Background

Delafloxacin is a novel generation quinolone with broad-spectrum activity against medically relevant enterobacteria (MRSA), susceptible gram-negative bacteria including ESBL-producing Enterobacteriaceae, and in Phase III development for ADR/IMX-resistant and multidrug-resistant gram-negative bacilli (e.g., CRE). Delafloxacin demonstrated improved penetration into the central nervous system, and may be a useful agent for the treatment of community-acquired and hospital-acquired infections.

Methods

This was a Phase 1, single-dose, randomized, open-label, 3-period, 4-sequence crossover study in 30 healthy subjects. After a 12-h fast of at least 10 h, subjects received a single dose of delafloxacin 900 mg as an enteric-coated tablet on treatment days 1, 2, and 3 of each cycle. Subjects were randomized to one of 6 treatment sequences with a balanced combination of treatment order and fasting state (first and second cycle) in a Latin square design. The primary outcome measure was pharmacokinetic (PK) characterization of delafloxacin following oral administration. Secondary outcomes included assessment of the effect of food on the PK parameters of delafloxacin.

Results

Delafloxacin was well tolerated in the fasted state. Cmax, tmax, AUC0-t, and AUC0-Inf were reduced by 30%, 30%, 22%, and 22%, respectively, when dosed under the fed state compared to the fasted state. Food did not affect the t1/2 of delafloxacin.

Conclusions

Delafloxacin exhibited lower exposure under the fed state compared to the fasted state. Food had no effect on the terminal elimination phase of delafloxacin. Delafloxacin is recommended for oral administration without regard to meals.

Abstract

Pharmacokinetics of a Single Dose of Oral Delafloxacin in Healthy Subjects

R. HOOVER1, L. LAWRENCE1, M. BENEDICT1, T. HUNT1, S. GUNDA2, D. LI1, E. SUN1, S. CAMMARATA1

1Melinta Therapeutics, Inc., New Haven, CT

2PPD Inc., Austin, TX

Introduction

Gonorrhea is a sexually transmitted disease (STD) caused by infection with N. gonorrhoeae in infections that are resistant to currently marketed fluoroquinolones and is in currently in a Phase 3 clinical study in the US. Of the 240,000 cases of gonorrhea reported to the Centers for Disease Control and Prevention (CDC) in 2011 (CDC, 2012b), more than 320,000 cases of gonorrhea reported to the Centers for Disease Control and Prevention (CDC) in 2011 (CDC, 2012b; 2013). The MIC of N. gonorrhoeae in infections that are resistant to currently marketed fluoroquinolones and in currently in a Phase 3 clinical study in the US.

Clinical Study Design

This study is a 2-period, 3-dose study, single-blind, randomized, double-blind, placebo-controlled, crossover study in 30 healthy subjects. Subjects randomized to one of 6 treatment sequences with a balanced combination of treatment order and fasting state (first and second cycle) in a Latin square design. The primary outcome measure was pharmacokinetic (PK) characterization of delafloxacin following oral administration. Secondary outcomes included assessment of the effect of food on the PK parameters of delafloxacin.

Methods

The study design was a Phase 1, single-dose, randomized, open-label, 3-period, 4-sequence crossover study in 30 healthy subjects. Subjects randomized to one of 6 treatment sequences with a balanced combination of treatment order and fasting state (first and second cycle) in a Latin square design. The primary outcome measure was pharmacokinetic (PK) characterization of delafloxacin following oral administration. Secondary outcomes included assessment of the effect of food on the PK parameters of delafloxacin.

Results

Delafloxacin was well tolerated in the fasted state. Cmax, tmax, AUC0-t, and AUC0-Inf were reduced by 30%, 30%, 22%, and 22%, respectively, when dosed under the fed state compared to the fasted state. Food did not affect the t1/2 of delafloxacin.

Conclusions

Delafloxacin exhibited lower exposure under the fed state compared to the fasted state. Food had no effect on the terminal elimination phase of delafloxacin. Delafloxacin is recommended for oral administration without regard to meals.

Abstract

Pharmacokinetics of a Single Dose of Oral Delafloxacin in Healthy Subjects

R. HOOVER1, L. LAWRENCE1, M. BENEDICT1, T. HUNT1, S. GUNDA2, D. LI1, E. SUN1, S. CAMMARATA1

1Melinta Therapeutics, Inc., New Haven, CT

2PPD Inc., Austin, TX

Introduction

Gonorrhea is a sexually transmitted disease (STD) caused by infection with N. gonorrhoeae in infections that are resistant to currently marketed fluoroquinolones and in currently in a Phase 3 clinical study in the US. Of the 240,000 cases of gonorrhea reported to the Centers for Disease Control and Prevention (CDC) in 2011 (CDC, 2012b), more than 320,000 cases of gonorrhea reported to the Centers for Disease Control and Prevention (CDC) in 2011 (CDC, 2012b; 2013). The MIC of N. gonorrhoeae in infections that are resistant to currently marketed fluoroquinolones and in currently in a Phase 3 clinical study in the US.

Clinical Study Design

This study is a 2-period, 3-dose study, single-blind, randomized, double-blind, placebo-controlled, crossover study in 30 healthy subjects. Subjects randomized to one of 6 treatment sequences with a balanced combination of treatment order and fasting state (first and second cycle) in a Latin square design. The primary outcome measure was pharmacokinetic (PK) characterization of delafloxacin following oral administration. Secondary outcomes included assessment of the effect of food on the PK parameters of delafloxacin.

Methods

The study design was a Phase 1, single-dose, randomized, open-label, 3-period, 4-sequence crossover study in 30 healthy subjects. Subjects randomized to one of 6 treatment sequences with a balanced combination of treatment order and fasting state (first and second cycle) in a Latin square design. The primary outcome measure was pharmacokinetic (PK) characterization of delafloxacin following oral administration. Secondary outcomes included assessment of the effect of food on the PK parameters of delafloxacin.

Results

Delafloxacin was well tolerated in the fasted state. Cmax, tmax, AUC0-t, and AUC0-Inf were reduced by 30%, 30%, 22%, and 22%, respectively, when dosed under the fed state compared to the fasted state. Food did not affect the t1/2 of delafloxacin.

Conclusions

Delafloxacin exhibited lower exposure under the fed state compared to the fasted state. Food had no effect on the terminal elimination phase of delafloxacin. Delafloxacin is recommended for oral administration without regard to meals.