Background

The New Era Study is an ongoing, prospective 7-year clinical trial initiated in 2009 using multi drug class (MDC) HAART in patients (pts) with primary HIV infection (PHI group) and in pts with chronic HIV-infection on suppressive PI-based HAART without prior virological failure (CHI group).

The primary objectives of the study were to halt residual viral replication in plasma and to achieve depletion of cell-associated HIV-DNA (‘proval’ DNA) as a step towards (functional) HIV cure.

Methods

Target sample size and major study eligibility criteria

- All patients (N=40) : CD4 nadir >200/μl, no history of AIDS, CRSS tropism
- PHI group (N=20) : Detectable plasma HIV-RNA, s2 Western blot bands
- CHI group (N=20) : Suppressive PI-based HAART for ≥3 years without history of virological failure

Study intervention

- PHI group: 2 NRTI + 1 PI + MVC (Maraviroc) + RAL (Raltegravir)
- CHI group: Intensification of stable HAART (2 NRTI + 1 PI) with MVC + RAL

Primary and secondary outcome measures

- Cell-associated HIV-DNA copies per 10⁶ peripheral mononuclear cells (PBMC), measurement was performed by the French ANRS group.⁵
- Plasma HIV-RNA levels (using standard assays and SCA, single copy assay)
- CD4⁺, CD8⁺, CD4/CD8 ratio, and CD8⁺CD38⁺ cell counts

Here we present virologic and immunologic outcomes after 24 months.

Statistical Analyses

- For comparing median values between groups, the Mann Whitney U test was used; the Wilcoxon signed-rank test was used to compared paired data. For comparing frequencies, the Fisher’s Exact test was used.
- The level of significance was p ≤0.05 (n.s. = not significant).

Results

Study population

- In total, 20 CHI and 22 PHI pts were included.
- PHI pts were started on MDC HAART within ≤6 weeks after HIV diagnosis. Western blot was negative in 12 PHI pts.

Table 1: Baseline characteristics

<table>
<thead>
<tr>
<th>Units</th>
<th>PHI group (N=22)</th>
<th>PHI group (N=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female gender</td>
<td>N, %</td>
<td>6, 30.0</td>
</tr>
<tr>
<td>Age</td>
<td>years</td>
<td>41.3 (28.0-61.2)</td>
</tr>
<tr>
<td>HIV-RNA</td>
<td>cop/mL</td>
<td>0.2 (0.1-12)</td>
</tr>
<tr>
<td>Proval-HIV-DNA</td>
<td>log cop/10⁶ PBMC</td>
<td>2.5 (1.8-3.0)</td>
</tr>
<tr>
<td>CD4+ cells</td>
<td>cells/μl</td>
<td>763 (400-1370)</td>
</tr>
<tr>
<td>CD4/CD8 ratio</td>
<td></td>
<td>0.9 (0.4-2.0)</td>
</tr>
<tr>
<td>CD8⁺CD38⁺</td>
<td>cell count %</td>
<td>14 (2-33)</td>
</tr>
</tbody>
</table>

Table 2: Antiretroviral combinations at baseline

<table>
<thead>
<tr>
<th>RVL + MVC plus NRTI... plus PI...</th>
<th>PHI group (N=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TDF + FTC + LPV/r</td>
<td>4</td>
</tr>
<tr>
<td>TDF + FTC + DRV/r</td>
<td>2</td>
</tr>
<tr>
<td>TDF + FTC + ATV/r</td>
<td>4</td>
</tr>
<tr>
<td>TDF + ATV + ETV</td>
<td>4</td>
</tr>
<tr>
<td>Other NRTI/PI combination partners</td>
<td>7</td>
</tr>
</tbody>
</table>

References


Immunologic response

After 24 months, significantly more PHI pts had a CD4⁺CD8⁺ ratio ≥1 (90% vs. 35%, p=0.001; Table 3). Proportions of CD8⁺CD38⁺ cells were comparable between groups (13% vs. 13%, however absolute CD8⁺CD38⁺ counts were still different (PHI vs. CHR pts: 72±1 vs. 133±µ, p=0.03).

Discontinuations and patient safety

By month 24, there were two study discontinuations in the PHI group. Reasons for discontinuation were ‘patient’s wish’ (n=1) and ‘virological failure’ (VF) (n=1), i.e. confirmed HIV-RNA >200 cop/mL after month 6, which was not attributed to a switch of viral tropism or the detection of resistance mutations. Based on the annual study reports, the independent Data Safety Monitoring Board (DSMB) did not raise concerns about the safety of the study.

Conclusions

- PHI patients receiving early treatment with multi drug class HAART achieved lower cell-associated HIV-DNA levels and a better immune reconstitution than chronically infected patients on intensified long term suppressive HAART.
- A study amendment implementing new strategies aiming to achieve post-treatment control in this selective patient group is planned.

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Participating Centers

- ICH Study Center (PD Dr. C. Hoffmann, Dr. K. Schwabe, Prof. Dr. H. Stellbrink, et al.), Hamburg; S. Hagemeyer: Private practice, Dr. W. Becker, Dr. R. Pauli, Munich; Prof. Dr. Christian Schulze; Munich; and MVZ Karlsruhe - HIV Research and Clinical Care Centre (Prof. Dr. C. Ohlenbusch, Dr. J. Giglia-Geudde, Dr. H. Jaeger), Munich, all Germany.

Contributors: S. Palmer for the single-copy HIV-RNA assay; V. Avettand-Fenoël for proviral HIV-DNA measurement.