High Mortality in African Infants Hospitalized with Severe Pneumonia and Advanced HIV #810

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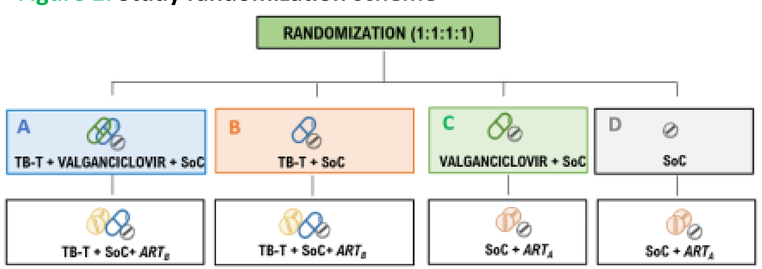
BACKGROUND

- Children with **advanced HIV disease** are known to have increased risk of **morbidity and mortality**.
- Death rates for **infants** hospitalized with **severe pneumonia** are not well-described.

METHODS

- **EMPIRICAL** is an ongoing Phase II-III, open-label randomized factorial (2×2) trial to assess the impact of empirical treatment against cytomegalovirus and tuberculosis.
- The **primary endpoint** is all-cause mortality at 15 days and 12 months post enrollment.
- **Inclusion criteria** are infants 28-365 days of age with confirmed HIV who are hospitalized with severe pneumonia
- **Exclusion criteria** include confirmed TB or known TB contact.
- **Recruitment** at 22 hospitals from 6 African countries (Côte d'Ivoire, Malawi, Mozambique, Uganda, Zambia, Zimbabwe).
- **Study visits** occur at days 0, 3, 15, discharge, 30, 60, 90, 180, and 360

Figure 1: Study randomization scheme



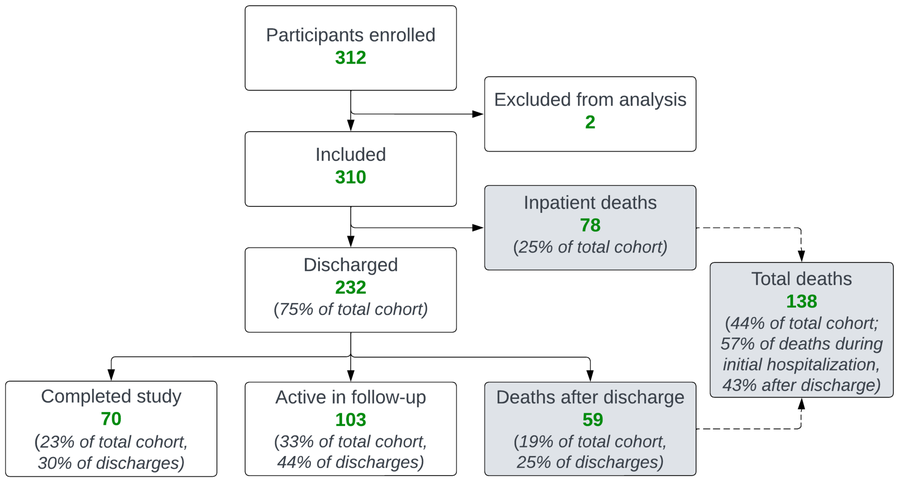
Key: TB-T: tuberculosis treatment; **SoC: s**tandard of care (antibiotics + therapeutic cotrimoxazole + steroids); **ART:** antiretroviral therapy

The probability of 15-day and 12-month survival was 71% and 50%, respectively

RESULTS

- In **interim analysis** as of July 7, 2022, 310 patients had been recruited with a median follow-up time of 4.5 months (IQR, 3.2-7.3)
- 226 patients (73%) were **newly diagnosed** with HIV during hospitalization, 199 (38%) had a history of maternal and/or infant **PMTCT**, and 93 (30%) were on **cotrimoxazole prophylaxis (CPT)** at admission.

Figure 2: Recruitment, follow-up, and mortality

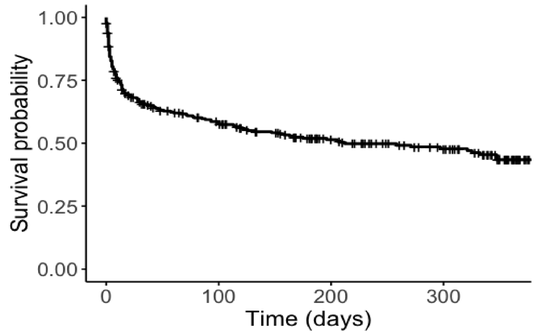


- The **probability of survival** at 15 days was 71% (95%CI: 66-76), and at 12 months was 50% (95%CI: 44-57).
- Pneumonia (48%) and sepsis (18%) were the most common **causes of death**.

Table 1: Baseline patient characteristics

	n = 310
Demographic	
Age (months, median)	4.5 (IQR, 3.2-7.3)
Sex (female)	50%
Clinical	
Chest indrawing	284 (92%)
Oxygen saturation <90%	199 (64%)
Lethargic or unconscious	80 (26%)
Unable to drink/breastfeed	97 (32%)
Severe malnutrition	226 (73%)
Laboratory	
HIV viral load (median)	6.3 logs cp/mL (IQR, 5.8-7.0)
CD4% (median)	14.4% (IQR, 9.9-21.6)
White blood cell count (median)	12.9 (IQR, 8.7-18.7)
Hemoglobin (median)	9.2 (IQR, 8.1-10.2)
ALT (median)	21 (IQR, 14-37)

Figure 3: Kaplan-Meier survival analysis



CONCLUSIONS

- Mortality is extremely high, and urgent measures are needed to **close gaps in PMTCT, Early Infant Diagnosis/EID, and ART programs** to prevent infants from reaching very advanced stages of HIV disease.
- For infants that fall through the cracks and develop HIV-associated severe pneumonia, EMPIRICAL will report on **the survival benefit of CMV and TB treatment** at trial conclusion.

EMPIRICAL
Better Treatment for Pneumonia in HIV-infected Infants

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