OUTCOMES IN CHILDREN LIVING WITH HIV WITH NON-SEROLOGICALLY NON-TUBERCULOSIS IN THE SHINE TRIAL

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BACKGROUND

• Children living with HIV (CLWH) are at high risk of developing tuberculosis (TB) and having poor treatment outcomes[1].
• We compared clinical outcomes between CLWH vs. HIV-negative children with non-severe TB in the SHINE trial; and describe viral suppression among CLWH.

METHODS

• SHINE trial (ISRCTN63579542) was an open-label, randomized controlled trial conducted in 3 African countries (Zambia, Uganda, South Africa) and in India.[2]
• Children aged <16 years with known HIV status, with smear-negative, non-severe TB were randomized to receive 4(2RHZE/2RH) vs. standard 6(2RHZE/4RH) months anti-tuberculosis treatment (ATT) and followed for 72 weeks.
• Anti-TB drugs were dosed according to standard WHO weight-bands using WHO-recommended paediatric fixed dose combination tablets.
• Among CLWH, CD4 and viral load (VL) were measured at 24 and 48 weeks or stored for retrospective testing.
• Anti-retroviral (ART)-naive children were initiated on Efavirenz (EFV) or Lopinavir/ritonavir (LPV/r) based regimens, 2 to 8 weeks after starting TB treatment based on national treatment guidelines.
• Logistic regression and Cox proportional hazards models were fitted to investigate predictors of clinical outcomes, defined as: mortality, hospitalization, and VL suppression in CLWH.
• TB treatment outcomes were defined as unsuccessful if there was death, treatment failure, TB treatment restarts, relapse or loss to follow-up.

RESULTS

• Of 1204 enrolled, 127 (11%) were CLWH who were of similar age compared to HIV-negative children (median[IQR] 3.6 [1.2, 10.3] vs. 3.5 [1.5, 6.9] years), but more overweight (WAZ=-2.3 [-3.3, -0.8] vs. -1.0 [-1.8, -0.2], p<0.01) and had lower haemoglobin (9.5 [8.7, 10.9] vs 11.5 [10.4, 12.3], p<0.01) (Table 1).
• Baseline median CD4% and counts [IQR] were 16% (10, 26) and 719 (241, 1134) cells/mm3, and 65 (54%) were ART-naive.
• CLWH had a lower proportion of microbiologically confirmed TB than HIV-negative children (8/127, 6.3% vs. 157/1077, 14.8%), p=0.01 (Table 1).
• Fewer CLWH had pulmonary disease (58% vs 67%, p<0.001) but more had mixed (pulmonary and lymph node) disease (42% vs 28%, p<0.001) (Table 1).
• There were 31/1204 (3%) deaths in the trial; of these 13 (42%) were among CLWH.
• Mortality risk was higher in CLWH (aHR [95%CI] 2.6 [1.2, 5.8]) compared to HIV-negative children (Table 2).

CONCLUSION

• Overall, the vast majority of CLWH (97%) with non-severe TB had favourable outcomes after 72 weeks of follow-up.
• The main trial results showed 4 months of TB treatment was as good as 6 months in the subgroup of CLWH with non-severe TB[3].
• Although deaths were infrequent in children with non-severe TB, (3%), CLWH had a higher risk of mortality than HIV-negative children.
• Young age, malnutrition and anemia independently predicted mortality only in both CLWH and HIV-negative children.
• Unfavourable TB outcomes were more frequent in CLWH.
• Suboptimal viral suppression was common among CLWH, with worst suppression on LPV/r-containing ART regimen.
• Earlier HIV diagnosis and initiation of ART in CLWH may improve outcomes, including mortality.

REFERENCES