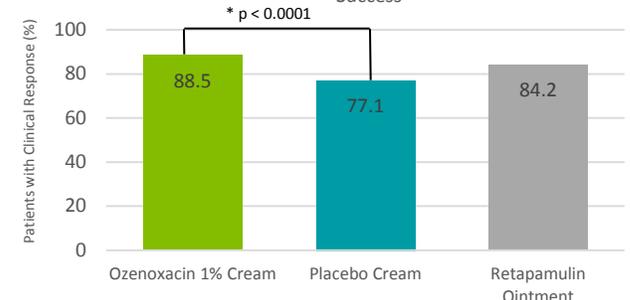
### Primary efficacy endpoint:

**Clinical success** was defined as total absence of treated lesions (SIRS score 0 for blistering, exudates/pus, crusting, itching/pain, and no more than 1 for erythema/inflammation), such that no additional antimicrobial therapy of the baseline affected area(s) was necessary. Improvement (defined as >10% decrease in total SIRS score compared with baseline, not fulfilling the criteria of individual SIRS scores for cure), as well as failure, were both considered Clinical Failure.

The clinical success rate in the ITTC population at the end of therapy (day 6-7, Visit 3) for the pooled analysis was 47.3% in the ozenoxacin 1% cream group and 31.4% in the placebo cream group. The statistically significant difference in success rates (15.9%; p<0.001; 95% CI=8.9–23.1) confirmed the significantly greater clinical success for ozenoxacin relative to placebo at the end of therapy.

### Key secondary efficacy endpoint:

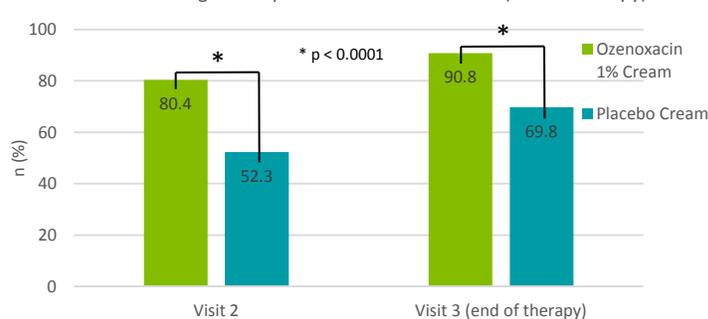
Clinical Response at Visit 3 with Combined Criteria of Clinical Success



Combined criteria of **clinical response** was defined as clinical success or improvement. **This broader measure reflects the same criteria for clinical success used in pivotal phase III clinical trials of other previously approved topical antibiotics for impetigo and includes 'improvement' in the definition of clinical success.** The difference in success rates (11.5%) was significant (p<0.001; 95% CI=6–17.0).

## MICROBIOLOGICAL RESULTS

Microbiological Response at Visit 2 and Visit 3 (End of Therapy)



**Microbiological success** was defined as eradication, a composite of documented eradication (absence of the original pathogen from the post-treatment culture of the specimen obtained from the original site of infection) and presumed eradication (complete resolution of signs and symptoms associated with absence of culturable material). The differences in the success rates between ozenoxacin 1% cream and placebo cream at Visit 2 (28%) and Visit 3 (21%) were significant (p<0.0001).

### Ozenoxacin vs. Retapamulin

There was evidence that ozenoxacin produced more rapid microbiological clearance than retapamulin after two days of therapy, as highlighted by success rates of 74.7% for ozenoxacin versus 60% for retapamulin (p=0.0087) in Study 1 (Gropper 2014).

## CONCLUSIONS

- In a pooled analysis of two phase III studies, ozenoxacin demonstrated a superior clinical and microbiological response compared to vehicle after 5 days of therapy.
- Ozenoxacin produced more rapid microbiological clearance than placebo after 2 days of therapy.
- The rapid clinical response of ozenoxacin could be clinically beneficial in terms of reducing the likelihood of disease spread to other parts of the body or to other persons; this is particularly important in the pediatric population.
- Data from this pooled analysis demonstrate that ozenoxacin has the potential to be a rapid and effective new treatment for impetigo.