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Directly Observed Therapy for Non-adherent HIV Infected Adolescents – Lessons Learned, Challenges Ahead

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Abstract

Background: Second to gaining access to antiretrovirals, maintaining medication adherence is perhaps the biggest global challenge to optimizing HIV care. Directly Observed Therapy (DOT) works for patients with tuberculosis, and shows promise for non-adherent HIV infected adults, but remains unexplored in HIV-infected adolescents. Given the unique needs/barriers to adherence for adolescents, a pilot study to examine feasibility of a DOT model was designed.

Methods: 4 US sites were selected for this 24-week Pediatric AIDS Clinical Trials Group (PACTG 1036B) pilot study. The DOT model incorporated feedback from HIV-infected adolescents (PACTG 1036A). Behaviorally infected adolescents with known medication adherence problems received once-a-day DOT from trained DOT facilitators at a site of their choice in the community. Medications taken more than once daily were self-administered. DOT frequency was weaned based on patient's ongoing adherence to medications (DOT/non-DOT). Assessment of CD4 count, HIV RNA PCR, mental health, barriers to adherence, and beliefs about medication was done at baseline, week 12 and week 24. Patient feedback (exit survey) was obtained at the end of DOT.

Results: 20 patients, 65% female, median age 21 years (range 18–24), median CD4 227 cells/µL (range 10–443), and median HIV-1 RNA level 4.6 log10 copies/ml (range 1.0–5.8) enrolled on study over one year. 10 (50%) patients had current/past history of major depression. For week 4, 8 and 12 study visits, 17, 14 and 14 patients came, respectively. Compliance with recommended DOT visits (e.g., able to meet the DOT facilitator) was a median (range): Week 4, 91% (64–100); week 8, 91% (33–100); and week 12, 83% (57–100). Overall, 6 patients (30%; 95% CI 11.9–54.3) completed >90% of their study specified frequency of DOT and successfully weaned to self-administered therapy. Per exit survey reports (n=14), 12 found meeting with the DOT facilitator easy, 11 felt DOT increased motivation to take medications, 7 felt sad when DOT ended, 10 were willing to continue or restart DOT given a choice, and 100% would recommend DOT to a friend with adherence problems.

Conclusions: This pilot study demonstrates community-based DOT for non-adherent HIV-infected adolescents is feasible. Ongoing analyses will identify characteristics of successful DOT candidates. Overall patient feedback for this intervention was positive, which combined with the logistical information gained, will inform future DOT studies.

Introduction

- Maintaining adherence to HIV medications is perhaps the biggest challenge to optimizing HIV care for adolescents in resource rich countries such as the US.
- Only 41% of HIV-infected adolescents, recruited from 13 U.S. cities into the Reaching for Excellence in Adolescent Care and Health (REACH) project, reported full adherence to HAART.
- A number of factors have been reported as reasons for poor adherence.
- Directly Observed Therapy has an established track record ensuring success of tuberculosis therapy.
- Existing experience with the use of Directly Observed Therapy as an intervention to improve adherence to medication in HIV infected patients has been encouraging.
- Given the unique needs/barriers to adherence for adolescents, a pilot study to examine feasibility of a DOT model was designed.

