E/C/F/TAF SINGLE TABLET REGIMEN FOR POST-EXPOSURE PROPHYLAXIS

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Background

Introduction: HIV post-exposure prophylaxis (PEP) completion rates are of major concern, as rates of individuals completing the 28-days course regimen range from 56 % to 78 %.
Recently, the elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide coformulation (E/C/F/TAF) was approved for HIV infection treatment. This single tablet regimen (STR) contains a new prodrug, tenofovir alafenamide, which could improve the safety profile of tenofovir [10].

Objectives: To describe PEP completion and safety of an E/C/F/TAF regimen.

Methods

Study settings and design: Prospective, open-label, single-arm trial in 15 French centers (NCT02998320). Individuals aged ≥ 18 years with potential HIV exposure (occupational or not) in the previous 48 hours who met criteria for PEP initiation received once-daily E/C/F/TAF for 28 days.

Assessments: The primary endpoint was PEP completion at day 28, excluding withdrawal after source patient was tested negative to HIV.
Secondary endpoints were:
(1) Adherence: through self report [day 14 and 28] and elvitergavir blood plasma level [day 14]
(2) Quality of life: through SF-12 questionnaire [baseline, day 14 and 28],
(3) Safety: through questionnaire [day 14 and 28] and biological parameters (creatinine, GFR, AST, ALT, phosphate) [baseline, day 14 and 28]
(4) Efficacy: through HIV serology [baseline, day 56 and 112]

Results

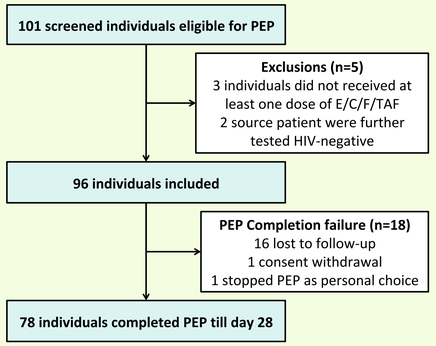
Study participants and Study Flowchart

96 individuals were included:
- No HIV positive test or active HBV or HCV at baseline
- 6 syphilis at initial screening

Participants were primarily male (n=75, 77 %) with a median age of 31 years (range, 18-69)

Exposures to HIV were:
- 8 occupational
- 88 sexual, of which 64% were MSM and 47% were unprotected

Six source patients were known to be HIV-infected (no HIV-RNA available)



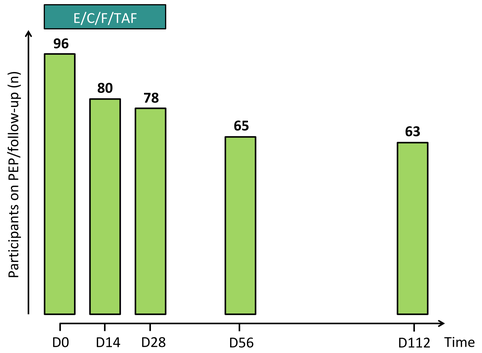
Treatment outcomes

81 % of individuals (95% CI, 73-89) completed PEP course till day 28 visit (n=78). Completion failure (n=18, 19%) was due to:
- lost to follow-up (n=16)
- individual's own choice (n=1)
- withdrawal of consent (n=1)

No PEP interruption due to adverse events was documented

14 additional participants (16%) were also lost to follow-up between day 28 to day 112, and pre-exposure prophylaxis was initiated for 1 participant (*see Figure*)

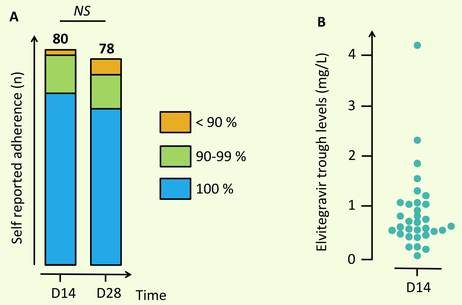
No HIV seroconversion was observed



Adherence

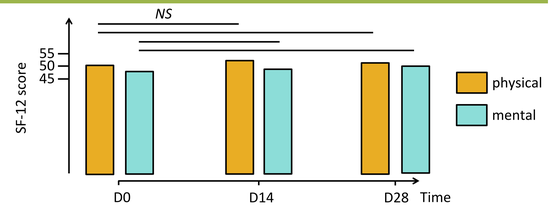
Self-reported adherence was 100%, between 90 and 99%, and <90% for 76%, 22% and 2% of individuals at day 14; and for 75%, 17% and 8% of individuals at day 28, respectively (p>0.05)
(*see Figure A*)

Median elvitegravir trough concentration at day 14 was 0.628 mg/L (range, 0-4.201), therefore above 0.190 mg/L for 88% of participants (*see Figure B*)



Health-related quality of life

Mean quality of life SF-12 measures of physical and mental health were of 50 (range, 27-64) and 47 (range, 17-65) at baseline, 52 (range, 25-64) and 48 (range, 25-67) on day 14, and 51 (range, 28-61) and 49 (range, 22-61) on day 28, respectively (p>0.05) (*see Figure*)

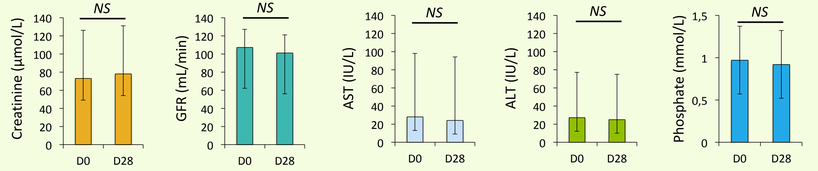


Safety

Overall, 226 adverse events were reported in 58 (68%) and 43 (59%) participants, at day 14 and 28 respectively (p>0.05).

At day 14; 93, 24 and 8 grade 1, 2 and 3 adverse events were observed, and 73, 21 and 7 on day 28, respectively (p>0.05). The most frequent reported adverse events were asthenia (19%), abdominal pain (16%), diarrhea (15%) and headache (14%). No renal or liver abnormalities occurred.

Non-significant variations in creatinine, GFR, AST, ALT and phosphate levels were observed (*see Figure*)



Conclusions

The PEP completion rate was of 81%, thus in the range of other recently approved STR when used in a PEP setting. PEP non-completion was not directly attributed to E/C/F/TAF, but mostly to losses of follow-up, which frequently hampers PEP care.
We also report a 100% efficacy rate, as no participant was subsequently tested HIV positive on study.
High adherence (> 90% of pills intake) to the E/C/F/TAF regimen was documented by both self-reports in 98% and 92% at day 14 and 28 respectively, as well as by pharmacological assessments (appropriate in 88% of cases). These results were similar than those obtained with other PEP STR.
Quality of life measures were not modified on E/C/F/TAF and were similar than those of the general population, suggesting that E/C/F/TAF is suitable for further PEP usage.
Although, no PEP discontinuations due to safety reasons were documented, even if adverse events rates were higher in PEP users than in HIV-infected individuals.
When comparing to other integrase inhibitors-based PEP regimen, E/C/F/TAF showed similar completion rates as the other elvitegravir-based and dolutegravir. This result could be further explained by low rates of adverse events with these compounds.

Overall, PEP E/C/F/TAF showed an acceptable safety profile and good completion rates. Self-reported and drug levels indicated good adherence, confirming that E/C/F/TAF could be a regimen of choice for PEP.

E/C/F/TAF PEP Study Group

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