

Simultaneity and adherence to multiple tablet regimens among patients starting once-daily atazanavir/ritonavir (ATV/r)-based therapy: the ANRS 134 - COPHAR 3 study

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Introduction

- Average adherence to boosted protease inhibitors-based antiretroviral therapy predicts virological suppression*
- Selective ritonavir nonadherence and dose-staggering may occur in recipients of boosted protease inhibitors (BPI)**

*Parienti JJ, *Clin Infect Dis* 2010

**Shuter J, *HIV Clin Trial* 2009

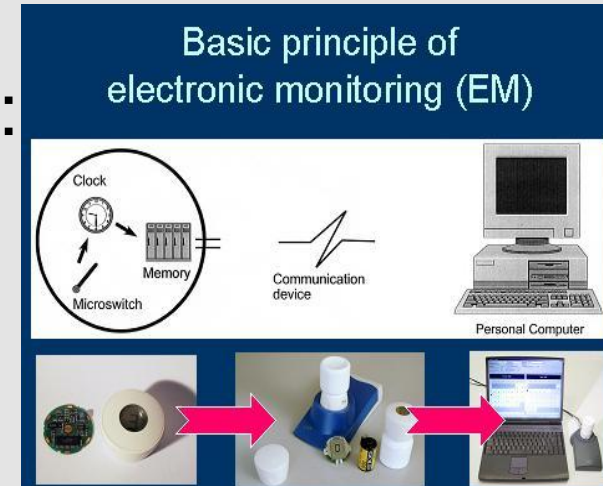
Objectives

- Assess simultaneity of drug intake for a once-daily 4-pill regimen including ritonavir
- Determine the relationships between
 - Adherence
 - Virological suppressionamong pts starting antiretroviral therapy

Methods

- HIV-infected pts starting QD MTR:

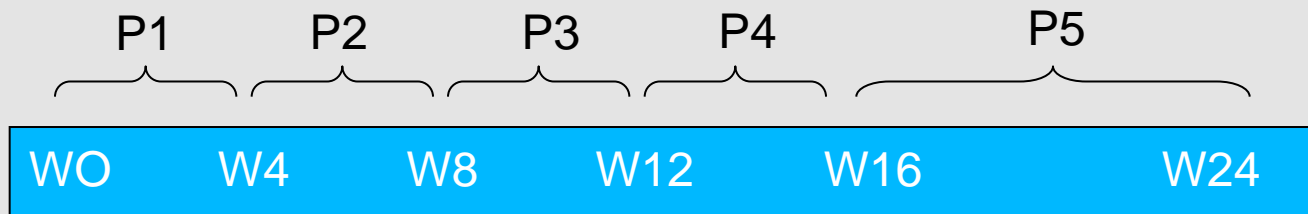
- Atazanavir 150mg
- Ritonavir 100 mg
- Tenofovir/emtricitabine (245/200 mg)



- Prospective 3 MEMS caps computing:
 - Taking Compliance (TAC): % of taken doses
 - Correct Dosing (COD): % days w correct dosing/total
 - Timing Compliance (TIC): % of doses taken on time (\pm 3 hours)

Methods

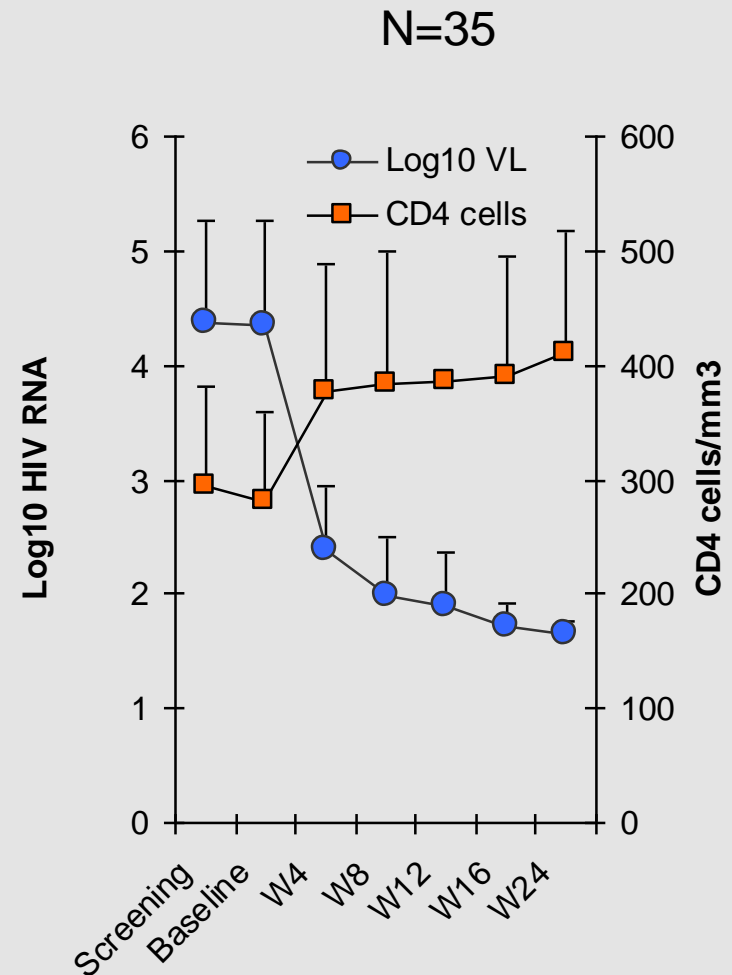
- Data collected at W0, W4, W8, W12, W16 and W24:
→ 5 periods of observation / pt



