

### BACKGROUND

- Last developed Protease Inhibitors (PIs) were the cornerstone of salvage therapy, being active when other PI have lost their activity.
- Tipranavir (TPV) and Darunavir ( DRV) presented different resistance profiles and the rules to interpret activity involved different mutations.
- Two genotypic interpretation systems have been validated taking into account viral response, TPV (J Scherer) and DRV (Meyer S).
- Both weighted each significant mutation.
- Disagreement between different interpretation systems may have impact in the design of the new regimen.

### OBJECTIVE

- To evaluate the agreement degree between TPV and DRV validated WS and Stanford HIVdb programme, to interpret antiviral activity linked to different mutational profiles

### METHODS

**Design:** Ongoing follow-up study.  
**Setting:** specialized outpatient clinic for patients with HIV infection  
**Period:** from April 2001 to April 2008.  
**Patients/treatment episodes:** All treatment episodes from pretreated virologically failing patients (>3 log HIV-RNA) in which rescue regimen included at least one new antiretroviral drug (TPV TPV-, DRV-,DRV- enfuvirtide - EFT-, raltegravir-RAL-, maraviroc-MRV- and etravirine-ETV-)

### METHODS

**Genotypic testing:** All treatment genotypes were interpreted using Stanford HIVdb program and additionally TPV (J Scherer) and DRV (Meyer S) scores were calculated.  
**Resistance Database:** all treatment episodes were collected in a database with their genotypic resistance testing, epidemiologic, virologic, immunologic and antiretroviral treatment information along with genotypic interpretation and the number of active drugs calculated according the different rules (see poster WEPEB204).  
**Análisis de Datos y estadística:** Kappa test and Landis scale were applied to evaluate agreement degree between TPV and DRV validated WS. STdb values were categorized as susceptible (S), intermediate (I) and resistant (R); and then in categories (S) and (I/R), to apply Kappa test. Virological response was defined as HIV-RNA<1.7 log c/mL. Univariate and multivariate models were created to test which variables predicted viral response.

Kappa	Agreement degree
<0,00	Poor
0,00-0,20	Slight
0,21-0,40	Fair
>0,41-0,60	Moderate
0,61-0,80	Substantial
0,81-1,00	Almost perfect

### RESULTS

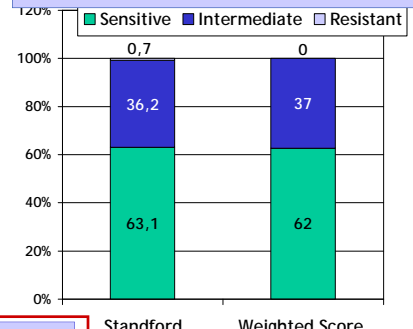
#### Baseline Characteristics

141 treatment Episodes corresponding to 75 patients		N
Age (years)	Median	43
	Range	24-74
Gender	Male (%)	61
AIDS	(%)	58
Risk Practice	IVDA%	38.3
CD4+ cell count (cells/mm <sup>3</sup> )	Median	253
	±SD	201
HIV RNA (log <sub>10</sub> copies/mL)	Median	4.54
	± SD	0.88
Exposure to 3 drug classes	%	100
Line of therapy	Median range	17.4 1-38
Exposure to ART (years)	Median range	11 2,4-18
Adherence (%) ± SD		88.9 ±24
Viral Response (HIV-RNA<1.7 log at 24 weeks) %		35.5

#### TIPRANAVIR resistance according to the interpretation system



#### DARUNAVIR resistance according to the interpretation system



TIPRANAVIR	STANDFORD		
	(%)	S	I/R
Weighted SCORE	S	37,6	14,9
	I/R	9,9	37,6

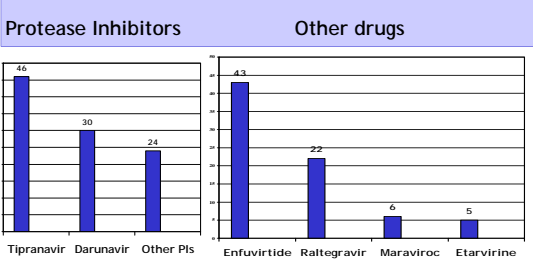
Kappa=0,505; moderate

DARUNAVIR	STANDFORD		
	(%)	S	I/R
Weighted SCORE	S	56	6,4
	I/R	7.1	30,5

Kappa=0,71; sustantial

1. Stanford interpretation for DRV and the DRV WS had a higher agreement degree than the same comparison for TPV.
2. Stanford interpretation for TPV considered a higher number of fully resistance patients than its WS.
3. After changing TPV susceptibility into a dichotomyc variable S and I/R, 24.8% genotypes were interpreted differently by Stanford and TPV SW, whereas this was only observed in 13.5% of DRV analysis.
4. Both WS considered fewer resistance genotypes than Stanford interpretation.

#### New drugs included in the salvage Regimen N/141 (%)



✓ Sixtyfive and 45 patients that had received TPV and DRV, respectively, were selected. Univariate analysis crossing viral response and baseline susceptibility to TPV and DRV were not significantly associated, using GSS or weighted GSS (as calculate in poster WEPEB204).

**Acknowledgements** We thank all of the patients, physicians, nurses, and data managers who took part in the project.  
**financial support** Instituto de Salud Carlos III through the Red Tematica de Investigación Cooperativa en Sida (RIS C03/173 to L.G.S.M.), also partially supported with unrestricted grants from Glaxo, Abbott, and Gilead.  
 Baseline

### Conclusions

- Using TPV and DRV Weighted Scored few patients were fully resistance.
- For TPV an important disagreement was found between STdb and its Weighted Score, while this is lower for DRV.
- Higher number of patients were needed to explore the impact of genotype interpretation and viral response.