

Supplementary Table 1. PCR assay and primer details; forward (F), reverse (R) and sequencing (s) primers for additionally created assays are shown giving the size and position of the amplicons as well as number of investigated CGs for each gene.

Primer name	Sequence 5' → 3'	Size (bp ³)	Position in the gene ⁴	No of CG sites	Annealing Temp(°)
EPB41L3 F	GGGGGATTTGTGTAAATTGG				
(B) EPB41L3 R	(B)- ACCTAAAAACCTCCCTAAAATC	83	376 to 458	3	54
EPB41L3 s	GGGATTTGTGTAAATTGG				

As reported in [1], Supplementary Table 2. ¹ bp = base pair; ² The position of 0 is start of the exon 1

Supplementary Table 2. Correlation* of EPB41L3 CpG sites 438, 427 and 425 among 362 women at baseline.

	CpG 438	CpG 427	CpG 425
CpG 438	1.0000		
CpG 427	0.9363	1.0000	
CpG 425	0.9404	0.9460	1.0000

*Pearson's correlation co-efficient

Supplementary Table 3. EPB41L3 median methylation levels (%) among 94 WLHIV in Burkina Faso and 268 in South Africa by CIN grade

	Burkina Faso			South Africa		
	N	Median % (IQR)	p ¹	N	Median % (IQR)	p ¹
<CIN1	34	0.97 (0.0-2.60)	Ref	85	0.0 (0.0-1.30)	Ref
CIN1	32	1.42 (0.32-3.83)	0.2486	59	0.0 (0.0-3.30)	0.0537
CIN2	17	6.40 (1.63-15.73)	0.0005	73	1.60 (0.0-9.87)	<0.001
CIN3+	11	8.93 (2.20-39.80)	0.0034	51	2.97 (0.0-12.80)	<0.001
p-trend ²			<0.001			

¹Mann-Whitney U test, p-value for difference in median values of CIN2/3 relative to ≤CIN1;

²Cuzick test for trend; p-value for trend in methylation levels by CIN grade

Supplementary Table 4. EPB41L3 median methylation levels (%) at baseline and endline for incident CIN2/3 over 16 months, among 57 WLHIV in Burkina Faso (BF) and 128 in South Africa (SA).

	Burkina Faso			South Africa		
	N	Baseline values	Endline values	N	Baseline values	Endline values
≤CIN1*	53	1.43 (0.73-2.63)	1.20 (0.63-3.63)	106	0.0 (0.0-1.43)	0.0 (0.0-1.10)
Incident CIN2/3	4	2.45 (0.85-12.62)	5.35 (2.98-18.45)	22	0.0 (0.0-2.70)	0.0 (0.0-9.80)
<i>p-value</i> [†]		0.42	0.05		0.68	0.07

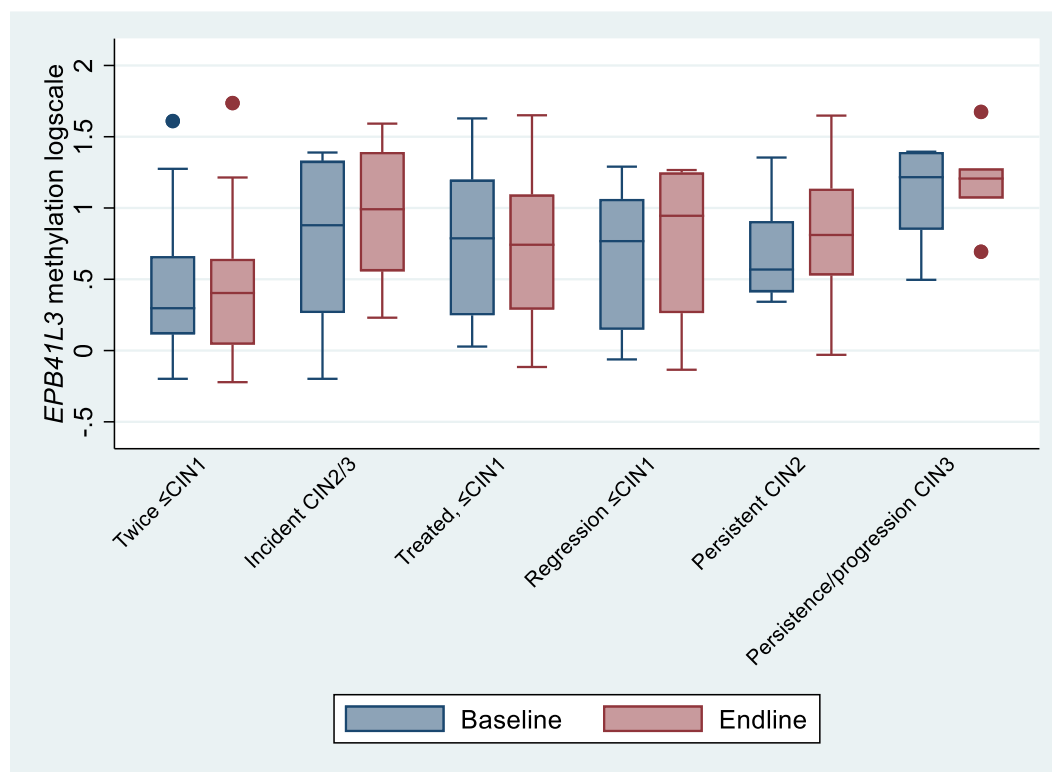
*≤CIN1 at both baseline and endline; [†]Mann Whitney U *p*-value for difference in median values of incident CIN2/3 vs. ≤CIN1

