CLINICALLY RELEVANT TUMOUR-BEARING ANIMAL MODEL TO EVALUATE CHEMOTHERAPY EFFICACY AND TOXICITY

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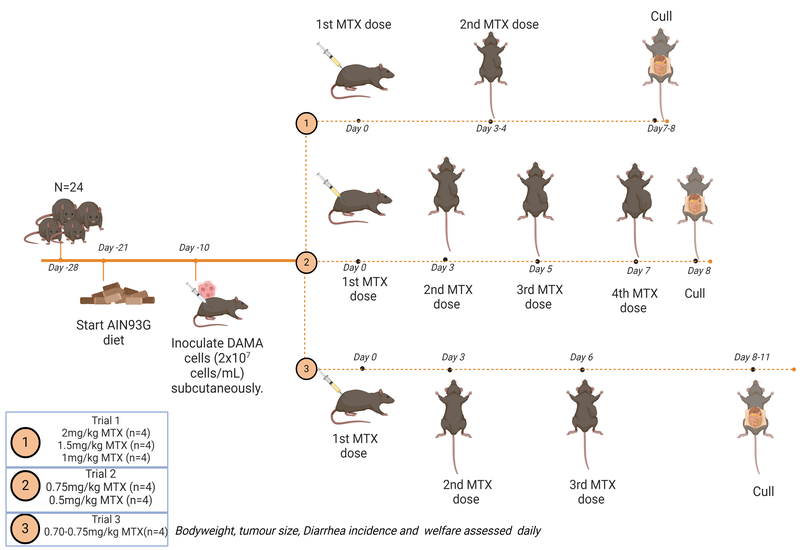
Introduction

- Studying interventions in animal cancer models mimicking clinical settings is difficult due to the challenging side effects of cyclical administration of chemotherapy[1].
- Although models exist, they are mostly large single doses which limit the ability to measure chemo-efficacy over time[2].

This study aimed to create a cyclical chemotherapy model using methotrexate (MTX) that balances animal welfare with long-term evaluation of breast cancer tumour growth and treatment response.

Methods



Bodyweight, tumour size, Diarrhea incidence and welfare assessed daily

Tumour burden was calculated as tumour volume relative to body weight (%BW, cm^3/g). Rats were euthanized if tumours ≥10% body weight or weight loss >15%.

Results

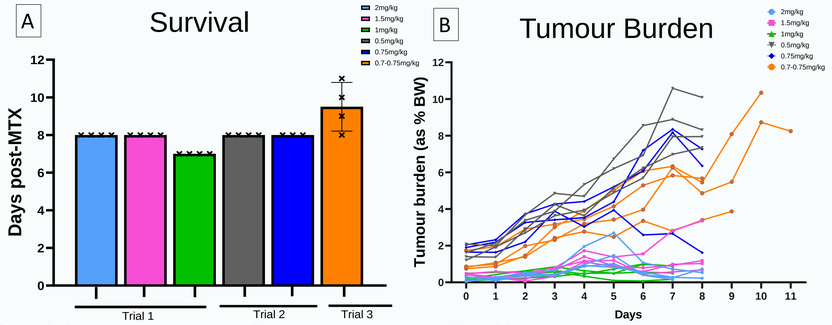


Figure A. Days of survival per group. Data shown is expressed as Mean±SD .
Figure B. Tumour Burden per group with Day 0 as first day of MTX. Data shown is expressed as individually aligned values.

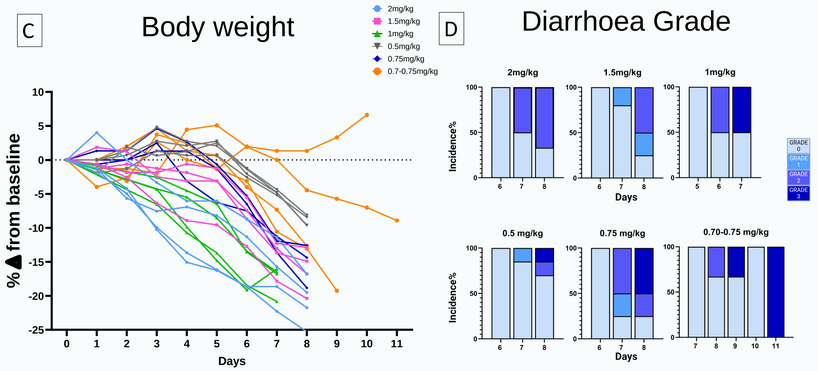
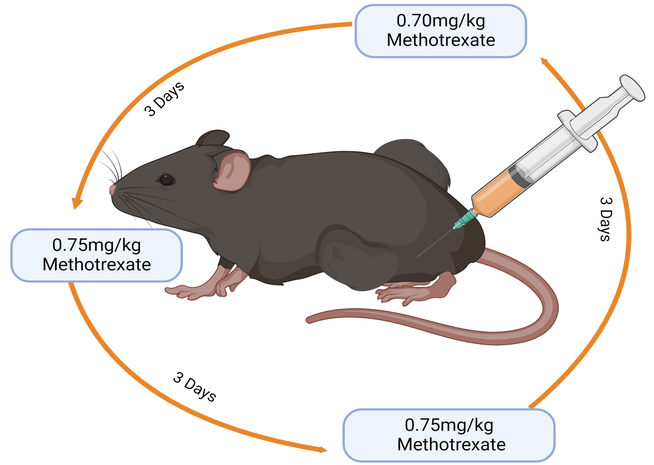


Figure C. %Change of bodyweight per group over time with Day 0 as first day of MTX. Data shown is expressed as individually aligned values .
Figure D. Diarrhoea proportions per group. Data shown is expressed as incidence of diarrhoea in each group.

- In **trial 1**, 100% of rats were euthanised due to **fast decline in welfare** and severe loss of body weight.
- In **trial 2**, the welfare of the rats in the 0.5mg/kg MTX group was **improved but no tumour control** hence rats were euthanised when tumour burden ≥10% BW. MTX at 0.75mg/kg showed promise.
- In the **3rd trial**, **efficacy** of the 0.70- 0.75mg/kg MTX was seen, the welfare of rats was **maintained**, and **tumour burden controlled**.



3 cycles of 0.70 - 0.75 mg/kg MTX was selected as optimal schedule that adequately balanced efficacy and toxicity.

Conclusion

- Cyclical chemotherapy can be administered to rats enabling both efficacy and toxicity responses to be evaluated simultaneously.
- This model offers a platform to investigate supportive care interventions to improve patient outcomes.

1. Lustberg, M.B., Kuderer, N.M., Desai, A. et al. Mitigating long-term and delayed adverse events associated with cancer treatment: implications for survivorship. Nat Rev Clin Oncol 20, 527–542 (2023).
2. Wardill HR, Da Silva Ferreira AR, Kumar H, Bateman EH, Cross CB, Bowen JM, Havinga R, Harmsen HJM, Knol J, Dorresteijn B, van Dijk M, van Bergenhenegouwen J, Tissing WJE. Whey-based diet containing medium chain triglycerides modulates the gut microbiota and protects the intestinal mucosa from chemotherapy while maintaining therapy efficacy. Cell Death Dis. 2023 May 23;14(5):338..

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