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Abstract

Adherence may be facilitated by reducing perceptual and practical barriers to antiretroviral therapy (ART). Practical barriers include the complexity of daily dosing, while perceptual barriers include perceptions of the need for treatment and concerns about adverse effects. The study aim was to assess the effect of switching zidovudine plus lamivudine twice-daily (Combivir, CBV) to once-daily tenofovir DF plus emtricitabine (Truvada, TVD), each plus efavirenz (EFZ), on adherence, beliefs about ART and quality of life (QoL). Subjects stable on CBV + EFV were randomised 1:1 to continue this regimen or switch to TVD + EFV. Adherence was measured using the Medication Adherence Self-Report Inventory (MASRI) at 4, 12, 24 and 48 weeks. Beliefs about ART (perceptions of necessity and concerns about adverse effects), treatment intrusiveness and QoL were measured by questionnaire at baseline 4, 12, 24 and 48 weeks. Viral load was assessed at each visit. Two hundred and thirty-four subjects initiated treatment. At week 48, the proportion of subjects reporting high adherence (≥95% taken as prescribed) was significantly greater in the TVD arm (p=0.049). Low adherence (reporting taking <95% as prescribed, discontinuing the study or having missing data) was associated with doubts about necessity (p=0.020), stronger concerns about adverse effects (p=0.010), greater treatment intrusiveness (p=0.010) and poorer mental health related QoL (p= 0.008). At week 48, both concerns about ART (p=0.038) and treatment intrusiveness (p=0.004) were lower among those who switched to TVD. Furthermore, there was a decline in both concerns about ART (p= 0.007) and treatment intrusiveness (p=0.057) over the 48 weeks among those who switched to TVD. There were no significant differences in necessity beliefs, QoL or viral load between randomised groups. Switching from CBV to TVD may improve patient reported outcomes including slightly better adherence, a greater reduction in concerns about adverse effects and less treatment intrusiveness.

Word count 300

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Introduction

While antiretroviral therapy (ART) has vastly improved morbidity and mortality associated with HIV (Mocroft et al., 2003; Palella et al., 1998; Sterne et al., 2005), its success is dependent on continuous, long-term treatment (El-Sadr et al., 2008; The Strategies for Management of Antiretroviral Therapy (SMART) Study Group, 2006) and high level of medication adherence (Bangsberg, 2006; Gross, Yip, Wood, & al., 2006; Paterson et al., 2000). Rates of persistence with ART and adherence are suboptimal: approximately 28% of patients discontinue treatment over the first year (Cooper et al., 2010) and studies using objective measures suggest approximately 30% of patients miss doses each day (Gross, Bilker, Friedman, & Strom, 2001; Liu et al., 2001; McNabb et al., 2001).

A multitude of barriers to ART adherence have been identified. These can be conceptualised as practical barriers (those that limit the patient's capacity to take their medication, leading to non-intentional non-adherence) and perceptual barriers (beliefs that impact on the individual's intention to take their medication as prescribed) (Horne, 2003). In order to facilitate adherence, both practical and perceptual barriers to ART need to be addressed (Horne, Weinman, Barber, Elliott, & Morgan, 2006).

In recent years, the complexity of antiretroviral regimens has been greatly reduced and there are now a number of reasonably well tolerated and efficacious once-daily, low pill burden antiretroviral treatment regimens (Johnson, 2006; Maggiolo et al., 2003; Molina, 2007; Santos et al., 2005). Once daily (QD) dosing is the preference of many patients (Moyle, 2003) and increases patient satisfaction with ART (Maitland et al., 2008). A recent meta-analysis comparing adherence to once daily Vs twice daily ART regimens showed a modest yet significantly greater rate of adherence (+2.9%) to once daily regimens over 11 published studies (Parienti, Bangsberg, Verdon, & Gardner, 2009).

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Despite its benefits, once-daily ART is unlikely to fully address the problem of non-adherence, since perceptual barriers to adherence may remain. A range of perceptual barriers to ART adherence have been identified, (Chesney et al., 2000; Gifford et al., 2000; Molassiotis et al., 2002; Spire, Duran, Souville, Leport C, & Raffi, 2002). These beliefscan be grouped under two categories: perceptions of necessity for treatment (necessity beliefs) and concerns about adverse effects (Horne, 2003; Horne & Weinman, 1999; Horne, Weinman, & Hankins, 1999). This 'necessity-concerns' framework has been found to predict adherence to medication across a variety of long-term illnesses (Horne & Weinman, 2002; Horne et al., 1999), including HIV (Cooper et al., 2010; Horne et al., 2004; Horne, Cooper, Gellaitry, Leake Date, & Fisher, 2007). Patients' perceptions of their personal necessity for treatment and concerns about adverse effects stem from their perceptions of illness and medicines in general (Horne, 2003) as well as their experiences of symptoms and side effects (Cooper, Gellaitry, Hankins, Fisher, & Horne, 2009)..,

