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Skin Rash Related to Once-daily Boosted Darunavir-Containing Regimens in HIV-infected Patients: Incidence and Associated Factor

Kuan-Yin Lin[1], Chia-Jui Yang[2], Mao-Song Tsai[2], Szu-Min Hsieh[1], Hsin-Yun Sun[1], Wang-Huei Sheng[1], Mao-Yuan Chen[1], Sui-Yuan Chang[1], Chien-Ching Hung[1]

[1]National Taiwan University Hospital and National Taiwan University College of Medicine, Taipei, Taiwan; [2]Far Eastern Memorial Hospital, New Taipei City, Taiwan

Chien-Ching Hung, M.D., Ph.D
E-mail: hcc0401@ntu.edu.tw

Abstract

Objectives: To investigate the incidence of and associated factors with rashes among HIV-infected Taiwanese patients who received once-daily darunavir (DRV) (800 mg) boosted by ritonavir (RTV) (100 mg) plus two NRTIs.

Methods: We reviewed the medical records of all HIV-infected patients who initiated once-daily DRV/RTV-containing regimens in 2012-2013. Information on clinical characteristics, follow-up evaluations, and adverse effects were collected.

Results: During the 20-month study period, 160 patients (mean age, 38.3 years) were enrolled. The mean plasma HIV RNA load (PVL) at switch was 5.26 $\log_{10}$ copies/ml and CD4 count 320 cells/μl. After a median interval of 13 days from starting DRV/RTV-containing regimens, 16 patients (10.0%) developed rashes and 11 (6.9%) had to discontinue DRV/RTV. In multivariate analysis, patients who had a history of rashes related to the previous PI-containing regimens before switch were more likely to experience adverse cutaneous reactions (adjusted odds ratio, 10.22; 95% CI, 2.59-52.63). For those who continued DRV/RTV-containing regimens, the proportion of patients with PVL<200 copies/ml increased from 34.6% at baseline to 91.7% at week 24; and CD4 count increased from 320 to 419 cells/μl.

Conclusions: Once-daily regimens containing DRV/RTV (800/100 mg) is associated with a higher rate of skin rashes that may result in discontinuation in HIV-infected ethnic Chinese. A history of rashes to the preceding PI-containing regimens before switch is associated with an increased risk for DRV/RTV-related rashes.

Introduction

1. Once-daily DRV/RTV (800/100 mg) is the preferred regimen for antiretroviral-naive patients without DRV resistance-associated mutations.
2. The most common adverse effects of DRV/RTV-containing regimens were gastrointestinal adverse effects (6.7% to 16%), skin rash (<3%), and headache, while the rate of adverse effect-related discontinuation ranged from 3% to 8%.
3. We aimed to examine the incidence and risk factors of skin rash to DRV/RTV-containing regimens when DRV/RTV (800/100 mg) was introduced into clinical use in Taiwan in 2012.

Methods

1. Design: retrospective cohort study, 2012-2013.
2. Study sites: two major designated hospitals for HIV care in northern Taiwan
3. Subjects: switched to or initiated once-daily DRV/RTV (800/100 mg)-containing regimens.
4. Primary endpoint: skin rash of any grade

Results

1. 160 patients were enrolled (Table 1).
2. In per-protocol analysis, the proportion of patients with plasma HIV RNA load <200 and <50 copies/ml increased from 34.6% (55/159) and 28.9% (46/159) at baseline, respectively, to 91.7% (55/60) and 73.3% (44/60) at week 24; the median CD4 cell count increased from 320 to 419 cells/μl.
3. The mean duration of DRV/RTV exposure was 39.4 weeks, and 23.8% of the patients developed any grade of adverse effects (Figure 1).
4. In multivariate analysis, the history of rash to the preceding PI-containing regimens before switch was independently associated with DRV/RTV-related rash (Figure 2).
5. During the same study period, 50 patients were switched from nNRTIs to other PIs than DRV/RTV and 3 (6%) experienced skin rash. In univariate logistic regression, the occurrence of skin rash was not affected by previous history of skin rash to other antiretroviral regimens.

Table 1. Baseline demographics and clinical characteristics of 160 patients who initiated DRV/RTV-containing antiretroviral regimens.

Male, n (%)		155 (96.9)
Mean age , years (SD)		38.3 (10.0)
Comorbidity, n (%)		
	Hypertension	10 (6.3)
	Hyperlipidemia	13 (8.1)
	Diabetes mellitus	6 (3.8)
	Chronic kidney disease	3 (1.9)
	Cerebral vascular accident	2 (1.3)
	Chronic hepatitis	27 (16.9)
	Others	19 (11.9)
Disease characteristics		
	Homosexual/bisexual, n (%)	135 (84.4)
	HBV/HCV-coinfected, n (%)	37 (23.1)
	Duration of previous ARV therapy, mean (SD), years	3.3 (4.1)
	PVL at switch, mean (SD), $\log_{10}$ copies/ml	5.26 (5.98)
	CD4 count at switch, median (range) cells/μl	320 (0-1253)
Latest ARV history before initiation of DRV/RTV-containing regimens		
	ARV-naive, n (%)	14 (8.8)
	NNRTIs + 2 NRTIs	64 (40.0)
	PI + 2 NRTIs	75 (46.9)
	Integrase inhibitor + 2 NRTIs	5 (3.1)

Figure 1. Summary of DRV/RTV-related adverse effects in 160 patients

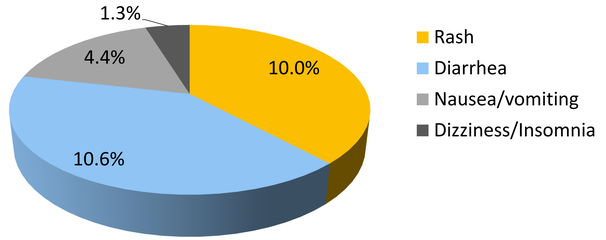
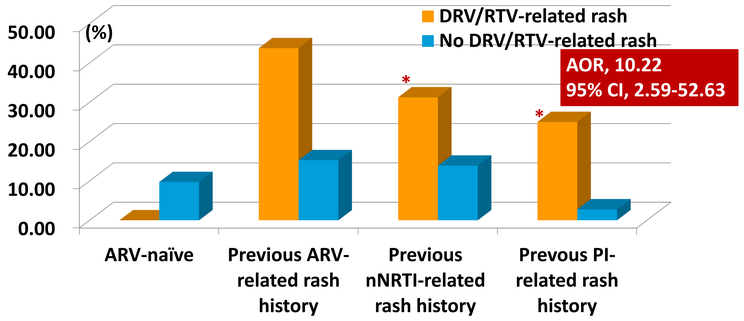


Figure 2. Incidence for DRV/RTV-related skin rash in different groups



Conclusions

1. Once-daily DRV/RTV (800/100 mg)-containing regimens cause a higher rate of rashes in HIV-infected ethnic Chinese.
2. A history of skin rash to the preceding PI-containing regimens before switch to DRV/RTV was independently associated with DRV/RTV-related rash (AOR, 10.22).
3. More pharmacogenetic investigations are warranted.