

LONG-TERM EFFICACY, SAFETY, AND METABOLIC IMPACT OF GENERIC DOLUTEGRAVIR IN TREATMENT-NAÏVE AND EXPERIENCED PEOPLE LIVING WITH HIV: A REAL-WORLD STUDY IN ARGENTINA

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Background:

- Dolutegravir (DTG) is a recommended integrase inhibitor for treatment-naïve (TN) and treatment-experienced (TE) people with HIV (PWHIV).
- Argentina has access to generic DTG, but long-term follow-up data are lacking.
- We aim to describe for generic DTG combined with NRTIs: 1) persistence, efficacy (viral load <50 c/mL), and safety; 2) metabolic impact; 3) body weight changes in both TN and TE PLHIV.

Methods:

- Real-world descriptive study of PLHIV initiating DTG + NRTIs in Argentina (DOLUMET study)
- The study has two components: a retrospective analysis (48-month follow-up) from 10/2019 to 05/2024, and a prospective cohort (24-month follow-up) from 10/2021 to 10/2023.

Results:

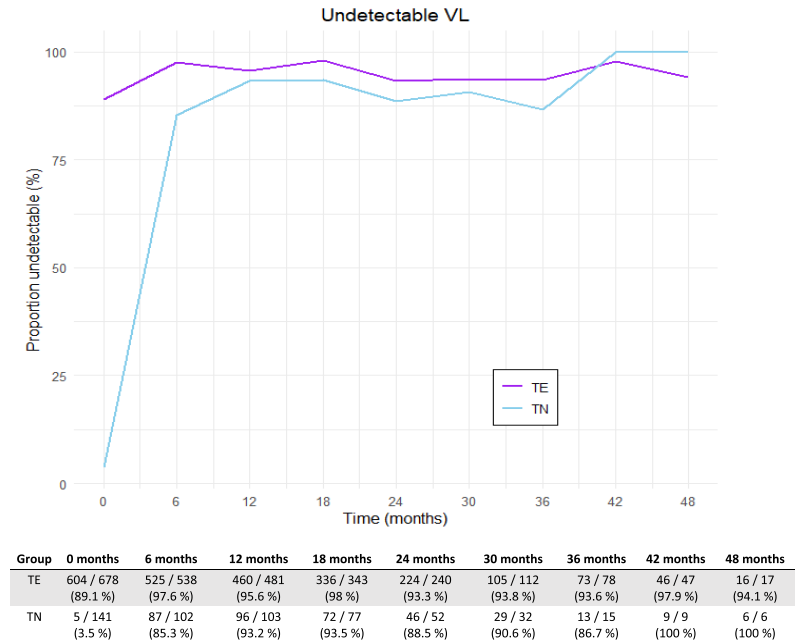
A) RETROSPECTIVE COHORT:

- Baseline characteristics are shown in **Table 1**.
- Combined results on persistence, immunevirological evolution and metabolic parameters are shown in **Table 2**.
- Virologic suppression rates are shown in **Figure 1**.

B) PROSPECTIVE COHORT:

- 123 PLWH were included: 73% TE, 69% male, 71% on triple therapy.
- Median age was higher in TE than TN (53 vs 39 years), as was baseline weight: 81 (71-92) vs 63 (55-70) kg.
- Persistence at 12 and 24 months was 99% and 100%; 93% were undetectable at 24 months.
- TE maintained stable weight: median of 81 (70-92) kg throughout follow-up.
- TN showed significant weight gain: baseline median 63 (55-70) kg vs 73 (57-82) kg at 12 and 76 (63-83) kg at 24 months.

Figure 1. Proportion of undetectable viral load (VL) in treatment naïve (TN) and experienced (TE) PLWH in DOLUMET retrospective cohort.



Conclusions:

1. Long-Term Efficacy and Safety: The results indicate high effectiveness in viral suppression over 48 months. The low prevalence of adverse events is crucial for patient adherence and quality of life.

2. Differentiated Metabolic Impact: There is a difference in metabolic impact between experienced and naive patients. In experienced patients, a sustained decrease in cholesterol and triglyceride levels was observed, suggesting a favorable metabolic profile. On the other hand, naive patients (propective cohort) experienced a significant weight gain, which aligns with existing literature in the context of return to health.

