In vivo efficacy of BV100 in mouse models of *Acinetobacter baumannii* infection

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Background: BV100 (rifabutin for infusion) is being developed by BioVersys for the treatment of serious infections due to *A. baumannii*. Screening of the ReFrame drug repurposing library under nutrient limiting conditions identified rifabutin as having potent antibacterial activity towards XDR *A. baumannii.* BV100 displays potent antimicrobial activity against clinical *A. baumannii* isolates with an MIC_{90} at 1 mg/L (n = 293). This study aimed to determine the efficacy of BV100 in mouse lung infection models.

Material/methods: Seven clinical *A. baumannii i*solates with MICs ranging from 0.004 – 2 mg/L were selected for efficacy testing in the murine lung infection model. Female CD-1 (ICR) mice were made neutropenic by injection of 150 & 100 mg/kg of cyclophosphamide, intraperitoneally, at 4 and 1 day prior to infection. Anesthetized mice were intranasally inoculated with 0.05 mL of the infecting inoculum (6-7 log_{10} CFU/animal). Animals were intravenously administered with BV100 or rifampicin 2 hrs post infection. Mice were euthanized at 26 hrs post-infection, lungs were removed aseptically, homogenized, diluted and plated for the determination of bacterial titers (log_{10} CFU/lung).

Results: All the neutropenic lung infection models had a high bacterial burden at start of treatment (ranging from 6.4-7.3 log_{10} CFU/lung) and provided a robust growth over 24 hours (mean = 2 log_{10} growth). BV100 reduced the bacterial burden in the lung for all strains tested. The mean maximum effect observed from start of treatment was -3.6 log_{10} CFU/lung and >2.4 log_{10} reduction was exhibited for all isolates after a 24 hrs.

Conclusions: BV100 displays potent *in vivo* activity towards *A. baumannii* with a broad MIC range in neutropenic lung models of infection. The safety and tolerability of BV100, a novel intravenous formulation of rifabutin, is currently investigated in Phase I clinical studies.

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