

# **Evaluating an enhanced adherence intervention among HIV positive adolescents failing 2<sup>nd</sup> line treatment**

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# Conflict of interest

- None

# Background

- 20-50% of adolescents fail bPI-based 2<sup>nd</sup> line ART
- Limited data on cause of treatment failure
- Identifying and addressing the cause/s will:
  - delay need for 3<sup>rd</sup> line and salvage regimens
  - prevent new and subsequent treatment failure
  - prevent propagation of drug resistant strains

# Research question

Will a home-based adherence intervention improve virological outcome in HIV-infected adolescents failing ATV/r-based 2<sup>nd</sup> line ART?

**Hypothesis-** mDAART improves VL suppression

**Treatment outcome-** VL suppression to <1 000 copies/ml

# Objectives

- To determine if mDAART improves virological suppression in adolescents failing ATV/r-based 2nd line treatment,
- To determine factors associated with virological failure in HIV+ adolescents on ATV/r-based 2nd line treatment,
- To compare ATV exposure between standard care and mDAART vs standard care alone in HIV+ adolescents who are failing ATV/r-based 2nd line treatment.

# Methods

- **Study setting-** HCH paediatric OI clinic
- **Design-** randomised, controlled trial
- **Ethical obligations-** met
- **Data collection-** January 2015-May 2016

## Screening

- Eligibility questionnaire
- Baseline viral load

## Phase 1

- Recruitment and randomisation (1:1)
- 2 baseline q'naires; hair sampling for [ATV] and [RTV]
- 3 months follow-up
- Viral load, 1 adherence q'naire and hair sampling at the end of follow-up

## Phase 2

- Genotypic HIV drug resistance testing for continued failure ( $VL \geq 1000$  cpm) from both arms

## Standard care and SAT

- ART intake with/out supervision
- 3 monthly clinic reviews and drug refills
- Adherence counselling at each review

## mDAART

### (home visits)

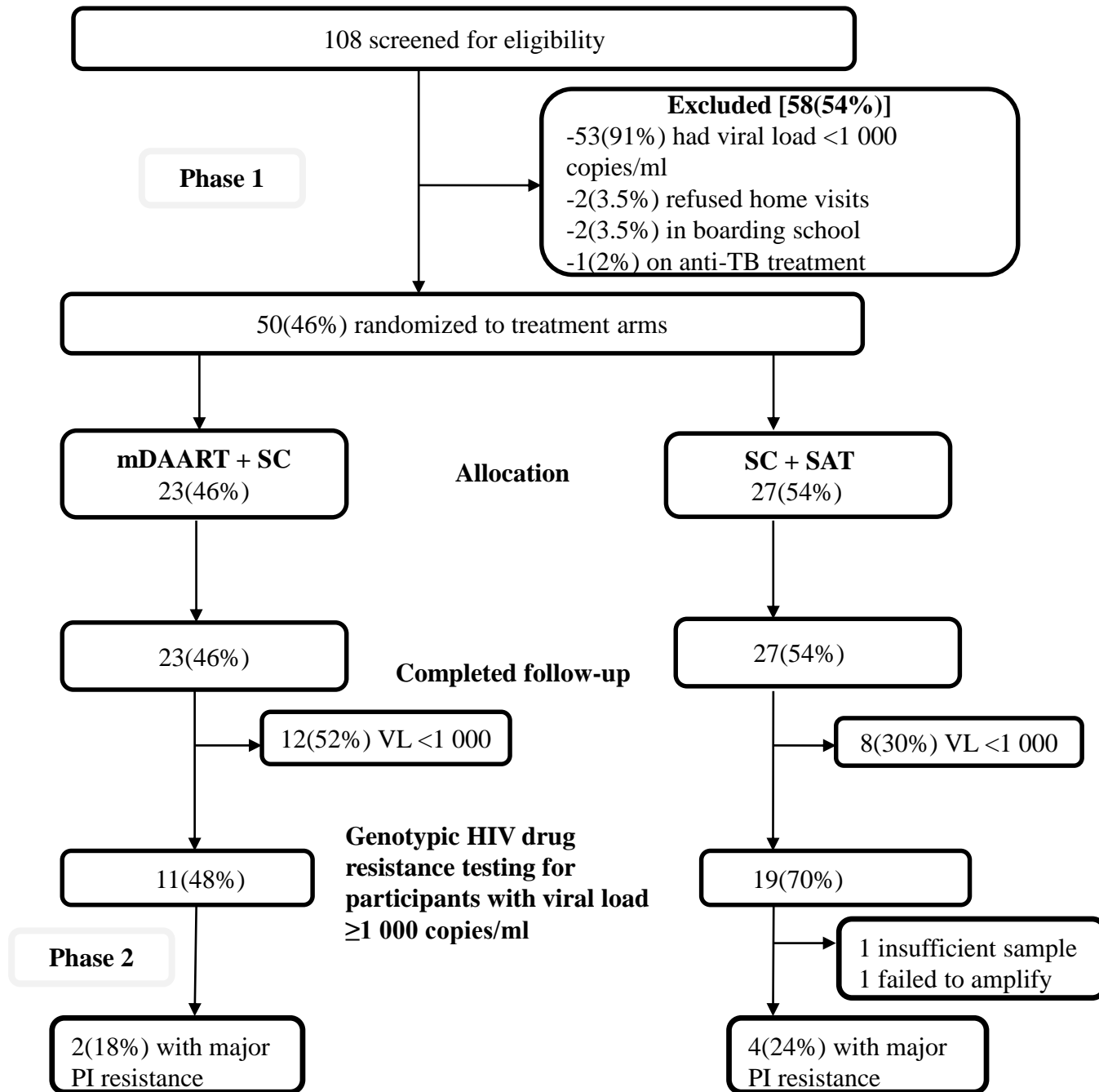
- Daily x 1st 10 week days
- Twice weekly x next 2 weeks
- Once weekly x next 2 weeks
- Once a fortnight x remainder of

