

In Vivo Determination of Tenofovir Antiviral Effect in the Presence of TAMs



F. Maggiolo^{1,2}, A. Callegaro³, G. Gregis^{1,2}, G. Quinzan^{1,2}, C. Arici¹, A. Goglio³, F. Suter¹

USC Malattie Infettive¹, US Terapia Antivirale², Laboratorio di Microbiologia e Virologia³, Ospedali Riuniti, Bergamo, Italy

E-mail franco31556@hotmail.com

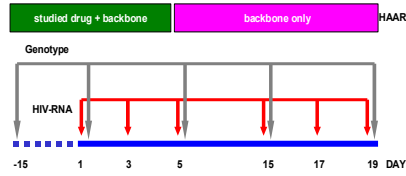
INTRODUCTION

For some antiretrovirals the assessment of virologic resistance in-vivo is difficult. When composite resistance patterns are present, the genotypic analysis can offer little information. We studied with an in-vivo model the effect of TAMs on tenofovir antiviral effect.

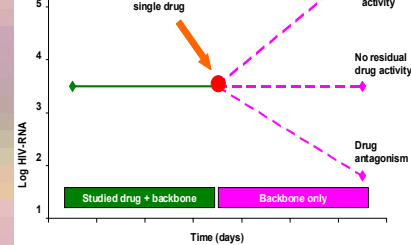
Single Drug Shortstop (SDS) Strategy

- Establish plasma HIV-RNA baseline (3 determination over a week)
 - Discontinue drug of interest (wash-out 10 days)
 - Determine effect on plasma HIV-RNA level (3 determination over a week)
 - Eventually re-start HAART (according to viral genotype)
- Outcome measure:** Change in HIV-RNA level

Single-drug shortstop strategy model

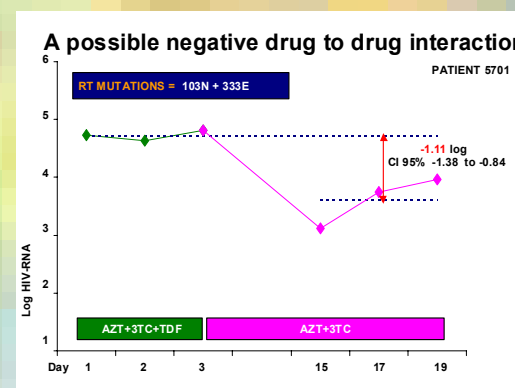
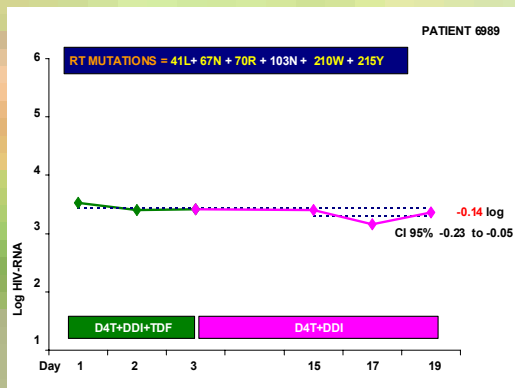
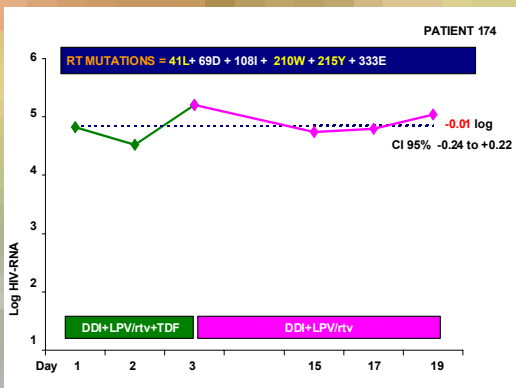
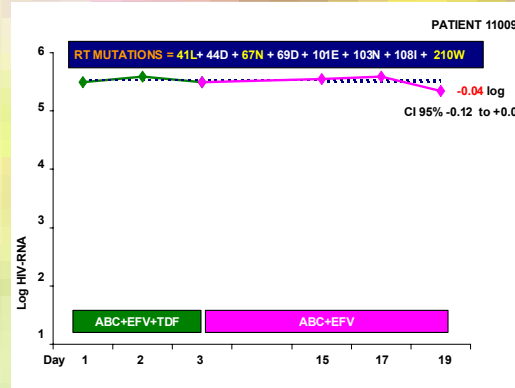
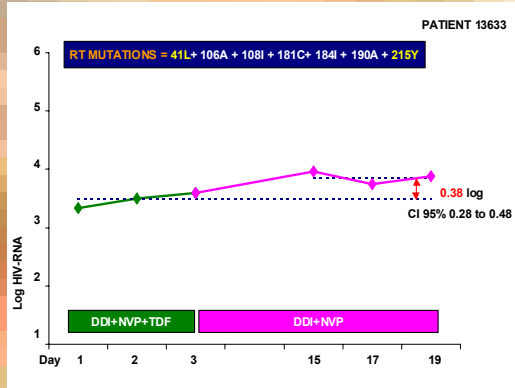
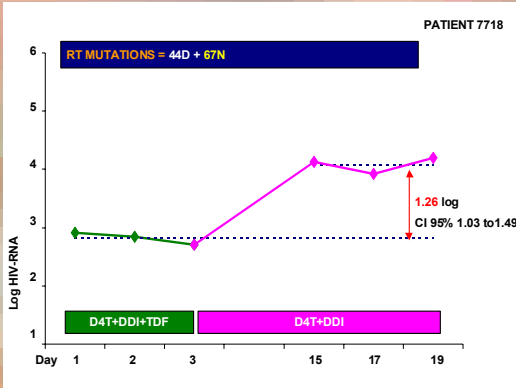


Potential outcomes



Patients at entry

PATIENT	Sex	age	CDC classification	HIV-RNA	CD4
7718	F	30	B3	811	216
13633	M	39	A3	2170	275
11009	M	21	C3	31887	640
174	M	37	C3	65947	445
6989	M	37	C3	3417	538
5701	M	34	A3	53728	416



CONCLUSIONS

SDS strategy allows the in-vivo study of the effective antiviral activity of a single drug.

SDS strategy is safe as the short stop of a single drug does not favor the selection of new mutations.

SDS strategy allows to document drug to drug interactions.

In the presence of multiple TAMs the antiviral activity of tenofovir is significantly reduced.

We documented how 41L + 215Y impairs tenofovir activity.

Three or more TAMs including mutations 41L and 210W lower tenofovir activity to negligible levels.

The effect of TAMs' pattern 2 (D67N + K70R + K219Q/E) has still to be studied.

We also documented a negative drug to drug interaction that might help to explain precox failures of 3 NRTIs HAART regimens including tenofovir.

A possible negative drug to drug interaction