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ACTG AIDS CLINICAL TRIALS GROUP

Partner-based Intervention for Adherence to Second-line ART: A Multinational Trial (ACTG A5234)

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Background

- The rollout of ART for treatment of HIV in developing world has resulted in remarkable gains in survival
- Adherence rates have, in general, been better in developing than developed countries
  - Treatment failures occur and threaten long-term viability of programs
  - Non-adherence is thought to be the main cause of 1st line failure
  - 2nd line therapy is typically more expensive, and often more difficult to take
- Few adherence interventions have effect
  - Directly observed therapy (DOT) has had some success in subpopulations
  - Conventional DOT is logistically challenging

Objective

- To test whether a partner-based modified DOT (mDOT) intervention would result in higher rates of virologic suppression compared with standard of care after first-line treatment failure

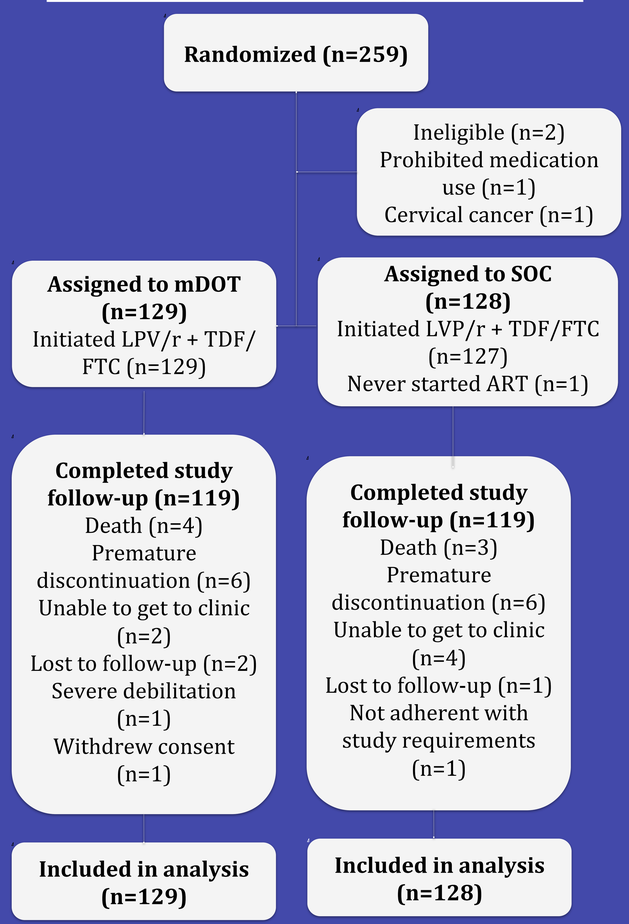
Methods

- Randomized clinical trial
  - 1:1 allocation to mDOT and standard of care (SOC)
  - Stratified by screening HIV RNA <10,000 cpm vs. ≥10,000 cpm
- Eligibility
  - Confirmed virologic failure (VF) (HIV RNA>1000 cpm)
  - 1st line: 1 NNRTI + 2 NRTI
  - Identifiable mDOT partner (family, friend, etc.)
- Study Sites: Brazil, Botswana, Haiti, Peru, South Africa, Uganda, Zambia, Zimbabwe
- Regimen: lopinavir/r (400 mg/100 mg) BID + TDF/FTC (300 mg/200 mg) qD
- Primary Endpoint
  - Confirmed HIV RNA>400 cpm by week 48
- Secondary Endpoints
  - Confirmed HIV RNA>400 cpm by week 24
  - Adherence measured using electronic monitors
    - Summarized quarterly as % of doses taken
- Sample Size Considerations (for ~90% power)
  - Assumed success rate in SOC= 60%
  - Desired detectable difference in success rate=20%
  - Target sample size=248 pairs (patients + partners)

mDOT Intervention Design

- mDOT partner chosen by patient
- Single training session of mDOT partner (1.5 hrs)
- Topics covered
  - Drug regimen details
  - Expected degree of adherence
  - Examples of +ve and –ve social support
  - Adverse drug effects and management
  - Handling missed doses
  - Documentation of observed doses
  - How and when to contact site for help
  - Provision of telephone cards to call
- Duration of active phase: 24 weeks
  - After active phase, mDOT could continue
  - After active phase, no telephone cards

Participant Flow Diagram



Results

Table 1. Baseline Characteristics

Characteristic	mDOT n=129	SOC n=128
Median age (IQR)	38 y (34,44)	37 y (33, 45)
Female sex	62 (48%)	65 (51%)
Black race	101 (78%)	103 (80%)
Hispanic ethnicity	27 (21%)	25 (20%)
Prior rx duration (IQR)	153 wks (82, 230)	144 wks (89, 245)
Entry CD4 (median) (IQR)	164 c/mm^3 (91, 250)	201 c/mm^3 (97, 292)
Nadir CD4 (median) (IQR)	122 c/mm^3 (37, 187)	109 c/mm^3 (45, 202)
HIV RNA (median) (IQR)	4.2 $_{log}$ cpm (3.8, 4.9)	4.2 $_{log}$ cpm (3.8, 4.9)

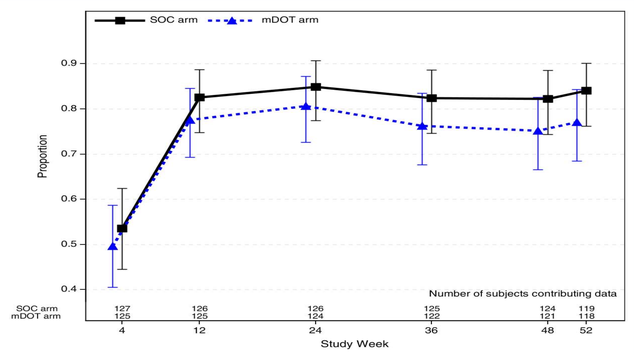
Results

Table 2. Endpoints by Study Arm

Endpoint	mDOT n=129	SOC n=128	p value*
VF wk 48	34 (26%)	23 (18%)	0.13
VF wk 24	24 (19%)	17 (13%)	0.31
Adherence Q1	95%	96%	0.38
Adherence Q2	91%	94%	0.30
Adherence Q3	90%	93%	0.17
Adherence Q4	90%	93%	0.36

* Fisher's Exact test for VF endpoints; Wilcoxon Rank Sum test for Adherence endpoints

Virologic suppression (HIV RNA ≤ 400 cpm) by arm over time (missing as failure)



Conclusions

- mDOT had no significant impact on virologic failure
  - High rate of suppression in both arms
- mDOT had no significant impact on adherence
  - High rate of adherence in both arms
- Other interventions to be tested in this setting still needed

Limitations

- Clinical trial volunteers at lower risk of subsequent non-adherence?
- Trial procedures may have served as co-intervention
- Single session training insufficient?

Study Sites

Botswana:	Botswana-Harvard Partnership, Gaborone
Brazil:	FIOCRUZ, Rio de Janeiro
Haiti:	GHESKIO, Port-au-Prince
Peru:	IMPACTA and INMENSA, Lima
South Africa:	University of Witwatersrand, Johannesburg
Uganda:	JCRC, Kampala
Zambia:	CIDRZ, Lusaka
Zimbabwe:	University of Zimbabwe, Harare

Disclosures

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