Burkina Faso

Mortality Reduction after Oral Azithromycin (MORDOR II)

The MORDOR II Burkina Faso trials were designed by the Centre de Recherche en Santé de Nouna and UCSF to confirm the results of the MORDOR I study in Niger, Tanzania, and Malawi. MORDOR I demonstrated a significant reduction in all-cause child mortality following biannual mass azithromycin administration (https://www.nejm.org/doi/full/10.1056/NEJMoa1715474 [1]). In addition to confirming these results, the MORDOR II studies aim to evaluate an alternative health systems distribution point for delivery of azithromycin to young children, and to assess potential mechanisms behind the effect of azithromycin. Funded by the Bill and Melinda Gates Foundation, this research will play an important role on informing future policy decisions regarding mass antibiotic distribution. Please see below for more information regarding each of the three MORDOR II trials:

Community Health Azithromycin Trial (CHAT)

In CHAT, the research team will assess childhood mortality over three years, comparing communities where children aged 1-59 months receive biannual oral azithromycin or placebo. Biological specimens will be collected from 48 random communities to assess infectious disease morbidity and macrolide resistance.

In addition, young children will be enrolled for targeted treatment at health centers or during vaccination outreach in the community. These children will be individually randomized to receive azithromycin or placebo during their 5^{th}-12^{th} week of life. The goal is to determine the efficacy of distributing azithromycin during a child?s first healthcare visits on infant mortality.

Overall, we hypothesize that biannual mass azithromycin treatments will reduce childhood mortality compared to placebo, and that this effect will be primarily driven by a reduction in infectious burden.

Neonates and Azithromycin: An Innovation in the Treatment of Children (NAITRE)

Although under-5 mortality rates are declining globally, neonatal mortality remains persistently high in many regions of sub-Saharan Africa. Mass azithromycin distribution to children aged 1-59 months has been shown to reduce childhood mortality in Niger, Tanzania, and Malawi. This study did not evaluate the effect of azithromycin administered during the neonatal period. Observational evidence from high income countries has suggested that macrolides, including erythromycin and azithromycin, may be associated with increased risk of development of infantile hypertrophic pyloric stenosis (IHPS). However, these studies are limited by confounding by indication, as infants only receive antibiotics when they are ill.

NAITRE aims to establish the efficacy and safety of administration of a single dose of azithromycin during the neonatal period. The investigative team hopes to generate evidence

that can later be utilized by child survival programs to reduce mortality among infants.

The study will be conducted in several regions across Burkina Faso where neonates aged between 8 and 27 days will be randomized to a dose of azithromycin or placebo. We hypothesize that neonates randomized to azithromycin will have a significantly lower all-cause mortality by 6 months of age, compared to those randomized to placebo.

Gut and Azithromycin Mechanisms in Infants and Neonates (GAMIN)

GAMIN is a longitudinal trial that will randomize 450 children aged 28 days to 59 months to a single dose of azithromycin or placebo. We hypothesize that a single dose of azithromycin will result in a significant difference in the intestinal microbiome and increase child growth over a 6-month period compared those receiving placebo. Our long-term goal is to answer questions surrounding how antibiotic administration can influence the intestinal microflora as well as to evaluate mechanisms behind azithromycin?s effect on all-cause mortality.

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Links
[1] https://www.nejm.org/doi/full/10.1056/NEJMoa1715474