Antimicrobial Activity of BC-3781, an Investigational Pleuromutilin, Tested Against Organisms Isolated From Patients with Community-Acquired Respiratory Tract Infections (CARTI) and Acute Bacterial Skin and Skin Structure Infections (ABSSSI)

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ABSTRACT

BC-3781 is a novel semi-synthetic pleuromutilin derivative developed by Nabriva Therapeutics AG with excellent antibacterial spectrum targeting the 50S ribosomal subunit. BC-3781 is a novel semi-synthetic pleuromutilin derivative developed by Nabriva Therapeutics AG with excellent antibacterial spectrum targeting the 50S ribosomal subunit. BC-3781 is a novel semi-synthetic pleuromutilin derivative developed by Nabriva Therapeutics AG with excellent antibacterial spectrum targeting the 50S ribosomal subunit.

INTRODUCTION

Pleuromutilin antibiotics are a new class of antibiotics for human use selectively inhibiting bacterial protein synthesis by specific interaction with the 50S ribosomal subunit. BC-3781 is a novel semi-synthetic pleuromutilin derivative developed by Nabriva Therapeutics AG with excellent antibacterial spectrum targeting the 50S ribosomal subunit. BC-3781 is a novel semi-synthetic pleuromutilin derivative developed by Nabriva Therapeutics AG with excellent antibacterial spectrum targeting the 50S ribosomal subunit. BC-3781 is a novel semi-synthetic pleuromutilin derivative developed by Nabriva Therapeutics AG with excellent antibacterial spectrum targeting the 50S ribosomal subunit.

MATERIALS & METHODS

Organism collection: The activity of BC-3781 was determined against bacterial pathogens causing ABSSSI and CARTI including Staphylococcus aureus, Group A and B streptococci, Staphylococcus epidermidis and S. agalactiae among others. Unique patient isolates were collected within the SENTRY Antimicrobial Surveillance Program during 2010 in 84 medical centers worldwide (28 countries), including 2,427 organisms from CARTI and 3,014 from ABSSSI.

RESULTS

Activity against isolates from CARTI (Tables 1 and 2):

- Against S. pneumoniae, BC-3781 was the most active compound with MIC90 values of 0.125–2 µg/mL. BC-3781 was four- to eight-fold more active than levofloxacin (MIC90 11/1 µg/mL) and inhibited strains resistant to the other tested antibiotics independent of susceptibility to penicillin, macrolides or fluoroquinolones. High rates of resistance were observed for azithromycin (35.8%), trimethoprim-sulfamethoxazole (23.2%) and doxycycline (25.2%).

- BC-3781 also displayed potent activity against the Gram-negative pathogens H. influenzae (MIC90 0.5 µg/mL) and M. catarrhalis (MIC90 0.125–2 µg/mL).

- Against S. aureus (including 37.0% MRSA), BC-3781 was the most active compound with MIC90 values of 0.125–2 µg/mL (range ≤0.03–0.5 µg/mL). BC-3781 was four- to eight-fold more active than vancomycin (MIC90 11/1 µg/mL). High rates of resistance were observed for oxacillin-S and -R (MSSA and MRSA) strains. Only 2 MRSA isolates (0.2%) had elevated BC-3781 MICs (2 and 4 µg/mL) compared to the MIC90, >16 µg/mL.

- BC-3781 was four- to eight-fold more active than vancomycin (MIC90 0.5 µg/mL) and linezolid (MIC90 1 µg/mL). BC-3781 was the most active compound with MIC50/90 values of 0.03/0.12 µg/mL, with only 2 isolates being inhibited at ≥16 µg/mL. BC-3781 exhibits potent activity against contemporary bacterial pathogens causing ABSSSI and CARTI including S. aureus, Group A and B streptococci, Staphylococcus epidermidis and S. agalactiae among others. Unique patient isolates were collected within the SENTRY Antimicrobial Surveillance Program during 2010 in 84 medical centers worldwide (28 countries), including 2,427 organisms from CARTI and 3,014 from ABSSSI. © 2011 ASM. All Rights Reserved.

CONCLUSIONS

- BC-3781 demonstrated excellent activity against contemporary pathogens collected worldwide in the course of 2010 SENTRY study from patients with CARTI and ABSSSI including those cases with multidrug-resistant Gram-positive cocci.

- BC-3781 was shown to be one of the most active compounds against the most prevalent respiratory and skin pathogens and its activity was not negatively influenced by other antimicrobial classes.

- No new resistance was noted for the BC-3781 activity by geographic region.

- There is good evidence (see results of the recently completed clinical Phase II trial, L-966, ICAAC 2011) that BC-3781 is a potent in vitro activity translated into potent clinical activity. Further clinical trials will define the role of BC-3781 for treatment of CARTI as well as other types of infection.

SELECTED REFERENCES

- BC-3781 exhibited potent activity against S. aureus (MIC, 0.125–12 µg/mL) with similar MIC distributions among MSSA and MRSA. Only 2 MRSA and 5 MSSA isolates had elevated BC-3781 MIC values (>16 µg/mL) compared to the wild-type population (MIC range, 0.03–0.5 µg/mL). Particularly against MRSA, displaying high resistance rates against macrolides, fluoroquinolones or linezolid, BC-3781 was the most active compound among those tested.

- A hitherto unknown staphylococcal compound with MIC50/90 values of 0.03/0.12 µg/mL and 99.8% and 100% of isolates being inhibited at ≤0.5 µg/mL, respectively. Among the tested antibiotics BC-3781 was the most active compound being 16- to 32-fold more active than vancomycin (MIC90 0.5 µg/mL) and linezolid (MIC90 1 µg/mL).

- Pleuromutilin antibiotics are a new class of antibiotics for human use selectively inhibiting bacterial protein synthesis by specific interaction with the 50S ribosomal subunit. BC-3781 is a novel semi-synthetic pleuromutilin derivative developed by Nabriva Therapeutics AG with excellent antibacterial spectrum targeting the 50S ribosomal subunit. BC-3781 is a novel semi-synthetic pleuromutilin derivative developed by Nabriva Therapeutics AG with excellent antibacterial spectrum targeting the 50S ribosomal subunit. BC-3781 is a novel semi-synthetic pleuromutilin derivative developed by Nabriva Therapeutics AG with excellent antibacterial spectrum targeting the 50S ribosomal subunit.