AAI101, a novel β-lactamase inhibitor: microbiological and enzymatic profiling

Christopher R. Bethel1,2, Michael J. Turley1,2, Joseph D. Rutter1,2, Magdalena A. Taracila1,2, Saralene Bajaksouzian2,3, Michael R. Jacobs2,3, and Robert A. Bonomo1,2

Background: AAI101 is a novel β-lactamase inhibitor, active against ESBLs and other β-lactamases. AAI101 combined with ceftazidime is in Phase 2 clinical trials. The objective of the present study was to determine differences between AAI101 and tazobactam in their inhibition of selected β-lactamases of clinical relevance. 

Methods: Inhibitory E. coli strains expressing single clinically relevant ESBLs were tested for susceptibility to AAI101 and tazobactam. β-Lactamase expression was monitored in the presence of AAI101 and tazobactam, and selected ESBLs were characterized by Western blotting.

Results: AAI101 more potently inhibited β-lactamase activity compared to tazobactam, with significant differences against CTX-M-15, KPC-2, and SHV-1. Western blotting revealed that AAI101 acylated SHV-1 faster than tazobactam, but similar to tazobactam.

Conclusions: AAI101 restores the activity of cephalosporin-resistant E. coli strains producing defined β-lactamases (Table 1). This study suggests that AAI101 represents a promising class of β-lactamase inhibitors.

Sensitivity Testing

Background: AAI101 is a novel β-lactamase inhibitor, active against ESBLs and other β-lactamases. AAI101 combined with ceftazidime is in Phase 2 clinical trials. The objective of the present study was to determine differences between AAI101 and tazobactam in their inhibition of selected β-lactamases of clinical relevance. 

Methods: Inhibitory E. coli strains expressing single clinically relevant ESBLs were tested for susceptibility to AAI101 and tazobactam. β-Lactamase expression was monitored in the presence of AAI101 and tazobactam, and selected ESBLs were characterized by Western blotting.

Results: AAI101 more potently inhibited β-lactamase activity compared to tazobactam, with significant differences against CTX-M-15, KPC-2, and SHV-1. Western blotting revealed that AAI101 acylated SHV-1 faster than tazobactam, but similar to tazobactam.

Conclusions: AAI101 restores the activity of cephalosporin-resistant E. coli strains producing defined β-lactamases (Table 1). This study suggests that AAI101 represents a promising class of β-lactamase inhibitors.

Sensitivity Testing

Background: AAI101 is a novel β-lactamase inhibitor, active against ESBLs and other β-lactamases. AAI101 combined with ceftazidime is in Phase 2 clinical trials. The objective of the present study was to determine differences between AAI101 and tazobactam in their inhibition of selected β-lactamases of clinical relevance. 

Methods: Inhibitory E. coli strains expressing single clinically relevant ESBLs were tested for susceptibility to AAI101 and tazobactam. β-Lactamase expression was monitored in the presence of AAI101 and tazobactam, and selected ESBLs were characterized by Western blotting.

Results: AAI101 more potently inhibited β-lactamase activity compared to tazobactam, with significant differences against CTX-M-15, KPC-2, and SHV-1. Western blotting revealed that AAI101 acylated SHV-1 faster than tazobactam, but similar to tazobactam.

Conclusions: AAI101 restores the activity of cephalosporin-resistant E. coli strains producing defined β-lactamases (Table 1). This study suggests that AAI101 represents a promising class of β-lactamase inhibitors.