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Poster presentation

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Atazanavir (ATV) plasma concentrations at different times after drug uptake: associations with virologic response and hyperbilirubinemia

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Purpose of the study

To explore the clinical significance of morning ATV plasma concentrations in HIV+ patients taking drugs at different day times.

Methods

HIV-infected patients on an ATV-containing cART regimen since >2 weeks, with an available ATV concentration obtained by a validated HPLC-UV (group i) 12 ± 2 hours (C12 h) and (group ii) 24 ± 2 hours (C24 h) after drug intake and 24 weeks subsequent virological follow-up, were retrospectively selected. Patients with genotypic resistance to ATV were excluded. Virological failure was defined as HIV-RNA >50 copies/ml after 24 weeks.

Summary of results

A total of 171 plasma samples from 112 patients (56% males, median age 46 years IQR 40–51) were analyzed. Median time from ATV initiation was 8.9 months (IQR 1.9–17.2). At ATV dosing, 79.5% of patients had a viral load <50 copies/ml. Overall, 27 (24.1%) showed virological failure at 24 weeks. No significant differences in terms of virological failures were seen between ritonavir-boosted and unboosted regimens. Median ATV plasma concentration was higher in patients using boosted regimens: 1.5 mg/L (IQR 0.58–2.30) vs. 0.27 mg/L (IQR 0.05–1.15), $p < 0.01$.

C12 h ATV concentrations were measured in 115 instances while C24 h in 56 samples. Median ATV plasma concentration was significantly higher in group (i) compared to group (ii): 1.5 mg/L (IQR 0.7–2.3) vs. 0.26 mg/L (IQR 0.07–0.67), $p < 0.01$. Plasma concentration showed a high interindividual variability in both groups (co-efficient of variation 83.3% and 146.8%, respectively).

In group (i), ROC curve test provided an ATV concentration cut-off of 0.23 mg/L to predict virological response at 24 weeks: instances (n = 17) with a C12 h ≤0.23 mg/L showed virological failure in 41.2%, whereas instances (n = 98) with a C12 h >0.23 mg/L failed in 16.3% of cases ($p = 0.042$). A total of 22.5% (20/89) of patients developed grade III/IV hyperbilirubinaemia. ATV C12 h correlated with concomitant unconjugated bilirubin ($r = 0.223$, $p = 0.037$). A concentration cut-off predictive of >grade III total bilirubin toxicity could not be identified. No correlations were identified between C24 h and virologic response or bilirubinemia.

Conclusion

Identification of an ATV C12 h efficacy threshold can be useful for the clinical application of morning TDM in patients receiving ATV at night.