

Successful management of gastrointestinal (GI) adverse events (AEs) in a prospective trial of ritonavir boosted saquinavir/lopinavir in heavily PI experienced patients

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Objectives Ritonavir boosted levels of PIs provide greater antiviral suppression as well as associated AEs. Strategies must be identified to minimize intolerance and achieve optimal adherence.

Methods AEs were evaluated & managed in a prospective, open label pilot of high dose (1000mg bid) saquinavir-sgc in combination with lopinavir/r and 2-3 nucleosides ±tenofovir in heavily PI experienced patients.

Results 28 subjects enrolled;32% female;46% Latino & African American. Concurrent meds 75% ABC,46% 3TC,43% ddI,43% TDF,21% ZDV & 14% d4T. 89% had an AE of any severity during the 1st month; 75% experiencing GI AEs. 96% (n=27) of subjects remained on study medication through week 12. 2 later stopped for GI AEs. 64% had nausea or vomiting, 43% diarrhea, 36% abdominal pain, indigestion or gas. Mean onset of AE was 1.1days. 8 subjects with GI meds prescribed prophylactically still had GI AEs. The most predictive factor for GI AEs is a history of intolerance to prior ART. (81%,p=.02). Other trends for having a GI AE but not reaching significance (p>0.05) include not on ART at study onset (89% had GI AE p=.06), depression (90%), concurrent use of psych meds (100%), and lack of social support (100%). No NRTI was predictive of GI AEs. Successful management of GI AEs included 43% resolved by SQV-sgc dose reduction with subsequent escalation to full dose. 21% switched from Fortovase to Invirase. 46% used symptom specific medications. 2 subjects' AEs resolved by stopping ABC. At week 24 87% on treatment had HIV viral load <400 copies/ml.

Conclusions Prior intolerance is a risk for future intolerance, although it does not preclude the use of boosted saquinavir/lopinavir. Factors such as depression, use of psych meds & social support may affect incidence of AEs. Strategies of saquinavir dose reduction with subsequent escalation can overcome intolerance and assist subjects in maintaining this effective regimen.
