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# It's Been a Long Time Running: The Era of Prolonged Infusion Beta-Lactams

## Background

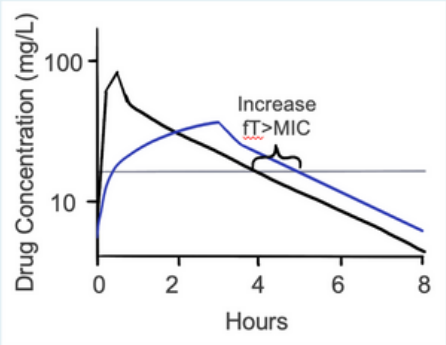
Beta-lactams exhibit time-dependent bacterial killing

- Amount of time free drug concentration exceeds the minimum inhibitory concentration (MIC) of the organism (fT>MIC)[1]

PK/PD targets of 40-70% fT>MIC have been extrapolated from in vitro studies and it's unclear if these targets correlate to positive clinical outcomes[2]

- Some PK/PD studies have found that 100% fT>MIC correlates to improved clinical outcomes

Prolonged infusions (infused over 2+ hours) increase the probability of target achievement for beta-lactams[3]




Prolonging infusion time

## Clinical Trials

| Trial | Population | Comparison | Outcomes |
|---|---|---|---|
| **MERCY Trial**[4] 2023 (RCT) | 607 critically ill adults | Continuous infusion versus standard infusion meropenem | **No difference** in primary outcome (composite of **all-cause mortality** and **emergence of drug-resistance**) at day 28 (*P*=0.60) |
| **BLING Trial**[5] 2016 (RCT) | 140 critically ill adults with severe sepsis | Continuous infusion versus standard infusion beta-lactams | Continuous infusions had **higher clinical cure rates** (*P*=0.01) and **better PK/PD target attainment** (*P*<0.001) than standard infusions |
| **BLING II Trial**[6] 2015 (RCT) | 432 critically ill adults with severe sepsis | Continuous infusion versus standard infusion piperacillin-tazobactam | **No difference in alive ICU-free days** at day 28 for all participants (*P*=0.38) or nested cohort (*P*=0.89) |

## Conclusions

All-comers design of RCTs make it difficult to determine which patients have improved clinical outcomes with prolonged infusions

Higher concentrations and fT>MIC may be necessary in certain patients than the PK/PD targets established in pre-clinical studies

Prolonged infusions should be considered in patients with augmented renal function, infections with high MIC organisms, and infections of tissues with limited drug penetration

## References

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