*Correspondence:
joaquin.burgos@vallhebron.cat,
mariajose.buzon@vhir.org

Lauric Acid Enhances T-Cell Recovery, Reduces Inflammation, and Impacts the HIV Reservoir on ART

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Joaquin Burgos[1], Judith Grau-Expósito[1], Irene Mota[1], Arnau Monforte[1], Jordi Navarro[1], Jorge Garcia[1], Adrià Curran[1], Paula Suanzes[1], Patricia Alvarez[1], Bibiana Planas[1], Marta Sanchiz[1], Vicenç Falcó[1], Meritxell Genescà[1], **María J. Buzón**[1]

[1]Infectious Diseases Department, Vall d'Hebron Institut de Recerca (VHIR), Vall d'Hebron Hospital Universitari, Vall d'Hebron Barcelona Hospital Campus, Passeig Vall d'Hebron 119-129, Barcelona, Spain

BACKGROUND

ART suppresses HIV replication but does not eliminate the viral reservoir. Persistent immune dysregulation and low-grade inflammation may contribute to reservoir stability, motivating interest in host-directed modulation strategies. Lauric acid (LA), a medium-chain saturated fatty acid, has been reported to modulate metabolic pathways and is orally administered, inexpensive, and non-toxic.

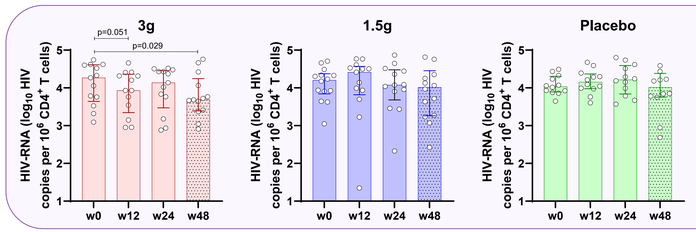
METHODS

In a randomized, placebo-controlled clinical trial, 45 PLWH on stable ART (median 8.7 years) received daily oral 3g LA (n=15), 1.5g LA (n=15) or placebo (n=15) for 24 weeks, followed by 24 weeks of follow-up. Primary endpoints: tolerance, HIV reservoir measures (total/intact HIV-DNA, intracellular HIV-RNA), lymphocyte counts, systemic inflammation indexes, plasma cytokines, and lipid profile Mixed-effects regression models (Wald test) were used for analysis.

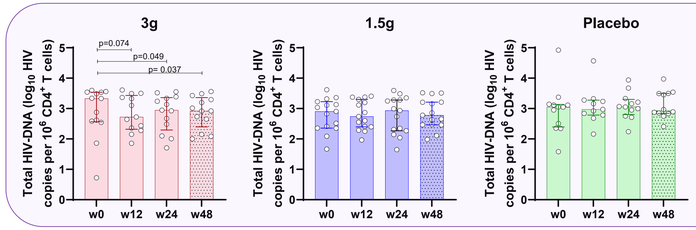
Baseline characteristics of the participants	Placebo group (n=15)	1.5 g LA group (n=15)	3 g LA group (n=15)
Characteristics of patients			
Sex male, n (%)	12 (80%)	10 (66.7%)	11 (73.3%)
Race, n (%) White	9 (60%)	11 (73.3%)	11 (78.6%)
Hispanic	5 (33.3%)	4 (26.7%)	3 (21.7%)
Age, median (IQR)	46.4 (46.1-56.2)	51.8 (41.7-56)	50.8 (39.5-61.3)
Current tobacco smoking, n (%)	4 (26.6%)	2 (13.3%)	6 (40%)
Nadir CD4⁺ T cell count, cells/µl, median (IQR)	400 (257-490)	370 (202-420)	386 (260-554)
Current CD4 ⁺ T celll count, cells/µl, median (IQR)	940 (670-1170)	750 (640-940)	730 (600-910)
Current CD8 ⁺ T cell count, cells/µl, median (IQR)	700 (410-840)	600 (400-910)	530 (390-640)
Zenith plasma HIV RNA, copies/mL, median (IQR)	189999 (46900-500000)	230000 (23800-530000)	51500 (19000-140000)
ART regimen (triple therapy)			
INSTI-based	11 (73.3%)	9 (60%)	9 (60%)
NNRTI-based	2 (13.3%)	2 (12.3%)	4 (26.6%)
PI-based	2 (13.3%)	4 (26.6%)	2 (13.3%)
Time virologically suppressed, months, median (IQR)	98.5 (60-155)	89.5 (59-138)	122 (59-172)

Twenty-four weeks of daily LA supplementation was safe, well tolerated, and associated with reductions in HIV Transcription and Reservoir Size with Immunological Recovery, that persisted after LA discontinuation.

