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BRIEF REPORT

Rapid Antiretroviral Therapy Among Individuals With Acute and Early HIV

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HIV transmission is increased during acute and early HIV (AEH). Rapid antiretroviral therapy may shorten the duration of infectivity. We show rapid antiretroviral therapy in AEH is acceptable and effective, with 69.0% of participants starting ART within 7 days of HIV diagnosis disclosure, and 88.1% achieving suppression by 48 weeks.

Keywords. rapid ART; HIV; acute HIV.

(See the Editorial Commentary by Coffey on pages 134–6.)

The HIV care continuum in the United States continues to show gaps, including a notable proportion of persons diagnosed with HIV who are not receiving antiretroviral therapy (ART) [1, 2]. One strategy to improve the proportion of individuals diagnosed with HIV who receive ART is to initiate same-day or rapid-ART (≤7 days from diagnosis) [3]. Several studies have demonstrated that rapid-ART is acceptable and is associated with improved rates of linkage to care, shorter time to viral suppression, and a greater proportion on ART with viral suppression at 1 year [3]. To date, this strategy has not been thoroughly evaluated in persons with acute and early HIV (AEH) infection.

Persons with AEH represent a challenging but important group of individuals to identify during HIV screening, given that increased infectivity during AEH may account for up to 50% of all HIV sexual transmission events [4, 5]. The early identification and treatment of individuals with AEH has the potential to reduce the period of infectivity and the number of secondary transmission events [6]. Additionally, initiation of ART in AEH leads to a greater immune system recovery and lower latent viral reservoirs [7, 8]. We report the outcomes of a rapid-ART initiation program among individuals diagnosed with AEH in San Diego, California.

METHODS

Participants were recruited from HIV testing sites in San Diego, California, including the Lesbian Gay Bisexual and Transgender Center and the NIH-funded Primary Infection Resource Consortium (PIRC) HIV testing program at the University of California San Diego. Testing sites recruitment occurred through community-based healthcare programs, print and social media advertisements, and dating/hookup website banner advertisements. Individuals presenting for testing underwent rapid HIV serological testing with negative antibody screens reflexing to qualitative HIV nucleic acid testing. Participants diagnosed with HIV were enrolled to the PIRC study [9] and an estimated date of infection (EDI) was derived as previously described [7]. Infection was characterized as acute (antigen/nucleic acid positive and antibody negative/indeterminate) or early (antibody positive and limiting-antigen avidity assay [10] or detuned assay [11] consistent with recent infection <133 days).

Between December 15, 2014 and October 31, 2018, adults (≥18 years old) newly diagnosed with AEH enrolled in the PIRC observational study were offered rapid-ART (defined as ART initiation ≤ 7 days from diagnosis disclosure; hereafter referred to as diagnosis) with provision of ART at their first study visit after HIV diagnosis (ideally same day). Day 0 was defined as the day that the person was informed of their diagnosis. The rapid-ART protocol was a modification of the RAPID care protocol used by Pilcher and colleagues [12] and included: same day medical visit lasting 2–3 hours with routine care laboratories; study supplied integrase strand transfer inhibitor (INSTI)-based ART; HIV provider visit within 24–48 hours of diagnosis; telephone/in-person follow-up with provider within 7–14 days to review labs and adherence; case management services (including insurance assessment); and linkage to care. Follow-up was performed at weeks 2, 4, 8, 12, 24, and 48 weeks.

Primary outcome measures were assessed on an intention-to-treat basis and included: the proportion of participants that started rapid-ART, the median duration from EDI to viral suppression (<50 copies/mL or undetectable), the duration from ART initiation to viral suppression, and the proportion of individuals with viral suppression by 12, 24, and 48 weeks. A "per-protocol" analysis was also performed for participants who started ART ≤7 days from diagnosis. For these participants we report the median duration from EDI to viral suppression, the median duration from ART initiation to viral suppression, and the proportion with viral suppression by 12, 24, and 48 weeks.

The UCSD Human Research Protections Program approved the study protocol and consent. All participants provided written informed consent.

Analysis

Descriptive data of participants with AEH during the rapid-ART intervention were collated. Analyses were performed on

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an intention-to-treat basis for primary outcomes, including all persons who were offered rapid-ART. Per-protocol analyses were performed on the subset of participants who started ART ≤7 days from diagnosis. A sensitivity analysis defining viral suppression as < 200 copies/mL was performed (data not shown).

RESULTS

A total of 84 individuals with AEH infection were included in the study. The mean age was 30 years, most participants were men (95.2%), and 61.5% were Black American or Hispanic (Table 1). By duration of infection, 39.3% had acute and 60.7% early HIV infection. Median peak viral load was 5.1 $\log_{10}$ copies/mL and median nadir CD4+ T cell count was 517.5 cells/μL. Substance use was reported in 46.4%, homelessness in 6.0%, and median household income was <$1000/month in 24.4%.

