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ALTERATION OF TRANSAMINASES IN PrEP USERS: INVESTIGATION OF POSSIBLE CAUSAL FACTORS OTHER THAN FTC/TDF

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INTRODUCTION

A grade 1 **increase in transaminases** has been reported among **side effects** during oral PrEP for HIV with FTC/TDF[1].
Still, transaminases alteration is a common finding and **can acknowledge multiple causes**: concomitant infections, alcohol consume and metabolic syndrome, major hepatotropic viruses, pharmacological therapies, and substance abuse, such as chems and steroids whose consumption may not be promptly reported by users due to stigma.

MATERIAL AND METHODS

Alanine aminotransferase (ALT) levels were collected at screening and follow-up visits of PrEP users from January 2022 to March 2024.
ALT values above the reference threshold were stratified according to severity, and the potential causes were explored by interview, if not previously reported.

RESULTS

A total of 145 ALT altered determinations, corresponding to a severity grade 1 or higher, were recorded (Figure 1, Table 1).

- In 88 cases **(61%) at least one possible alternative cause to FTC/TDF** for the transaminase elevation **could be identified.**
- In particular, in 49 cases there was a use of **chems** and in 30 of **steroids** as physical enhancers.
  The use of them was reported **in 43% of the altered ALT detections**. However, also other possible causes were identified as shown in Table 1.

	ALT (n)	Chems (n)	Physical enhancers (n)	Daily alcohol use (n)	Chronic liver disease (n)	Drug therapy (n)	Infections (n)	Unknown (n)
Grade 1 (mild)	112	36	15	2	8	19	3	50
Grade 2 (moderate)	24	9	9	-	1	10	1	7
Grado 3 (severe)	7	3	5	-	-	2	1	-
Grado 4 (potentially life-threatening)	2	1	1	-	-	-	1	-
Total	145	49	30	2	9	31	6	57

Table 1. Grades of transaminase alterations and correlation with possible causes
Grade 1 (ALT 50 UI/ml – 99 UI/ml), Grade 2 (ALT 100 UI/ml – 199 UI/ml), Grade 3 (ALT 200 UI/ml – 399 UI/ml), Grade 4 (ALT ≥ 400 UI/ml)

- Among possible infectious causes of ALT alteration, two findings were consistent with **secondary syphilis**, whose possible liver involvement could explain ALT alterations, while the other cases included one **Mpox infection**, one acute **CMV infection**, one acute **toxoplasmosis**, and finally one case of ***C. difficile* colitis**.
- Of the 73 users for whom a **pre-PrEP screening** determination was available, 44 (**60%) had an ALT alteration at the baseline.**
- In the cases **where no other cause could be identified** (**39%**, n 57), **the alterations were all mild or moderate**.

It was also assessed whether the increase remained stable during FTC/TDF prophylaxis over time; cases with at least 4 ALT determinations were included, representing a total of 21 users, of which only 5 had a stable elevation, suggesting a possible role for the drug as a cause.

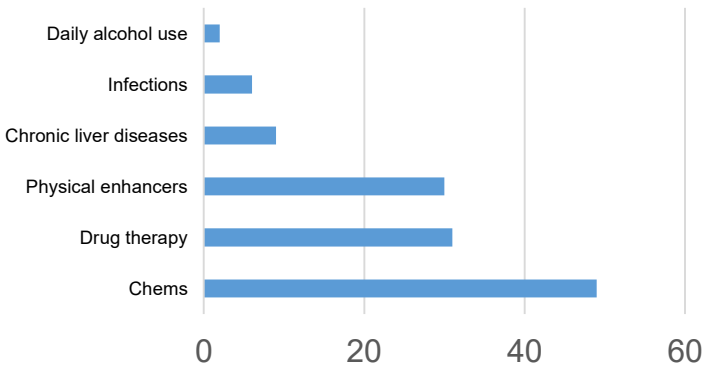

Figure 1. Stratification of possible causal factors in ALT alteration (n 145). More than 1 factor can be indicated for each alteration.

CONCLUSIONS

- Oral **PrEP with FTC/TDF** is confirmed to be very **well tolerated.**
- In nearly half of the cases a **use of chems or steroids** was reported, which was **often not spontaneously disclosed by the users**, unless they were specifically questioned after the alteration was detected.

Our study therefore also highlights the **importance of proactively investigating the use of chems and steroids** in PrEP population in order to **optimize** their clinical management, **avoid** misinterpretation of the toxicity of FTC/TDF, and ultimately **allow** appropriate counselling on the risks associated with their use.

Reference

1. Molina, J. M. *et al.* Daily and on-demand HIV pre-exposure prophylaxis with emtricitabine and tenofovir disoproxil (ANRS PREVENIR): a prospective observational cohort study. *Lancet HIV* **9**, e554–e562 (2022).