## mDAART

### (SMS)

- SMS texts on weekends

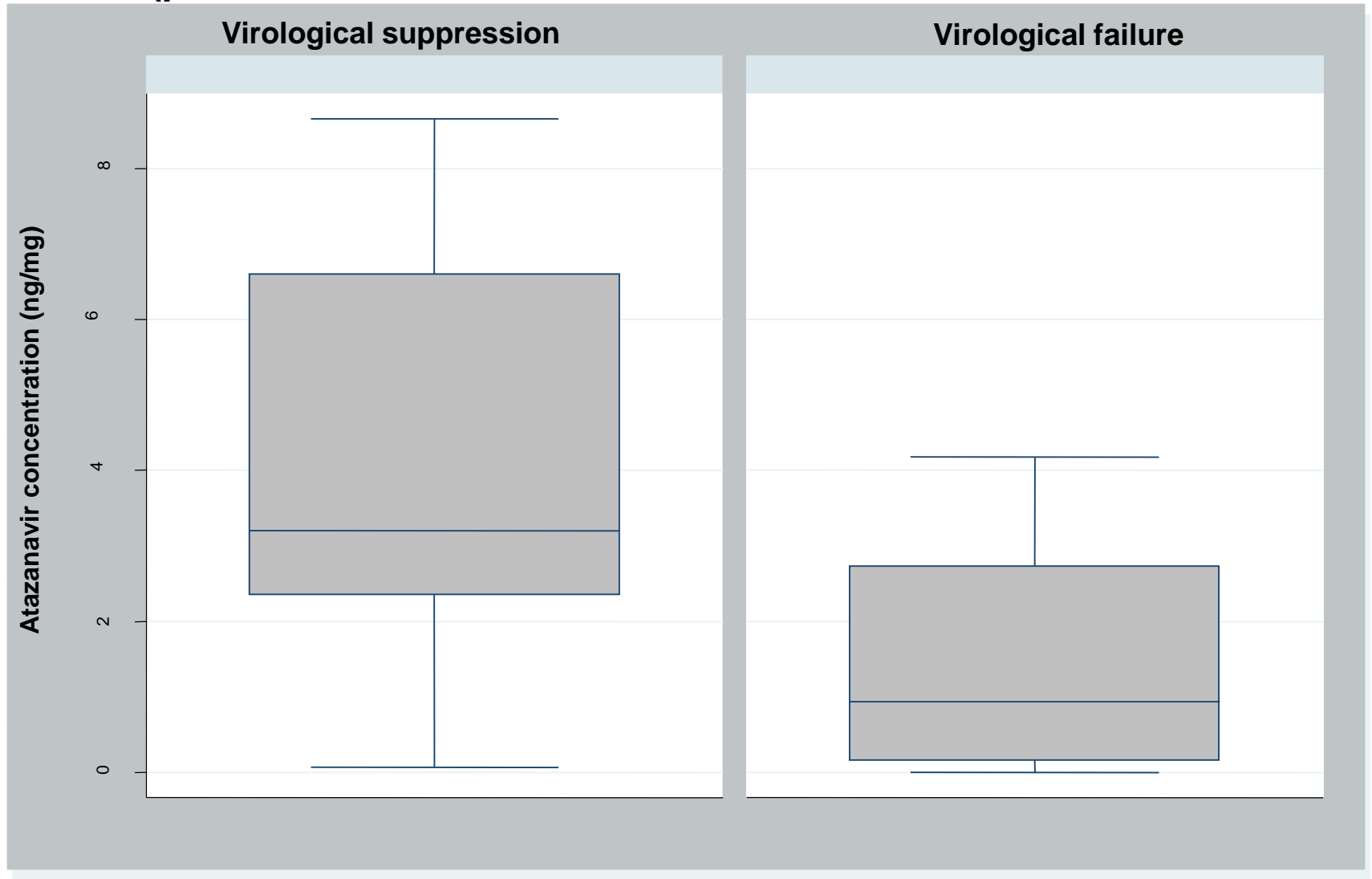




Variable	Total (n=50) n(%) or mean(SD)	mDAART (n=23) n(%) or mean(SD)	Standard care (n=27) n(%) or mean(SD)
Age (years)	15.8(1.8)	15.5(1.95)	16(1.7)
Gender: Female	27(54)	12(52)	15(56)
Male	23(46)	11(48)	12(44)
Total time on ART (months)	78(26)	80.9(21.6)	75.3(29.3)
Orphan status:			
Non-orphan	7(14)	5(22)	3(11)
Single orphan	20(40)	6(26)	13(48)
Double orphan	23(46)	12(52)	11(41)
BMI-for-age:			
Normal	25(55)	12(55)	13(54)
Underweight	14(30)	6(27)	8(33)
Overweight	7(15)	4(18)	3(13)
Viral load (log <sub>10</sub> copies/ml)	4.8(0.8) (70 500)	4.8(0.8)	4.7(0.9)
Average self-reported adherence: ≥95%	15(30)	6(26)	9(33)
80-94%	15(30)	9(39)	6(22)
<80%	20(40)	8(35)	12(45)
Self-reported closely following dosing schedule in past 4 days: Yes	22(44)	10(43)	12(44)
No	28(56)	13(57)	15(56)
Hair [ATV] (ng/mg) (n=44); mean(SD); 95% CI	1.4(1.5); 0-3.92	1.1(1.4); 0-3.79	1.7(1.6); 0-3.98

Variable	mDAART (n=23) n(%) or mean(SD); 95% CI	Standard care (n=27) n(%) or mean(SD); 95% CI	p-value
Viral load at follow-up: <1 000 copies/ml ≥1 000 copies/ml	12(52) 11(48)	8(30) 19(70)	<b>0.105</b>
Follow-up VL (log <sub>10</sub> copies/ml)	3.3(1.5); 2.6-3.9	4(1.5); 3.4-4.6	<b>0.048</b>
VL decrease (log <sub>10</sub> copies/ml)	-1.5(1.6); -2.2 - -0.9	-0.8(1.3); -1.3 - -0.3	<b>0.031</b>
Viral load change: ≥1 log <sub>10</sub> decrease <1 log <sub>10</sub> decrease	12(52) 11(48)	11(41) 16(59)	0.399