The primary analysis of the SWEET (Simplification With Easier Emtricitabine and Tenofovir) study (Fisher, Moyle, Shahmanesh & Orkin, 2009) demonstrated maintenance of virological control, increases in haemoglobin, declines in proatherogenic lipids and limb fat preservation among stable, virologically suppressed efavirenz-recipients who switched from combivir (CBV) (zidovudine plus lamivudine) to truvada (TVD) (emtricitabine and tenofovir).

The aim of this analysis was to assess the effect of switching from twice daily CBV to once daily TVD, each plus efavirenz (EFZ), on adherence, beliefs about ART (perceptions of necessity for ART, concerns about adverse effects and perceived treatment intrusiveness) and quality of life.

Methods

These data were collected as part of phase IV, open-label, UK-based, multi-centre, randomised, 48-week trial, which compared the continuation of CBV with substitution with TVD in patients treated with EFV-based ART. Eligibility criteria included being aged ≥18 years, being stable on

AZT and 3TC or CBV plus EFV therapy for ≥6 months, with RNA <50 copies/ml on two consecutive visits and <400 copies/ml for ≥3 months prior to screening. Eligible subjects were randomised 1:1 to a) stop CBV and start TVD once-daily, or b) continue CBV twice-daily. Both TVD and CBV were taken as one tablet per dose, with or without food. All subjects continued EFV once-daily. The overall study methods are described elsewhere (Fisher et al., 2009).

Measures

Adherence

Adherence was measured using the Medication Adherence Self-Report Inventory (MASRI) (Walsh, Mandalia, & Gazzard, 2002) at weeks 4, 12, 24 and 48. Subjects were asked to indicate the percentage of ART medication taken over the previous month on a visual analogue scale (VAS). The VAS has demonstrated good validity against objective measures (electronic monitoring: r = 0.63, P =0.001; pill count: r = 0.75, p= 0.001; and viral load: p= 0.01) (Walsh et al 2002). Low adherence was defined as taking <95% of ART over the past month. Subjects with missing data were defined as having low adherence.

Beliefs about ART were assessed at baseline and weeks 4, 12, 24 and 48 using the Beliefs about Medicines Questionnaire (Horne et al., 1999) which has previously been adapted for antiretroviral therapy (BMQ-ART; Horne et al., 2004; Horne et al., 2007)). The BMQ-ART comprised 2 scales: The ART-necessity scale consists of 8 items assessing patients' beliefs about their personal need for ART for controlling their HIV, maintaining their health, preventing illness and keeping them alive, while the ART-concerns scale consisted of 15 items bringing together a range of concerns about the potential adverse effects of ART that have been identified across studies, including fears about short- and long-term side effects, concerns about the timing of pills and the disruptive effects of the ART regimen on daily life, concerns about lacking information about ART and more abstract concerns about becoming dependent on ART, feeling that ART is a ''mystery,'' embarrassment surrounding taking ART and a general feeling of worry about taking the

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treatment. For the specific purposes of this study, an additional four items were included to elicit concerns about unwanted changes to the shape of buttocks, hips, face and arms.

Participants were presented with a series of statements about which they were told, ‘‘These are statements that other people have made about combination therapy.’’ They were then asked to rate their level of agreement with each necessity belief or concern on a scale, where responses ranged from strongly agree (scored 5) to strongly disagree (scored 1). Three items (2 concerns and 1 necessity belief) were reverse scored. Scores for the individual items within each scale were summed to give a total scale score. To facilitate comparison of scores between scales, a mean scale score was computed by dividing each scale by the number of items, giving a range of 1 to 5 for necessity and concerns scales with higher scores indicating stronger necessity beliefs or concerns.

Treatment intrusiveness

Perceived intrusiveness of the ART regimen was assessed at baseline and weeks 4, 12, 24 and 48 using the HAART Intrusiveness Scale (HIS) (Newell, Mendes, & Horne, 2002). This scale consisted of 12 items addressing the degree to which ART is perceived to interfere with ten aspects of daily life (e.g. social life, ability to work, relationships). Participants were asked to indicate the degree to which ART interfered with each aspect of their daily life on a scale from 1-5, where 1 indicated low interference and 5 indicated high interference. A total score was computed by adding up responses to each item. For comparison with other scales, an average score was computed by dividing the total score by the number of items. Possible responses ranged from 1-5 with higher scores indicating higher perceived intrusiveness.

