

## Intensive Adherence Interventions Improve Virologic Response to Antiretroviral Therapy (ART) in Treatment Naïve Patients

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### ABSTRACT

**Background:** Despite use of potent ART, failure rates of initial regimens are reported as high as 50%. Adherence appears to be a strong predictor of durability of ART; however, virologic outcomes data evaluating the effect of adherence interventions are lacking.  
**Objective:** To evaluate the impact of intensive adherence interventions by a pharmacist on ART adherence and virologic response in naïve patients.

**Methods:** This was a prospective, case-controlled study. All ART naïve patients were eligible for the intervention (ADH); however, those not offered the service by their provider and those refusing to participate served as controls, receiving only standard of care (SOC). An additional group of matched historic controls were included for comparison. ADH patients were assessed for readiness and educated with an individualized, 3 module educational program focussing on basic understanding of HIV infection, psychosocial factors, and proper administration instructions. Potential adherence barriers, anticipated toxicities, pill burdens, dosing intervals and regimen preferences were discussed in detail with each patient, evaluated, reported to their provider, and used to select an individualized ART. Patients were given tools such as pill boxes, dose cards, daily dosing schedule, and beepers, if needed. We provided intensive coaching for the first 16 wks and had a phone line dedicated to these patients for questions. Adherence (self-report), side effects and VL were evaluated and addressed at each visit (wks 2, 4, 8, 16, 24). Demographics and VL were compared to a cohort of patients who did not receive the intervention (SOC) using Chi-squared. Continuous variables were compared using the Kolmogorov-Smirnov Two Sample Test.

**Results:** 61 patients with similar demographics (n=24 ADH; 37 SOC) were evaluated for 24 wks. Median baseline VL (log<sub>10</sub>) is 5.29 c/mL (3.06-5.88, ADH) vs 5.26 c/mL (4.00-5.88, SOC). At week 16, 83% vs 35% had VL<400, for ADH and SOC, respectively (p<0.001). Of those with 32 wk follow-up (16 ADH, 14 SOC), 100% in ADH remained <400, but only 20% in SOC. 93% vs 82% reported 100% adherence at week 16. Regimen modifications to improve tolerance or adherence were made in 35% of ADH patients vs. 11% of SOC in the first 16 wks (p<0.05).

