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In Vivo Activity of CXA-101 Against _Pseudomonas aeruginosa_(PA) in a Rabbit Experimental Model of Pneumonia: Comparison with Ceftazidime (CAZ), Piperacillin/Tazobactam (TZP), and Imipenem (IMP)

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Background: The aim of this work was to assess the in vivo activity of CXA-101, a novel oxyimino-aminothiazolyl cephalosporin, and comparators against a PA strain using a rabbit experimental pneumonia model. **Methods**: MICs for the PA strain were 0.5, 1, 4, and 0.5 mg/L for CXA-101, CAZ, TZP, and IMP, respectively. Experimental pneumonia was induced by endobronchial administration of 1 mL of 10^9CFU/mL of PA. Antibiotics were started 5hr after bacterial challenge and given for 2 days. Animals were randomly assigned to either no treatment (control), CXA-101 1g (computer-controlled infusion syringe pump simulating a human-equivalent [HE] dose of 1g q8hr), CXA-101 2g (simulating a HE dose of 2g q8hr), CAZ (simulating a HE dose of 2g q8hr), TZP (simulating a HE dose of 4/0.5g q6hr), and IMP (simulating a HE dose of 1g q8hr). Surviving bacteria at the end of therapy were counted in lungs and spleen and evaluated for resistance development on antibiotic containing media. **Results:** Results were as follows.

Treatment (n)	Mean ± SD $\log_{10}$ CFU/g of lung
Controls (10)	6.3 ± 0.8
CXA-101 (1g q8hr) (5)	4.8 ± 0.3[a]
CXA-101 (2g q8hr) (6)	3.6 ± 0.3[a, b]
CAZ (2g q8hr) (5)	4.8 ± 0.2[a]
TZP (4/0.5g q6hr) (6)	5.5 ± 0.9
IMP (1g q8hr) (6)	3.9 ± 0.3[a]
(n) = no. of animals. [a] $P<0.001$ vs controls; [b] $P<0.05$ vs CAZ, CXA-101 (1g q8hr), and TZP; Bonferroni's test after analysis of variance.	

Conclusions: 1. CXA-101, CAZ and IMP demonstrated significant in vivo activity against PA strain. 2. TZP was poorly active against PA after a 2-day treatment in this model. 3. CXA-101 (2g q8hr) was significantly more active than CXA-101 (1g q8hr) and CAZ (2g q8hr) in this model. 4. None of the agents tested selected for resistant variants on media containing antibiotics at 4× MIC. 5. These data strongly support CXA-101 as a therapeutic option for the treatment of severe PA infection.