Methods

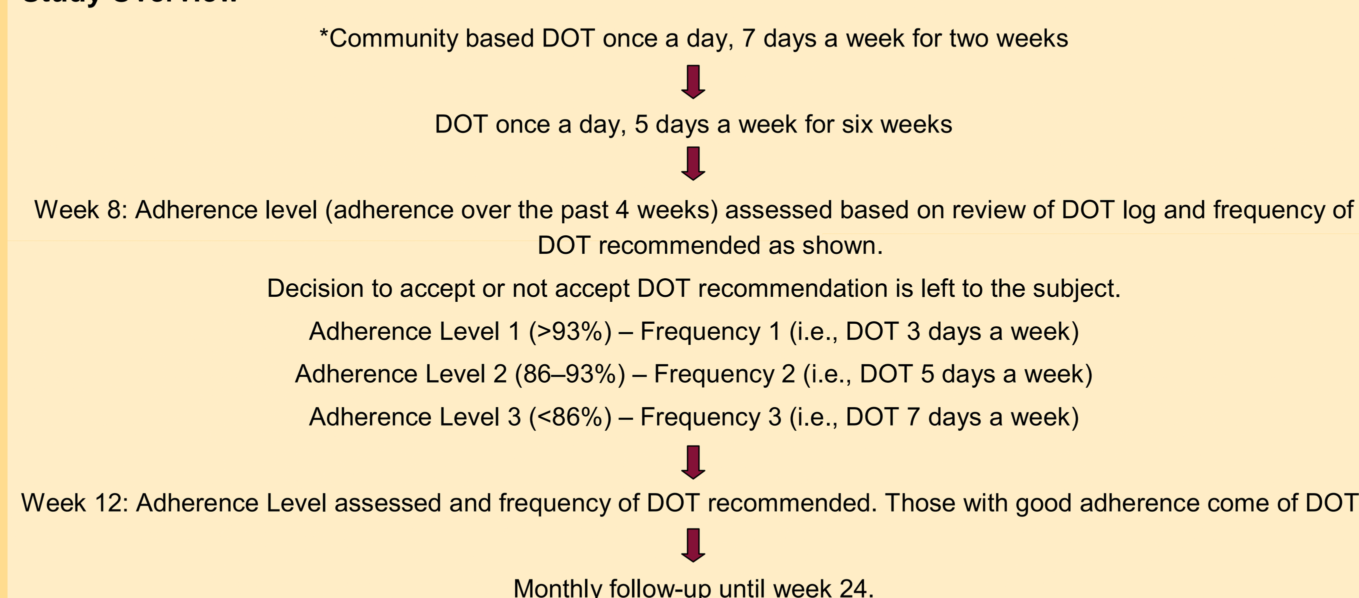
PACTG 1036B Study Overview

- Primary Objective: To examine feasibility of providing DOT to HIV-1-infected adolescents.
- Pilot study; study duration 24 weeks
- DOT model based on findings of PACTG 1036A (focus groups)
- 20 participants from 4 PACTG sites — Detroit, Memphis, Los Angeles, San Diego
- Study Population
  - HIV-1-infected subjects 16 to <22 years of age who are either continuing, changing, or re-initiating HAART regimens and have demonstrated adherence problems (less than 85% of prescribed doses taken, as clinically disclosed, on two consecutive occasions, at least one month apart)
- Primary care physician prescribes the best once daily or twice daily HAART.
- DOT provided in the community
- DOT wean based on patient adherence

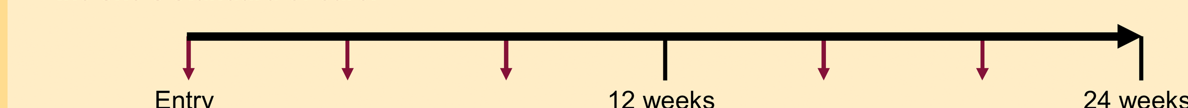
DOT Facilitators

Individuals hired by each site to provide DOT to each patient at a site in the community (including the patient's home) chosen in mutual agreement with the patient. These individuals were trained in providing DOT and in study specified procedures using a DOT facilitator training program developed by the PACTG 1036B team.

Study Overview



*** Note: DOT once a day. While receiving DOT other doses unobserved but prompted by automatic pager reminders. Subjects to return pagers (automated prompts stop) once DOT phase is completed unless it is the site's standard of care.**



Study Related Assessments

- Viral load (entry, week 8, 12, and 24)
- CD4 counts, CBC (entry week 12, and 24)
- Pregnancy test at screening
- Adherence assessment by
  - Monthly review of DOT log while patient on DOT
  - Four week recall (monthly visit) throughout study)
  - Pill count at week 24
- Beck Depression Inventory – II (BDI-II) (entry, 12 weeks, 24 weeks)
- Beck Hopelessness Scale (BHS) (entry, 12 weeks, 24 weeks)
- Coping Responses Inventory (CRI) (entry, 12 weeks, 24 weeks)
- Youth Self-Report (YSR)/Adult Self Report (ASR) (entry, 12 weeks, 24 weeks)
- Assessment of patient beliefs about medication (entry, 12 weeks, 24 weeks)
- Use of Support Services (monthly visit)
- Exit Survey (after completion of DOT)

Results

Table 1. Baseline Characteristics

Characteristic	Value
Study participants (total)	20
Detroit	3
Memphis	8
Los Angeles	8
San Diego	1
Age in years (median, range)	21 (18 – 24)
Female	13 (65%)
Race/Ethnicity	
White (non-hispanic)	1 (5%)
Black (non-hispanic)	15 (75%)
Hispanic (regardless of race)	4 (20%)
Education and Employment	
Currently un-employed	15 (75%)
Grades 1–12 education completed	15 (75%)
Mental Health (psychiatric related diagnosis)	
Major depressive disorder	10 (50%)
Other	1(5%)
Substance use (> 1-2 times a week)	
Alcohol	5 (25%)
Marijuana	9 (45%)
Viral load in log10 copies/mL (median, range)	4.61 (1.04 – 5.75)
Absolute CD4 count cells/mm^3 (median, range)	227 (10 – 443)

