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Efficacy of Dolutegravir versus Lopinavir-based Antiretroviral Treatment Regimens for Infants

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INTRODUCTION

In 2021, WHO updated antiretroviral treatment (ART) recommendations for infants from **lopinavir/r (LPV/r)** to **dolutegravir (DTG)**-based regimens from 4 weeks of age and 3kg body weight. DTG-based regimens are expected to result in improved treatment efficacy due to **increased potency, high resistance barrier, and improved practicality**.

PLAIN LANGUAGE SUMMARY

- Testing newborns for HIV soon after birth helped health facilities start lifesaving treatment with minimal delays.
- Infants given newer dolutegravir-based treatment were more likely to achieve viral control by 3 and 6 months of age compared to those receiving older lopinavir/r-based treatment.
- These results support recent treatment guideline changes from WHO recommending dolutegravir for young infants with HIV.

CONCLUSION

- PoC test-and-treat at birth was successfully implemented in primary and secondary healthcare settings and enabled rapid ART initiation in neonates with HIV.
- In both studies, viral suppression was similarly low while infants received nevirapine-based ART.
- DTG-based regimens were associated with improved viral suppression compared to LPV/r granule-based regimens at months 3 and 6.
- Differences in study periods and implementation contexts mean that improvements in adherence, service delivery, or other unmeasured factors may have also contributed.

ACKNOWLEDGEMENTS

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METHODS

We conducted 2 cluster-randomized trials at primary and secondary healthcare facilities in Mozambique and Tanzania.

- **LIFE** (2019-2021): n=6602
- **LIFE2Scale** (2023-2025): n=3853

Point-of-care (PoC) testing (Abbott mPIMA or Cepheid Xpert) was utilized for **early infant diagnosis (EID)** and **viral load (VL)** monitoring.

The LIFE2Scale delivered EID and VL testing via a **hub-and-spoke** model, with spoke facilities sending samples to nearby hub facilities with PoC testing infrastructure **(near PoC)**, while LIFE implemented **true PoC** EID and VL.

In both studies, the neonatal ART regimen was zidovudine (AZT), lamivudine (3TC), and nevirapine (NVP) at birth and abacavir and lamivudine (ABC/3TC) plus LPV/r in LIFE or pediatric DTG (pDTG) in LIFE2Scale at 4-6 weeks of age and at least 3kg body weight.

We measured infant viral load at 4-6 weeks and 3, 6, and 12 months of age and present risk ratios (RR) and 95% confidence intervals (CI) of infants **virally suppressed (<1000 copies/mL) at 4-6 weeks and 3 and 6 months for DTG versus LPV/r**.

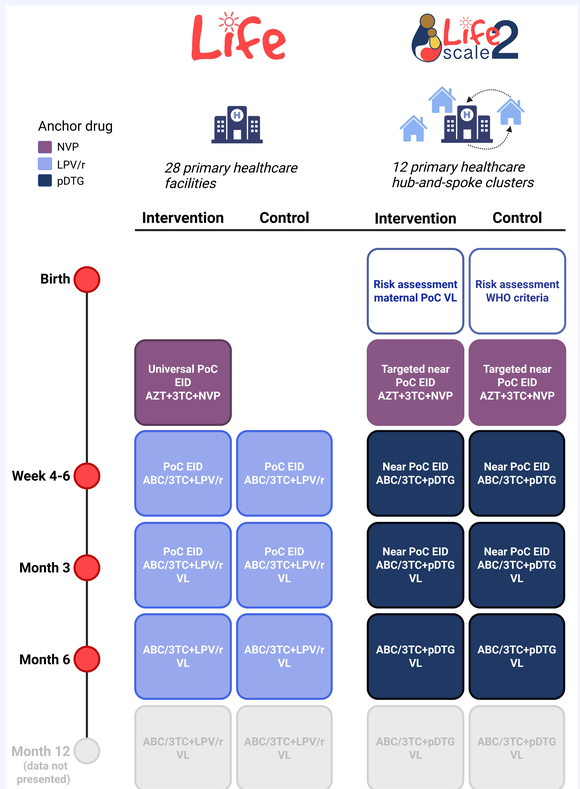


Figure 1: Study schema. LIFE implemented PoC test-and-treat at birth in the intervention arm and at 4-6 weeks in the control arm. LIFE2Scale implemented test-and-treat at birth based on high-risk criteria for vertical HIV transmission. Testing in the LIFE2Scale study was delivered via a hub-and-spoke model, with 12 hubs and 49 health facilities total.

RESULTS

DTG-based ART was associated with improved viral suppression at months 3 and 6 compared to LPV/r-based regimens among infants with HIV.

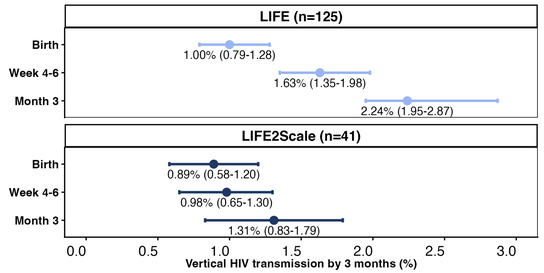


Figure 2: Vertical HIV transmission rates. Cumulative incidence up to 3 months of age expressed as percentage (95% CI).

