



VIROLOGICAL RESPONSE TO SALVAGE THERAPY AT 6 MONTHS IN PATIENTS WITH B OR NON-B SUBTYPES

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ABSTRACT

Background : We already described the polymorphisms in resistance of PI and RT mutation in B and non-B HIV-1 subtypes among a cohort of highly experienced patients failing HAART. (1) Despite similar prior ART, there were different patterns in primary and mostly secondary RT and PI resistance mutations. It is unknown whether these differences have clinical implications.

Objectives : To assess the virological response of a genotypically driven salvage therapy according to HIV-1 subtype.

Methods : In patients failing HAART PI, RT sequence analysis performed by HIV-Seq and confirmed by phylogenetic analysis (PHYLIP). For each patient salvage therapy was discussed according to prior treatment history and genotypic resistance results. Retrogram 1.4 was used for genotypic resistance mutations on PI and RT genes. An intent-to-treat analysis was performed (with missing value= failure) to evaluate the virological response according to HIV-1 clades. Response to HAART was defined as VL < 400 and < 50 copies/ml at 6 months.

Results : 121 patients with a median baseline VL of 12900 copies/ml (50-850 000) and 290 CD4/ml³(1-1042) were prospectively evaluated. Sixty-four p. had B clades and 57 non-B clades. Mean age was 40 years (22-71). There were 79 males and 35 patients were of African origin. Virologic response was :

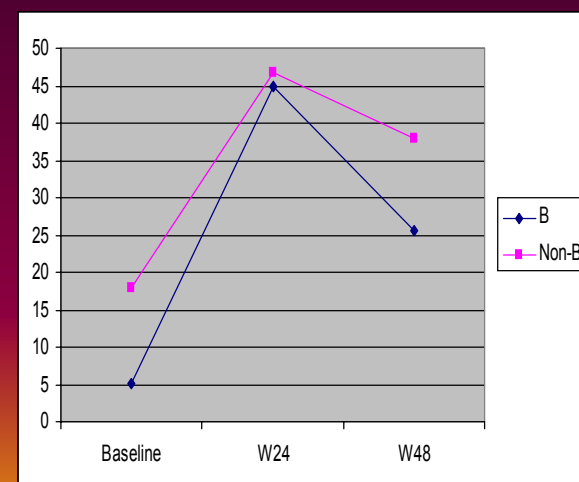
	< 400	<50
Clade B	44.9%	28.2%
Clade non-B	46.7%	35.5%

Follow up data at W 48 and subanalyses comparing clades A and C will be presented.

Conclusion : This study suggests that virological response to therapy is similar in patients carrying B and non-B clades.

B – Non B at W24, W48 (HIV-RNA < 400 cp/ml)

Subtype	Baseline	W24	W48
B	5,1	44,9	25,6
Non-B	17,8	46,7	37,8



Baseline statistics (1)

- N pts = 127
- Sex:
 - 78 Male (61%)
 - 49 Female (39%)
- Origin:
 - 82 African (65%)
 - 40 Caucasian (31%)
 - 5 Other + Asian (4%)
- Risk factors:
 - 59 heterosexual (46%)
 - 52 MSM (41%)
 - 8 blood transfusion (africa) (6%)
 - 4 IDU (3%)
 - 3 blood transfusion (2%)

INTRODUCTION

Viral resistance testing is often used as a guide to assess appropriate future antiviral therapy (ART) and to predict long term response to therapy. So far, studies on the emergence of HIV-1 resistance have been predominantly concentrated on HIV subtype B infections. The imbalance of resistance mutation patterns in different subtypes might not only confound statistical analysis of long term therapy failure prediction, but more importantly might reduce drug efficacy to specific subtypes. The global spread of HIV-1 subtypes other than B highlights the need to study the genetic diversity of circulating strains.

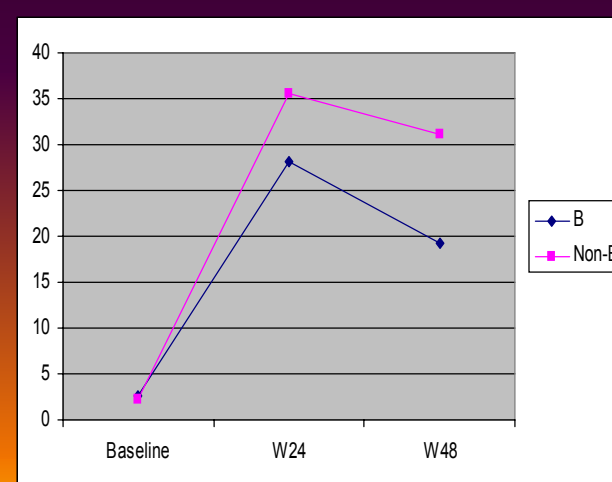
We already showed that there were different patterns in primary and mostly secondary resistance mutations between B and non-B strains. (1)

OBJECTIVE :

The aim of this study was to assess the virological response of a genotypically driven salvage therapy according to HIV-1 subtypes.

