



Efficacy of boosted amprenavir in the salvage therapy of highly antiretroviral experienced HIV-1 infected patients.

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BACKGROUND : Amprenavir is a recently released protease inhibitor (PI) which remains active against HIV resistant to multiple PI. It is formulated as 150 mg gels. Its major inconvenience is the number of pills (8 BID) to be taken by the patients. Inhibition of the cytochrome P450 using low dose ritonavir leads to great improvement in the pharmacokinetics of amprenavir allowing a reduced 4 pills BID burden. However, safety and efficacy of this combination has been poorly studied. We assessed efficacy and safety of low dose ritonavir boosted amprenavir (APV/rtv) based regimens in highly antiretroviral experienced patients.

METHODS : PharmAdapt is a prospective randomized study to evaluate the benefit of TDM combined with genotypic resistance testing in antiretroviral experienced patients during a 32 weeks period. Patients receiving a ritonavir boosted APV containing regimen at baseline were included in this substudy. At week 32, we evaluated the changes in HIV-RNA, in CD4 and the proportion of patients with HIV-RNA <200 copies/ml or >1 log₁₀ decrease compared to baseline. Intention-to-treat (ITT,missing=failure) and on-treatment analyses were performed. Grade 3-4 side effects were also recorded.

RESULTS : Of the 252 patients included in PharmAdapt, 40 received an APV/rtv containing regimen. There were 38 males (95%), risk factors: MSW 4(10%)/MSM 31(78%)/IVDU 4(10%), CDC stages A(27%)/B(38%)/C(35%), baseline CD4 313 [211;414], baseline HIV-RNA 4.4 log₁₀ copies/ml [3.7;4.9]. Patients were exposed to a median number of 4.5 [4;5] NRTIs; 1 [0;1] NNRTIs, 2 [2;3] PIs for a median number of 3.8 [3.3;4.3] years. Baseline number of resistance mutations was 4 [3;5] for the NRTIs, 1 [0;2] for the NNRTIS and 6 [5;8] for the PIs. At week 32, median changes in HIV-RNA was 1.2 [0.7-2.0] log₁₀ copies/ml, 55% (22/40) were in success (ITT), 61% (17/28) (OT). Median increase in CD4 cell count was 66 [-15;111]. Grade 3-4 side effects occurred in 3/40 (7.5%) patients.

CONCLUSIONS : These two BID PI-based combinations as initial therapy were similar in terms of efficacy and impact on lipids at 12 month. However, the rate of treatment discontinuations was significantly higher in the IDV/RTV group and mainly due to side effects.

CONCLUSIONS : Low dose ritonavir boosted amprenavir based regimen is effective and safe in highly ARV experienced patients.

Abstracts