Discontinuation of dolutegravir containing regimens due to adverse reactions: real world data

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BACKGROUND
• We have observed a number of people living with HIV (PLWH) discontinuing dolutegravir (DTG) containing regimens due to adverse drug reactions (ADRs).
• Rates of discontinuation in phase III trials were low (2%) but post-marketing data show higher rates, particularly due to central nervous system (CNS) effects
• A previous cohort study has found CNS ADRs to be more frequent in females, older patients and when DTG is co-administered with abacavir.
• We present real world data of DTG use in our large, urban cohort of 10,371 patients.

OBJECTIVES
To assess:
• ADR-related discontinuation rates
• Nature of ADRs
• Influence of NRTI backbone
• Whether stopping DTG led to resolution of symptoms

METHODS
• All PLWH ever prescribed DTG from Apr 2011 to Sept 2018 were identified using electronic patient records
• Data was extracted as follows: basic demographics, ARV combination details including ARV regimen prescribed DTG from time of starting DTG and type of DTG regimen, discontinuation of DTG and type of DTG regimen, discontinuation of DTG and gender

RESULTS
• 2543 patients were prescribed a DTG-containing regimen over the 7.5 year period

Figure 1: Baseline demographics (n=2543)

<table>
<thead>
<tr>
<th>Median age</th>
<th>% male (n)</th>
<th>% White</th>
<th>Median CD4 at time of starting (cells/mm³)</th>
</tr>
</thead>
<tbody>
<tr>
<td>44</td>
<td>91</td>
<td>75</td>
<td>651</td>
</tr>
</tbody>
</table>

Figure 2: Demographics of PLWH who discontinued DTG (n=308)

<table>
<thead>
<tr>
<th>Median age</th>
<th>% male</th>
<th>% White</th>
<th>Median CD4 at time of discontinuation (cells/mm³)</th>
</tr>
</thead>
<tbody>
<tr>
<td>44</td>
<td>89</td>
<td>79</td>
<td>674</td>
</tr>
</tbody>
</table>

• 308 patients discontinued DTG due to ADRs
• Overall ADR related discontination rate = 12% (308)
• 69 patients stopped DTG due to other reasons and were thus excluded from the analysis
• Median time to discontinuation was 132 days (4.4 months)

• There was an association between DTG discontinuation and type of DTG regimen prescribed

Discontinuation rate: Triumeq (Abacavir/Lamivudine/Dolutegravir) 13.9% (255/1831) vs. other DTG containing regimens 7.4% (53/712); p-value <0.001

• Figure 3: Discontinuations by ARV regimen

DISCUSSION
We observed considerably higher rates of ADR-related discontinuation than those reported in several RCTs
• This could be due to higher rates of mental health issues and recreational drug use in real-world cohorts
• The higher rate of discontinuation in women, especially if older, has been demonstrated in a previous study
• This requires further work to assess significance, and analysis of DTG pharmacokinetics in these patient groups
• Our data reinforces the need for inclusion of underrepresented populations in clinical trials
• As Triumeq was associated with higher rates of discontinuation compared with other regimens, further work is needed to directly compare tolerability of DTG when coupled with different NRTI backbones

LIMITATIONS
• The study did not capture patients who experienced side effects but persevered with treatment
• Resolution of symptoms post-switch was difficult to assess as patients switching off DTG may also have switched other agents in their ARV regimen
• Due to retrospective design, it was not possible to account for confounding factors (e.g. persisting CNS effects in patients switching off efavirenz, psychiatric history, co-medications)

REFERENCES