OA-83 EARLY BACTERICIDAL ACTIVITY OF MEROPENEM, ERTAPENEM, AMOXICILLIN/CLAVULANATE AND OPTIMIZED RIFAMPICIN IN PULMONARY TUBERCULOSIS

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Background Repurposing established antibiotics for TB has been successful, notably for fluoroquinolones, linezolid, and clofazimine. Meropenem co-administered with amoxicillin/clavulanate (A/Clav) demonstrated early bactericidal activity (EBA) in clinical trials (Diacon 2016; de Jager 2020; de Jager 2022). This study evaluated different regimens of carbapenems, A/Clav, and rifampicin, alone or in combinations.

Methods This phase 2a, open-label, randomized trial recruited 132 HIV-negative adults with newly diagnosed, smear-positive, rifampicin-susceptible pulmonary TB. Participants received 14 days of treatment in one of 8 experimental arms, or standard-of-care (HRZE). EBA was determined with mixed effects modelling and reported as change in time (hours) to sputum culture positivity (TTP0-14) of samples collected overnight with 95% confidence intervals. Adverse events (AE) were assessed daily.

Results A/Clav 2x1000/62.5mg orally twice daily showed no activity. TTP0-14 of other drugs in combination with A/Clav was, for meropenem 6g over 6 hours(6Mero6): 58.02 hours (18.72–192.92), meropenem 6g over 1 hour(6Mero1): 58.13 hours (27.26–121.83), meropenem 3g over 1 hour twice daily (3x2Mero): 60.07 hours (19.89–884.71), and meropenem 4g over 1 hour(4Mero1): 35.28 hours (25.31–84.74). Ertapenem 1g daily intravenously (ErtaIV) or intramuscularly (ErtaIM) was not active. The activity of rifampicin 35mg/kg daily plus A/Clav was 136.92 hours (103.21–400.64) and HRZE 134.30 hours (106.28–160.23). In 58 participants, 111 adverse events were reported. Most commonly diarrhoea (15 participants: four ErtaIM, three ErtaIV, four 6Mero6, two rifampicin, one each A/Clav and HRZE), injection site reactions (six participants: four ErtaIM, one each 6Mero6 and 3x2Mero), and raised transaminases (four participants: A/Clav, ErtaIM, Erta IV, rifampicin). Three SAEs occurred (pneumonia in ErtaIV, haemoptysis in rifampicin and 6Mero1) unrelated to treatment.

Conclusion Rifampicin-based treatments showed the highest EBA. A/Clav and meropenem given at 6g per day, in single or divided doses, had higher EBA than lower doses, and shorter infusions were better tolerated. Ertapenem-based treatments and A/Clav alone showed no anti-TB activity.

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OA-87 RESEARCH ETHICS COMMITTEES IN MOZAMBIQUE: OPERATIONAL AND FUNCTIONAL CHARACTERISTICS EVALUATED FROM A SELF-ASSESSMENT TOOL IN 2019

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Background In the past decades, Africa witnessed increased biomedical research and transnational collaborations making the continent vulnerable to exploitation. Research ethics committees (REC) are the cornerstone; however, many lack an accreditation system. A self-assessment tool can be feasible for reviewing processes and policies against recognized standards. This study aimed to describe Mozambique's RECs network and its operational and functional characteristics.

Methods A descriptive cross-sectional study was conducted. In 2019, Mozambique had seven RECs; the study population was the president of each existing REC. A self-assessment tool developed by researchers from Africa was used. Participants were recruited by telephone, and after informed consent, the questionnaire was emailed to each participant and returned to the investigators. A descriptive statistical analysis was done to describe the frequency of the events.

Results The existing seven RECs in 2019 accepted to participate in the study. A total of six RECs has a policy for appointing the president. The most common criteria for the president's selection were prior training in ethics (six), followed by prior research experience (five). Regarding resources, only one of the seven RECs reported having a yearly budget, and only one has a full-time administrative staff. The reported number of RECs that meet as a full committee to review research studies once a month was four, and two referred meeting once a week. All the RECs stated they have policies for protocol reviewing. Out of seven, six RECs have a policy on expedited review, on how decisions are made and communicated to investigators.

Conclusion This study is the first attempt to document Mozambique's RECs network. The process of self-assessment raises knowledge regarding strengths and challenges. Results can serve as a quality improvement mechanism detecting specific areas needing upgrading and as a reference on how they are operating compared to others.

OA-92 CLINICALLY RELEVANT ENANTIOMER SPECIFIC R- AND S-PRAZIQUANTEL PHARMACOKINETIC DRUG-DRUG INTERACTIONS WITH EFAVIRENZ AND RITONAVIR: IMPLICATIONS FOR HIV AND SCHISTOSOMIASIS CO-INFECTION

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Background HIV and schistosomiasis are the most widespread infections worldwide. The two diseases share the same epidemiological space, especially in poor regions where endemicity is high. Co-infections are therefore common. We conducted a clinical study to determine the effect of efavirenz and ritonavir on the pharmacokinetics of R- and S-praziquantel (PZQ) in healthy male participants. The aim was to increase knowledge towards the safe and efficacious use of PZQ especially in cases of coinfection and mass drug treatment programs where HIV status and concomitant drug intake is not considered prior to administration.

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