3. Treatment Persistence: Treatment persistence was high and sustained over time. This highlights PLWH's acceptance of generic dolutegravir-based treatment in HIV management, which may contribute to reducing virus transmission.

4. Clinical Considerations: Generic dolutegravir is a viable and effective treatment option for HIV patients in Argentina. The combination of efficacy, safety, and a favorable metabolic profile makes this treatment a first-line option, especially in a context where access to antiretroviral medications may be challenging.

Table 1. Baseline characteristics of treatment experienced PLWH who switched to co-packed 3TC/DTG (dual therapy) vs. DTG-based triple therapy, Argentina.

	Total, N = 884 ¹	TE N = 738 ²	TN N = 146 ²	p-value ²
Sex at birth, male	628/883 (71%)	514/737 (70%)	114/146 (78%)	0.042
Age at DTG start (years)	46 [37-54]	47 [40-55]	36 [29-44]	<0.001
Presence of comorbidities ²	406/692 (59%)	372/578 (64%)	34/114 (30%)	<0.001
Viral load <50 c/mL	609/819 (74%)	604/678 (89%)	5/141 (3.5%)	<0.001
Viral load (absolute value):	19 [19-63]	19 [19-44]	34,900 [7,210-133,000]	<0.001
CD4 T-cell count (cell/mm ³)	591 [379-796]	628 [430-830]	341 [151-621]	<0.001
Prior Treatment				<0.001
PI	294/884 (33%)	294/738 (40%)	-	
NNRTI	288/884 (33%)	288/738 (39%)	-	
INSTI	130/884 (15%)	130/738 (18%)	-	
Other	26/884 (2.9%)	26/738 (3.5%)	-	
None	146/884 (17%)	-	146/146 (100%)	
NRTI-backbone				<0.001
3TC/TDF or FTC/TDF	390/878 (44%)	283/733 (39%)	107/145 (74%)	
3TC	290/878 (33%)	268/733 (37%)	22/145 (15%)	
3TC/ABC	162/878 (18%)	151/733 (21%)	11/145 (7.6%)	
FTC/TAF	25/878 (2.8%)	20/733 (2.7%)	5/145 (3.4%)	
Other	11/878 (1.3%)	11/733 (1.5%)	-	

¹n/N (%); Median [Q1-Q3]

²Pearson's Chi-squared test; Wilcoxon rank sum test; Fisher's exact test

²dyslipidemia: 226 (55.67%), hypertension: 107 (26.42%), obesity: 78 (19.35%), neuropsychiatric: 74 (18.23%), osteopenia-osteoporosis: 51 (12.59%), diabetes: 48 (11.85%), gastrointestinal disorders: 43 (10.62%), other cardiovascular (MI, peripheral cardiovascular disease): 40 (9.9%), renal disorders: 39 (9.61%), asthma/COPD: 26 (6.4%), solid neoplasia: 26 (6.44%), blood dyscrasias: 18 (4.43%), autoimmune disease: 12 (2.96%), cirrhosis: 7 (1.72%)

Table 2. Evolution of immunevirological and metabolic parameters in DOLUMET retrospective cohort, Argentina.

