Pharmacokinetics of darunavir/cobicistat in an Italian observational, multicenter, prospective study (The STart Of REzolsta "ST.O.RE" study - TMC114FD1HTX4003).

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Background

The ST.O.RE. study is an observational, multicenter, single-arm, prospective study carried on HIV1-positive, virologically suppressed out-patients already in treatment with an antiretroviral (ARV) regimen based on ritonavir boosted protease inhibitors (PI/r), switching to a treatment based on darunavir/cobicistat (DRV/c) 800/150 mg taken once daily. The primary objective of this study is to describe the effectiveness of DRV/c-based regimens, measured as maintenance of virological suppression 48 weeks after the day when the treatment with DRV/c-based regimen is started, through collection of daily practice data in the Italian setting. Between the secondary objectives, there is the collection of DRV Ctrough data.

Methods

In the centers that collect, as per their routine clinical practice, the patients blood samples to perform DRV Ctrough analysis, these data were registered and reported in the electronic Case Report Form (eCRF). These values, collected 24-hours after the previous DRV/c dose intake, were subsequently analyzed and compared with the data coming from the previous DRV/c registration studies (1).

Results

So far, DRV Ctrough values from blood samples in 17 patients were collected. All of them were caucasian and virologically suppressed (Viral Load < 50 copies/ml); twelve were males and five females. The mean (±SD) age was 44,9 (±8,5) years overall, 43,25 (8,24) in male patients; 48,80 (8,53) in females; the mean (±SD) Body Mass Index was 23,5 (±3,8) kg/mq overall, 28,24 (3,83) in males and 22,18 (3,90) in females. Two patients were treated with DRV/c+ abacavir (ABC) and lamivudine (3TC) FDC (both males), three with DRV/c+3TC (one male and two females); the remaining patients were treated with DRV/c + tenofovir disoproxyl fumarate (TDF) / emtricitabine (FTC) FDC. The Cthrough mean (± SD) was 2285,12 (±1557,67) ng/ml overall, compared with the 2917 (±1658) ng/ml (N = 17 - experienced subjects) reported in the DRV/c phase III study (1); a two-sides t-test was performed and the difference between these values was not statistically significant (p=0,26). The Ctrough values registered in male were 2245±1124,04 ng/ml and 2381 ±2359,82 ng/ml in female patients. No subject had values below the 55 ng/ml, the protein-binding adjusted EC50 for wild-type HIV; two of them reported values below the threshold of 550 ng/ml (one male 296 ng/ml, BMI equal to 27 kg/mq and one female, 496 ng/ml, BMI equal to 17,2 kg/mq), the protein-binding adjusted EC50 for PI-resistant HIV. Concomitant medications

administered in some of these subjects were also recorded (mainly vitamin D and anti-hypertensive drugs) and none of them seem to alter the pharmacokinetics of DRV.

Conclusions

This is the first observational study collecting data on cobicistat boosted DRV Ctrough values in a real world setting. The results here reported are comparable to the data reported in the previous registration studies carried out with DRV/c (1).

Bibliographic references:

1) Tashima et al. Cobicistat-boosted darunavir in HIV-1-infected adults: week 48 results of a Phase IIIb, open-label single-arm trial AIDS Research and Therapy 2014, 11:39