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HIV/AIDS

Prospective observational study of effectiveness and rate of discontinuation of lead-in dosing of efavirenz-containing regimens in HIV-infected antiretroviral-naive patients in Taiwan

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Objectives: Efavirenz plus 2 NRTIs remains one of the most commonly used antiretroviral (ARV) regimens in most of the developing countries. Efavirenz may cause significant adverse effects, which may increase the risk of virological failure. A previous Spanish study investigating lead-in dosing of efavirenz (200 mg daily for 7 days, 400 mg daily for 7 days, followed by 600 mg daily) showed a lower incidence of short-term adverse effects and similar efficacy in achieving viral suppression at week 24 compared to full-dose efavirenz started upfront. This observational study aimed to assess the effectiveness and discontinuation rate in ARV-naive HIV-infected patients who started lead-in dosing of efavirenz (300 mg daily for 7 days followed by 600 mg daily) plus 2 NRTIs.

Methods: Between June 2012 and October 2014, ARV-naive patients who started efavirenz-containing antiretroviral therapy were enrolled in this observational study. Lead-in dosing strategy was adopted during the study period to improve the short-term tolerability of efavirenz. The decision to adopt lead-in dosing was made at the discretion of treating physicians after counseling sessions were provided to the patients. Monitoring of CD4 and plasma HIV RNA load (PVL) was performed at baseline, week 4 and subsequently every 12 weeks in the first year of ARV therapy. Transmitted drug resistance of HIV-1 to nNRTI was determined retrospectively. The primary endpoint was rate of discontinuation of efavirenz and PVL<400 copies/ml at week 24 in intention-to-treat analysis.

Results: During the study period, 316 ARV-naive patients initiated efavirenz-containing regimens, 154 on full-dose efavirenz upfront and 162 on 300-mg lead-in dosing. The two groups of patients were similar in terms of mean age (33.9 vs 32.6 years) and baseline PVL, (5.0 vs 4.9 $\log_{10}$ copies/ml) and the proportions of male gender (98.1 vs 98.8%), homosexual males (92.2 vs 95.1%), and patients with chronic HBV (16.3 vs 11.8%) or HCV infection (5.3 vs 3.1%). Patients on lead-in efavirenz had a higher CD4 count (252 vs 327 cells/mm^3) and a lower proportion of patients with PVL>5 $\log_{10}$ (36.4 vs 47.4%). Overall, 48 (31.2%) and 31 (19.1%) of patients on full-dose efavirenz upfront and lead-in dose, respectively, discontinued efavirenz before week 24 after excluding the patients infected with HIV-1 resistant to nNRTIs at baseline. Of 277 patients who have completed at least 24 weeks of follow-up, 74 of 141 (52.5%) and 86 of 136 (63.2%) patients on full-dose and lead-in efavirenz, respectively, achieved PVL<400 copies/ml at week 24 in intention-to-treat analysis.

Conclusions: While a significant proportion of ARV-naive patients initiating efavirenz-containing regimens have to discontinue efavirenz because of intolerance or toxicity, lead-in dosing of efavirenz plus 2 NRTIs in ARV-naive patients may decrease the discontinuation rate of efavirenz without compromising the effectiveness of viral suppression.