Quality of life

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Quality of life was measured by the SF-12 v2 Health Survey (Ware, Kosinski, & Keller, 1996) at baseline and weeks 4, 12, 24 and 48. This scale has previously been used (Viswanathan, Anderson, & Thomas, 2005) and validated (Delate & Coons, 2000) with people with HIV. It contains either one or two items from each the following health concepts: physical functioning, role limitations arising from problems with physical health, bodily pain, general health, vitality (energy/fatigue), social functioning, role limitations arising from emotional problems and mental health (psychological distress and well-being). Two summary scales were generated: the physical component summary (PCS-12) and the mental component summary (MCS-12). Possible scores ranged from 0–100, with higher scores indicating better health. The scale has demonstrated acceptable validity and reliability (Ware et al., 1996).

Viral load was recorded at each visit.

Statistical methods

Analyses were conducted using SPSS version 15.0. Significance was evaluated using two-tailed non-parametric tests at alpha=0.05.

The primary outcome of this analysis was adherence at 48 weeks. In an intention to treat analysis, where missing = nonadherent, subjects reporting ≥95% adherence were allocated to a 'high adherence' group and those who reported <95% adherence, discontinued the study or had missing adherence data were allocated to a 'low adherence' group (Horne et al., 2007). A chi-square test was used to test for differences in adherence (high versus low) between randomised treatment groups. Change in the proportion of subjects reporting high (≥95%) adherence over time was assessed within each randomised group between week 4 and week 48 using McNemar's test.

For all other variables, missing data were treated as missing. Differences in beliefs about ART (ART-Necessity and ART-Concerns), ART-intrusiveness and quality of life (PCS-12 and MCS-12) were assessed between randomised groups at baseline and week 48 using the Mann Whitney U

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test. Changes in these variables between baseline and week 48 (48 week scores minus baseline scores) were compared between randomised groups using the Mann Whitney U test. Associations between continuous variables were assessed using the Spearman's Rho test.

Viral load

In order to compare viral load efficacy, the proportion of subjects with HIV RNA <50 copies/ml at week 48 was compared between randomised groups using the Chi-Square test. Subjects with missing viral load data were considered to have a detectable viral load (≥50 copies/ml).

Results

234 participants (84% male) took at least one dose of study medication, 117 continued CBV (CBV arm) and 117 switched to TVD (TVD arm).

Insert Table 1 about here

Comparisons at baseline

At baseline, there were no significant differences in beliefs about ART (Necessity or Concerns), ART-intrusiveness, or quality of life (PCS-12 or MCS-12) between randomised groups (all p>0.05; Table 3). Subjects randomised to receive TVD reported less concern about unwanted changes to the shape of their buttocks compared to those randomised to continue on CBV (Table 4).

Change over time

Adherence

At week 48, 87/117 (74.4%) subjects in the TVD arm reported ≥95% adherence compared to 73/117 (62.4%) of those randomised to remain on CBV (p=0.049; Table 2). The proportion of subjects reporting ≥95% adherence decreased significantly between weeks 4 and 48 for the group as a whole (McNemar's test, p<0.0001). Within groups analyses showed a significant

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decrease within those who remained on CBV (McNemar's test p<0.0001) but not among those who switched to TVD (McNemar's test p=0.137).

Insert Table 2 about here

Beliefs about ART

ART-Necessity

Perceptions of necessity for ART did not differ between randomised groups at week 48, and there was no difference between the two groups in the extent to which perceptions of necessity changed over time (Table 3).

ART-Concerns

Subjects who switched to TVD reported fewer concerns about ART at the 48 week follow-up than those remaining on CBV (p=0.038). Furthermore, there was a greater decline in ART-concerns between baseline and 48 weeks among those who switched to TVD (p=0.007) (Table 3).

Insert Table 3 about here

Specific Concerns about unwanted changes to body shape

Switching to TVD resulted in a reduction of concerns about unwanted changes to the shape of their hips (p=0.032), buttocks (p=0.002), face (p=0.004) and arms (p=0.011) between baseline and week 48 (Table 4). These concerns decreased between baseline and 48 weeks among those who switched to TVD and increased among those who remained on CBV.