During follow-up, 81 (96.4%) participants initiated ART after a median duration of 4 days from diagnosis (IQR 1–8): 29/84 (34.5%) within 2 days, and 58/84 (69.0%) ≤7 days. Among 26 participants who did not start ART within 7 days, 23 initiated ART within 60 days of diagnosis. Three participants were lost to follow-up after only a baseline visit. No association between starting ART within 7 days and age, race/ethnicity, household income, substance use, or homelessness was found.

In the intention-to-treat analysis, the median duration from EDI to viral suppression was 15.3 weeks (IQR 12.9–24.4) and the median duration from ART initiation to viral suppression 7.5 weeks (IQR 4.0–12.4). The proportion of participants who achieved viral suppression by 12, 24, and 48 weeks after diagnosis was 58.3%, 79.8%, and 88.1%, respectively. Persons who initiated ≤7 days from diagnosis were more likely to achieve viral suppression by 24 weeks, compared to persons who did not (86.2% vs 65.4%, $P = .03$). Ten individuals did not have follow-up results available or did not suppress viral load during follow-up: none had resistance mutations at baseline. Three of the 10 moved away and did not attend any follow-up; 5 were removed from study due to nonadherence with visits; 1 was admitted to inpatient psychiatric care; and 1 did not achieve viral suppression after 48 weeks of follow-up.

A total of 58 participants with AEH started ART ≤ 7 days from diagnosis and were included in the per-protocol analysis. The median duration from EDI to viral suppression was 14.7 weeks (IQR 11.1–23.9) and the median duration from ART initiation to viral suppression 7.7 weeks (IQR 4.0–12.4). The proportions of per-protocol participants with viral suppression by 12, 24, and 48 weeks after diagnosis were 67.3%, 90.9%, and 98.1%, respectively. The proportion of persons with viral suppression by 24 weeks was not significantly different between persons who started ART ≤ 7 days vs >7 days ($P = .23$). Outcomes among persons with acute HIV who initiated ART within 7 days of diagnosis are also shown in Table 1.

DISCUSSION

Our study shows that, on an intention-to-treat basis, the implementation of a rapid-ART program among individuals diagnosed with AEH resulted in over two-thirds (69.0%) of participants initiating ART within 7 days of diagnosis and viral suppression in 88.1% by week 48. Among the subset of participants with AEH that initiated ART ≤7 days from diagnosis, ART was found to be highly effective, despite relatively high baseline viral load values, with a median time from ART initiation to viral suppression of 7.7 weeks and 90.9% achieving viral suppression within 24 weeks of diagnosis.

While only two-thirds of participants started ART within 7 days of diagnosis, almost all participants (96.4%) eventually initiated ART within 60 days, potentially due to the additional support, drug availability, and case management included in the rapid-ART program. Interestingly, ART uptake within 7 days was not associated with any socioeconomic or demographic factors and persons with AEH who started ≤7 days from diagnosis, were more likely to virally suppress by 24 weeks compared to those that did not ($P = .03$).

Prior rapid-ART studies demonstrated improved uptake of ART, immunological benefits, improved engagement in care, and improved time to viral suppression with rapid-ART, but have not discussed the potential prevention benefit of rapid-ART [3, 13–15]. Our study extends rapid-ART to the AEH population and shows that, using a case-finding strategy and rapid-ART program, the time from EDI to viral suppression can be limited to a median of just 15.3 weeks. While AEH case finding and rapid-ART is resource intensive, this reduction in the highly infectious period potentially could reduce transmission events and thus, if widely implemented, reduce population incidence.

Our study had limitations: our study population was comprised of mostly white and Hispanic men, reflecting the HIV epidemic in Southern California, which may limit its generalizability to other populations with more Black/African Americans and/or women. In addition, detailed qualitative data from participants in this study was not included; however, prior work within the PIRC study has highlighted concerns about insurance and drug coverage, and needing time to "absorb the diagnosis" as reasons for delayed ART initiation [16].

In conclusion, AEH case-finding and rapid-ART is effective and can minimize the time from EDI to viral suppression. Our results support further work evaluating the impact of rapid-ART among AEH on HIV transmission networks and long-term outcomes for participants. These data support the recommendation of rapid-ART for persons with AEH, including persons reporting low socioeconomic status, substance, or homelessness, in settings with appropriate infrastructure and resources.

Table 1. Demographics and ART Initiation Details for Rapid-ART Participants.

