These data suggest that DLX has activity in ABSSSI where anaerobes may be involved.

Methods
Activities of all antimicrobials tested against 93 anaerobic isolates are shown in Table 1. All 21 isolates in the DLX treatment arm were eradicated, including 1 MXF-resistant isolate. Interestingly, DLX demonstrated potent activity against Clostridium sordellii and Fusobacterium nucleatum, with >90% of isolates susceptible. In addition, DLX had improved activity against polymicrobial infections at pH 6.0 compared with MXF.

DLX is also in clinical development for community-acquired bacterial pneumonia (CABP) and other polymicrobial infections at pH 6.0 compared with MXF.

Figure 1: MIC distributions of 93 anaerobes tested against delafloxacin and comparators moxifloxacin, metronidazole, and clindamycin.

Figure 2: Comparison of delafloxacin activity in medium pH 7.0 vs. pH 6.0 when tested against 93 anaerobic isolates.

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

D SHORTRIDGE, S MCCURDY, PR HOMBURG, MD HUDH, RK FLAMM

JMI Laboratories, North Liberty, Iowa, USA; 1Melinta Therapeutics, Morristown, New Jersey, USA

Abstract

- Background: Delafloxacin (DLX) is a broad-spectrum fluoroquinolone (FQ) antibacterial approved in 2017 by the Food and Drug Administration for treatment of skin and skin structure infections (ABSSSI). DLX is an FQ with a neutral pKa, which allows its activity to be maintained in acidic environments (pH 6.0).
- Methods: A total of 43 anaerobic isolates were collected during Phase 3 ABSSSI clinical trials and an additional 29 cultures were collected as part of the 2017 SENTRY Antimicrobial Surveillance Program. The isolates tested included 11 Bacteroides fragilis (BF), 13 Clostridium (CP), 10 Bacillus (B), and 9 Fusobacterium (Fusobacterium nucleatum, Fnu) isolates. Activities of all antimicrobials were determined by CLSI agar dilution methodology (M11, 2012). For all isolates combined, DLX activity was unchanged at lower pH while MXF MIC values increased 2-fold at pH 6.0. Other antimicrobials tested included clindamycin (CD), metronidazole (MTZ), and moxifloxacin (MXF). In vitro susceptibility (S) for DLX and comparator agents for gram-negative (GN) and gram-positive (GP) anaerobic isolates from Phase 3 ABSSSI clinical trials were determined and compared with the microbiologic response for evaluable isolates.
- Results: DLX had the least MIC values against both CP and GN species and was potent against many gram-positive and gram-negative anaerobic isolates tested, including BF and CP, and was active more than MTZ (pH 7.0). For all isolates combined, DLX activity was unchanged at lower pH while MXF MIC values increased 2-fold. These data suggest that DLX activity remains potent at a lower pH, consistent at sites of infection.

Figure 1: MIC distributions of 93 anaerobes tested against delafloxacin and comparators moxifloxacin, metronidazole, and clindamycin.

Figure 2: Comparison of delafloxacin activity in medium pH 7.0 vs. pH 6.0 when tested against 93 anaerobic isolates.

Table 2: Delafloxacin MIC when tested against 93 anaerobic isolates.

Table 3: Susceptibilities, monomicrobial or polymicrobial infection, and microbiologic outcomes of isolates from the delafloxacin treatment arm.

Figure 2: Comparison of delafloxacin activity in medium pH 7.0 vs. pH 6.0 when tested against 93 anaerobic isolates.

Materials and Methods
- Delafloxacin (DLX) is a broad-spectrum fluoroquinolone (FQ) antibacterial approved in 2017 by the Food and Drug Administration for treatment of skin and skin structure infections (ABSSSI).
- DLX is also in clinical development for community-acquired bacterial pneumonia (CABP) and other infections.
- In vitro susceptibility (S) for DLX and comparator agents for gram-negative (GN) and gram-positive (GP) anaerobic isolates from Phase 3 ABSSSI clinical trials were determined and compared with the microbiologic response for evaluable isolates.

Introduction

- Delafloxacin (DLX) is a broad-spectrum fluoroquinolone (FQ) antibacterial approved in 2017 by the Food and Drug Administration for treatment of skin and skin structure infections (ABSSSI).
- DLX is also in clinical development for community-acquired bacterial pneumonia (CABP) and other infections.
- In vitro susceptibility (S) for DLX and comparator agents for gram-negative (GN) and gram-positive (GP) anaerobic isolates from Phase 3 ABSSSI clinical trials were determined and compared with the microbiologic response for evaluable isolates.

Materials and Methods
- A total of 93 anaerobic isolates were collected from both test arms during 2 Phase 3 ABSSSI clinical trials.
- The anaerobic isolates (93 BF, 13 CP, 10 B, and 9 Fnu) were collected during the 2017 SENTRY Antimicrobial Surveillance Program.
- The isolates tested included 11 BF, 11 CP, 11 B, and 9 Fnu. (Table 2).
- The isolates were obtained from patients with large, complex wounds that were susceptible to multiple classes of antimicrobials.
- Other antimicrobials tested included clindamycin (CD), metronidazole (MTZ), and moxifloxacin (MXF).
- Interpretation criteria from CLSI (M100-S24, 2014) were applied where appropriate.
- Delafloxacin and moxifloxacin were tested at an acid pH using pH 6.0.

Results
- The M11-A8. Methods for antimicrobial testing was performed according to CLSI agar dilution methodology (M11, 2012).
- For all isolates combined, DLX activity was unchanged at lower pH while MXF MIC values increased 2-fold at pH 6.0. Other antimicrobials tested included clindamycin (CD), metronidazole (MTZ), and moxifloxacin (MXF).
- In vitro susceptibility (S) for DLX and comparator agents for gram-negative (GN) and gram-positive (GP) anaerobic isolates from Phase 3 ABSSSI clinical trials were determined and compared with the microbiologic response for evaluable isolates.
- Results: DLX had the least MIC values against both CP and GN species and was potent against many gram-positive and gram-negative anaerobic isolates tested, including BF and CP, and was active more than MTZ (pH 7.0). For all isolates combined, DLX activity was unchanged at lower pH while MXF MIC values increased 2-fold. These data suggest that DLX activity remains potent at a lower pH, consistent at sites of infection.

References

Clinical and Laboratory Standards Institute (CLSI). Performance standards for antimicrobial susceptibility testing. 25th informational supplement. Wayne, PA: CLSI.

Clinical and Laboratory Standards Institute (CLSI). Methods for antimicrobial susceptibility testing of anaerobic bacteria, 9th edn. Wayne, PA: CLSI.

Contact Information:
Doo-Soon Shortridge, PhD
JMI Laboratories
345 Beaver Knolls Centre, Suite A
North Liberty, IA 52317
Phone: (319) 665-3370
Fax: (319) 665-3371
Email: dsho@jmlabs.com

Acknowledgements

This study was sponsored by Melinta Therapeutics, Inc., Morristown, N.J. Originally presented at MAD-ID 2019, 10th European IDA, Uxbridge, UK, October 24, 2019.