Evaluation of Delafloxacin Activity and Treatment Outcome for Phase 3 Acute Bacterial Skin and Skin Structure Infection Clinical Trial Anaerobic Isolates

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Abstract

Background: Delafloxacin (DLX) is a broad-spectrum fluoroquinolone (FQ) antibacterial approved in 2017 by the Food and Drug Administration for treatment of aerobic bacterial and skin microorganisms (AABSMSSIs, AABSSIs). DLX was studied in two comparative Phase 3 clinical trials (TRB, 390-001) for the treatment of community-acquired bacterial skin and skin structure infection (CABSSIs).

The objective of this study was to analyze the activity of DLX in vitro and in vivo against anaerobic isolates (AABSMSSIs, AABSSIs) in a Phase 3 clinical trial and to compare the outcomes of infections caused by these isolates with the microbiologic response for evaluable at follow-up in the microbiologically evaluable-at-follow-up (MEFU) population. All of the subjects in the study were considered evaluable.

Methods: A total of 84 clinical and non-clinical isolates were collected during Phase 2A (TRB, 004) and Phase 2B (TRB, 193) clinical trials and 9 additional isolates were colleted during Phase 2B. All isolates were tested for susceptibility against DLX. Other antimicrobials tested included clindamycin (CD), metronidazole (MTZ), and moxifloxacin (MXF). The activity of DLX and MXF were compared at standard pH 7.0 and pH 6.0.

Results: DLX had the lowest MIC values against both CP and OP species and was excellent against all other anaerobic isolates tested, including CD, CP, and was more active than MXF. Of all clinical isolates, DLX activity was unchanged at lower pH while MXF MIC increased 2-fold. These data suggest that DLX activity remains potent at a lower pH, common at sites of infection.

Conclusions: DLX demonstrated excellent in vitro and in vivo activity against anaerobic species of AABSSIs and is an active drug against MXF-nonsusceptible isolates grown at pH 6.0.

Introduction

Delafloxacin (DLX) is a broad-spectrum fluoroquinolone (FQ) antibacterial approved in 2017 by the Food and Drug Administration for treatment of aerobic bacterial and skin microorganisms (AABSMSSIs, AABSSIs). DLX is also in clinical development for community-acquired bacterial pneumonia (CABP). In AABSSIs, anaerobic isolates may be recovered and may be significant pathogens, depending on site and type of infection. Anaerobic infections generally have a poor clinical outcome.

Materials and Methods

A total of 117 anaerobic isolates were collected from both trials during 2 Phase 3 clinical trials: TRB, 004 and TRB, 193.

The aerobic isolates grew in 21/2 agar and were collected during the 2017 SENTRY Antimicrobial Surveillance Program.

In the clinical trials, the isolates were identified by molecular testing as Gram-negative (GN) and Gram-positive (GP) species. The isolate identifiers were used to determine the susceptibility to the antimicrobial for in vivo isolates.

The in vivo isolates were compared with the sensitivity results at standard pH 7.0 and pH 6.0.

In this study, in vitro susceptibility for DLX was done against anaerobic agents using enhanced broth (E-test) and E-test strips. The in vivo isolates were determined for the susceptibility to the antimicrobial for in vivo isolates.

The susceptibility testing was performed according to CLSI guidelines. In vitro activity was assessed by MicroScan WalkAway (MAST). The MICs were determined and compared with the microbiologic response for evaluable at follow-up.

Results

The activity of DLX and MXF were compared at standard pH 7.0 and pH 6.0. The activity of DLX had the lowest MIC values against both CP and OP species and was excellent against all other anaerobic isolates tested, including CD, CP, and was more active than MXF. Of all clinical isolates, DLX activity was unchanged at lower pH while MXF MIC increased 2-fold. These data suggest that DLX activity remains potent at a lower pH, common at sites of infection.

Conclusions

DLX demonstrated excellent in vitro and in vivo activity against anaerobic species of AABSSIs and is an active drug against MXF-nonsusceptible isolates grown at pH 6.0. The in vivo isolates were compared with the sensitivity results at standard pH 7.0 and pH 6.0. The activity of DLX and MXF were compared at standard pH 7.0 and pH 6.0. The activity of DLX had the lowest MIC values against both CP and OP species and was excellent against all other anaerobic isolates tested, including CD, CP, and was more active than MXF. Of all clinical isolates, DLX activity was unchanged at lower pH while MXF MIC increased 2-fold. These data suggest that DLX activity remains potent at a lower pH, common at sites of infection.

References

Acknowledgements

This study was sponsored by Melinta Therapeutics, Inc., North Haven, CT.

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