

The FOTO study: 24 week Results Support the Safety of a 2-day Break on Efavirenz-based Antiretroviral Therapy

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Background

- Daily treatment adherence is an ongoing challenge for some patients
- Treatment interruptions *with* viraemia have negative clinical consequences
- *Some* antivirals have long half lives which makes less than daily dosing plausible
- Short interruptions, if they prevent rebound viraemia, provides flexibility in dosing while preserving the benefits of virus suppression

Tested Regimen: TDF+FTC+EFV

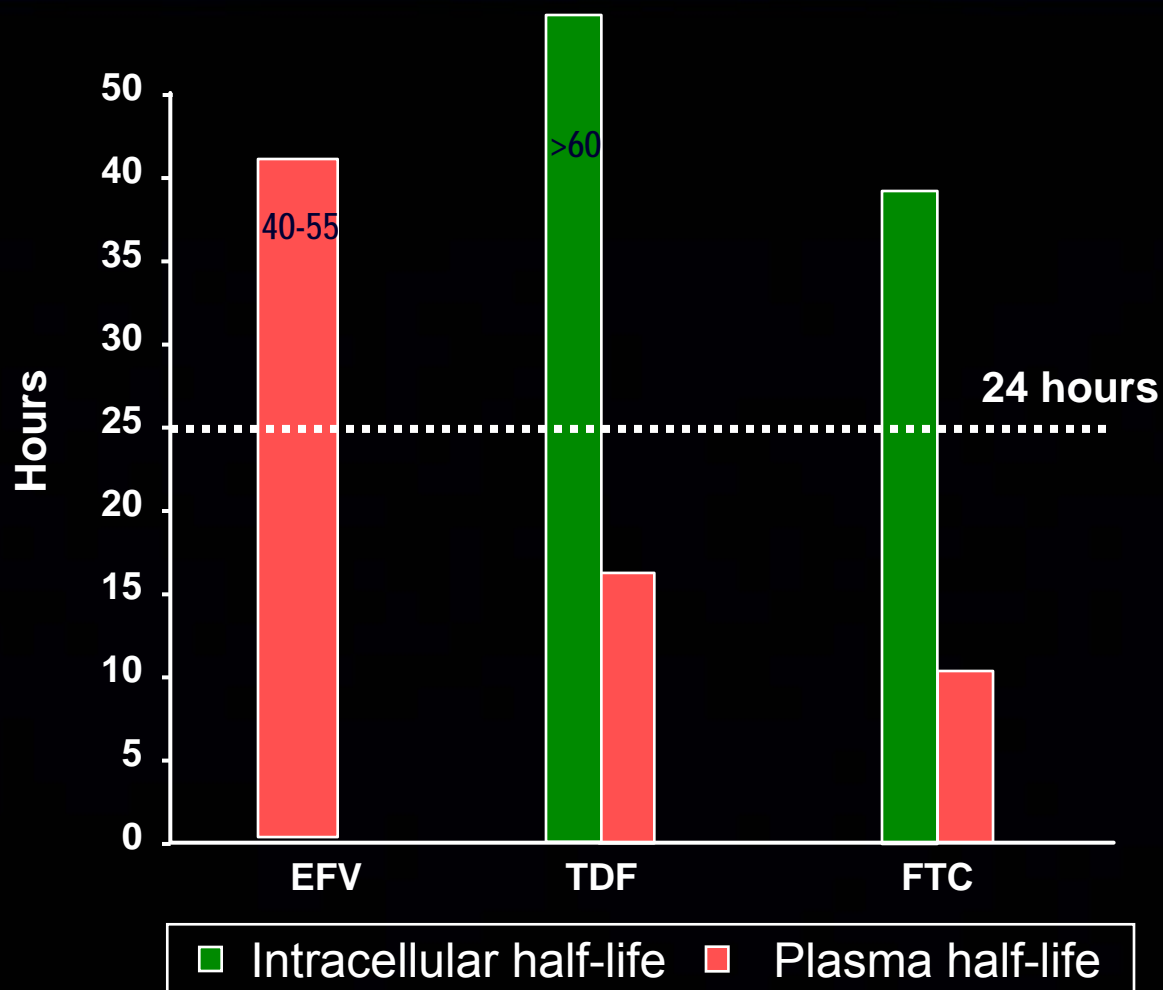
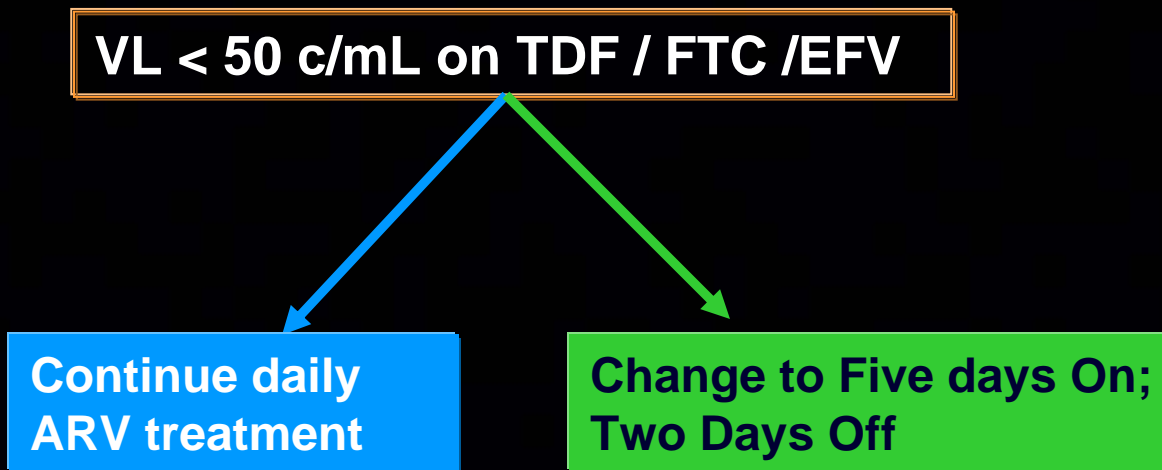


