Treatment with finafloxacin is effective in a murine model of melioidosis.

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Introduction

The antibiotic treatment of infections with *Burkholderia pseudomallei* is lengthy and relapse often occurs. Finafloxacin, a novel fluoroquinolone, has good antimicrobial activity against a wide range of bacterial species including MRSA and MDR Gram-negative pathogens1; this activity is enhanced in acidic conditions, where other fluoroquinolones are significantly less active. Finafloxacin may therefore exhibit an advantage in treating bacteria residing in these conditions, including intracellular bacteria that rely on the host cell to replicate and proliferate, such as *B. pseudomallei*.

The window of opportunity for initiating finafloxacin treatment was evaluated in a murine model of inhalational melioidosis and compared to co-trimoxazole.

Further analysis is detailed in the poster presented by Sarah Harding.

Methods

- Balb/c mice were challenged with approximately 98 CFU of *B. pseudomallei* by the inhalational route.
- Treatment was initiated at 24, 36 or 48 hours post-challenge and continued for 14 days; finafloxacin (37.5 mg/kg) and the vehicle control were administered every 8 hours, co-trimoxazole (78 mg/kg) was administered every 12 hours, all by the oral route.
- Following 1 day and 14 days of treatment, 5 mice per group were culled and their spleen, liver and lungs harvested for bacterial enumeration.
- Ten animals per group were left for survival until day 59.

Results

Cull 1 – 1 day of treatment

- Finafloxacin treated mice (initiated at 24 hours post-challenge) had a significantly reduced bacterial load in the liver and spleen (where no bacteria was detected) and the lungs in comparison to mice treated with co-trimoxazole.
- Finafloxacin treated mice (initiated at 36 hours post-challenge) had a significantly reduced bacterial load in the liver in comparison to co-trimoxazole and in all 3 organs in comparison to the vehicle control.

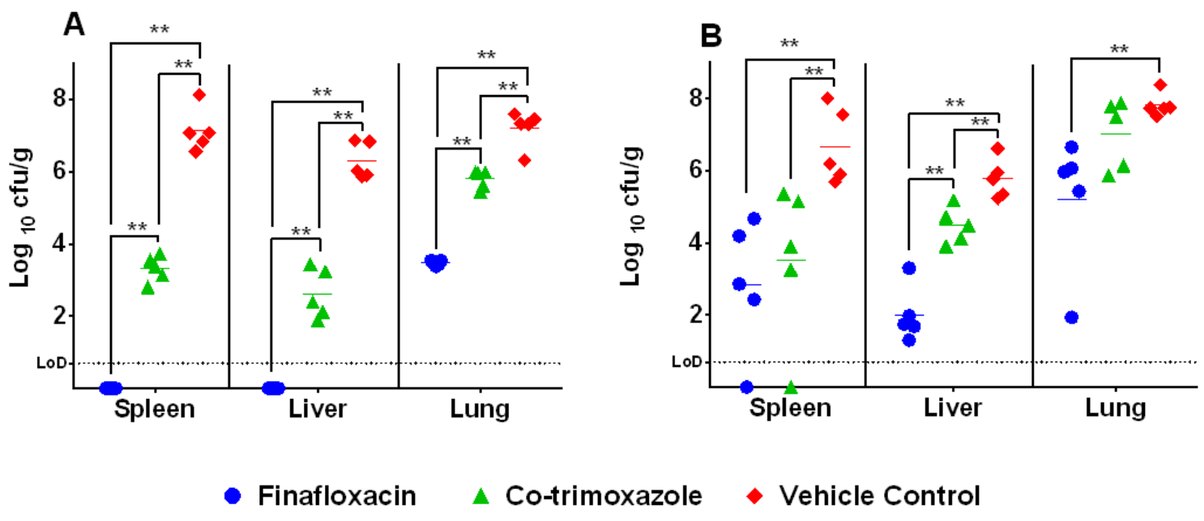

Figure 1. The bacterial load in organs following 1 day of antibiotic treatment. Bacterial counts (CFU/g) in the spleen, liver and lungs of 5 mice per group following 1 day of antibiotic treatment initiated at 24 (A) or 36 (B) hours post-challenge. (p<0.01)**

Cull 2 – 14 days of treatment

- No *B. pseudomallei* was detected in organs harvested from mice treated with finafloxacin or co-trimoxazole when treatment was initiated at 24 hours post-challenge.
- When treatment was initiated at 36 hours post-challenge, two mice treated with finafloxacin were colonised compared to three mice treated with co-trimoxazole.

