Pharmacy and Poisons Board
Online clinical trials
Submitted Application : (ECCT/17/10/01)

Protocol No:	**ECCT/17/10/01**	Date of Protocol:	**23-08-2017**

Abstract of Study:

Antimicrobial resistance (AMR) has become a major issue in global health. Despite progress in the reduction of under 5 mortality rates in recent decades, the proportion of neonatal deaths occurring within this age group has increased, with almost one quarter of all neonatal deaths occurring due to serious bacterial infection. Common bacteria causing neonatal sepsis are now exhibiting widespread resistance to several classes of antibiotics. There is an urgent need to discover new, effective treatments and re-evaluate existing therapeutic agents to treat infections potentially caused by multi-drug resistant (MDR) pathogens. Gram-negative bacteria (GNB) predominate as the cause of neonatal sepsis, and are increasingly associated with high rates of resistance to the currently recommended WHO empirical therapy regimen of ampicillin/penicillin and gentamicin. There is therefore a need to develop an updated empiric regimen with improved efficacy in the context of increasing MDR sepsis in neonates. New antimicrobials under development will be expensive once licensed, and there are currently virtually no planned trials to assess their efficacy in neonates in low- and middle-income countries (LMICs).

One potential strategy is utilising an existing off-patent (and therefore affordable) antibiotic available in intravenous and oral formulations – fosfomycin. Fosfomycin has a wide spectrum of activity against Gram-positive and Gram-negative bacteria causing neonatal sepsis. It is mainly used for resistant urinary tract infections in adults, but has licenced neonatal and paediatric doses in Europe (though dosing regimens vary between countries). Both oral and IV formulations are available. A large clinical trial to assess the efficacy of a fosfomycin plus an aminoglycoside combination (compared to the current WHO recommended ampicillin and gentamicin) is anticipated, including sites in Kenya. The ultimate aim is for fosfomycin to be included in the WHO Essential Medicines List for children (EMLc) and be available for use in developing countries, where rates of resistance to ampicillin and gentamicin have been estimated at over 40%. The first steps before this trial are to clarify the pharmacokinetics (PK) and safety profile of fosfomycin in neonates, as well as generating further information regarding local patterns of bacterial susceptibility to fosfomycin. The aim of this study is to fulfil both these steps. Fosfomycin (IV and oral) PK will be investigated among 60 babies admitted to hospital and being treated for presumed sepsis; administered alongside the standard antibiotics. Another 60 babies receiving standard treatment only (without PK sampling) will be monitored in the same way to compare adverse events. In the laboratory at CGMR-C, previoiusly archived bacterial isolates will be tested for their sensitivity to fosfomycin.

Study Title:

Intravenous and Oral Fosfomycin in Hospitalised Neonates with Clinical Sepsis: an open-label safety and pharmacokinetics study