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Effects of NRTI backbone on HIV RNA, CD4 counts and lipids for first-line boosted PI-based HAART: meta-analysis of 12 clinical trials in 4,896 patients

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Background

Several ritonavir-boosted PIs (PI/r) are currently recommended for use in first-line therapies for HIV infection. TDF/FTC and ABC/3TC are widely used with these PI/r, but there is conflicting evidence on their relative efficacy: the ACTG 5202 and BICOMBO trials suggest higher efficacy for TDF/FTC, whereas the HEAT trial shows no efficacy difference between the NRTI backbones.

Methods

A systematic MEDLINE search identified 21 treatment arms in 12 clinical trials of 4,896 antiretroviral naïve patients, where TDF/FTC (n = 3,340) or ABC/3TC (n = 1,556) was the NRTI backbone used with PI/r. For each NRTI backbone and PI/r, the percent HIV RNA <50 copies/mL at week 48 by standardised ITT TLOVR analysis were combined using inverse-variance weighting. The effect of baseline HIV-RNA, CD4 count and choice of NRTI backbone were examined using a weighted analysis of covariance. Changes in CD4 counts and lipids (TCHOL, TRIGS, HDL, LDL) were also assessed with the same methods.

Summary of results

For the TDF/FTC and ABC/3TC groups, there were no significant differences in median baseline CD4 (204 and 195, respectively) and mean log10 HIV-RNA (4.9 and 5.0, respectively). The efficacy of first-line HAART correlated with baseline HIV-RNA and CD4 count. Use of TDF/FTC was associated with higher rates of HIV-RNA suppression in each of the three third agents where data were available (LPV/r, fAPV/r and ATV/r). (Table 1.)

There was no difference in CD4 change to week 48 by type of PI or NRTI used. All lipid parameters showed significantly greater increases when ABC/3TC was used, vs. TDF/FTC. TCHOL and TRIGS showed significantly higher increases for LPV/r and fAPV/r, vs. ATV/r, SQV/r or DRV/r.

Conclusion

This systematic meta-analysis of standardised HIV-RNA <50 copy efficacy data at week 48, using the FDA TLOVR algorithm, suggests higher efficacy for first-line use of a TDF/FTC NRTI backbone, relative to use of ABC/3TC. However, CD4 increases were similar across the range of NRTIs and PIs used. Lipid profiles also differed by choice of NRTI backbone or boosted PI.

Table 1:

NRTI backbone	**TDF/FTC**			**ABC/3TC**		
PI	**N**	**RNA<50**	**95% CI**	**N**	**RNA<50**	**95% CI**
LPV/r	2285	74%	72–76%	722	66%	63–70%
fAPV/r	53	75%	63–87%	722	67%	63–70%
ATV/r	493	79%	75–82%	112	77%	68–85%
SQV/r	166	65%	58–72%	no data	-	-
DRV/r	343	84%	80–88%	no data	-	-