- Dynamic Virological Suppression (DVS) defined as Δ HIV RNA >1log every 4W or HIV RNA < 40 cp/mL *
- Longitudinal DVS was modeled by Logistic Mixed Models (Proc GLIMMIX in SAS)

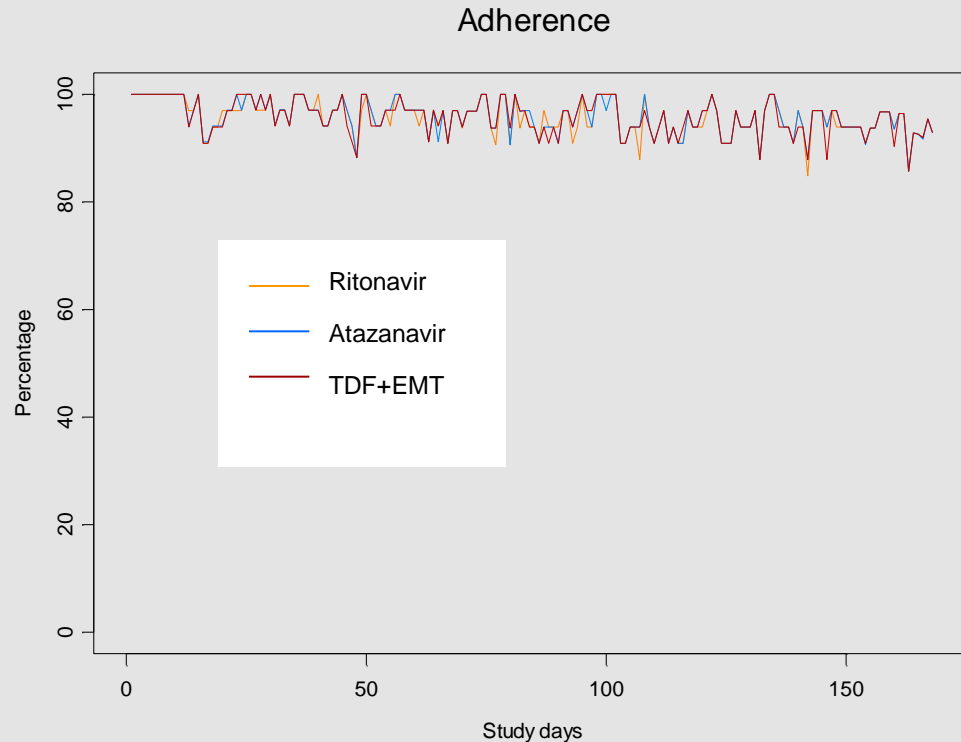
Results

Variable	n=35
Age, median [range]	36 [24-66]
Male, n (%)	29 (83)
Level of education, n (%)	
High school, n (%)	30 (86)
Smokers, n (%)	12 (34)
Alcohol >4 times/week, n (%)	4 (11)
AIDS, n (%)	3 (9)
Contamination route	
Sexual, n (%)	34 (97)
CD4 < 200	5 (14)
HIV RNA > 100,000	10 (29)