Insert Table 4 about here

Treatment Intrusiveness

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Subjects who switched to TVD reported less treatment intrusiveness than those who stayed on CBV at week 48 (p=0.004), however, the difference between groups in the change in intrusiveness from baseline to week 48 did not reach significance (p=0.057) (Table 3).

Quality of life

There were no significant differences between randomised groups in physical component summary (PCS) or mental component summary (MCS) scores at week 48, and no difference in the extent to which these variables changed over time (Table 3).

Associations between adherence, beliefs about ART and quality of life

Lower adherence at week 48 was associated with doubts about necessity for ART (p=0.020), stronger concerns about adverse effects (p=0.010), greater treatment-intrusiveness (p=0.010) and poorer mental health-related quality of life at week 48 (p=0.008) (Table 5).

Insert Table 5 about here

Viral load

99/117 (84.6%) of those randomised to remain on CBV and 102/117 (87.2%) of those who switched to TVD recorded an undetectable viral load (<50 copies/ml) at 48 weeks (p=0.573).

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Discussion

Long-term adherence to antiretroviral therapy is pivotal to treatment success (Bangsberg, 2006; Gross et al., 2006; Paterson et al., 2000). In this study, switching from twice daily CBV to once daily TVD in people established on EFV resulted in higher levels of adherence and reduced both patients' concerns about adverse effects and the degree to which ART was perceived to intrude into daily life. We found no significant effect of switching from CBV to TVD on viral load or quality of life.

The results of this study concur with those of previous studies showing a benefit of once-daily ART for adherence (Parienti et al., 2009). Reducing the frequency of ART to once-daily may reduce practical barriers to adherence by minimizing the opportunity to miss doses and facilitating the assimilation of treatment into daily routines. The effect of the change in regimen frequency on practical barriers to adherence is reflected in less reported intrusiveness at week 48 and a reduction of intrusiveness between baseline and week 48 among those who switched to TVD (although this result was of borderline significance).

Switching from CBV to TVD also reduced perceptual barriers to adherence. Several previous studies (Cooper et al., 2010; Horne et al., 2004; Horne et al., 2007) have shown that patients who have strong concerns about adverse effects of ART are less likely to be highly adherent. In this study, switching from CBV to TVD reduced patients' concerns about their treatment. The concerns measure encompassed patients' concerns about side effects and potential long term effects, as well as concerns about the disruption of treatment to daily life and embarrassment about taking ART. The reduction in the overall score may therefore reflect both the reduction in the number of daily dosing and an improvement in side effects and longer-term effects including lipodystrophy (Fisher et al., 2009). In this case, switching from CBV to TVD also reduced specific concerns about changes to the shape of hips, buttocks, face and arms. This finding reflects the findings of the primary analysis of the SWEET study (Fisher et al., 2009) in which switching from CBV to TVD preserved limb fat and led to limb fat recovery. Previous studies have shown

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changes in fat distribution to cause psychological distress (Rajagopalan, Laitinen, & Dietz, 2008) and a reduction in quality of life (Kavouni, Catalan, Brown, Mandalia, & Barton, 2008). These types of side effects have also previously been linked to non-adherence (Ammassari et al., 2002).

Both individuals randomised to switch to TVD and those who remained on CBV remained convinced of their necessity for ART over the 48 weeks. In contrast to previous data showing an inverse relationship between persistent symptoms and perceptions of necessity for ART (Cooper et al., 2009), the higher prevalence of side effects among those who remained on CBV (Fisher et al., 2009) did not impact on perceptions of necessity. This may be due to relatively strong perceptions of the need for ART among this highly adherent sample.

Despite the benefit of switching to TVD on adherence, we found no significant effect of switching from CBV to TVD on viral load at 48 weeks. The lack of a corresponding effect of regimen on viral load may be a result of the relatively high adherence threshold used. In setting our cut-off point for high adherence, we adopted the convention of 95% (Paterson et al., 2000). Viral suppression may be achieved at lower rates of adherence nonnucleoside reverse transcriptase inhibitor (NNRTI)–based regimens (Bangsberg, 2006). Despite a greater level of adherence, fewer concerns about side-effects and less perceived treatment intrusiveness among those who switched to TVD, we did not find a difference in quality of life. It could be that the SF-12, a generic (rather than HIV specific) measure of quality of life lacked sensitivity to detect differences in physical and mental wellbeing resulting from the different regimens, since it does not include some of the relevant aspects of quality of life such as somatic symptoms and body image (Grossman, Sullivan & Wu, 2003). It is also worth noting that quality of life was good at baseline for the subjects in this study, with very little room for improvement.

