



Clinical outcomes associated with once daily ritonavir-boosted darunavir in HIV infected patients harboring single or multi-class resistant virus

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Background

Resistance to antiretrovirals may be transmitted or may also be acquired due to poor adherence. M184V/I, a common resistance mutation, can limit the availability of daily regimens with low pill burdens. Limited data exist on the use of a potent boosted protease inhibitor in combination with <2 active nucleotide reverse transcriptase inhibitors without the use of additional classes of ART in treatment experienced patients with background resistance. We evaluated the clinical outcomes in HIV-infected patients harboring single/multi-class resistant virus (M184V/I ± NRTI ± PI and/or NNRTI resistance) treated with once daily darunavir/ritonavir (DRV/r) plus tenofovir disoproxil fumarate/emtricitabine (TDF/FTC).

Methods

Objective

- To assess virologic and clinical outcomes in HIV-1-infected patients prescribed once daily ritonavir-boosted darunavir with tenofovir disoproxil fumarate (TDF)/emtricitabine while harboring single or multi-class resistant virus including an M184V/I mutation.

Study Design

- Retrospective chart review of HIV-infected patients receiving care at the University of Toledo Medical Center (UTMC) Ryan White Clinic. The study was approved by the UTMC Institutional Review Board.

Setting and Population

- UTMC Ryan White Clinic, an outpatient clinic providing care to individuals living with HIV in Northwest Ohio.

Inclusion Criteria:

- HIV-1 positive
- ≥18 years of age
- Patient enrolled in the UTMC Ryan White Clinic between 1/2008 and 12/2015.
- Prescribed darunavir 800 mg/ritonavir 100 mg plus TDF/emtricitabine administered once daily for a minimum of 24 weeks
- M184V/I mutation by genotype/phenotype identified prior to start of study regimen

Exclusion Criteria:

- HIV-1 negative
- <18 years of age
- Use of antiretrovirals other than darunavir, ritonavir, TDF, and emtricitabine
- High level resistance to darunavir or tenofovir (interpretation based on Stanford HIV Drug Resistance Database Genotypic Resistance Interpretation algorithm)

Methods

Data Collection

- Data collected over the study period included the following:
 - Demographics: age, gender, prior ART, baseline antiretroviral resistance mutations, adherence (self-reported), baseline CD4 counts and viral loads, and reason for discontinuation of a prescribed regimen

Endpoints
Achieve VL < 40 copies/ml
Achieve VL < 200 copies/ml
<i>Virologic Resuppression</i> defined as viral load >200 copies/ml after achievement of viral suppression followed by return of viral load to undetectable levels in subsequent assays
<i>Virologic Rebound</i> defined as achievement of viral load < 200 copies/ml but with rebound to > 200 copies/ml on successive viral loads and last available viral load
<i>Virologic Failure</i> defined as failure to achieve a viral load < 200 copies/ml
Acquisition of additional resistance mutations

Results

Months on therapy	1-6	7-12	13-18	19-24
N (%) with VL <40 cp/ml	17/29 (59%)	15/27 (56%)	16/25 (64%)	15/21 (71%)
N (%) with VL <200 cp/ml	22/29 (76%)	19/27 (70%)	20/25 (80%)	17/21 (81%)
Number with no follow-up VL drawn during time period	5	6	6	10
Number no longer taking DRV/r plus TDF/FTC	ND	1	3	3

Results (cont.)

- 19/34 (56%) with VL < 40 on last reading
- 25/34 (74%) with VL < 200 on last reading
- 23/34 (68%) achieved < 40 at least once
- 18/23 (78%) achieved and maintained VL < 40 during the remainder of the study period
- 1/34 (3%) had virologic resuppression
- 2/34 (6%) had virologic rebound
- 7/34 (21%) had virologic failure
- 10 subjects were baseline TDF resistance/DRV susceptible
 - 9/10 subjects achieved/maintained VL < 200
 - 7/10 achieved/maintained VL < 40
 - 1/10 experienced virologic rebound
- 2 subjects had baseline TDF and DRV mutations
 - Pt. 8: TDF – Intermediate, DRV – Intermediate
 - Pt. 30: BL – TDF – Low Level, DRV – Low Level
 - Both were virologic failures
 - Follow-up genotypic data showed the following:
 - Pt. 8: TDF-Intermediate; DRV – High Level
 - Pt. 30: TDF – Low Level, DRV - Intermediate
- 4 other subjects had follow up genotypic data available
 - 3 subjects had no new mutations
 - 1 subjects had one new PI mutation which did not change sensitivities (susceptible to DRV)

Conclusion

- Simple, once daily options for patients with poor history of adherence and multiclass resistance have been limited
- TDF/FTC plus RTV-boosted DRV may provide a reasonable option for subjects with baseline M184V resistance
- Adherence remains a key to success
- Additional acquired resistance may occur with continued poor adherence

Disclosure

Authors of this presentation have the following to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation: Nothing to disclose