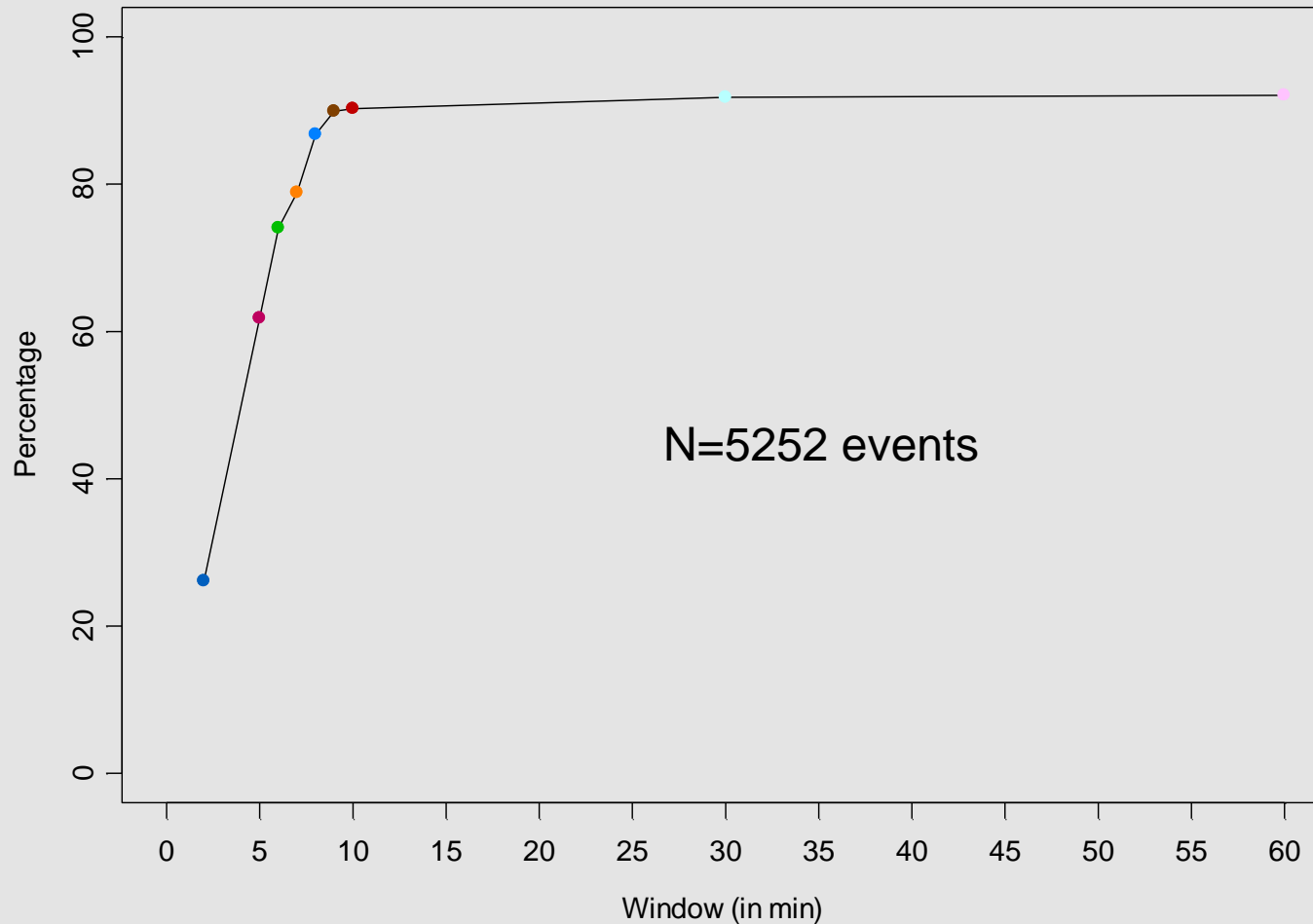
MEMS Adherence, %, median [Range]

	TAC	COD	TIC
Ritonavir	100 [51-100]	98 [43-100]	87 [30-100]
Atazanavir	100 [50-102]	95 [41-100]	86 [32-100]
TDF/EMT	100 [49-102]	98 [42-100]	86 [31-100]



