IMPORTANT SEX DIFFERENCES IN OUTCOMES FOR INDIVIDUALS PRESENTING FOR THIRD LINE ART

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Introduction

Real-time HIV drug resistance results, treatment history and, if available, any historical resistance results, were used to assign participants to one of four treatment cohorts. Ritonavir boosting was part of every cohort.

This analysis combined cohorts B, C and D (BCD) as all three involved any historical resistance results, were used to assign participants to one of individual cohorts for meaningful analysis. Sex differences were evaluated using logistic regression and proportional hazards models adjusted for cohort (A or BCD), and were further evaluated in multivariate models adjusted for cohort, baseline age, weight, HIV-1 RNA and CD4 count, and country of enrollment.

Methods

Important sex differences in ART drug exposure and tolerability that lead to treatment discontinuation and unfavorable outcomes for women have been reported.

- Ritonavir’s clearance is decreased in women leading to increased levels.
- Nevirapine is associated with a fatal hepatitis in women.

Women have been reported to lead to treatment discontinuation and unfavorable outcomes for individuals experiencing virologic failure on their second regimen. This analysis evaluated differences in safety and tolerability between men and women taking third-line ART regimens.

AS288 was an open-label phase IV, prospective intervention study strategy at 19 urban sites in 10 countries1 evaluating third-line therapy options for individuals experiencing virologic failure on their second regimen. This analysis evaluated differences in safety and tolerability between men and women taking third-line ART regimens.

Key inclusion/exclusion criteria:

- HIV-infected adults age ≥18 years.
- Two prior ARV regimens, including one NNRTI-based regimen replaced with a PI-based regimen; with the change due to toxicity or failure.
- Current receipt of a PI-based regimen for a minimum of 24 weeks prior to screening, with confirmation of virologic failure at screening.

Results

Table displays the N(%) and results from models assessing each of the outcomes and groups specified.

<table>
<thead>
<tr>
<th>Sex</th>
<th>Grade 3 signs and symptoms (n=545)</th>
<th>Grade 3 laboratory abnormalities (n=545)</th>
<th>Grade 3 diagnoses (n=545)</th>
<th>Serious Adverse Events (n=545)</th>
<th>AIDS-defining events (n=545)</th>
<th>Deaths (n=545)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>12 (4%)</td>
<td>59 (22%)</td>
<td>26 (20%)</td>
<td>40 (14%)</td>
<td>12 (4%)</td>
<td>1 (4%)</td>
</tr>
<tr>
<td>Female</td>
<td>60 (17%)</td>
<td>80 (22%)</td>
<td>56 (22%)</td>
<td>20 (16%)</td>
<td>16 (5%)</td>
<td>12 (5%)</td>
</tr>
<tr>
<td>Difference</td>
<td>OR 1.87 (1.17, 2.99)</td>
<td>OR 1.47 (1.04, 2.06)</td>
<td>OR 1.87 (1.05, 3.36)</td>
<td>OR 1.23 (0.94, 1.81)</td>
<td>OR 1.48 (1.04, 2.09)</td>
<td>OR 0.97 (0.42, 2.21)</td>
</tr>
</tbody>
</table>

‡ Multivariate proportional/hazards models were not fitted for some outcome measures with too few events

Table above displays the cumulative incidence function for the Grade ≥3 sign by outcome and Cohort Group and Sex.

Discussion

- Women failed therapy without resistance on a regimen containing a boosted PI more commonly than men.
- Women experienced grade ≥3 signs and symptoms more frequently than men without concomitant diagnoses or laboratory values.
- Subjective tolerability may be different for women and men, and interventions designed to improve tolerability may improve adherence and clinical outcomes.

Implications

- Women experienced grade ≥3 signs and symptoms more frequently than men without concomitant diagnoses or laboratory values.
- Subjective tolerability may be different for women and men, and interventions designed to improve tolerability may improve adherence and clinical outcomes.

References