	LIFE (N=125)	LIFE2Scale (N=41)
Female sex – N (%)	69 (55.2%)	21 (51.2%)
Twin – N (%)	7 (5.6%)	4 (9.8%)
Corrected gestational age (weeks) - Median [IQR]	38 [37, 40]	40 [38, 41]
Weight (g) – Mean (SD)	2900 (478)	2900 (529)
1 min APGAR – Mean (SD)	8.36 (0.66)	8.47 (0.65)
5 min APGAR – Mean (SD)	9.51 (0.64)	9.00 (0.55)
High risk for vertical HIV transmission	112 (89.6%)	36 (90.0%)
Time of HIV infection [a]		
Birth	65 (52.0%)	19 (46.3%)
Week 4-6	40 (32.0%)	16 (39.0%)
Month 3	20 (16.0%)	6 (14.6%)
Time of HIV diagnosis		
Birth	38 (30.4%)	12 (29.3%)
Week 4-6	61 (48.8%)	22 (53.7%)
Month 3	20 (16.0%)	7 (17.1%)
Time of ART initiation		
Birth [b]	35 (28.0%)	8 (19.5%)
Week 4-6	62 (49.6%)	22 (53.7%)
Month 3	22 (17.6%)	9 (22.0%)
Did not start ART [c]	7 (5.6%)	2 (4.9%)
Baseline viral load – Mean (SD) log10 copies/mL	4.97 (1.42)	4.15 (1.88)

Table 1: Infant baseline characteristics and timing of HIV detection, diagnosis, and ART initiation. [a]First sample with detectable HIV; [b]Within the first week of life. [c]Reasons for not starting ART were death or loss to follow-up before EID testing (with retrospective positive HIV test).

Infant diagnosis and treatment cascade

LIFE

- In the true PoC implementation, most infants were initiated on ART within 1 day (median 0 [IQR: 0, 1] days) of HIV diagnosis.

LIFE2Scale

- In the hub-and-spoke, near PoC implementation, infants were started on ART at median 4 [0, 14] days after diagnosis and 8 [2, 22] after the first positive HIV sample.
- Delays in EID testing and therefore ART initiation were primarily driven by laboratory processing times and sample transport.

	LIFE	LIFE2Scale	
	Virally suppressed on NVP – N (%)	Virally suppressed on NVP – N (%)	RR (95% CI) NVP LIFE2Scale vs. LIFE
Week 4-6	19 (23.8%)	10 (34.5%)	1.45 (0.77, 2.74); p=0.250
	Virally suppressed on LPV/r – N (%)	Virally suppressed on DTG – N (%)	RR (95% CI) DTG vs. LPV/r
Month 3	23 (26.1%)	17 (54.8%)	2.10 (1.31, 3.37); p=0.002
Month 6	24 (31.1%)	16 (59.3%)	1.90 (1.20, 3.00); p=0.006

Table 2: Risk ratios (RR) comparing viral suppression between LIFE and LIFE2Scale at 4-6 weeks and 3 and 6 months. At 4-6 weeks of age, all infants had received NVP. By 3 months, infants had transitioned to or initiated LPV/r (LIFE) or DTG (LIFE2Scale).Virally suppressed was defined as <1000 copies/mL and infants with a viral load result were included in denominators. Risk ratios and 95% confidence intervals (CI) are presented for LIFE2Scale versus LIFE.

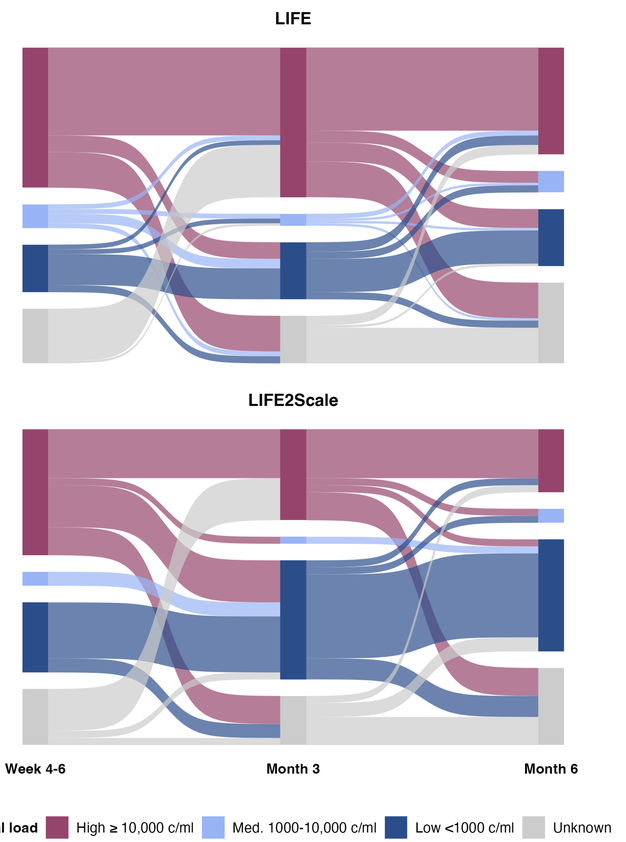


Figure 3: Sankey diagrams showing infant viral suppression at 4-6 weeks and 3 and 6 months in the LIFE (LPV/r-based antiretroviral treatment) and LIFE2Scale (DTG-based antiretroviral treatment) studies. The height of each bar represents the proportion of infants in each viral load category at each time point. The flow illustrates how infants moved between viral load categories over time.

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