Adherence to ART and acceptability of planned treatment interruptions (PTI) in the PENTA 11 trial

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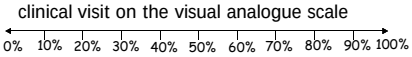
Introduction

- Complete HIV suppression requires a high level of adherence[1,2] and for children this will be difficult to sustain over a lifetime
- In addition, antiretroviral drugs have appreciable risks[3]
- Therefore, children and their carers may welcome a PTI, and subsequently compliance to ART may be improved.
- However, results from the SMART[4] trial suggest CD4-guided episodic use of ART results in an inferior quality of life compared to continuous therapy (CT)
- Within PENTA 11[5], a randomised trial comparing CD4-guided PTI to CT in 109 children, we assessed carer and child adherence to ART and acceptability of PTI

Methods

- Carers, and children if appropriate, completed:
  - **adherence questionnaires (Qs)** at
    - CT: baseline, weeks 24, 48, 72
    - PTI: baseline, 4, 12, 24, 48 weeks after each ART re-start
  - **acceptability questionnaires (Qs)** at
    - PTI: baseline and end-of-study (protocol amendment)
- Due to possible bias from the unreturned Qs in Europe/USA, graphs and tables are shown by region as well as arm
- **Non-adherence** was defined as either reporting missed doses in the last three days OR recording <100% adherence since the last clinical visit on the visual analogue scale



- Multilevel logistic regression accounted for multiple Qs per child

Table 1

	Europe/USA CT	Europe/USA PTI	Thailand CT	Thailand PTI
N	41 (1 in USA)	45 (3 in USA)	12	11
Age group				
2-<7 yrs	10 (24%)	13 (29%)	5 (42%)	4 (36%)
7-<12 yrs	21 (51%)	21 (47%)	3 (25%)	5 (45%)
12-<16 yrs	10 (24%)	11 (24%)	4 (33%)	2 (18%)
CD4%				
<30	3 (7%)	3 (7%)	0 (0%)	0 (0%)
30-40	25 (61%)	27 (60%)	12 (100%)	8 (73%)
40+	13 (32%)	15 (33%)	0 (0%)	3 (27%)
median [IQR]	37 [35-41]	37 [33-43]	35 [32-39]	34 [32-41]
Cumulative exposure median[IQR] (yrs)				
NRTIs	7.5 [5.3-9.2]	6.1 [4.3-8.3]	2.9 [1.8-3.9]	2.8 [2.5-3.1]
NNRTIs	1.4 [0.0-4.3]	3.2 [0.0-5.1]	2.9 [1.8-3.9]	2.8 [2.5-3.1]
PIs	4.3 [0.0-5.7]	2.7 [0.0-5.3]	0.0	0.0
Main carer				
mother	28 (68%)	26 (59%)	3 (25%)	1 (9%)
other carer	5 (12%)	13 (29%)	9 (75%)	10 (91%)
unknown	8 (19%)	6 (13%)	0 (0%)	0 (0%)

Table 2

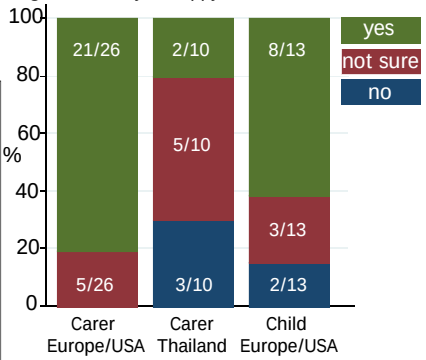
	Carer Europe/USA	Carer Thailand	Children (>10 yrs) Europe/USA
ADHERENCE CT			
Qs returned during follow-up	80/123 (65%)	36/36 (100%)	31/69 (45%)
returned at least one Q	37/41 (90%)	12/12 (100%)	21/26 (81%)
ADHERENCE PTI			
Qs returned after 1st re-start	50/123 (41%)	34/36 (94%)	27/62 (44%)
Qs returned after 2nd re-start	4/14 (29%)	3/3 (100%)	8/14 (57%)
returned at least one Q	35/45 (78%)	11/11 (100%)	22/26 (85%)
ACCEPTABILITY PTI			
Qs returned at baseline	15/26 (58%)	3/9 (33%)	9/15 (60%)
Qs returned at end-of-study	27/45 (60%)	10/11 (91%)	14/23 (61%)
returned at least one Q	33/45 (73%)	10/11 (91%)	19/25 (76%)

Table 3

Confirmed HIV RNA >100 c/ml while on treatment	
Reported non-adherence *	6/31 (19%)
Reported full adherence	10/64 (17%)
Did not complete Qs	3/14 (21%)

* missed doses in the last 3 days OR < 100% adherence on the visual analogue scale

Figure 3: Are you happy to have further PTIs?