Consistent with other studies, lower adherence was associated with patients' doubts about their necessity for ART and strong concerns about adverse effects (Cooper et al., 2010; Horne et al., 2004; Horne et al., 2007), a higher level of perceived treatment intrusiveness (Newell, Mendes da Costa, & Horne, 2002) and reduced mental health-related quality of life (Mannheimer et al.,

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2005). We found no significant relationship between adherence and physical health-related quality of life. Again, this may be explained by the use of a generic rather than HIV specific quality of life scale, or to the fact that the study only included people who were already doing well on ART. A previous study found increases in quality of life over the first 12 months of ART among individuals who consistently reported higher adherence and a decrease in quality of life among patients reporting <80% adherence (Mannheimer et al., 2005).

The results of this study should be interpreted in light of its limitations. Adherence was not measured at baseline, therefore it was not possible to determine whether adherence differed between randomised groups at baseline, or to examine change from baseline within or between the two groups. The fact that this was a clinical trial with inclusion criteria of undetectable viral load on two consecutive visits means that the sample were biased in terms of being highly adherent. Although further studies with different populations would be useful, we would speculate that the benefits of TVD over CBV in terms of once daily dosing (Parienti et al., 2009) and fewer side effects (Fisher et al., 2009) would also reduce perceptual and practical barriers to ART and improve adherence among broader clinic populations. Additional bias may have resulted from the fact that the trial was open-labelled, however, we are confident that our findings are not solely due to more positive expectations of the newer drug (TVD) because beliefs about ART became increasingly positive over the 48 weeks the participants were receiving TVD. The differences between randomised groups were modest. A further limitation was our reliance on self-report questionnaires. To minimize the possibility that individuals would give socially desirable responses, emphasis was placed on the fact that the individuals' responses were confidential and questionnaires were carefully worded in a nonjudgmental manner. Self-report measures have advantages over other methods of measuring adherence, including high face validity and high specificity for nonadherence; however, they are subject to self-presentation and recall bias. Our rating of adherence may underestimate the true extent of nonadherence (some people may be giving socially desirable responses, reporting higher adherence rates than they actually attain in practice), however, this bias was likely to be similar between randomised groups.

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The findings of this study present a clear rationale for the implementation of interventions to maintain higher levels of adherence by addressing perceptual and practical barriers to ART. Switching to a once daily, lower toxicity regimen is one way of addressing these barriers. Given that our classification of low adherence included both taking less than 95% of doses, and stopping treatment completely, and the link between taking less than prescribed and discontinuation of treatment (Vrijens, Vincze, Kristanto, Urquhart, & Burnier, 2008), these findings are particularly important in light of the current recommendation of continuous ART (Gazzard et al., 2008).

In summary, patients on long-term, twice daily CBV may benefit from switching to once daily TVD in order to reduce concerns about ART, facilitate integration of treatment into daily life and optimise adherence over the long-term.

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Table 1: Demographics and Baseline Characteristics (Treated Analysis Set)

Characteristic	FTC/TDF + EFV (N = 117)		AZT+3TC + EFV (N = 117)		Total (N = 234)	
Sex (n, %)						
Male	101	86%	96	82%	197	84%
Female	16	14%	21	18%	37	16%
Age (years)						
Mean (SD)	42 (8.8)		42 (9.1)		42 (8.9)	
Min, Max	20, 69		24, 72		20, 72	
Race (n, %)						
White	77	66%	68	58%	145	62%
Black	36	31%	44	38%	80	34%
Asian	3	3%	4	3%	7	3%
Other (Black Caribbean, Mixed heritage)	1	< 1%	1	< 1%	2	< 1%

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Table 2: Proportion of subjects reporting ≥95% adherence at each assessment during study

	FTC/TDF + EFV (N = 117)	AZT/3TC + EFV (N = 117)	Pearson's chi-square	p-value
4 weeks (n,%)	96 (82.1)	95 (81.2)	0.028	0.866
12 weeks (n,%)	93 (79.5)	86 (73.5)	1.165	0.281
24 weeks (n,%)	92 (78.6)	81 (69.2)	2.683	0.101
36 weeks (n,%)	87 (74.4)	74 (63.2)	3.365	0.067
48 weeks (n,%)	87 (74.4)	73 (62.4)	3.874	0.049

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Table 3: Median scores for beliefs about ART, ART-intrusiveness and quality of life at baseline and week 48 and changes between baseline and week 48 in each treatment group, and p values for differences between groups (Mann Whitney U Test).