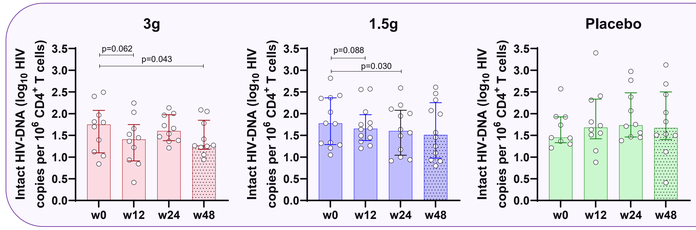
RESULTS



HIV RNA declined progressively in 3g LA over follow-up, with a marked reduction at week 12 (−54% relative to baseline; p=0.051), becoming statistically significant by week 48 (−74%; p=0.029)



Total HIV DNA declined progressively in 3g LA, with significant reductions at week 24 (−58.6%; p=0.049) and week 48 (−60.8%; p=0.037)

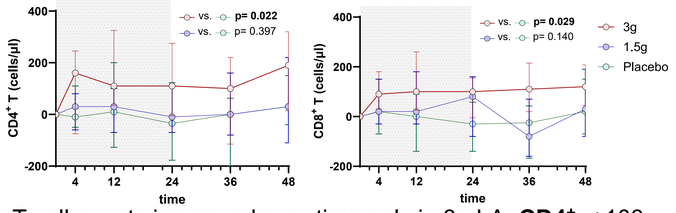


IPDA declined by 54.7% at week 12 (p=0.062) in 3g LA and reached a significant reduction of 67.1% at week 48 (p=0.043). 1.5g LA showed a transient IPDA reduction, significant only at week 24 (−33%; p=0.031)

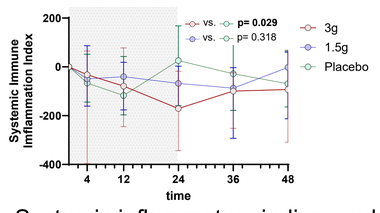
Safety outcomes	Placebo group (n=14)	1.5 g LA group (n=15)	3g LA group (n=14)	*p*-value [a]
At least one adverse event, n (%)	2 (14.3%)	4 (26.6%)	6 (42.8%)	0.24
Treatment-related adverse events, n (%)	2 (14.3%)	3 (20%)	4 (28.6%)	0.65
Serious adverse events, n (%)	0	0	1 (7.1) *	0.35
Patients with adverse events leading to discontinuation, n (%)	0	0	0	-
Treatment-related adverse events for total adverse events				
Nausea, n (%)	0/4	0/4	1/7 (14.3%)	1
Dyspepsia, n (%)	1/4 (25%)	1/4 (25%)	1/7 (14.3%)	1
Diarrhea, n (%)	0/4	1/4 (25%)	1/7 (14.3%)	1
Abdominal distension, n (%)	0/4	1/4 (25%)	0/7	1
Gastroesophageal reflux, n (%)	1/4 (25%)	0/4	1/7 (14.3%)	1

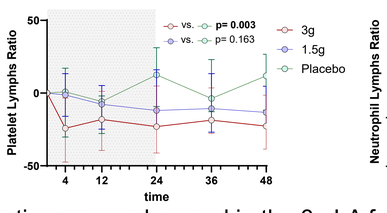
[a] Difference between the three groups, Fisher's exact test
* Patient hospitalized for knee prosthesis surgery, not related to the study intervention

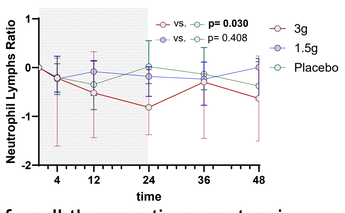
RESULTS



T-cell counts increased over time only in 3g LA. **CD4⁺:** +103 cells/µL wk4, +146 cells/µL wk12, +128 cells/µL wk24, +209 cells/µL wk48 (p<0.001). **CD8⁺**: +155 cells/µL wk4, +128 cells/µL wk12, +110 cells/µL wk24, +159 cells/µL wk48 (p=0.002).







Systemic inflammatory indices reductions were observed in the 3g LA for all three ratios: systemic immune–inflammation index (SII), platelet–lymphocyte ratio (PLR), and neutrophil–lymphocyte ratio (NLR) . For **SII**, all weeks p≤0.023. For **PLR**, all weeks p ≤ 0.022. For **NLR**, all weeks; p ≤ 0.002.

CONCLUSIONS

Our findings are consistent with a **reshaping of immune tone and cellular homeostasis** in a manner unfavorable to long-term HIV persistence. The observed expansion of circulating CD4⁺ and CD8⁺ T cells occurred without evidence of systemic immune activation or HIV reactivation, distinguishing LA from classical cure-directed strategies based on immune stimulation. Notably, both T-cell expansion and reductions in HIV reservoir measures persisted beyond the supplementation period, suggesting an association with sustained alterations in immune homeostasis. ***Overall, LA supplementation was safe and well tolerated, enhanced CD4⁺ and CD8⁺ T-cell recovery, reduced systemic inflammation, and was associated with decreases in the HIV reservoir, supporting further evaluation of LA as an adjunctive strategy targeting chronic inflammation and HIV persistence.***

PLAIN LANGUAGE SUMMARY

In people living with HIV on effective treatment, lauric acid supplementation was safe and associated with improved immune cell recovery, lower inflammation, and reductions in the HIV reservoir. These findings suggest that a low-cost dietary supplement may help modify immune conditions that support long-term HIV persistence.

Funding: This work was funded by Instituto de Salud Carlos III, grant PI20/01080 cofinanced by European Regional Development Fund (ERDF). MJB was supported by the Miguel Servet program funded by the Spanish Health Institute Carlos III (CPII22/00005).