Average self-reported adherence at follow-up: ≥95% 80-94% <80%	15(65) 6(26) 2(9)	10(37) 8(30) 9(33)	<b>0.050</b>
Closely followed dosing schedule in past 4 days at follow-up: Yes No	19(83) 4(17)	10(37) 17(63)	<b>&lt;0.001</b>
Hair [ATV] (ng/mg) (n=42)	2.9(2.2); 0.5-7.2	2.3(2.5); 0-6.6	<b>0.203</b>

# Box and whisker plots showing atazanavir concentration in hair by virological outcome (p<0.001)



n=18; median hair level 3.21, IQR 2.35-6.61ng/mg)

n=24; median hair level 0.94, IQR 0.16-2.73ng/mg

Variable	VL<1 000cpm (n=20) n(%) or mean(SD); 95% CI	VL ≥1 000cpm (n=30) n(%)or mean(SD); 95% CI	p-value
Age (years)	15(1.98); 14.4-16.3	16(1.66); 15.4-16.7	<b>0.080</b>
Gender: Female	10(50)	17(57)	0.643
Male	10(50)	13(43)	
Caregiver: Parent/s	3(15)	7(23)	0.470
Other	17(85)	23(77)	
Initial WHO stage: 1-2	8(40)	8(27)	0.322
3-4	12(60)	22(73)	
Latest CD4 count: <200	7(35)	19(63)	0.133
200-350	6(30)	6(20)	
>350	7(35)	5(17)	
Total time on ART (months)	81.3(17.6); 73-90	75.3(30.8); 63-87	0.217
BMI-for-age: Normal	12(63)	13(48)	0.499
Underweight	4(21)	10(37)	
Overweight	3(16)	4(15)	
Average self-reported adherence, at follow-up, VAS: ≥95%	10(50)	15(50)	0.143
80-94%	8(40)	6(20)	
<80%	2(10)	9(30)	
Self-reported following dosing schedule in past 4 days at follow-up: Yes	14(70)	15(50)	0.160
No	6(30)	15(50)	
Hair [ATV] (ng/mg) (n=42): ≤2.35	5(28)	16(67)	<b>0.013</b>
>2.35	13(72)	8(33)	

