DISCONTINUATIONS & VIROLOGIC RESPONSE IN LATE PRESENTERS WITH INSTI- OR PI-BASED ART

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Background

• The optimal antiretroviral (ART) regimen for treatment naive patients with advanced HIV is unknown[1]

• Active opportunistic infections and/or low CD4+T-cell count are exclusion criteria in most clinical trials

• Protease inhibitors (PI) are commonly used in advanced disease, however there are few data on outcomes associated with integrase inhibitors (INSTI) in this population [2,3]

Aims

• To compare the tolerability of PI-based vs INSTI-based regimens in those with advanced HIV

• To compare the efficacy of PI-based vs INSTI-based regimens in those with advanced HIV at 12 and 48 weeks after treatment initiation
Methods

• Retrospective multicentre European cohort

• Inclusion criteria:
  • CD4+ T-cell count <200 cells/µL and/or AIDS defining disease at the time of starting ART
  • Treatment naive starting either PI or INSTI based ART (any backbone)
  • >18 years old
  • Commenced ART between January 2014- December 2016

• Primary endpoint:
  • ART discontinuation at 12 and 48 weeks following start of therapy
Methods

• Secondary endpoints measured at 12 and 48 weeks
  • HIV viral load < 50 copies/ml
  • Mortality
  • AIDS defining illness
  • Adverse events
  • CD4 cell count

• Statistics
  • Differences between PI and INSTI groups will be assessed using Mann-Whitney tests, Chi-squared tests or Fisher’s exact tests, as appropriate
## Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>INSTI (N=131)</th>
<th>PI (N=87)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years, median (SD)</td>
<td>42 (33, 42)</td>
<td>44.9 (36, 44.8)</td>
</tr>
<tr>
<td>Male, N %</td>
<td>111 (84.7)</td>
<td>77 (88.5)</td>
</tr>
<tr>
<td>European ethnicity, N %</td>
<td>105 (80.2)</td>
<td>61 (70.1)</td>
</tr>
<tr>
<td>AIDS defining illness, N %</td>
<td>75 (57.3)</td>
<td>46 (52.9)</td>
</tr>
<tr>
<td>CD4 cell count (cells/µl), median (IQR)</td>
<td>103.5 (42, 180)</td>
<td>90 (33, 144)</td>
</tr>
<tr>
<td>CD4:CD8 ratio, median (IQR)</td>
<td>0.12 (0.08, 0.2)</td>
<td>0.10 (0.06, 0.2)</td>
</tr>
<tr>
<td>HIV viral load log_{10} (cps/ml), mean (SD)</td>
<td>5.8 (1.2)</td>
<td>5.7 (1.2)</td>
</tr>
</tbody>
</table>
Antiretroviral regimens at baseline

Total N=218

Integrase Inhibitor
N= 131
- Dolutegravir N=82
- Raltegravir N=34
- Elvitegravir N=15

Protease Inhibitor
N=87
- Darunavir/r N=54
- Atazanavir/r N=28
- Lopinavir/r N=8

• Backbone: 78% tenofovir disoproxil fumarate/emtricitabine
% discontinuation of first line ART by week 12

Reason for discontinuation

<table>
<thead>
<tr>
<th></th>
<th>INSTI (N=23)</th>
<th>PI (N=14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Side effects N (%)</td>
<td>5 (21.7)</td>
<td>4 (28.6)</td>
</tr>
<tr>
<td>Patient wishes N (%)</td>
<td>0 (0)</td>
<td>1 (7.1)</td>
</tr>
<tr>
<td>Non-compliance N (%)</td>
<td>1 (4.4)</td>
<td>1 (7.1)</td>
</tr>
<tr>
<td>Other N (%)</td>
<td>0 (0)</td>
<td>2 (14.3)</td>
</tr>
<tr>
<td>Not documented N (%)</td>
<td>17 (73.9)</td>
<td>6 (42.9)</td>
</tr>
</tbody>
</table>

