Note: This is Online Appendix 1 of Zhao Y, Voget, J, Singini, I, et al. Virologic outcomes with tenofovir-lamivudine-dolutegravir in adults failing protease inhibitor-based second-line antiretroviral therapy. S Afr J HIV Med. 2024;25(1), a1567. https://doi.org/10.4102/sajhivmed.v25i1.1567

Supplementary Table S1. Resistance profile of patients with PI resistance at the time of second-line failure

Variable	Patients, No. (%)	
	TLD group (n = 47)	**DRV/r group (n = 99)**
Lopinavir resistance[a]		
Fully active[b]	2 (4.3)	6 (6.1)
Potential low-level resistance	3 (6.4)	8 (8.1)
Low-level resistance	4 (8.5)	7 (7.1)
Intermediate-level resistance	8 (17.0)	22 (22.2)
High-level resistance	30 (63.8)	56 (56.6)
Atazanavir resistance[a]		
Fully active[b]	0 (0.0)	0 (0.0)
Potential low-level resistance	3 (6.4)	8 (8.1)
Low-level resistance	5 (10.6)	8 (8.1)
Intermediate-level resistance	9 (19.1)	14 (14.1)
High-level resistance	30 (63.8)	69 (69.7)
Darunavir resistance[a]		
Fully active[b]	24 (51.1)	54 (54.5)
Potential low-level resistance	4 (8.5)	2 (2.0)
Low-level resistance	13 (27.7)	30 (30.3)
Intermediate-level resistance	4 (8.5)	12 (12.1)
High-level resistance	2 (4.3)	1 (1.0)

PI, protease inhibitor; GART, genotypic antiretroviral resistance testing; TLD, tenofovir-lamivudine-dolutegravir; DRV/r, ritonavir-boosted darunavir.
[a]Resistance was classified with the Stanford algorithm, with potential low-level, low-level, intermediate-level, and high-level resistance defined as Stanford score 10–14, 15–29, 30–59, and >59, respectively.
[b]Stanford score was <10 indicating susceptibility.

Supplementary Table S2. Summary of patients switched to TLD with tenofovir resistance at the time of second-line failure

Age (years)	HIV-1 RNA at the time of second-line failure (log_{10} copies/mL)	CD4+ cell count at the time of second-line failure (cells/μL)	Resistance mutations at the time of second-line failure	Virologic suppression <400 copies/mL	Virologic rebound with virologic failure*	Emergent resistance mutations
48	4.96	283	NRTI mutations: D67N and K70R	Yes (at month 3)	No	Not done
42	5.19	22	NRTI mutations: M184V, T215Y, and M41L/M	Yes (at month 2)	Yes (at month 10)	NRTI mutations: M184V, T215Y, and M41L; INI mutations: E138K, G140A, and Q148K
34	5.34	13	PI mutations: I54M, N88S, and K20T; NRTI mutations: L210W, M184V, M41L, T215Y, and V75M; NNRTI mutations: E138A and K103N	Yes (at month 7)	No	Not done
18	3.44	152	NRTI mutations: T215D and M41L/M; NNRTI mutations: K101R, K103N, Y181C, and V179I/V	Yes (at month 4)	No	Not done

TLD, tenofovir-lamivudine-dolutegravir; ART, antiretroviral therapy; NRTI, nucleoside reverse transcriptase inhibitors; INI, integrase inhibitor; PI, protease inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitors.
*Virologic failure was defined as two consecutive HIV-1 RNA ≥1000 copies/mL after at least 3 months on the TLD regimen.