## Multivariate logistic regression to determine factors associated with virological treatment failure

Variable	Relative risk (95% confidence interval)	p-value
Hair [ATV] at follow-up (ng/mg): ≤2.35	7.2(1-50.9)	<b>0.049</b>
Study arm: mDAART	0.26(0.04-1.62)	0.148
WHO clinical stage at ART initiation: 3-4	1.5(0.3-7.6)	0.613
Closely followed dosing schedule in past 4 days at follow-up: Yes	1.05(0.19-6)	0.953
Gender: Male	1.6(0.26-10.1)	0.598
Latest CD4 cell count (cells/mm <sup>3</sup> ): 200-350	1.3(0.2-8.8)	0.770
>350	0.6(0.09-4)	0.591
Average self-reported adherence, VAS, at follow-up:		
80-94%	0.28(0.05-1.7)	0.162
<80%	0.61(0.05-6.8)	0.689

Variable	[ATV] ≤2.35ng/mg (n=18) n(%) or mean(SD); 95% CI	[ATV]>2.35ng/mg (n=24) n(%) or mean(SD); 95% CI	p-value
Age (years)	15.7(1.9); 14.8-16.5	15.6(1.4); 15-16.3	0.464
Gender: Female	15(71)	8(38)	<b>0.030</b>
Male	6(29)	13(62)	
Time on ART (months)	75(28); 61.5-87.4-90.7	81(23); 70-91.6	0.218
BMI-for-age: Underweight	6(30)	5(26)	0.476
Normal	9(45)	12(63)	
Overweight	5(25)	2(11)	
Viral load: <1,000 copies/ml	5(24)	13(62)	<b>0.013</b>
≥1,000 copies/ml	16(76)	8(38)	
Viral load decrease (log <sub>10</sub> copies/ml)	-0.7(1.3); -1.2- -0.08	-1.8(1.5); -2.5- -1.1	<b>0.006</b>
Study arm: mDAART	10(48)	11(52)	0.758
Standard care	11(52)	10(48)	
Average self-reported adherence, VAS: ≥95%	9(43)	12(57)	0.507
80-94%	7(33)	7(33)	
<80%	5(24)	2(10)	
Change in average self-reported adherence, VAS:			<b>0.031</b>
No change	1(5)	6(28)	
Increased	12(57)	13(62)	
Decreased	8(38)	2(10)	
Closely followed dosing schedule in past 4 days: Yes	9(43)	15(71)	<b>0.061</b>
No	12(57)	6(29)	

## Multivariate logistic regression to determine factors associated with atazanavir concentrations in hair $\leq 2.35$ ng/mg

Variable	Relative risk (95% confidence interval)	p-value
Gender: Male	0.019(0.0008-0.44)	<b>0.013</b>
Latest CD4 cell count (cells/mm <sup>3</sup> ): 200-350	0.04(0.003-0.75)	<b>0.031</b>
>350	0.26(0.03-2.7)	0.259
Change in average self-reported adherence, VAS: Increased	7.4(0.38-143.8)	0.187
Decreased	295(2.6-33 921)	<b>0.019</b>
Study arm: mDAART	7(0.09-47.66)	0.644



# PI resistance

10 PI resistance, 6(21%)- high level:

- 5 with intermediate and/or low level ATV resistance + 1 with single I50L mutation
- 3(11%)- high level resistance to ATV, LPV and DRV (V32I, I50L, I54V, I47V and V82A)- switched to 3<sup>rd</sup> line
- 3(11%)- no resistance to LPV, switched to LPV/r, (alternative 2<sup>nd</sup> line)

# Discussion

mDAART resulted in:

- modest increase in virological suppression
- significant decrease in viral load
- lower viral load after follow-up
- significant increase in self-reported adherence (average and close following dosing schedule)
- \*modest VL suppression- ↓ing intensity of home visits, short mDAART time, ATV resistance

# Factors associated with VL failure

- [ATV] in hair strongest predictor of VL suppression (bi- and multivariate)
- Defined [ATV] associated with viral suppression ( $>2.35\text{ng/mg}$ )
- Although not statistically significant, SRA improved modestly in mDAART
- Clinically significant PI resistance was demonstrated

# Conclusion

## mDAART:

- Modestly improved VL suppression
- Significantly decreased VL
- Significantly increased average SRA
  
- Sub-optimal adherence was seen
- High level PI resistance was demonstrated
- Sub-optimal [ATV] seen