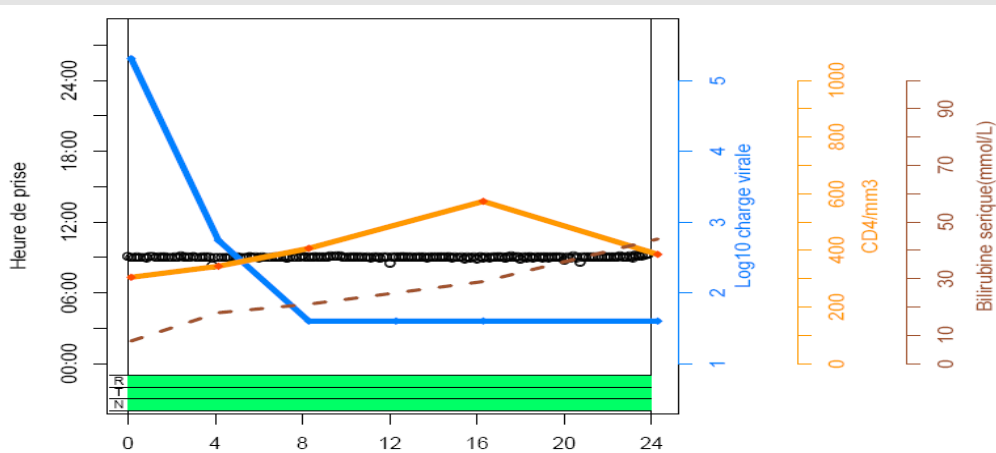
Simultaneous intakes

3 simultaneous drug intakes within given interval



Adherence and outcomes for 2 pts

A



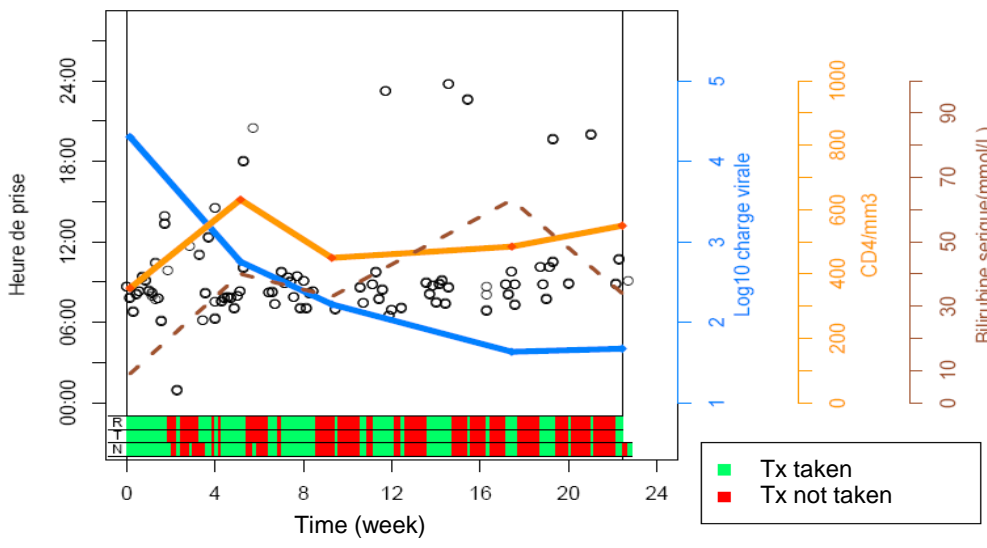
- HIV RNA (Log10)
- CD4 (cell/mm3)
- - - Bilirubinemia (mmol/L)

