Session PX-2
Poster #1048

48-Week Outcomes in Adults Starting ART at CD4 ≥350 Using Streamlined Care in Rural Uganda

Vivek Jain[1], Dathan Byonanebye[2], Gideon Amanyire[2], Doug Black[1], James Rooney[3], Gabriel Chamie[1], Elvin Geng[1], Edwin Charlebois[1], Moses Kamya[2], Diane Havlir[1] and the SEARCH Collaboration

[1]University of California, San Francisco, USA; [2]Makerere University, Kampala, Uganda; [3]Gilead Sciences, Foster City, USA

Vivek Jain, MD, MAS
UCSF Box 0874
HIV/AIDS Division
San Francisco, CA 94143
Tel: (415) 326-3402
Email: vivek.jain@ucsf.edu

Background

- As WHO guidelines recommend earlier ART initiation, concerns persist about whether healthy asymptomatic individuals with high CD4+ cell counts in resource-limited settings will adhere well to antiretroviral therapy (ART) and achieve high rates of viral suppression.
- Some prior studies have raised concerns about higher CD4+ counts predicting lower ART efficacy due to lower adherence, however these have primarily been conducted in individuals with lower CD4+ cell counts.
- **Very few data on asymptomatic high CD4+ count individuals exist to inform the question of how strong adherence and viral suppression will be.**

Methods:

- The **EARLI Study (NCT01479634):** an open-label study of ART administration via a streamlined care model to ART-naïve, HIV-positive Ugandan adults (age≥18) receiving care at a prototypical Level-IV government health facility in Mbarara, Uganda.
- **Recruitment:** via clinic database queries, file reviews of patients attending clinic visits, and HIV diagnosis/linkage from a community-wide health campaign in the geographic parish served by the health center.
- **Antiretroviral Therapy:** Truvada (TDF) + efavirenz (EFV) or Aluvia (ritonavir/lopinavir [RTV/LPV]). Substitution of TDF if eGFR≤50, of EFV to RTV/LPV if pregnancy occurred, or any ARV at study staff discretion.

Methods (cont'd)

- **Inclusions:** HIV-positive, CD4≥350, ART-naïve (except for PMTCT or ≤7d duration), living within 30km radius of health center, able to swallow oral medication, able to give written consent. **Exclusions:** intent to relocate to >30km distance, WHO stage 3/4 illness, pregnant, neutrophil count <500 cells/uL, hemoglobin ≤7.0 g/dL, platelets ≤50,000, ALT>5x upper normal value, eGFR≤60 mL/minute (MDRD), positive Gene Xpert test.
- **Assessments:** Week 0 & week 4 by medical officer; weeks 8, 12, 24, 36, 48 by nurse. Toxicity/adverse event screening at every visit with conversion of visit to medical officer as needed. Pregnancy screening at every visit.
- **Adherence:** 3-day self-reported ART recall.
- **Laboratory Evaluations:** Chemistries at weeks 0/48, BUN/creatinine at weeks 8/48, CBC and LFTs at weeks 12/48. Plasma viral load at weeks 0, 24, 48. CD4+ count at weeks 24/48.
- **Retention / Participant Tracking:** 7-day window before/after target date for visit to be counted as made. After failure to present on visit date, telephone contact attempted. Defaulter tracking performed after missed visits.
- **Telephone Access for Participants:** Mobile phone number of study clinician provided to all participants with offer of availability for questions on ART, side effects, clinical status, appointments, or any concerns.
- **Clinic Flow:** rapid transit through clinic, pharmacy window medication refills, 3-month return visits.
- **Incentives:** none provided.

Results: Demographics

CD4≥350 (n=200)	
Age, median (IQR)	35 years (29-41)
Sex, %	65.1% F / 34.9% M
CD4, median (IQR)	**564/uL** (448-712)
HIV RNA, median (IQR)	**22,400 c/mL** (4,137-87,759)

Results: 48 Week Retention



Results: Adherence

Visit	CD4>350 (n=197)	
Week 4	94.4%	(186/197)
Week 8	97.8%	(182/186)
Week 12	99.4%	(183/184)
Week 24	98.9%	(188/190)
Week 36	98.3%	(176/179)
Week 48	98.9%	(178/180)
Total	**97.9%**	**(1093/1116)**

visits with no missed ARV doses in past 3 days (by recall)

Results: Virologic Suppression

Week 24	Week 48
95.4% (188/197)	**96.9%** (186/192)

Results: Adverse Events

Adverse Events	Cumulative (by Week 48)	Details
Grade 3/4 Laboratory Abnormalities	22 (18 participants)	neutropenia, n=11 creatinine, n=2 (both resolved)
Deaths	2	inoperable gastric carcinoma cholecystectomy complications
Hospitalizations	12 (6.1%)	pneumonia (5; 1 with sepsis), malaria (1), malignancy complications (2), dyspepsia (2), cholecystitis (1), anxiety (1)

Results: Medical Officer Usage

Reason for MO Visit	Converted from RN	Un-sched.	Sched by MO	Missed Last Visit	Other
n (% of total)	n=92 (24%)	n=193 (51%)	n=28 (7%)	n=65 (17%)	n=6 (2%)

Results: Transit through Clinic

Visit Type	Week 8 n=6	Week 12 n=14	Week 24 n=89	Week 36 n=90	Week 48 n=29	Un-sched. n=40
Total time (m)	**35**	**32**	**35**	**25**	**54**	**30**
Waiting time (m)	15	14	19	13	28	11

Conclusions

- **48-week HIV RNA suppression rates exceeded 95% in an open label study of ART in 197 adults with CD4>350 receiving streamlined care in a rural Ugandan clinic.**
- **These high CD4+ individuals showed robust retention in care, strong ART adherence, and little medication toxicity.**
- **These data challenge current views that asymptomatic HIV-infected adults will not be interested or able to comply with ART when initiated at high CD4+ cell counts.**
- Durability of model and results will continue to be assessed in years 2-3.

Acknowledgments

We thank the EARLI Study participants, and Makerere Joint AIDS Program and IDRC staff. This work is supported by NIH/NIAID U01 AI069502 to DH, P30 AI027763 to Paul Volberding/UCSF, and NIH UCSF-CTSI KL2TR000143 to VJ. EARLI also received material support via donated HIV antiretroviral medication (Truvada) and research grant support from Gilead Sciences, Inc.