P=0.76
% discontinuation of first line ART by week 48

<table>
<thead>
<tr>
<th>Reason for discontinuation</th>
<th>INSTI (N=42)</th>
<th>PI (N=33)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Side effects N (%)</td>
<td>3 (7.1)</td>
<td>6 (18.2)</td>
</tr>
<tr>
<td>Patient wishes N (%)</td>
<td>3 (7.1)</td>
<td>3 (9.1)</td>
</tr>
<tr>
<td>Non-compliance N (%)</td>
<td>2 (4.8)</td>
<td>1 (3.0)</td>
</tr>
<tr>
<td>Comorbidity N (%)</td>
<td>7 (16.7)</td>
<td>1 (3.0)</td>
</tr>
<tr>
<td>Treatment failure N (%)</td>
<td>4 (9.5)</td>
<td>3 (9.1)</td>
</tr>
<tr>
<td>Drug interactions N (%)</td>
<td>0 (0)</td>
<td>2 (6.1)</td>
</tr>
<tr>
<td>Other N (%)</td>
<td>1 (2.4)</td>
<td>1 (3.0)</td>
</tr>
<tr>
<td>Not documented N (%)</td>
<td>22 (52.4)</td>
<td>16 (48.5)</td>
</tr>
</tbody>
</table>

P=0.52

% discontinuation of Antiretroviral regimen:

- INSTI: 39.3
- PI: 44.0
Virological outcomes at week 48

% HIV viral load <50 copies/ml

Week 12
- INSTI: 63.5
- PI: 42.9

Week 48
- INSTI: 86.1
- PI: 81.1

P=0.009 (between Week 12 and Week 48 for INSTI)

P=0.36 (between Week 12 and Week 48 for PI)
# Clinical outcomes at week 48

<table>
<thead>
<tr>
<th>Outcome at 48 weeks</th>
<th>INSTI</th>
<th>PI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD4 cell count, median (IQR)</td>
<td>360 (243.5, 461)</td>
<td>315 (234, 461)</td>
<td>0.41</td>
</tr>
<tr>
<td>CD4:CD8 ratio, median (IQR)</td>
<td>0.33 (0.24, 0.43)</td>
<td>0.31 (0.2, 0.47)</td>
<td>0.68</td>
</tr>
<tr>
<td>HIV VL&lt;50 cps/ml*, N (%)</td>
<td>93 (86.1)</td>
<td>60 (81.1)</td>
<td>0.36</td>
</tr>
<tr>
<td>Adverse events, N (%)</td>
<td>30 (24.8)</td>
<td>27 (32.9)</td>
<td>0.21</td>
</tr>
<tr>
<td>Category B diagnosis, N (%)</td>
<td>11 (8.6)</td>
<td>3 (3.5)</td>
<td>0.17</td>
</tr>
<tr>
<td>Category C diagnosis, N (%)</td>
<td>12 (9.4)</td>
<td>6 (6.9)</td>
<td>0.52</td>
</tr>
<tr>
<td>Mortality, N (%)</td>
<td>3¹ (2.2)</td>
<td>3² (3.5)</td>
<td>0.45</td>
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</tbody>
</table>

¹ Multifocal leukoencephalopathy, non-AIDS defining cause of death (1 cause death not reported)
² PCP + Kaposi’s sarcoma, PCP + Kaposi’s sarcoma + CMV, Kaposi + primary effusion lymphoma
*N=167
Adverse events

- Jaundice
- Sleep disorder
- Exanthema
- Pruritus
- Dizziness
- Joint pain
- Fatigue
- Pancreatitis
- Kidney failure
- Gastrointestinal intolerances

Total number of reported adverse events

Legend:
- PI
- INSTI
Limitations

• Many limitations of retrospective studies
  • Reliant on documentation
  • Loss to follow up
  • Confounders

• No information on factors that led to choice of 3rd agent (for example drug interactions, resistance testing, need for immediate treatment)

• No data specifically looking at IRIS
Conclusion

• No significant differences in discontinuation rates and virological response at week 48

• Choice between INSTI and PI can be made on an individual basis

• Future research will focus on the identifying factors associated with regimen selection in this cohort
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