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Genotypic susceptibility to tipranavir of HIV-1 isolates in treatment-experienced patients

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Purpose of the study

Tipranavir (TPV) is a ritonavir-boosted HIV protease inhibitor (PI) indicated for use in treatment-experienced patients (TEP) with PI resistance. TPV has shown superior virologic and immunologic responses in TEPs compared with first-generation PIs. In the Utilization of HIV Drug Resistance in Treatment-Experienced Patients (UTILIZE) study, we assessed the presence of susceptibility to TPV among HIV-1 isolates in TEPs.

Methods

UTILIZE was conducted at 40 US sites and examined clinician use of HIV drug-resistance testing in TEPs failing a PI-based regimen. In this observational study, patients were randomized to have either a genotype (GT; Monogram GeneSeq) or combined phenotype-genotype test (PGT; Monogram Phenosense GT) to assist with treatment decision-making. Resistance data were evaluated to assess TPV susceptibility among isolates from patients failing a PI-based regimen.

Summary of results

246 patients enrolled and 236 had resistance testing. Median HIV-RNA and CD4 count were 30,538 copies/mL and 197 cells/mm^3 with no significant differences between GT and PGT groups. There were 139 and 69 patients who had GT or PT evidence of reduced susceptibility to at least one PI, respectively. Table 1 shows the percentage of isolates from these patients (both overall and by number of prior PIs) demonstrating genotypic and phenotypic susceptibility to TPV.

Conclusion

In this cohort of TEPs failing a PI-based regimen, a majority of patient isolates showed full or partial susceptibility to TPV. Even in the most PI-experienced patients, one-third to one-half had virus that remained fully or partially susceptible to TPV. An advantage of phenotypic testing is that it reports both full and partial drug susceptibility which may help guide clinician choice of TPV. When constructing a new regimen in PI-experienced patients, resistance testing should guide the use of TPV as a potential therapeutic option.

Table 1:

	Genotypic TPV susceptibility* (n = 139)	Phenotypic TPV susceptibility** (n = 69)
Overall	58%	79%
1–2 previous PIs	83%	90%
3–4 previous PIs	60%	71%
5+ previous PIs	36%	52%

*includes only full susceptibility
**includes full and partial susceptibility

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