Table 2. Proportion of patients receiving DOT who completed their DOT interaction

Study week (Patients receiving DOT)	DOT interactions completed: median (range)
Week 4 (17)	91% (64 – 100%)
Week 8 (14)	91% (33 – 100%)
Week 12 (14)	83% (57 – 100%)
Week 16 (5)	100% (57 – 100%)
Week 20 (4)	62% (43 – 79%)
Week 24 (3)	50% (20 – 75%)

DOT Success

Overall 6 of 20 patients (30%; 95% CI 11.9–54.3) were considered a "DOT success" i.e. completed > 90% of their study specified frequency of DOT and successfully weaned to self-administered therapy.

Three of the above patients were able to maintain a >93% adherence to medications at week 24 (end of study).

Table 3: Self-reported adherence to medications (four week recall)

Patients who were a "DOT Success" as defined before

Medication adherence	Week 4 (N=6)	Week 8 (N=6)	Week 12 (N=6)	Week 16 (N=6)	Week 20 (N=4)	Week 24 (N=6)
> 93%	6	6	6	6	4	3
86 – 93%	0	0	0	0	0	0
< 86%	0	0	0	0	0	3

Patients who were not a "DOT Success" as defined before

Medication adherence	Week 4 (N=10)	Week 8 (N=9)	Week 12 (N=8)	Week 16 (N=6)	Week 20 (N=6)	Week 24 (N=5)
> 93%	8	6	4	3	1	2
86 – 93%	1	1	1	2	2	2
< 86%	1	2	3	1	3	1

Table 4: HIV RNA suppression in study participants

Study Week	Patients scheduled	Patients with < 400 copies/mL	Patients with < 50 copies/mL	Proportion (95% CI) < 400 c/mL	Proportion (95% CI) < 50 c/mL
8	14	8	3	0.57 (0.29, 0.82)	0.21 (0.05,0.51)
12	14	9	5	0.64 (0.35, 0.87)	0.36 (0.13, 0.65)
24	12	6	5	0.50 (0.21, 0.79)	0.42 (0.15, 0.72)

- Median drop in viral load from baseline to week 12 was -1.92 logs (P value 0.09)
- There was no statistically significant difference in number of patients achieving an undetectable viral load at week 24 between those who had >90% adherence to DOT visits versus those who were not as adherent to the protocol specified DOT process.

Patient feedback regarding DOT (from 14 participants):

- Majority of the respondents found choosing a place to receive DOT, remembering to be there, and taking medications in the presence of the DOT facilitator easy.
- Most felt more motivated to take medications after receiving DOT and reported increased regularity of taking them.
- 100% reported they would recommend DOT to a friend
- Majority felt DOT helped them in ways more than just taking medications. Support and encouragement were some of the sentiments reported in this regards.
- 50% of respondents reported feeling sad when DOT ended and >90% reported missing meeting the DOT facilitator.

Conclusions

- Community based Directly Observed Therapy (DOT) in HIV infected adolescents is feasible and acceptable.
- Overall feedback from adolescents who received community based DOT was very positive and supportive of future interventions using this approach.
- A sub-group of youth were unable or unwilling to continue with DOT and further analysis and randomized controlled studies are needed to determine in whom this intervention is most applicable.
- Twelve weeks of DOT was not adequate for some youth to maintain adherence, as illustrated by the increased self reported non-adherence at weeks 20 and 24. Future studies may need longer duration or repeated cycles of DOT, provision of simultaneous interventions, and possible sustained support from the DOT facilitator post completion of DOT doses to address adherence barriers.

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Participating sites:

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St. Jude Children's Research Hospital – Joyce Fields and Abby Verbist (DOT facilitators), Jill Utech (Study coordinator), Aditya Gaur (PI)

University of Southern California, LA and Children's Hospital of LA –Roman Hernandez (DOT facilitator), Cathy Salata and Cecilia Lind (Study coordinators), Michael Neely MD (PI)

University of California, San Diego – Roberto "Hugo" Escudero (DOT facilitator), Kim Norris (study coordinator), Stephen Spector MD (PI)

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