The VMVN Study:
Virological Monitoring in Vietnam

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Routine VL (RVL) monitoring is recommended for patients on ART. Randomized clinical trials (in Uganda, Zambia, and Thailand) failed to demonstrate a benefit of VL monitoring in clinical outcomes. We conducted a clinical trial of RVL monitoring vs Targeted VL monitoring in a patient population starting ART in Vietnam.

**Hypothesis:** RVL monitoring would result in higher rates of virological suppression and decreased incidence of death or new or recurrent AIDS-defining illnesses within 3 years.
Methods

• Prospective, randomized controlled trial of RVL monitoring every 6 months versus standard targeted VL (TVL, VL testing to confirm suspected treatment failure) in patients starting ART between 4/2011 and 4/2014.
• 647 subjects initiating ART were randomized to either RVL monitoring (n=305) or TVL monitoring (n=342) and followed for 3 years.
• Both arms were management according to national guidelines; only difference was VL monitoring.
• Primary endpoints were death or WHO clinical stage IV events after 6 months of ART and rate of virological suppression at 3 years.
• Proportions were calculated and compared using Chi-squared test or Fisher’s exact test.
• Survival analysis was used to compare time to occurrence of death or stage IV event between two groups.
## Select Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Intervention N (%)</th>
<th>Control N (%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total</strong></td>
<td>305 (47.1%)</td>
<td>342 (52.9%)</td>
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<tr>
<td>Male Gender</td>
<td>190 (62.3%)</td>
<td>217 (63.4%)</td>
<td>0.761</td>
</tr>
<tr>
<td>Mean Age</td>
<td>34.9 +/- 8.0</td>
<td>35.2 +/- 9.3</td>
<td>0.622</td>
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<tr>
<td><strong>Clinical Stage</strong></td>
<td></td>
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<tr>
<td>I</td>
<td>134 (44.0%)</td>
<td>166 (48.5%)</td>
<td>0.415</td>
</tr>
<tr>
<td>II</td>
<td>26 (8.5%)</td>
<td>22 (6.4%)</td>
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<tr>
<td>III</td>
<td>37 (12.1%)</td>
<td>32 (9.4%)</td>
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<tr>
<td>IV</td>
<td>108 (35.4%)</td>
<td>122 (35.7%)</td>
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<tr>
<td><strong>CD4 at enrollment</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>&lt; 100</td>
<td>140 (45.9%)</td>
<td>161 (47.1%)</td>
<td>0.490</td>
</tr>
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<td>101 - 250</td>
<td>73 (23.9%)</td>
<td>69 (20.2%)</td>
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<tr>
<td>&gt; 250</td>
<td>92 (30.2%)</td>
<td>112 (32.7%)</td>
<td></td>
</tr>
<tr>
<td><strong>Prior ART</strong></td>
<td>10 (3.3%)</td>
<td>16 (4.7%)</td>
<td>0.366</td>
</tr>
</tbody>
</table>

## Study Outcomes Summary

### TVL (n=342)
- **Deaths:** 26 (7.6%)
- **OIs:** 6 (1.8%)
- **Others:** 46 (13.4%)
  - Transferred: 26
  - Stopped ART: 15
  - LTFU: 3
  - Withdrew: 2
- **No event on ART:** 264 (77.2%)

### RVL (n=305)
- **Deaths:** 24 (7.9%)
- **OIs:** 5 (1.6%)
- **Others:** 34 (11.2%)
  - Transferred: 21
  - Stopped ART: 8
  - LTFU: 4
  - Withdrew: 1
- **No event on ART:** 242 (79.3%)

### VL
- **Completed (alive):** 270 (79.0%)
  - VL < 4000 cps/ml: 267 (98.9%)
  - VL ≥ 4000 cps/ml: 3 (1.1%)
- **Completed (alive):** 247 (80.9%)
  - VL < 4000 cps/ml: 240 (97.2%)
  - VL ≥ 4000 cps/ml: 7 (2.8%)
Among patients on ART at 6-mo, death or stage IV event occurred in 3.6% of RVL and 3.9% of TVL (p=0.823).

Survival analysis showed no significant difference between the two groups (p=0.825).

44% of study events (death, lost to follow up, withdrawal, or new or recurrent stage IV event) and 68% of deaths occurred within the first 6-months of ART.

There was no difference in switching to 2nd-line ART (3.6% in RVL; 2.1% in TVL, p=.228).

Trends of CD4 recovery were similar in both arms.

### Proportion of patients with VL <400 cps/ml or < 1,000 cps/ml at 36 months (n=517)

<table>
<thead>
<tr>
<th>Cut off (cps/ml)</th>
<th>Intervention N (%)</th>
<th>Control N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total</strong></td>
<td>247 (100%)</td>
<td>270 (100%)</td>
</tr>
<tr>
<td>1,000 cps/ml</td>
<td>&lt;1,000</td>
<td>242 (98.0%)</td>
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<tr>
<td></td>
<td>≥ 1,000</td>
<td>5 (2.0%)</td>
</tr>
<tr>
<td>400 cps/ml</td>
<td>&lt;400</td>
<td>240 (97.2%)</td>
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<tr>
<td></td>
<td>≥400</td>
<td>7 (2.8%)</td>
</tr>
<tr>
<td>ITT Analysis*</td>
<td>&lt;400</td>
<td>240 (78.7%)</td>
</tr>
<tr>
<td>400 cps/ml</td>
<td>≥400</td>
<td>65 (21.3%)</td>
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</tbody>
</table>

* ITT Analysis: Those without a VL at 36 mo of ART (deaths, LTFU) were assigned as non VL suppression.
Conclusions

- RVL monitoring every 6 months did not improve clinical outcomes compared to a TVL strategy after 3 years of follow-up.
- We found no difference in death, stage IV events, virological failure, CD4 recovery, or 2\textsuperscript{nd} line switching in patients with RVL monitoring compared to those monitored with a TVL strategy.
- Most deaths occurred within the first 6-months of ART suggesting that earlier HIV diagnosis, use of enhanced OI prophylaxis, and rapid initiation of ART may be needed to improve treatment outcomes in this group.
- Overall, there were high rates of viral suppression and relatively few adverse outcomes among patients alive and on ART after 6 months.
- These data suggest that the VL monitoring strategy may have less impact on patient outcomes compared to efforts to reduce early mortality and improve ART retention.