The penetration of antiretroviral drugs in deep compartments, like the central nervous system (CNS), is a crucial part of strategies toward HIV cure.

This study aimed to estimate cerebrospinal fluid (CSF) diffusion of bictegravir (BIC), that has high protein binding which could limit diffusion, entecavir (FTC) and tenofovir alafenamide (TAF) in patients with HIV-related CNS impairment (HCl) enrolled in a real-life observational study.

### Patients and methods

**Monocenter, prospective, single arm, open label, observational study**

- **Inclusion criteria:**
  - Admitted to the Neuro-HIV Rehabilitation Care Unit, (AP-HP, Hôpital Bicêtre, France)
  - At least 1 HIV-related CNS impairment
  - Treated by an optimized antiretroviral therapy including BIC/FTC/TAF since at least 1 month
- **Enrolment:** 2019 January to 2020 January
- **Simultaneous samples in the setting of routine care:**
  - 1 blood sampling & 1 cerebrospinal fluid (CSF) sampling

### Biologic parameters

**HIV-RNA (RT-PCR, Abbott Realtime®)**
- Plasma & cerebrospinal fluid

**Albumin**
- Plasma & cerebrospinal fluid
  - Quotient albumin Qₐ
  - Qₐ = CSF albumin (mg/L) / Plasma albumin (g/L)
  - Assesses blood-brain barrier (BBB) integrity

### Baseline characteristics

<table>
<thead>
<tr>
<th>Sex – M (♂)/ F (♀)</th>
<th>12 ♂ / 8 ♀</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age (IQR) – years</td>
<td>45 (15)</td>
</tr>
<tr>
<td>Median CD4 cell count (IQR) – /µL</td>
<td>204 (202)</td>
</tr>
</tbody>
</table>

**Plasma HIV-RNA**

<table>
<thead>
<tr>
<th>&lt; 40 copies/mL – n (%)</th>
<th>14 (70)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median (IQR) if &gt; 40 copies/mL – log₁₀ copies/mL</td>
<td>1.9 (2.2)</td>
</tr>
</tbody>
</table>

**CSF HIV-RNA**

<table>
<thead>
<tr>
<th>&lt; 40 copies/mL – n (%)</th>
<th>18 (90)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median (IQR) if &gt; 40 copies/mL – log₁₀ copies/mL</td>
<td>1.9 (1.2)</td>
</tr>
</tbody>
</table>

**HIV-related CNS impairment – n (%)**

- Progressive multifocal leukoencephalopathy (PML) 9 (45)
- Cerebral toxoplasmosis (CT) 6 (30)
- HIV encephalitis 2 (10)
- CT combined with HIV encephalitis 1 (5)
- Acute disseminated encephalomyelitis (ADEM) 1 (5)
- VZV meningoencephalitis 1 (5)
- Antiretroviral therapy (ART) – n (%) 15 (75)
  - BIC/FTC/TAF 4 (20)
  - BIC/FTC/TAF + maraviroc 1 (5)
  - Median (IQR) duration of the current ART regimen – days 32 (11)

| IQQR: interquartile range |

### Results

There are correlations between:
- CSF and Total plasma concentrations for BIC and FTC
- HIV-related CNS impairment:
  - PML (2), HIV encephalitis (1)
- Not related with a higher CSF BIC/FTC/tenofovir diffusion.

### Conclusion

Total plasma concentrations remained as previously reported. Almost all CSF BIC concentrations and most of CSF FTC concentrations were above the in vitro 50% inhibitory concentration (IC50). CSF tenofovir concentrations, administered as TAF, are even lower than administered as TDF. This suggests a limited effect of TAF in the CNS.

BIC with FTC/TAF backbone should be effective to target HIV replication in the CNS, which is a deep reservoir, even though BBB is undamaged.