Supplementary Table 5. Baseline *EPB41L3* DNA methylation (%) as a predictor of histological outcomes at endline/M16 among 78 WLHIV in BF and 215 WLHIV in SA with *EPB41L3* methylation and histology data at both baseline and endline

	Burkina Faso			South Africa		
	N	Baseline <i>EPB41L3</i> DNA methylation	p-value	N	Baseline <i>EPB41L3</i> DNA methylation	p-value ¹
≤CIN1 at both baseline & endline	53	1.43 (0.73-2.63)	Ref	106	0.0 (0.0-1.43)	Ref
Incident CIN2/3	4	2.45 (0.85-12.62)	0.423	22	0.0 (0.0-2.70)	0.680
Treated and ≤CIN1 at endline ^a	21	5.67 (1.80-15.73)	0.0006	53	1.57 (0.0-8.83)	0.0000
Spontaneous regression: CIN2/3 to ≤CIN1 ^b	0	-	-	15	0.0 (0.0-3.83)	0.280
Persistent CIN2, or CIN3 regression to CIN2	0	-	-	12	2.83 (0.0-4.55)	0.038
Persistent CIN3, or CIN2 progression to CIN3 ^c	0	-	-	7	15.67 (3.13-24.70)	0.0002

¹Mann-Whitney U test, p-value for difference in median values of relative to ≤CIN1 at both baseline and endline; ^a1 women who was treated for CIN2+ at baseline had missing methylation values at baseline in BF; ^b1 woman with CIN2 regression to ≤CIN1 with missing methylation values at baseline in SA; ^c1 woman with persistent CIN3 with missing methylation value at baseline.

Supplementary Figure 1. Change in median EPB41L3 methylation between baseline and endline among 78 WLHIV in BF and 215 WLHIV in SA, according to endline CIN status*



*Twice \leq CIN1 = \leq CIN1 at both baseline and endline; Incident CIN2/3 = newly detected CIN2/3 at the endline visit among those without CIN2/3 at baseline; Treated, \leq CIN1 = \leq CIN1 at endline among women who received management for prevalent CIN2+ diagnosis before the second biopsy visit at endline; spontaneous regression to \leq CIN1 = \leq CIN1 at endline among those participants that did not receive management for prevalent CIN2/3 diagnosis before the second biopsy visit at endline; Persistent CIN2 (persistent CIN2 or CIN3 regression to CIN2) and persistent CIN3 and progression from CIN2 to CIN3 were similarly described.

1. Vasiljevic N, Scibior-Bentkowska D, Brentnall AR, Cuzick J, Lorincz AT. Credentialing of DNA methylation assays for human genes as diagnostic biomarkers of cervical intraepithelial neoplasia in high-risk HPV positive women. *Gynecol Oncol.* 2014;132(3):709-14.