Avibactam renders piperacillin effective against *Mycobacterium abscessus* in vitro.

and in an *in vivo* *Galleria mellonella* infection model

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**Introduction**

*Mycobacterium abscessus* is a multi-drug resistant pathogen, harboring the *Class A* β-lactamase BlaMAB that is resistant to clavulanic acid, sulbactam and tazobactam inhibition. *Piperacillin* is readily hydrolyzed by BlaMAB.

We aimed to determine whether the addition of *avibactam*, a non-β-lactam, β-lactamase inhibitor, enables the use of piperacillin against *M. abscessus*.

We used a recombinant, luminescent *M. abscessus* to show the augmentation of piperacillin (and ampicillin) activity against *M. abscessus* in vitro.

We then used our *G. mellonella* infection model¹ to evaluate the efficacy of avibactam containing combinations in vivo.

**Avibactam lowers the MIC of piperacillin for *M. abscessus***

Addition of avibactam (4 μg/ml) consistently decreased the MIC of piperacillin and ampicillin by 16-32 fold. As expected, avibactam had no significant effect on meropenem MIC, as meropenem is very poorly hydrolyzed by the β-lactamase BlaMAB.

**Piperacillin/avibactam effectively treats *M. abscessus* infection in vivo***

60 *G. mellonella* larvae were inoculated with luminescent *M. abscessus* on day 0, and treated with meropenem, piperacillin, avibactam alone, or piperacillin combined with avibactam on days 2 and 3. Using IVIS® imaging, we measured infection progression in live infected larvae on day 4.

**Conclusion**

The piperacillin-avibactam combination is effective against *M. abscessus* infections. This novel combination may hold a great promise for patients with cystic fibrosis suffering from *M. abscessus*, *Pseudomonas aeruginosa* and/or *Staphylococcus aureus* co-infections.

¹ Meir M et al. Antimicrob Agents Chemother. 2018

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