FOTO: Five days On, Two days Off Study Design

- N = 60; virologically suppressed (<50 copies/mL for at least 90 days) on TDF / FTC / EFV



Primary Outcome: 24 weeks

At week 24 – pts. on Continuous arm offered change to FOTO; all followed for ≥ 48 weeks

Study Hypothesis and Power

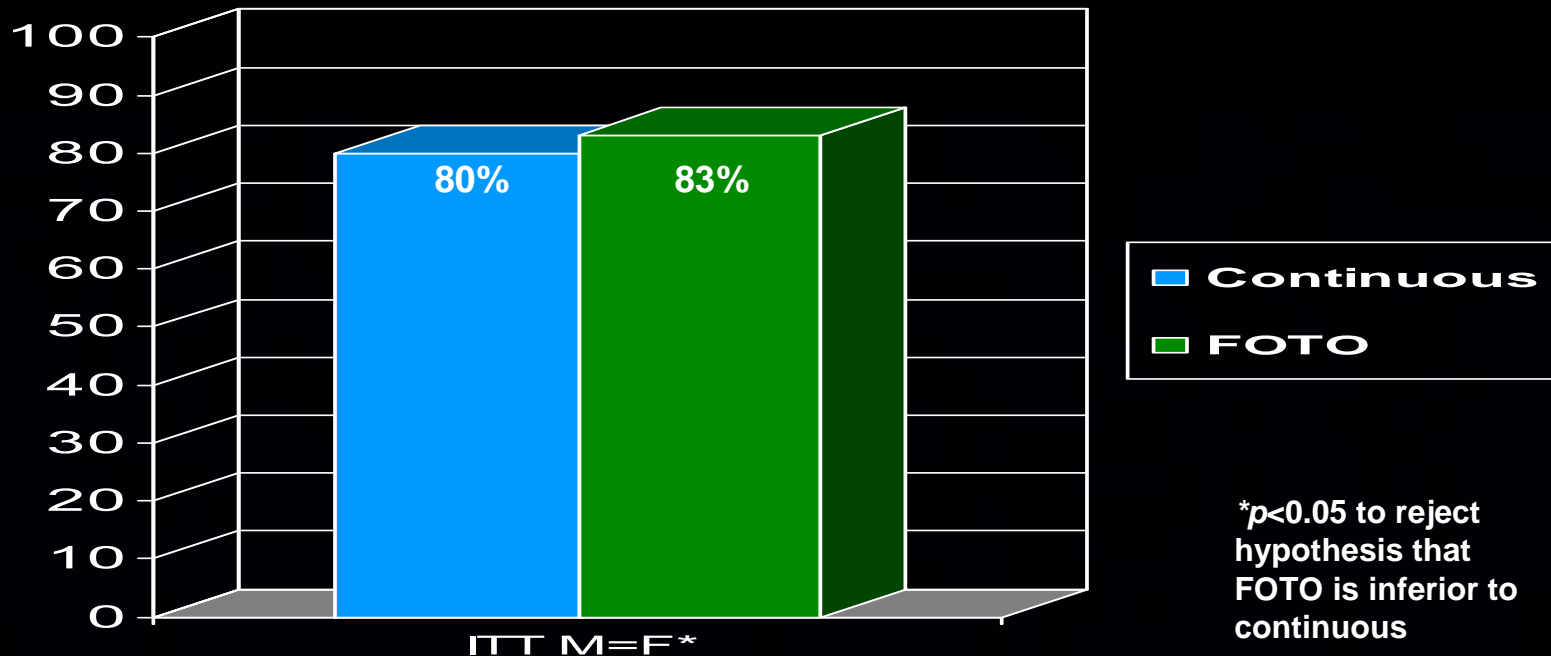
- Primary Outcome: Test for equivalence of maintaining suppression at week 24
 - Virologic Failure: Confirmed consecutive VL >400 c/mL
 - 5% one-sided significance
 - Farrington and Manning test used
- N=60 provides 80% power to conclude that the FOTO strategy is not inferior to the control strategy
 - 15% set as definition of inferiority
 - Allowing 10% drop outs