Baseline Participant characteristics[a]	Rapid-ART ITT[b] (n = 84)	Rapid-ART per protocol (n = 58)	Rapid-ART per protocol acute HIV (n = 26)
Median age—yr. (range)	30 (25.0–38.5)	28.5 (24.0–34.0)	27 (24.0–31.0)
Gender—no. (%)			
Male	80/84 (95.2)	54/58 (93.1)	24/26 (92.3)
Female	3/84 (3.6)	3/58 (5.2)	1/26 (3.8)
Transgender	1/84 (1.2)	1/58 (1.7)	1/26 (3.8)
Race/ethnicity—no. (%)			
White (non-Hispanic)	26/78 (33.3)	15/53 (28.3)	8/23 (34.8)
Black (non-Hispanic)	4/78 (5.1)	4/53 (7.5)	2/23 (8.7)
Hispanic	44/78 (56.4)	30/53 (56.6)	11/23 (47.8)
Other (including multi-racial)	4/78 (5.1)	4/53 (7.5)	2/23 (8.7)
Highest level of education—no. (%)			
<High School (n = 1) or HS diploma	17/83 (20.5)	12/58 (20.7)	5/26 (19.2)
Some college (incl Assoc Degree)	34/83 (41.0)	26/58 (44.8)	12/26 (46.2)
College degree (incl postgrad)	32/83 (38.6)	20/58 (34.5)	9/26 (34.6)
Monthly household income—no. (%)			
<$1000	19/78 (24.4)	12/55 (21.8)	3/24 (12.5)
$1000–$1999	22/78 (28.2)	17/55 (30.9)	8/24 (33.3)
$2000–$3999	20/78 (25.6)	17/55 (30.9)	7/24 (29.2)
$4000+	17/78 (21.8)	9/55 (16.4)	6/24 (25.0)
Homeless—no. (%)	5/83 (6.0)	3/58 (5.2)	0/26 (0.0)
Recreational drug use in past month—no. (%)			
Any drug	39/84 (46.4)	27/58 (46.6)	1/26 (3.8)
Stimulants	22/84 (26.2)	15/58 (25.9)	6/26 (23.1)
Heroin	0/84 (0)	0/58 (0)	0/26 (0)
Injection drug use	4/84 (4.8)	3/58 (5.2)	1/26 (3.8)
STI diagnoses—no. (%)			
Any STI	32/76 (42.1)	21/55 (38.2)	10/24 (41.7)
Syphilis[c]	15/72 (20.8)	21/55 (38.2)	4/24 (16.7)
Gonorrhea (any site)	9/83 (10.8)	6/57 (10.5)	4/25 (16.0)
Chlamydia (any site)	12/83 (14.5)	7/57 (12.3)	3/25 (12.0)
Stage of HIV infection—no. (%)			
Acute (Ab−, Ag+)	33/84 (39.3)	26/58 (44.8)	26/26 (100.0)
Early	51/84 (60.7)	32/58 (55.2)	0/26 (0.0)
Lab results			
Median peak viral RNA (IQR) $\log_{10}$ copies/mL	5.1 (4.4–5.7)	5.1 (4.6–5.8)	5.7 (5.1–6.0)
Nadir CD4—cells/μL	517.5 (367–635)	462.5 (350–625)	366.5 (330–572)
Disclosure of HIV diagnosis, median (IQR)			
Days since EDI	70 (15.0–70.0)	62 (15.0–70.0)	14.5 (12.0–16.0)
Days since HIV testing	0 (0.0–5.0)	0 (0.0–5.0)	5 (3.0–6.0)
ART treatment, median (IQR):	n = 81 started ART	n = 58 started ART	n = 26 started ART
Days from EDI to ART initiation	70 (20.0–89.0)	63 (17.0–76.0)	17 (15.0–20.0)
Days from diagnosis disclosure to ART	4 (1.0–8.0)	2.5 (0.0–5.0)	3 (1.0–4.0)
Days from enrollment to ART	0 (0.0–5.0)	0 (0.0–1.0)	0 (0.0–0.0)
Viral Suppression (<50/ND)	N = 74 suppressed	N = 53 suppressed	N = 24 suppressed
Weeks since EDI	15.3 (12.9–24.4)	14.7 (11.1–23.9)	10.7 (6.4–14.3)
Weeks since diagnosis disclosure	8.9 (4.7–12.8)	8.0 (4.3–12.7)	8.3 (4.2–12.7)
Weeks since ART	7.5 (4.0–12.4)	7.7 (4.0–12.4)	8.1 (4.0–12.1)
Virologic suppression (<50/ND) - no. (%)			
From diagnosis			
Suppressed at 12 weeks	49/84 (58.3)	37/55 (67.3)	12/25 (48.0)
Suppressed at 24 weeks	67/84 (79.8)	50/55 (90.9)	23/25 (92.0)
Suppressed at 48 weeks	74/84 (88.1)	53/54 (98.1)	24/24 (100.0)
From ART initiation			
Suppressed 12 weeks	56/84 (66.7)	41/55 (74.5)	21/25 (84.0)
Suppressed at 24 weeks	69/84 (82.1)	50/55 (90.9)	23/25 (92.0)
Suppressed at 48 weeks	74/84 (88.1)	53/54 (98.1)	24/24 (100.0)

[a] Due to missingness, categorical variables include denominators for full context.

[b]Rapid-ART provided beginning mid-December 2014. Stribild® (Elvitegravir/Cobicistat/Emtricitabine/Tenofovir Disoproxil Fumarate), Genvoya® (elvitegravir, cobicistat, emtricitabine & tenofovir alafenamide), and Biktarvy® (bictegravir, emtricitabine & tenofovir alafenamide) were provided to rapid-ART participants sequentially as they were FDA-approved.

[c]Active infection defined as RPR ≥ 1:8

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

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Potential conflicts of interest. S. Little received an honorarium and travel support from Gilead Sciences. She also received grant support paid to her institution from Gilead Sciences. All other authors report no potential

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