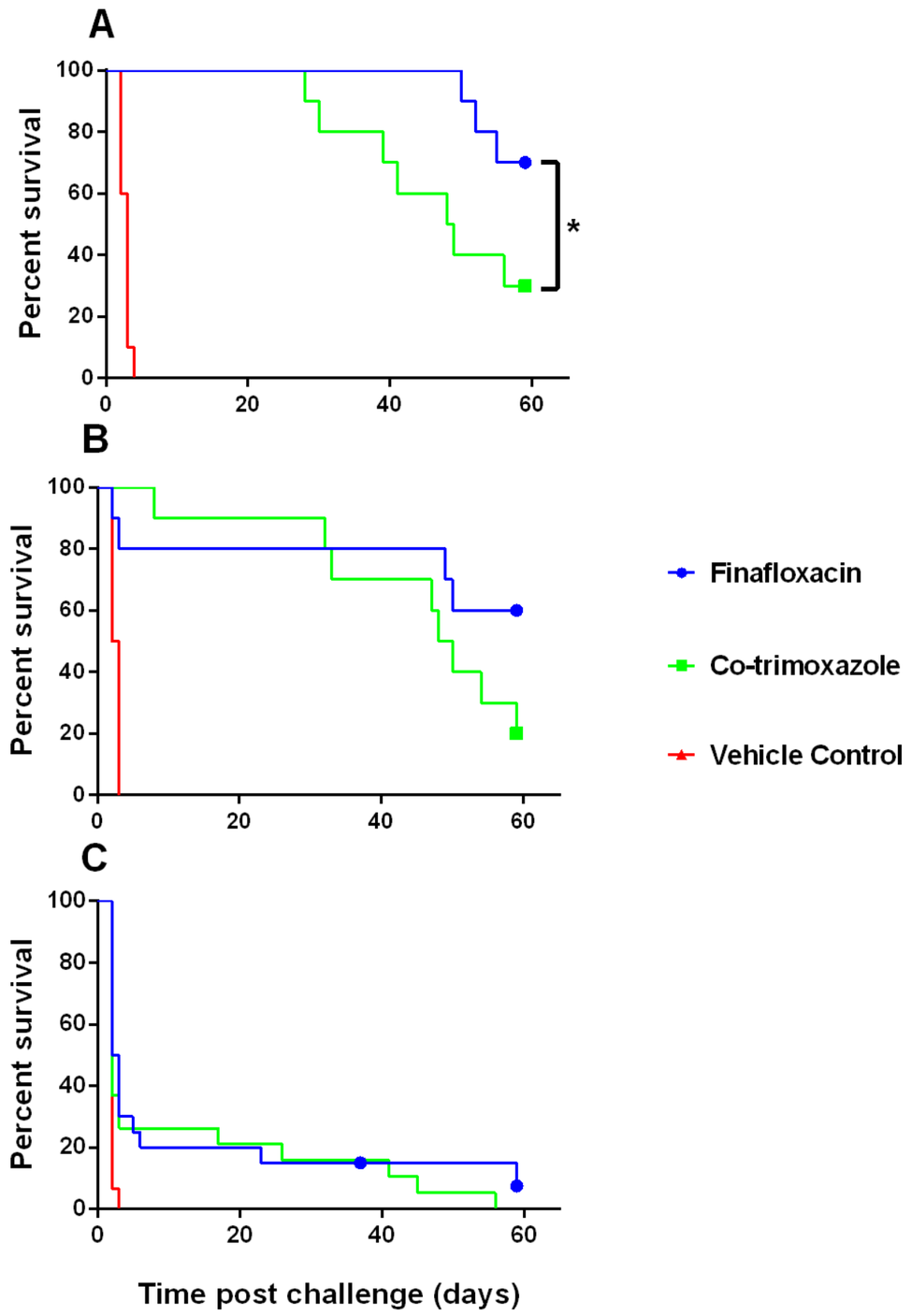

Figure 2. The percentage survival of mice following challenge with *B. pseudomallei*. Mice were challenged with approximately 98 CFU of *B. pseudomallei* by the inhalational route and treated with finafloxacin or the vehicle control every 8 hours, or with co-trimoxazole every 12 hours. Treatment was initiated at 24 hours (A), 36 hours (B) or 48 hours (C) post-challenge.

- Both antibiotics offered significant protection compared to the vehicle control ($p<0.0001$).
- When treatment was initiated at 24 hours post-challenge, finafloxacin offered a significant benefit in comparison to co-trimoxazole ($p<0.05$).
- There was no significant difference between antibiotic treatment when initiated at 36 or 48 hours post-challenge ($p>0.05$).
- Initiating treatment at either 24 or 36 hours post-challenge was better than at 48 hours post-challenge ($p<0.001$ and $p<0.01$).
- However, all surviving animals were colonised with *B. pseudomallei* at the end of the study.

Discussion

Treatment with finafloxacin has offered significant protection in comparison to co-trimoxazole, against acute melioidosis in mice when administered at 24 hours post-challenge and a high level of protection when administered at 36 hours post-challenge. Further studies are required to determine the localisation of colonising bacteria in mice before they succumb to disease.

Reference

1. Lemaire S, Van Bembeke F and Tulkens P. Activity of finafloxacin, a novel fluoroquinolone with increased activity at acid pH, towards extracellular and intracellular *Staphylococcus aureus, Listeria monocytogenes* and Legionella *pneumophila*. *Int J Antimicrob Agents* (2011) 38: 52-59.

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