Factors Associated With Weight Loss or Stable Weight After Continuing or Switching to a Doravirine-Based Regimen

Background
Weight loss has become an important aspect in the management of HIV.

- Use of reverse transcriptase inhibitors (RTIs) and protease inhibitors (PIs) is associated with increased weight loss
- Risk factors for weight gain with RTI therapy include female sex, lower CD4+ T-cell count, and disease duration
- Weight gain can have numerous consequences, including development of cardiovascular disease, diabetes mellitus, dyslipidemia, and other metabolic disorders

- Minimal weight gain has been observed with doravirine (DOR)-based regimens as first-line therapy (Table 1).

Objective
- To characterize predictive factors of participants who maintained or lost weight after continuing or switching to a DOR-based regimen in the DRIVE-FORWARD, DRIVE-AHEAD, and DRIVE-SHIFT phase 3 clinical trials.

Methods
Study design
- DRIVE-FORWARD (NCT02772078) and DRIVE-AHEAD (NCT02784449) were randomized, double-blind, active-controlled, double-dummy placebo-controlled trials in treatment-naive participants (~70%) who were randomized to and continued their DOR regimen in the extension phase in DRIVE-FORWARD and DRIVE-AHEAD, and the DOR continued group (Figure 1).

- DRIVE-SHIFT (NCT03473006) was a randomized, open-label, active-controlled, noninferiority study of adults who were virologically suppressed and on a stable antiretroviral regimen for ≥50 years.

Participants were randomly assigned to a DOR regimen (DOR with 2 nucleos(t)ide reverse transcriptase inhibitors [NRTIs]) in DRIVE-FORWARD or DOR/TDF in DRIVE-AHEAD or the respective comparator regimen (placebo-based arm in DRIVE [with 2 NRTIs] or efavirenz + TDF; FTC/TDF, respectively) for 96 weeks of double-blind treatment.

- Both groups continued DOR-based regimen for 96 weeks.

- A comparison of DOR-based phase 3 trials showed that participants who switched to DOR-based therapy had greater weight loss at week 96 compared to week 24.

Table 1. Participant characteristics by weight change group, DRIVE-FORWARD and DRIVE-AHEAD

<table>
<thead>
<tr>
<th>Weight Change Group</th>
<th>Number (%)</th>
<th>Baseline Median (Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lost weight</td>
<td>11 (9.7)</td>
<td>24.4 (14.9-48.0)</td>
</tr>
<tr>
<td>Stable weight</td>
<td>124 (51.0)</td>
<td>33.0 (19-67)</td>
</tr>
<tr>
<td>Gained weight</td>
<td>29 (40.8)</td>
<td>30.5 (18-69)</td>
</tr>
</tbody>
</table>

Results

DOR continued group: DRIVE-FORWARD (DOR + 2 NRTIs) and DRIVE-AHEAD (DOR/TDF).

- The combined DOR continued groups consisted of 466 participants: 55.1% lost weight, 30.5% (55.7%) had stable weight, and 10.6% (37.3%) had gained weight. 3

- No statistical significance was noted between the weight change categories; the weight loss group had a higher proportion of females (56.5%) compared to the stable weight group (40.2%) (Table 1).

Table 2. Participant characteristics by weight change group, DRIVE-SHIFT

<table>
<thead>
<tr>
<th>Weight Change Group</th>
<th>Number (%)</th>
<th>Baseline Median (Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lost weight</td>
<td>10 (9.4)</td>
<td>28.8 (15.6-46.2)</td>
</tr>
<tr>
<td>Stable weight</td>
<td>31 (22.1)</td>
<td>34.0 (17.5-64.0)</td>
</tr>
<tr>
<td>Gained weight</td>
<td>1 (1.4)</td>
<td>37.0 (20.0-50.0)</td>
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Conclusions

- Weight loss (5% or stable weight) was observed in the majority of participants who continued DOR or switched to DOR in the DRIVE-FORWARD, DRIVE-AHEAD, and DRIVE-SHIFT phase 3 trials.

- Treatment-naive participants who were randomly assigned to and continued their DOR regimen in the extension phase in DRIVE-FORWARD and DRIVE-AHEAD, none of the factors examined had a significant association with weight loss or stable weight (Table 1).

- Participants were more likely to have weight loss at 144 weeks if they immediately switched to DOR/3TC/TDF (p < 0.05) than those who continued DOR (p > 0.05) (Figure 4A, Table 3).

- Non-Black females were more likely to have weight loss than Black non-Malaysian and Black females after switching to DOR (Table 3).

- Weight loss was also more likely to occur in participants who switched from PI in those who remained on NNRTI (Figure 4A).

- Stable weight was more likely to occur in participants aged ≥50 years (Table 3).

Figure 4. Analysis of factors impacting the probability of (A) weight loss or (B) stable weight versus weight gain from week 24 to week 144, DRIVE-SHIFT

<table>
<thead>
<tr>
<th>Timepoint</th>
<th>Odds Ratio (95% CI)</th>
</tr>
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<tbody>
<tr>
<td>Week 96</td>
<td>0.892 (0.730-1.106)</td>
</tr>
<tr>
<td>Week 144</td>
<td>0.793 (0.644-0.979)</td>
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</table>

Acknowledgments
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References

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