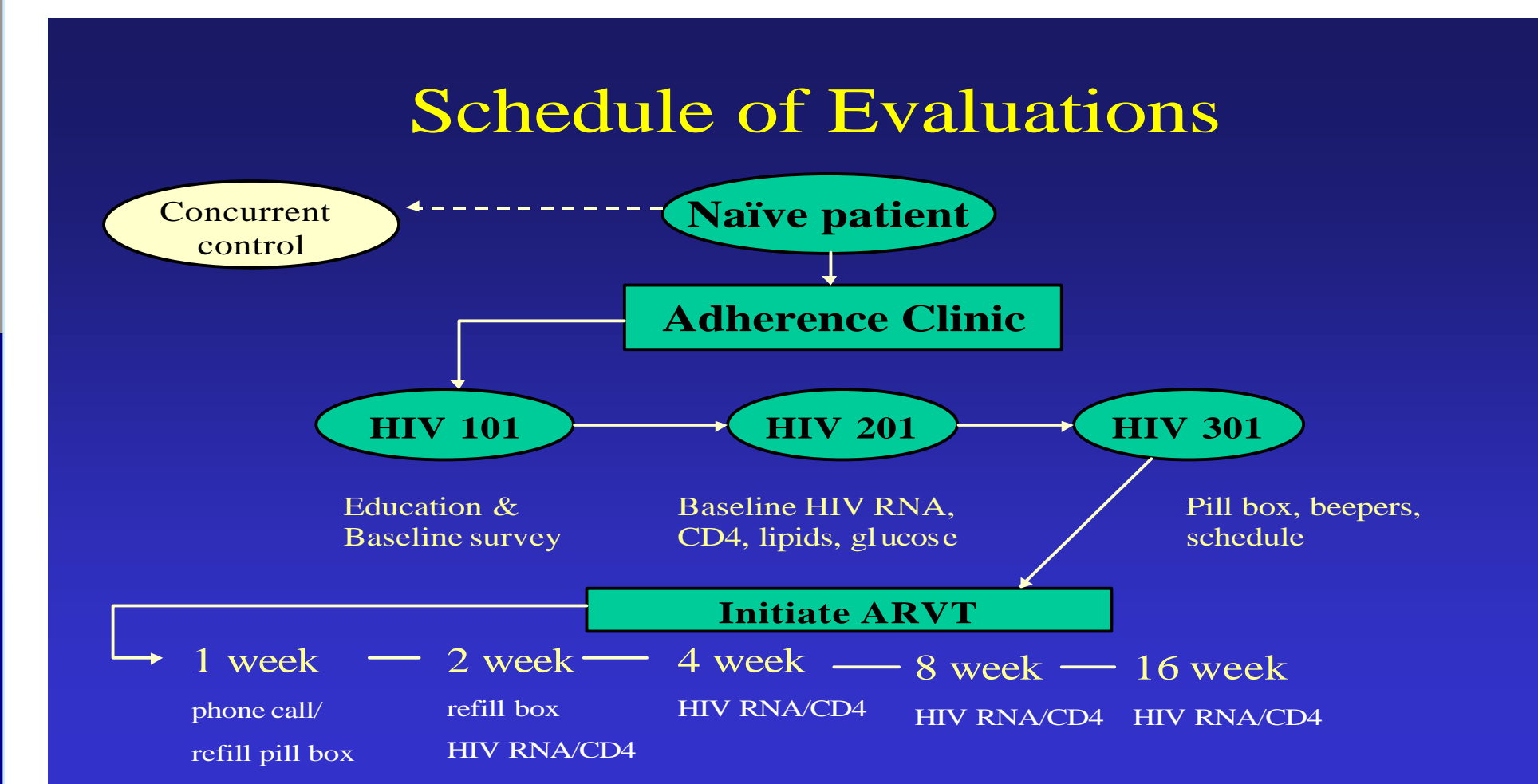
**Conclusions:** Tailored ART regimens, and intensive adherence interventions during the first 16 wks of therapy are associated with increased self-reported adherence and enhanced virologic response compared to standard of care in antiretroviral naïve patients.

### INTRODUCTION

- Despite use of highly active antiretroviral therapy, failure rates of initial regimens have been reported to be as high as 50%.
- Adherence appears to be a strong predictor of virologic response and durability of HAART.
- The initial regimen has the greatest chance of suppressing viral load and determining disease outcome.
- Care should be exercised in determining who should begin therapy and at what point they are ready.
- Few studies have evaluated the impact of structured adherence interventions on virologic outcomes in patients on potent antiretroviral therapy.
- The primary objective of this study was to evaluate the impact of intensive adherence interventions by a pharmacist on adherence to antiretroviral therapy and virologic response in naïve patients.

### METHODS

- This was a prospective, case-controlled study. All ART naïve patients were eligible for the intervention (ADH); however, those not offered the service by their provider and those refusing to participate served as controls, receiving only standard of care (SOC). An additional group of matched historic controls were included for comparison.
- ADH patients were assessed for readiness and educated with an individualized, 3 module educational program focussing on basic understanding of HIV infection, psychosocial factors, and proper administration instructions. Potential adherence barriers, anticipated toxicities, pill burdens, dosing intervals and regimen preferences were discussed in detail with each patient, evaluated, reported to their provider, and used to select an individualized ART.
- Patients were given tools such as pill boxes, dose cards, daily dosing schedule, and beepers, if needed. We provided intensive coaching for the first 16 wks and had a phone line dedicated to these patients for questions. Adherence (self-report), side effects and VL were evaluated and addressed at each visit (wks 2, 4, 8, 16, 24). Demographics and VL were compared to a cohort of patients who did not receive the intervention (SOC) using Chi-squared. Continuous variables were compared using the Kolmogorov-Smirnov Two Sample Test. All analyses were intention-to-treat.



### RESULTS

61 patients (n=24 ADH; 37 SOC) with similar demographics were evaluated for 24 wks. There were no significant differences between baseline viral load (VL) or CD4 counts (Table 1).