Supplementary Table S3. Predictors of virologic suppression (HIV-1 RNA <50 copies/mL) by 12 months in patients with PI resistance

Variable	Univariate HR (95% CI)	P-value	Multivariate HR (95% CI)	P-value
Switched to TLD	0.88 (0.60 – 1.30)	0.528	0.73 (0.38 – 1.40)	0.345
Male sex	1.21 (0.90 – 1.64)	0.202	0.82 (0.48 – 1.40)	0.469
Receiving tenofovir at the time of first-line failure	0.98 (0.73 – 1.32)	0.893	1.26 (0.75 – 2.11)	0.389
Age (per year)	1.00 (0.98 – 1.01)	0.562	0.99 (0.97 – 1.02)	0.642
Duration of PI exposure (per year)	1.00 (0.96 – 1.05)	0.970	1.11 (1.02 – 1.21)	0.018
CD4+ cell count at the time of second-line failure (per square root cells/µL)	1.02 (0.98 – 1.05)	0.332	0.98 (0.94 – 1.03)	0.442
HIV-1 RNA at the time of second-line failure (per $\log_{10}$ copies/mL)	0.87 (0.81 – 0.94)	0.001	0.83 (0.72 – 0.96)	0.010

PI, protease inhibitor; HR, hazard ratio; CI, confidence interval; TLD, tenofovir-lamivudine-dolutegravir; ART, antiretroviral therapy.

Supplementary Table S4. Predictors of virologic suppression (HIV-1 RNA <50 copies/mL) by 12 months in patients without PI resistance

Variable	Univariate HR (95% CI)	P-value	Multivariate HR (95% CI)	P-value
Switched to TLD	4.95 (2.97 – 8.24)	<0.001	6.56 (3.04 – 14.2)	<0.001
Male sex	1.21 (0.90 – 1.64)	0.202	0.61 (0.31 – 1.18)	0.139
Receiving tenofovir at the time of first-line failure	0.98 (0.73 – 1.32)	0.893	1.09 (0.55 – 2.13)	0.809
Age (per year)	1.00 (0.98 – 1.01)	0.562	1.02 (0.99 – 1.05)	0.239
Duration of PI exposure (per year)	1.00 (0.96 – 1.05)	0.970	1.03 (0.92 – 1.15)	0.581
CD4+ cell count at the time of second-line failure (per square root cells/µL)	1.02 (0.98 – 1.05)	0.332	1.00 (0.94 – 1.06)	0.898
HIV-1 RNA at the time of second-line failure (per $\log_{10}$ copies/mL)	0.87 (0.81 – 0.94)	0.001	0.83 (0.69 – 0.99)	0.035

PI, protease inhibitor; HR, hazard ratio; CI, confidence interval; TLD, tenofovir-lamivudine-dolutegravir; ART, antiretroviral therapy.

Supplementary Table S5. Summary of plasma HIV-1 RNA outcomes at 6 and 12 months

	PI resistance[a]		No PI resistance[a]	
Variable	**TLD group (n = 47)**	**DRV/r group (n = 99)**	**TLD group (n = 86)**	**Continue PI group (n = 120)**
HIV-1 RNA <400 copies/mL (n, % [95% CI])[b]				
6 months	33/38 (87 [72 – 96])	75/84 (89 [81 – 95])	43/70 (61 [49 – 73])	19/77 (25 [16 – 36])
12 months	23/26 (88 [70 – 98])	55/60 (92 [82 – 97])	41/58 (71 [57 – 82])	20/72 (28 [18 – 40])
HIV-1 RNA <50 copies/mL (n, % [95% CI])[b]				
6 months	24/38 (63 [46 – 78])	59/84 (70 [59 – 80])	26/70 (37 [26 – 50])	7/77 (9 [4 – 18])
12 months	17/26 (65 [44 – 83])	47/60 (78 [66 – 88])	31/58 (53 [40 – 67])	10/72 (14 [7 – 24])

PI, protease inhibitor; TLD, tenofovir-lamivudine-dolutegravir; DRV/r, ritonavir-boosted darunavir; CI, confidence interval.
[a]Resistance was classified with the Stanford algorithm, with a score of ≥10 indicating at least potential low-level resistance.
[b]Missing HIV-1 RNA within window (±3-months) were excluded from the analysis.