FOTO: Demographics

	Control n=30	FOTO n=30	Total n=60
Male (n,%)	25 (83%)	25 (83%)	50 (83%)
Female (n,%)	5 (17%)	5 (17%)	10 (17%)
White (n,%)	23 (77%)	19 (63%)	42 (70%)
Afr-Amer (n,%)	5 (17%)	8 (27%)	13 (22%)
Other Race (n,%)	2 (7%)	3 (10%)	5 (8%)
Age (mean, min-max)	47 (23-67)	42 (22-56)	44 (22-67)
CD4 count/mm ³	679	660	670

FOTO Results: Primary Outcome % with Virologic Suppression Wk 24

Week 24: % VL < 50 c/mL



Early Terminations:

— FOTO: n=5

- Psych (2), time burden (3)

-- All had VL < 50 c/mL at last visit

— Continuous: n=2

- Pregnancy (1), LTFU (1)

FOTO: Virologic Failure and “Blips”

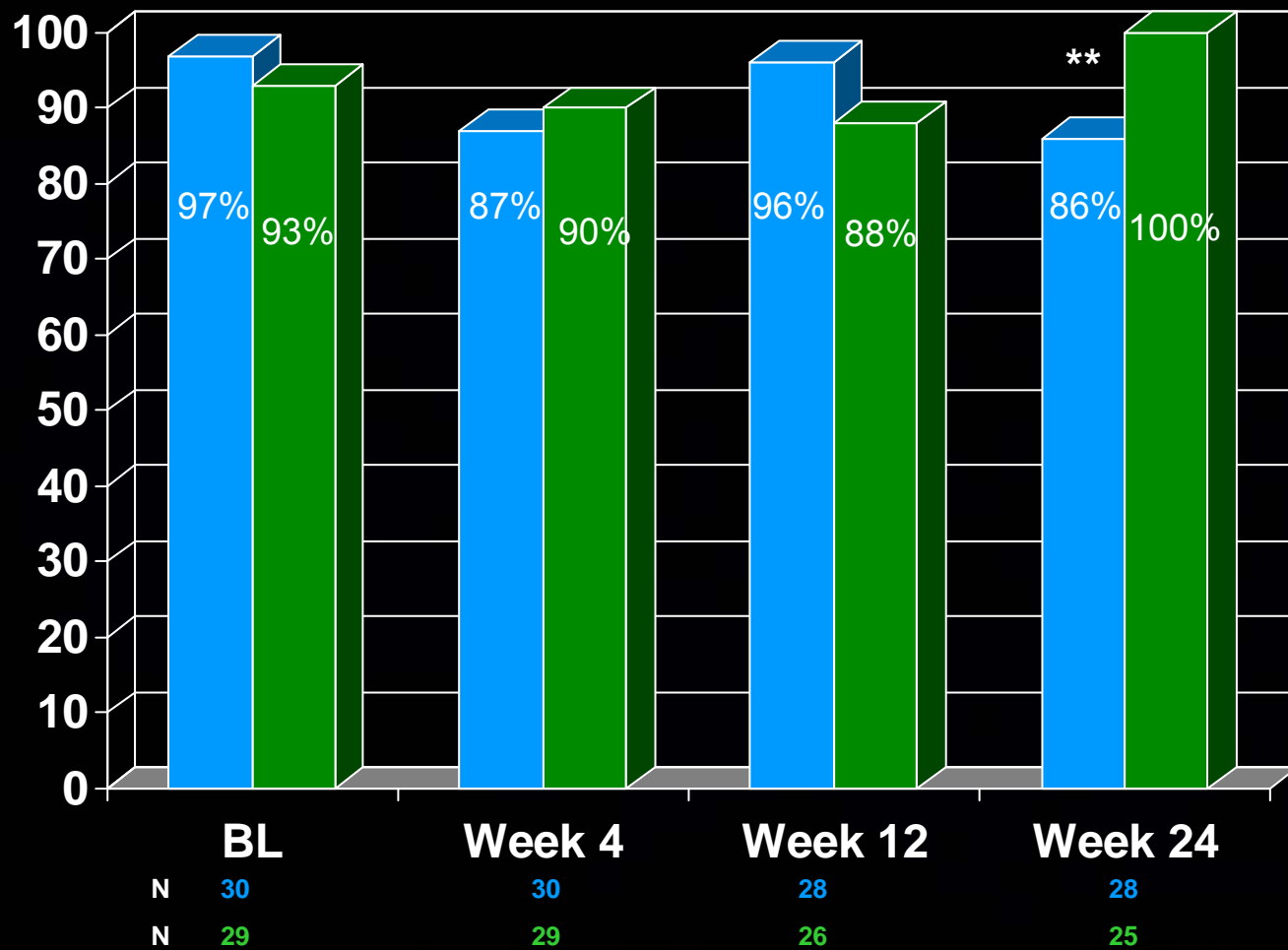
Virologic Failure: Confirmed VL >400 c/mL

— No failures either arm through Week 24

Virologic “blips”: >50 – <500 c/mL

# pts with Blips	Continuous	FOTO	Value
Baseline	1	2	142 50,60
Wk 4	4	3	52,57,68,80 77,130,146
Wk 12	1	3	225 56,61,160
Wk 24	4	0	58,66,165,465 ---

FOTO: Virologic Suppression %<50 c/mL to week 24 (OT*)



*Missing = Excluded

■ Continuous
■ FOTO

**p<0.05 to exclude inferiority

FOTO: CD4 cell outcomes

Mean with 95% CI



Adverse Events, Pt. Preference and Adherence to Strategy

— Adverse Events

- SAEs: Continuous (n=1); FOTO (n=1) judged unrelated
- Adverse Events: No grade ≥ 3 AEs in either arm
 - AE considered at least *possibly related*:
 - N=2 on FOTO: Grade 1 CNS AE (insomnia, dizzy)
 - Labs: No \geq Grade 2 in either arm

— Pt. Preference Questionnaire – Week 4 on FOTO arm

- Scale: 0 (prefer Continuous) to 10 (prefer FOTO)
- Result: Median 9.5 (range 2-10)

— Adherence to Strategy (FOTO arm)

- N = 3 took >5 doses per week
- N = 8 took >2 days off

Study Conclusions

- For patients virologically suppressed on TDF/FTC/EFV, 5 days on per week / 2 days off is not inferior to continuous treatment
 - No virologic failures seen (due to prolonged $\frac{1}{2}$ life of regimen?)
 - Number / pattern of “blips” similar
 - No significant difference in CD4 count changes
- Few AEs noted
 - Two mild CNS AE noted on FOTO
- Strong patient preference by Likert Scale for FOTO
- This schedule conserves 29% of the cost of ARVs while maintaining virologic suppression

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