R: Atazanavir

T: Tenofovir+emtricitabine

N: Ritonavir

B



■ Tx taken
■ Tx not taken

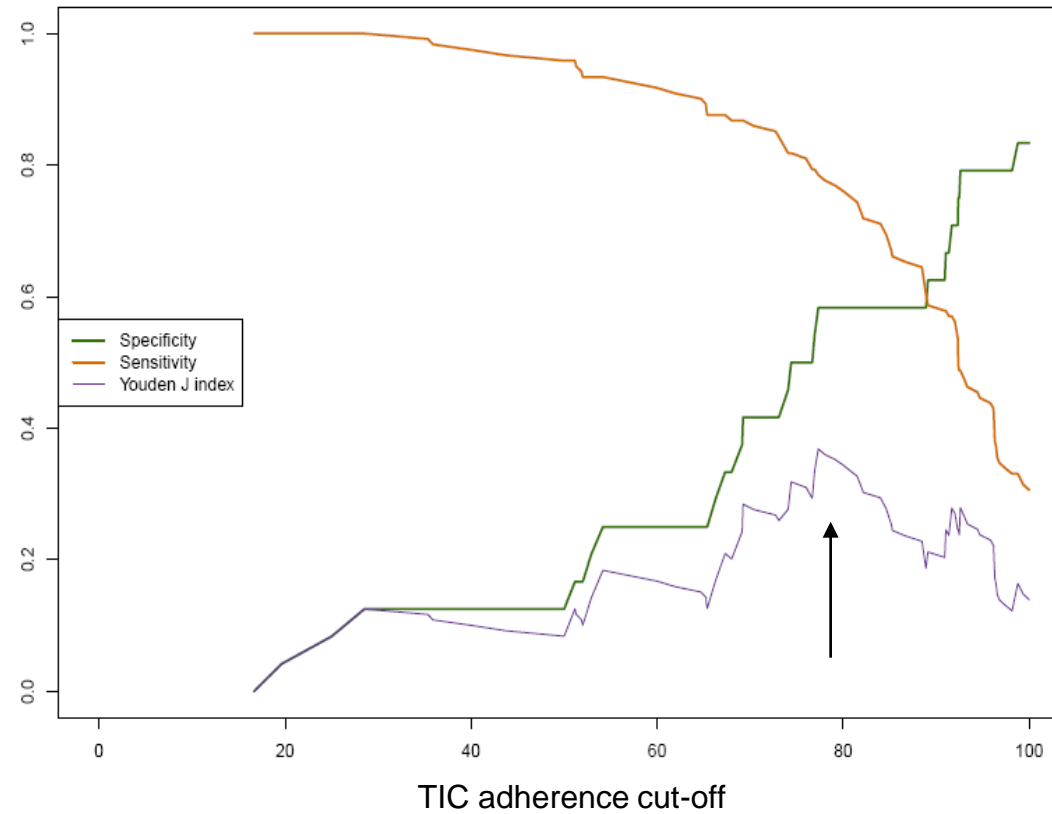
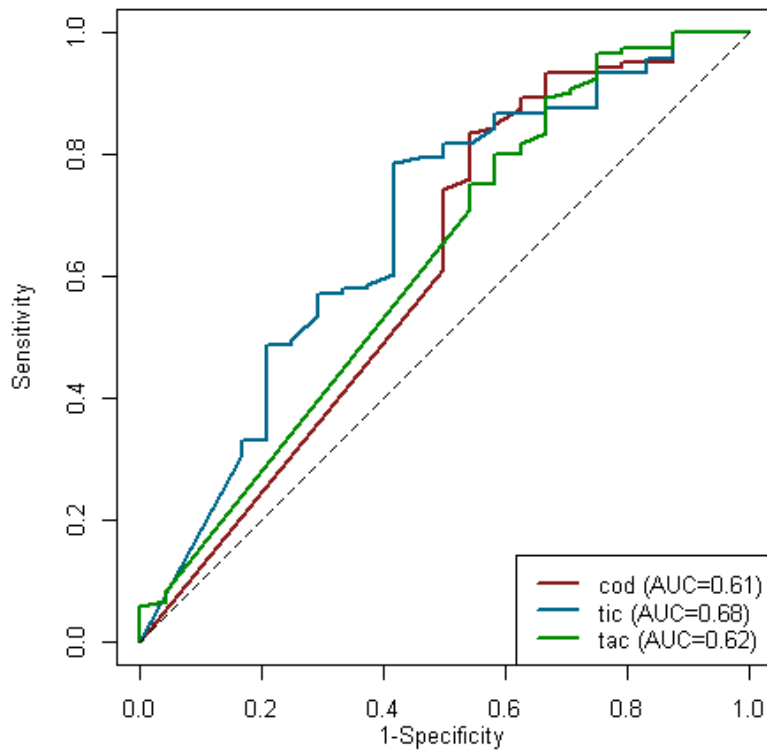
MEMS Adherence and DVS

Adherence definition	Odds Ratio [§]	95% confidence Interval	P-value
Taking compliance	1.7	[1.1 to 2.9]	0.04
Correct dosing	1.6	[1.1 to 2.5]	0.03
Timing compliance	1.4	[1.1 to 1.8]	0.02

[§] A value > 1 indicates an increased probability of DVS corresponding to +10% adherence

ROC curve and adherence cutoff

Dynamic virological suppression



Limitations

- Follow-up is limited
- Results specific to the antiretroviral regimen and population studied
- The protocol may have induced better adherence (Hawthorne effect)

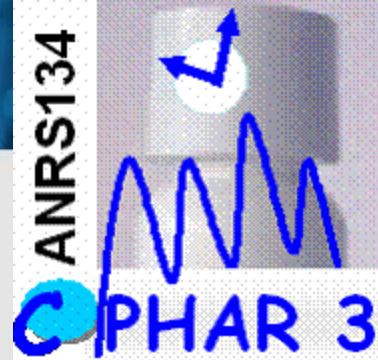
Conclusion

- Excellent simultaneity and high adherence in the absence of fixed dose regimen in naive HIV-infected subjects

Nevertheless,

- Average adherence (Timing compliance +/- 3 hours) appeared relevant to explain DVS

Acknowledgments



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- AARDEX: B. Vrijens

- Patients
- Investigators in each centre
- Pharmacists et pharmacologists

- Industry: BMS and Gilead for providing the drugs
- ANRS for supporting the study

Back-up SLIDES

Virological outcomes

