Long-Term Use of Darunavir/r QD Containing Regimens in Daily Practice in Europe: Retrospective Observational Cohort Data of 1,701 HIV-Patients

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Background

- DRV/r QD, in combination with other ARVs, is recommended as a first-line option for HIV-infected patients in different guidelines
- Once daily DRV/r (800mg/100mg) is available and reimbursed in Belgium for the treatment of HIV-infected patients since 2010
- DRV/r QD showed good efficacy and tolerability in treatment-naïve patients in a long-term clinical trial (192 week ARTENMS study)1 as well as in treatment-experienced patients with no DRV resistance-associated mutations (ODN study)2
- However, long-term data in real life clinical settings are limited

Belgian Cohort

Data from 1,701 HIV-infected patients were collected and analyzed. The majority of patients were male (66.5%), from Caucasian origin (48.6%), and had a mean age of 42.9 years. 33.1% were treatment-naïve (44.2% with baseline VL ≥1000 copies/mL) and 66.9% were ART-experienced (of which 48.5% were suppressed with VL <50 copies/mL).

Methods

Objectives

- Observation, non-interventional, non-comparative, retrospective, multicenter cohort study
- Data were collected from the existing databases on HIV-infected patients of 8 AIDS Reference Centers in Belgium

Inclusion Criteria:

- HIV-1 infected adults ≥18 years (treatment-naïve or experienced patients)
- Duration of DRV/r QD treatment in various regimes from 01/2010 to 01/2014, with a minimum follow-up of 6 months

Endpoints:

- Primary Endpoints: Time to discontinuation of DRV/r QD treatment and reasons for discontinuation of DRV/r QD containing regimens (using D.A. classification)3
- Secondary Endpoints: Virological suppression (viral load (VL) <50 copies/mL), change from baseline of CD4, lipids and kidney function

Results

Baseline Characteristics

Table 1: Baseline characteristics.

<table>
<thead>
<tr>
<th>Trait</th>
<th>All</th>
<th>NRTI</th>
<th>NNRTI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>27.1 (8.5)</td>
<td>26.5 (8.4)</td>
<td>27.4 (8.7)</td>
</tr>
<tr>
<td>Gender, %</td>
<td>Female 56.2%</td>
<td>53.0%</td>
<td>61.3%</td>
</tr>
<tr>
<td>Race, %</td>
<td>White 82.6%</td>
<td>82.3%</td>
<td>83.6%</td>
</tr>
<tr>
<td>CD4 T cell count, cells/mm³</td>
<td>518.0 (260)</td>
<td>551.0 (268)</td>
<td>450.0 (247)</td>
</tr>
<tr>
<td>baseline VL, copies/mL</td>
<td>≥50  (95% CI) 80%–100%</td>
<td>≥50  (95% CI) 70%–100%</td>
<td>≥50  (95% CI) 50%–100%</td>
</tr>
</tbody>
</table>

Probability to remain on treatment overall

Table 2: Probability to remain on treatment (%).

Overall, 1,242 patients (73.0%) remained on DRV/r QD treatment as part of their ART during a median follow-up of 2.45 years. The probability to remain on treatment was 87.0% for the first year and 78.9% for the second year (Table 2).

Time to treatment discontinuation

The time to DRV/r treatment discontinuation, defined as the time from first treatment initiation until the end of treatment, is shown in Figure 1 for naïve patients and in Figure 2 for experienced patients.

Reasons for treatment discontinuation

The main reasons for treatment discontinuation were treatment simplification (6.7%), adverse events (6.9%, of which 4.0% were from the GI tract), and patients or physicians decide (3.5%), with small differences in treatment discontinuation between naïve and experienced patients. Discontinuation due to virological failure was only noted in 13 patients (0.8%). A reason for discontinuation was missing in 53 patients (3.1%).

Secondary Endpoints

Probability to maintain virological suppression

The vast majority of the 1504 subjects, which responded to treatment (VL <500 copies/mL), remained virologically suppressed. At the end of the follow-up period, 81% of the patients maintained virological suppression (Figure 2).

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References

2. Caillot F et al. AIDS 2011, PMID: 21436124

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Summary and Discussion

- This retrospective cohort analysis summarizes the long-term outcomes and experience with once-daily DRV/r-containing regimens in a diverse patient population (treatment-naïve vs. experienced) in Belgium
- Despite the general limitations associated with observational retrospective studies, the results from this study confirm previous trials’ outcomes and show the robust long-term efficacy and good tolerability of DRV/r QD in real life settings
- The study showed that the DRV/r QD-based regimens have a documented virological efficacy and a good tolerability with no substantial differences between naïve and experienced patients
- The rate of discontinuation of DRV/r QD in daily practice was low, and rarely due to lack of efficacy. No unexpected adverse events (AEs), and predominantly gastrointestinal (GI)-based AEs were reported

Detailed reasons for treatment discontinuation are shown in Table 3:

Table 3: Reasons for treatment discontination.

- Discontinuation rates (%) were calculated using the Kaplan-Meier method. Rates were calculated for all patients and for naïve patients (stratified by BL VL ≥50 copies/mL).
- Overall, 3.2% of patients discontinued treatment due to adverse events (6.9%, of which 4.0% were from the GI tract), and patients or physicians decide (3.5%), with small differences in treatment discontinuation between naïve and experienced patients.
- Discontinuation due to virological failure was only noted in 13 patients (0.8%). A reason for discontinuation was missing in 53 patients (3.1%).

Secondary Endpoints

Infection

- CD4 count increased by an average of 164.4 cells/mm³ from baseline to end of follow-up

Lipids

- TG, Tchol, HDL-C and LDL-C remained stable throughout the observation period

Renal parameters

- Renal parameters (eGFR) remained stable throughout the observation period

No significant differences were observed between BL VL < or ≥1000 copies/mL in naive patients (p=0.3129 log-rank test) and BL VL < or ≥250 copies/mL in experienced patients (p=0.3859 log-rank test). There were also no differences observed when stratified by gender, race, NRTI backbone or baseline CD4 count.

Secondary Endpoints

- Immunological response
- Lipids
- Renal parameters
- Adverse events (AEs), Toxicity
- Drug interaction
- Adherence
- Pregnancy
- Virological failure
- Laboratory
- Definite
- Esr
- Other
- Missing

No patients were lost to follow-up, 81% of the patients maintained virological suppression (Figure 2).

Figure 1. Time to DRV/r treatment discontinuation (Kaplan-Meier) for all naïve patients (stratified by BL VL ≥500 copies/mL and ≤500 copies/mL) and all experienced patients (stratified by BL VL <500 copies/mL and ≥500 copies/mL) related to DRV/r QD

Figure 2. Probability of maintaining virological suppression over time (Kaplan-Meier) for all patients (N=1504) and patients indicated as DRV/r QD. Loss of virological response was defined as viral load >50 copies/mL on two consecutive occasions.