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TIME TO VIRAL REBOUND AFTER STOPPING ART IN CHILDREN TREATED FROM INFANCY IN CHER

Clinical: (Q) Pediatrics and Adolescents

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Background: We investigated factors associated with time to viral rebound in children in CHER who started ART at age <12 weeks and received 40 (ART-40W) or 96 weeks (ART-96W) of primary therapy.

Methods: HIV RNA viral load (VL) from stored samples was assessed 8 weeks after interruption and 12 weekly thereafter. Included were children with VL<400 c/ml at interruption and ≥1 VL measurement within 12 months. Multivariable stepwise Cox regression models (backwards elimination, exit probability p=0.05) were used to identify factors associated with time to viral rebound (confirmed VL≥400 c/ml). Follow-up was censored at ART reinitiation (if VL had not rebounded) or last VL measurement. Results: Of 183 children virally suppressed (VL<400) at interruption, 54% were from ART-40W and 61% were female. At enrolment, 81% received PMTCT, 81% had CDC stage N; median [IQR] birth weight was 3 [2.7,3.3]Kg. At ART start, median [IQR] age was 1.8 [1.5,2.1] months, CD4% 34 [29,40]%, CD4 count 1982 [1445,2745], CD8% 28 [22,34]% and VL 750000 [376000,750000] copies/ml. Median VL at rebound was 354615 [91040,750000] copies/ml, not significantly different between arms [ART-40W=418760; ART-96W=325000 copies/ml; P=0.19]. 86% of children suppressed within 40 weeks of ART start [88% ART-40W; 83% ART-96W; P=0.38]. Overall estimated cumulative probability of rebound (95% CI) at 2, 4, 6 and 8 months were 70% (63,76)%, 80% (74, 85)%, 94% (90,97)% and 99% (96,100)%, respectively. Median time to rebound was 1.8 (range: 0.9-13.1) months. One child (ART-40W) maintained viral suppression until last VL available. Five children were censored due to ART restart. In univariable analysis, among baseline demographic and clinical factors, CD4% was the strongest predictor of longer time to rebound based on the log likelihood ratio. In multivariable analysis, longer time to rebound was associated with higher birth weight, baseline CD4% and viral suppression within 40 weeks of ART start (Table). There was no evidence of significant effect of gender, baseline VL and CD8%, CDC stage, PMTCT, age at ART initiation (6-12weeks) and length of therapy (arm) or site. Sensitivity analyses produced similar results.

Conclusion: Most children rebounded by 13 months while one remained suppressed until the end of follow up. Age at ART initiation ranging from 6 to 12 weeks and length of therapy were not associated with longer time to rebound. Our findings may inform the design of clinical trials involving analytic treatment interruption in paediatric HIV.