At week 16, 83% vs 35% had VL<400, for ADH and SOC, respectively (p<0.001) and at 24 weeks 75% vs 35% had VL <400 c/mL (Table 2). Of those with 32 wk follow-up (16 ADH, 14 SOC), 100% in ADH remained <400, but only 20% in SOC.

93% vs 82% reported 100% adherence at week 16 (Table 3). Minor regimen modifications to improve tolerance or adherence were made in 35% of ADH patients vs. 11% of SOC in the first 16 wks (p<0.05).

Since ARV regimens were individualized in the intervention group, a comparison of regimens is illustrated in Table 4.

	Adherence intervention total n=24	Standard of Care total n=37	p-value
median age (y)	40	35	0.446
female (%)	10 (42)	12 (32)	0.94
non-caucasian (%)	15 (63)	21 (57)	0.753
<b>HIV RISK</b>			0.062
injection drug use	8 (33)	5 (14)	
heterosexual	13 (54)	19 (51)	
homosexual	3 (13)	13 (35)	
<b>baseline parameters</b>			
median log <sub>10</sub> HIV RNA (range)	5.29 (3.06-5.88)	5.26 (4.00-5.88)	0.76
median CD4 (range)	97 (4-690)	164 (3-610)	0.58

**TABLE 1.** Baseline demographic, virologic and immunologic factors between the Adherence Intervention and the Standard of Care control groups.

Viral Load (VL) Response	Adherence intervention total n=24	Standard of Care total n=37	p-value
<b>VL &lt;400 @ 16 wks (%)</b>	<b>20/24 (83)</b>	<b>13/37 (35)</b>	<0.001
subset < 50c/mL	12/16	6/7	
lost to follow-up*	1	0	
VL unavailable*	2	0	
<b>VL &lt;400 @ 24 wks (%)</b>	<b>18/24 (75)</b>	<b>13/37 (35)</b>	<0.001
subset < 50c/mL	13/15	9/10	
lost to follow-up*	3	3	
discontinued treatment*	1	5	

\*lost to follow-up or unavailable VL or discontinued treatment=failure

**TABLE 2.** Viral load responses at weeks 16 and 24 in the Adherence Intervention and the Standard of Care control groups.

**TABLE 3.** Comparison of Median Number of Clinic Visits and Patient Reported Adherence between Adherence Intervention and Standard of Care Groups

	Adherence Intervention	Standard of Care
<b>Total Clinic Visits at 16 wks</b>	5 (4-11)	3.25 (2-7)
Median (range)		
<b>Missed doses reported (%)*</b>	5/68 (7%)	18/98 (18%)

\* Adherence was determined as the total number of times that any patient reported any missed doses in the previous 48h prior to their appointment divided by the number of patient visits at which the question was asked across the entire group.

**Table 4.** Comparison of the antiretroviral regimens used in the Adherence Intervention and Standard of Care groups.

ANTIRETROVIRAL REGIMEN	Adherence Intervention n=24	Standard of Care n=37
<b>triple containing PI</b>	<b>9</b>	<b>34</b>
nelfinavir	7	31
indinavir	2	3
<b>triple containing EFV</b>	<b>8</b>	<b>3</b>
<b>triple NRTI + PI</b>	<b>4</b>	<b>0</b>
<b>triple NRTI + NNRTI</b>	<b>0</b>	<b>0</b>
<b>dual NRTI + NNRTI &amp; PI</b>	<b>3</b>	<b>0</b>

PI: protease inhibitor; EFV: efavirenz; NRTI: nucleoside reverse transcriptase inhibitor; NNRTI: non-nucleoside reverse transcriptase inhibitor

### DISCUSSION

In this study there was a lack of consistency among ARV regimens; therefore it is difficult to discriminate effect of intervention vs. individual regimens. However, it is possible that *not* standardizing the initial regimen aided in our intervention group's success.

Those refusing Adherence Clinic may pre-select for individuals more likely to fail. Our recommendation to defer starting therapy in those deemed not ready to begin, selects for those more likely to succeed and may account partly for our high success rate.

### CONCLUSIONS

Tailored antiretroviral regimens and intensive adherence interventions during the first 16 wks of therapy are associated with increased self-reported adherence and enhanced virologic responses compared to standard of care in antiretroviral naïve patients.