	Total				p-value ²	Treatment experienced (TE)				p-value ²	Treatment Naïve (TN)				p-value ²
	Baseline N = 907 ¹	24 months N = 415 ²	36 months N = 146 ²	48 months N = 42 ²		Baseline N = 738 ²	24 months N = 335 ²	36 months N = 117 ²	48 months N = 32 ²		Baseline N = 146 ²	24 months N = 80 ²	36 months N = 29 ²	48 months N = 10 ²	
Persistence	-	384/394 (97%)	141/144 (98%)	42/42 (100%)	>0.9	-	311/319 (97%)	112/115 (97%)	32/32 (100%)	>0.9	-	73/75 (97%)	29/29 (100%)	10/10 (100%)	>0.9
Viral load <50 c/mL	609/819 (74%)	270/292 (92%)	86/93 (92%)	22/23 (96%)	<0.001	604/678 (89%)	224/240 (93%)	73/78 (94%)	16/17 (94%)	0.2	5/141 (3.5%)	46/52 (88%)	13/15 (87%)	6/6 (100%)	<0.001
CD4 T-cell count (cell/mm ³)	591 [379-796]	652 [494-838]	637 [494-786]	599 [441-681]	0.002	628 [430-830]	655 [508-842]	651 [505-783]	594 [379-643]	0.054	341 [151-621]	640 [400-828]	511 [294-822]	689 [665-915]	<0.001
Weight	76 [65-85]	78 [66-87]	78 [73-83]	70 [68-78]	0.9	78 [66-87]	79 [66-87]	78 [73-86]	70 [68-78]	0.9	71 [59-79]	75 [73-78]	70 [61-79]	NA [NA-NA]	0.6
Adverse events attributable to DTG ²	-	5/385 (1.3%)	-	-	0.5	-	2/312 (0.6%)	-	-	>0.9	-	3/73 (4.1%)	-	-	0.7
Therapy type															
3TC	290/878 (33%)	96/411 (23%)	27/145 (19%)	6/42 (14%)		268/733 (37%)	91/331 (27%)	27/116 (23%)	6/32 (19%)		22/145 (15%)	5/80 (6.3%)	-	-	
3TC/ABC	162/878 (18%)	84/411 (20%)	26/145 (18%)	1/42 (2.4%)		151/733 (21%)	77/331 (23%)	23/116 (20%)	1/32 (3.1%)		11/145 (7.6%)	7/80 (8.8%)	3/29 (10%)	-	
3TC/TDF or FTC/TDF	390/878 (44%)	218/411 (53%)	83/145 (57%)	34/42 (81%)		283/733 (39%)	151/331 (46%)	58/116 (50%)	24/32 (75%)		107/145 (74%)	67/80 (84%)	25/29 (86%)	10/10 (100%)	
FTC/TAF	25/878 (2.8%)	12/411 (2.9%)	9/145 (6.2%)	1/42 (2.4%)		20/733 (2.7%)	11/331 (3.3%)	8/116 (6.9%)	1/32 (3.1%)		5/145 (3.4%)	1/80 (1.3%)	1/29 (3.4%)	-	
Other	11/878 (1.3%)	1/411 (0.2%)	-	-		11/733 (1.5%)	1/331 (0.3%)	-	-		-	-	-	-	
Glucose	92 [87-99]	92 [86-99]	95 [87-103]	95 [87-103]	0.4	92 [87-100]	92 [87-100]	95 [86-106]	93 [86-105]	0.7	90 [81-96]	90 [84-96]	93 [88-99]	101 [98-102]	0.12
Total cholesterol	191 [160-222]	178 [149-201]	171 [148-192]	151 [125-203]	<0.001	195 [163-226]	181 [154-203]	173 [148-202]	152 [126-209]	<0.001	162 [133-183]	160 [138-186]	170 [146-181]	150 [114-197]	>0.9
HDL Cholesterol:	46 [38-57]	42 [36-50]	43 [36-54]	38 [33-42]	<0.001	46 [39-58]	43 [37-50]	43 [37-49]	37 [33-41]	<0.001	39 [31-51]	42 [33-48]	44 [31-62]	40 [33-63]	0.9
LDL Cholesterol:	114 [92-142]	106 [85-123]	97 [84-116]	86 [64-123]	<0.001	117 [95-145]	106 [87-128]	97 [84-120]	86 [72-129]	<0.001	97 [81-118]	100 [75-115]	95 [85-103]	85 [44-110]	0.8
Triglycerides:	132 [95-200]	112 [89-161]	100 [81-142]	118 [31-124]	<0.001	138 [98-205]	115 [95-165]	94 [81-144]	NA [NA-NA]	<0.001	104 [81-139]	101 [72-133]	104 [75-120]	118 [31-124]	>0.9

¹n/N (%); Median [Q1-Q3]

²Fisher's exact test; Kruskal-Wallis rank sum test

²weight gain: 4 (80%), digestive intolerance: 1 (20%)