Incidence and Severity of COVID-19 in HIV-Positive Persons Receiving Antiretroviral Therapy
A Cohort Study

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SA HIV Clinicians Society
Covid-19 Webinar
16 July 2020
Background

• Spain
  • 257,494 COVID-19 cases and 28,413 deaths
  • Highest HIV prevalence in Europe
  • More than 90% of HIV+ people in Spain on ART and 95% suppressed
  • More than 75% of HIV+ people are men and co-morbidities common

• ART
  • Certain NRTIs may have activity against SARS-CoV-2 RNA-dependent RNA polymerase based on molecular docking and other lab studies
Antiviral Efficacies of FDA-Approved Drugs against SARS-CoV-2 Infection in Ferrets


(A)

Viral titer in turbinate (Log_{10} TCID_{50}/g)

(B)

Viral titer in lung (Log_{10} TCID_{50}/g)

Days post infection

PBS control
Lopinavir/Ritonavir
Hydroxychloroquine sulfate
Emtricitabine/Tenofovir
Azathioprine

FIG 3 Virus titers in respiratory tissues. Groups of ferrets (3/group) were sacrificed at 4 and 8 dpi. Viral titers were measured in turbinate (A) and lung (B) by determining the numbers of TCID_{50} per gram. The limit of detection is 1 Log_{10} TCID_{50}/g and indicated by the dotted line for each representation.
Methods

• Conducted between 1 Feb and 15 April 2020 (75-day risk)
• 60 ART clinics
• PCR-confirmed COVID-19 diagnoses ascertained
• Variables included in analyses
  • Age, sex, ART regimen
  • Not comorbidities, CD4, HIV viral load or ART duration
• Outcomes
  • COVID-19 diagnosis, hospital admission, ICU admission, death
• Comparison also made to general population, aged 20-79
  • National COVID-19 Health Information System (age and sex-standardized)
Figure. Study flow chart of 77,590 HIV-positive persons receiving ART in Spain from 1 February to 15 April 2020.

- Patients receiving ART (n = 77,590)
- Patients with PCR-confirmed diagnosis (n = 236)
  - Hospitalized patients (n = 151)
    - ICU admissions (n = 15)
      - Died (n = 5)
        - ABC/3TC (n = 2)
          - TAF/ FTC (n = 3)
        - Recovered (n = 10)
          - ABC/3TC (n = 4)
            - TAF/ FTC (n = 4)
            - Dual therapy (n = 2)
    - Non-ICU admissions (n = 136)
      - Died (n = 12)
        - ABC/3TC (n = 5)
          - TAF/ FTC (n = 5)
          - Dual therapy (n = 2)
      - Recovered (n = 124)
        - ABC/3TC (n = 36)
          - TAF/ FTC (n = 40)
          - TDF/ FTC (n = 13)
          - Dual therapy (n = 29)
          - Others (n = 6)
  - Nonhospitalized patients (n = 85)
    - Died (n = 3)
      - ABC/3TC (n = 1)
        - TAF/ FTC (n = 2)
    - Recovered (n = 82)
      - ABC/3TC (n = 9)
        - TAF/ FTC (n = 46)
        - TDF/ FTC (n = 8)
        - Dual therapy (n = 17)
        - Others (n = 2)

151 hospitalized (64%)
15 admitted to ICU (6%)
20 died (8%)

3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; FTC = emtricitabine; ICU = intensive care unit; PCR = polymerase chain reaction; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate.
HIV+ versus general population comparison
Age and sex standardized; per 10,000 individuals

<table>
<thead>
<tr>
<th></th>
<th>COVID-19 diagnosis</th>
<th>COVID-19 death</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV+</td>
<td>30.0</td>
<td>3.7</td>
</tr>
<tr>
<td>General pop</td>
<td>41.7*</td>
<td>2.1</td>
</tr>
</tbody>
</table>

*33.0 after health care workers excluded
Table 2. Risk per 10 000 Persons for PCR-Confirmed COVID-19 Diagnosis, Hospital Admission, ICU Admission, and Death Among 77 590 HIV-Positive Persons Receiving ART, 1 February to 15 April 2020, Spain

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<tr>
<th>Characteristics</th>
<th>COVID-19 Diagnosis (95% CI)</th>
<th>COVID-19 Hospital Admission (95% CI)</th>
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<td>Overall</td>
<td>30.4 (26.7-34.6)</td>
<td>19.5 (16.5-22.8)</td>
<td>1.9 (1.1-3.2)</td>
<td>2.6 (1.6-4.0)</td>
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<td>Standardized*</td>
<td>30.0 (29.8-30.2)</td>
<td>17.8 (17.7-18.0)</td>
<td>2.5 (2.4-2.6)</td>
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<td>Sex</td>
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<td>Men</td>
<td>35.1 (30.4-40.3)</td>
<td>23.4 (19.6-27.7)</td>
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<td>Women</td>
<td>16.4 (11.2-23.2)</td>
<td>7.7 (4.3-12.7)</td>
<td>1.5 (3-4.5)</td>
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<td>Age, y</td>
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<td>28.3 (20.3-38.3)</td>
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<td>27.9 (20.9-36.4)</td>
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<td>16.9 (10.5-25.9)</td>
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* Standardized to the age and sex of the general population of Spain aged 20 to 79 y.
† One-sided 97.5 CI.
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**NRTI**

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Potential explanations for TDF effect

• Those receiving TDF in 2020 are a select group of patients
  • On ART longer with better immune reconstitution?
  • Fewer co-morbidities?

• Biological explanation
  • Tenofovir diphosphate fits better into RNA\text{dRNA}\text{p} pocket than other NRTIs
  • But what might explain differences between TAF and TDF?
TFV = Tenofovir
TDF = Tenofovir disoproxil fumarate
TAF = Tenofovir alafenamide fumarate
TFV-MP = Tenofovir monophosphate
TFV-DP = Tenofovir diposphosphate

Plasma tenofovir levels are associated with bone and renal effects

Fernandez-Montero, Expert Opin Pharmacother 2014
Hypothesis: Higher exposure of SARS-CoV-2 to tenofovir disphosphate in epithelial and endothelial cells with TDF than TAF
Future research

• Evaluation of TDF/FTC effect on COVID-19 in HIV-PrEP studies

• COVID-19 treatment and prophylaxis trials with TDF/FTC