	FTC/TDF + EFV (N = 117)		**AZT/3TC + EFV (N = 117)**		**p-value**
Measure	n	Median (IQR)	n	Median (IQR)	
Baseline					
ART-Necessity	107	4.37 (3.88, 4.63)	111	4.38 (3.75, 4.75)	0.935
ART-Concerns	107	2.33 (2.00, 2.67)	111	2.47 (2.00, 2.87)	0.329
ART-intrusiveness	109	1.25 (1.00, 1.58)	111	1.33 (1.00, 1.83)	0.376
SF-12 Physical component	101	55.1 (48.9, 57.5)	108	53.7 (46.3, 57.5)	0.405
SF-12 Mental component	101	49.1 (38.1, 54.7)	108	48.6 (40.5, 55.1)	0.548
Week 48					
ART-Necessity	104	4.37 (3.75, 4.75)	97	4.50 (3.88, 4.88)	0.276
ART-Concerns	104	2.31 (1.93, 2.31)	97	2.53 (2.13, 2.93)	0.038
ART-intrusiveness	104	1.17 (1.00, 1.42)	97	1.33 (1.00, 1.88)	0.004
SF-12 Physical component	97	53.2 (46.7, 56.7)	92	52.3 (42.6, 56.4)	0.191
SF-12 Mental component	97	47.4 (40.9, 54.5)	92	47.6 (40.9, 54.3)	0.694
Change to Week 48					
ART-Necessity	96	-0.00 (-0.25, 0.15)	93	0.13 (-0.13, 0.25)	0.159
ART-Concerns	97	-0.05 (-0.50, 0.25)	93	0.07 (-0.13, 0.40)	0.007
ART-intrusiveness	97	0.00 (-0.25, 0.00)	93	0.00 (-0.25, 0.21)	0.057
SF-12 Physical component	85	0.00 (-2.79, 3.26)	86	-1.29 (-5.83, 2.84)	0.211
SF-12 Mental component	85	0.46 (-4.92, 6.03)	86	-0.04 (-6.32, 5.43)	0.318

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Table 4: Median scores for concerns about unwanted changes in body shape at baseline and week 48 and changes between baseline and week 48 in each treatment group, and p values for differences between groups (Mann Whitney U Test)

	FTC/TDF + EFV (N = 117)		**AZT/3TC + EFV (N = 117)**		
Type of concern	n	Median (IQR)	n	Median (IQR)	p-value
Baseline					
Shape of hips	107	2.00 (1.00, 3.00)	111	2.00 (2.00, 3.00)	0.171
Shape of buttocks	107	2.00 (1.00, 3.00)	110	2.50 (2.00, 3.00)	0.039
Shape of face	107	2.00 (2.00, 3.00)	111	2.00 (2.00, 3.00)	0.177
Shape of Arms	106	2.00 (2.00, 3.00)	111	2.00 (2.00, 3.00)	0.114
Week 48					
Shape of hips	104	2.00 (1.00, 3.00)	97	2.00 (2.00, 3.00)	0.061
Shape of buttocks	102	2.00 (1.00, 3.00)	97	2.00 (2.00, 4.00)	0.016
Shape of face	104	2.00 (1.00, 3.00)	97	2.00 (2.00, 3.00)	0.007
Shape of Arms	104	2.00 (1.00, 3.00)	97	2.00 (2.00, 3.00)	0.063
Change from baseline to Week 48					
Shape of hips	97	0.00 (-1.00, 0.00)	93	0.00 (0.00, 1.00)	0.032
Shape of buttocks	95	0.00 (-1.00, 0.00)	92	0.00 (0.00, 1.00)	0.002
Shape of face	97	0.00 (-1.00, 0.00)	93	0.00 (0.00, 1.00)	0.004
Shape of Arms	96	0.00 (-1.00, 0.00)	93	0.00 (0.00, 1.00)	0.011

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Table 5: Associations between adherence, beliefs about ART and quality of life

	Self-reported adherence (MASRI-VAS)	
	Spearman's rho	*p-value*
ART-Necessity (BMQ-ART)	0.169	0.020
ART-Concerns (BMQ-ART)	-0.188	0.010
ART-Intrusiveness (HIS)	-0.188	0.010
Quality of life (SF12-PCS)	-0.044	0.567
Quality of life (SF12-MCS)	0.199	0.008

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