Results

- Table 1 shows baseline characteristics by arm and region
- Carer Qs were completed more often in Thailand than Europe/USA (table 2)
- Only children in Europe/USA completed Qs (table 2)
- Number of adherence Qs returned did not differ over time
- Figure 1 shows carer and child reported non-adherence during follow-up by arm and region
- Overall, non-adherence was reported on 21% (24/113) and 15% (12/82) of carer Qs in the CT and PTI arms (P=0.71), and there was no difference in reported non-adherence over time on CT (P=0.31) or after first re-start (P=0.85)
- Carers reported non-adherence more often in Europe/USA (28%, 35/123) than in Thailand(1%, 1/73) (P=0.002)
- Children reported no difference in non-adherence between arms or over time (arms: CT 30% (9/30), PTI 41% (14/34), P=0.31; time: CT P=0.58, after first re-start P=0.33)
- Table 3 suggests there was no link between confirmed HIV RNA>100 c/ml while on treatment and carer reported adherence (P=0.83)
- Figures 2 and 3 show carer and child acceptability of PTI by region
- Overall, carers and children thought PTIs made life easier, however a higher proportion said PTIs had made things 'no different' or 'more difficult' at the end-of-study than at baseline (figure 2)
- Most carers (81%, 21/26) and children (62%, 8/13) in Europe/USA were happy to have further PTIs, whereas carers in Thailand had a split opinion (yes 20% (2/10), no 30% (3/10), not sure 50% (5/10)) (figure 3)
- Carers (Europe/USA 48% (12/25), Thailand 30% (3/10)) and children (50%, 6/12) disliked more clinic visits during PTIs
- A higher proportion of children (64%, 7/11) reported problems re-starting medications than carers (Europe/USA 35% 7/20, Thailand 20% 2/10)

Figure 1: Non-adherence during follow-up by arm and region

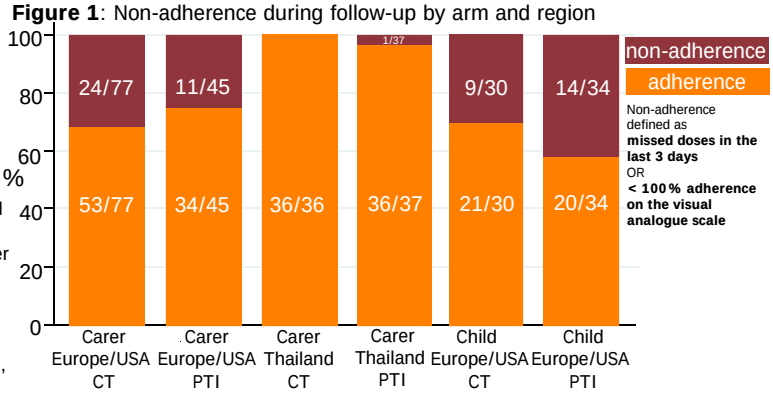
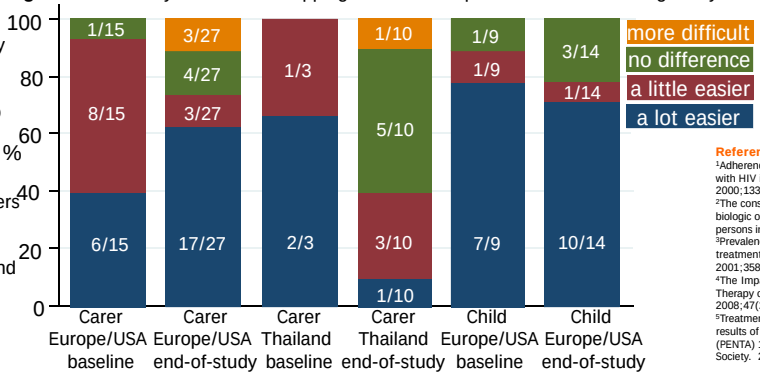


Figure 2: How do you think/did stopping medicines as part of a PTI make things for you?



Conclusions

- Reported adherence on ART was similar in the CT and PTI arms
- Better adherence was reported in Thailand than Europe/USA
- Carer reported adherence was not related to HIV RNA rebound
- In general, PTIs made life easier, and children and carers were happy to have further PTIs
- However, data suggests, PTIs were more acceptable in Europe/USA
- Analysis may be biased by the low Q return rate, particularly in the PTI arm within Europe/USA

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