B – Non B at W24, W48 (HIV-RNA < 50 cp/ml)

Subtype	Baseline	W24	W48
B	2,6	28,2	19,2
Non-B	2,2	35,5	31,1



Baseline Statistics (2)

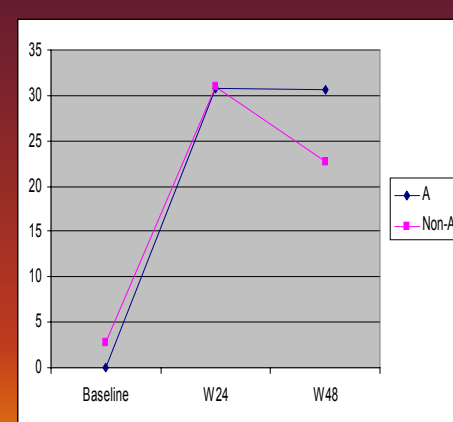
- Age:
 - Median = 42; IQR = [38;48]
 - Mean = 43,5 ± 8,6
- Subtype:
 - B = 65 (51%)
 - Non B = 58 (46%)
 - A = 13 (10%) (22%)
 - C = 11 (9%) (19%)
 - Other = 34 (27%) (59%)
 - Missing = 4 (3%)
- Data retrieved from 01/2000 to 09/2001
- Baseline VL : 13690 co/ml (50-750.000)
- Baseline CD₄ : 291 (1-1042)

Methods

- Intention-to-treat (ITT) analysis for treatment outcome (Missing data was considered as failure)
- Uni and multivariate analyses
 - Response variable:
 - undetectable at week 24 (400 cp/ml)
 - Variables:
 - baseline vira load, origin, sex, risk factors, resistant to fortovase and use or fortovase
 - Subtype
 - B / non-B
 - A / non-A
 - C / non-C

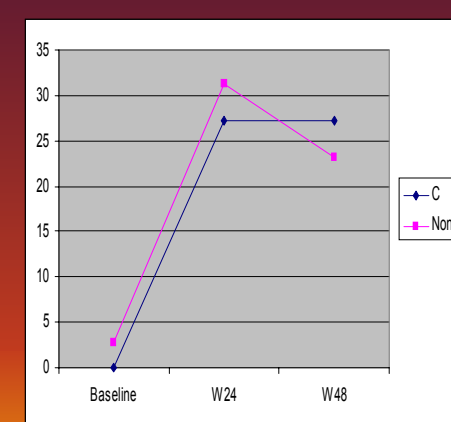
A – Non A at W24, W48 (HIV-RNA < 50 cp/ml)

Subtype	Baseline	W24	W48
A	0	30,8	30,7
Non-A	2,7	30,9	22,7



C – Non C at W24, W48 (HIV-RNA < 50 cp/ml)

Subtype	Baseline	W24	W48
C	0	27,3	27,3
Non-C	2,7	31,3	23,2



CD4 count (cell/mm³)

- Baseline
 - Missing = 13
 - Min / Max = 1 / 1,042
 - Median / IQR = 291 [177-448]
 - Mean = 331 ± 224
- W24
 - Missing = 45
 - Min / Max = 1 / 1,141
 - Median / IQR = 354 [235-497]
 - Mean = 373 ± 225
- W48
 - Missing = 83
 - Min / Max = 4 / 933
 - Median / IQR = 379.5 [238-573]
 - Mean = 423 ± 230

Uni and multivariate analyses

Explanatory variables	Odds-Ratios	95% Confidence Limits	P
Subtype b/non-b	0,93	0,45 1,94	0,8472
Use Fortovase	3,02	1,46 6,25	0,0029
Resistant	0,43	0,21 0,88	0,0215
Origin	1,26	0,65 2,42	0,4956
Sex	1,00	0,49 2,05	0,9977
Risk Factor	1,09	0,86 1,38	0,4744
Baseline vl	0,68	0,47 0,99	0,0439
Use Fortovase	3,17	1,06 9,46	0,0390
Resistant	1,09	0,36 3,25	0,8811
Baseline vl	0,73	0,50 1,08	0,1176
Use Fortovase	3,22	1,52 6,82	0,0023
Subtype b/non-b	1,12	0,52 2,45	0,7682
Subtype b/non-b	1,06	0,49 2,26	0,8860
Resistant	0,42	0,20 0,88	0,0214
Subtype b/non-b	0,95	0,45 2,03	0,8997
Baseline vl	0,70	0,48 1,02	0,0622
Use Fortovase	3,74	1,17 12,00	0,0265
Resistant	1,22	0,38 3,92	0,7412
Baseline vl	0,75	0,50 1,11	0,1441
Subtype b/non-b	1,13	0,51 2,52	0,7630
Subtype A/non-A	0,72	0,22 2,35	0,5897
Subtype C/non-C	0,66	0,18 2,38	0,5247

Conclusions

- This study suggests that virological response to salvage therapy is similar in patients carrying B and non-B strains, despite a different pattern in PI and RT mutations at baseline
- Preliminary results on clade A and clade C give similar results suggesting that in this population of patients, the treatment outcome is not related to HIV-1 subtypes

(1) P. Hermans et al. : In Patient Failing HAART, Patterns of PI and RT Mutations Differ in B Versus non-B Subtypes : 1st IAS Conference on HIV Pathogenesis & Treatment, 8-11 July 2001, Buenos-Aires, Argentina.