AIDS

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# Quality of life improvement in resource-limited settings after one year of second-line antiretroviral therapy use among adult men and women

**Running head: Quality of life improvement on second-line therapy in resource-limited settings**

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**Abstract**

**OBJECTIVE**: We evaluated improvement of quality of life (QoL) after one year of second-line antiretroviral therapy (ART) use in resource-limited settings (RLS) among adult men and women, comparing two randomized treatment arms.

**DESIGN**: ACTG A5273 was a randomized clinical trial of second-line ART comparing lopinavir/ritonavir (LPV/r) + raltegravir (RAL) with LPV/r + nucleos(t)ide reverse transcriptase inhibitors (NRTIs) in participants failing a non-nucleoside reverse transcriptase inhibitor (NNRTI)-containing regimen at 15 sites in 9 RLS. Participants completed the ACTG SF-21 which has 8 QoL domains with a standard score ranging from 0 (worst) to 100 (best).

**METHODS**: Differences in QoL by randomized arm, as well as by demographic and clinical variables, were evaluated by regression models for baseline and week 48 QoL scores fitted using the generalized estimating equations method (GEE).

**RESULTS**: 512 individuals (49% male, median age 39 years) were included. 512 and 492 participants had QoL assessments at baseline and week 48, respectively. QoL improved significantly from week 0 to 48 ($p<0.001$ for all domains). There was no significant difference between treatment arms for any domain. Individuals with higher VL and lower CD4 at baseline had lower mean QoL at baseline but larger improvements such that mean QoL was similar at week 48.

**CONCLUSIONS**: Improvements in QoL were similar after starting second-line ART of LPV/r combined with either RAL or NRTIs in RLS. QoL scores at baseline were lower among participants with worse disease status prior to starting second-line, but after one year similar QoL scores were achieved.

**Key words**: quality of life; HIV; raltegravir; second-line therapy; antiretroviral therapy; resource-limited settings; randomized clinical trial

## Introduction

Antiretroviral therapy (ART) has dramatically changed the course of the HIV/AIDS epidemic by reducing morbidity and mortality [1]. Once a terminal disease, HIV infection is now considered a chronic medical condition, with individuals on effective ART having life expectancies similar to those who do not have HIV [2].

Therefore, long-term complications of HIV infection and its treatment, including quality of life (QoL), are important considerations for HIV-infected individuals. QoL is a multidimensional concept and can be influenced by many factors such as income, housing, social support, and life situation. Health-related QoL is a dimension of broader QoL that reflects the impact of disease and treatment on a person's well-being and ability to carry out daily activities, taking into account the biological and psychological effects of the disease. It includes physical, social, cognitive, and psychological functioning, as well as subjective sense of health, comfort, and well-being. QoL measurements are important to assess a person's perception of his/her own health [3, 4].

Health-related QoL measures were introduced for HIV-infected individuals in higher income settings in the early 1990s [5], and were used to evaluate factors associated with QoL as well as effects of ART on the QoL 6-8]. Poorer immunological status, HIV-related symptoms, depression, lack of social support, unemployment and low adherence to ART were most frequently and consistently associated with low QoL in these rich settings [9].

QoL at first-line ART initiation in resource-limited settings (RLS) has varied with disease severity, demographic characteristics and country [3, 10, 11] and it improves over time after starting ART [10-13]. Previous studies have shown improvements in QoL

among HIV-infected individuals taking PI-containing regimens [14] and among individuals taking a raltegravir-containing regimen [15, 16].

We previously reported cross-sectional results of QoL among individuals with virologic failure (VF) on first-line ART before starting second-line ART [17]. However, QoL during second-line ART has not been extensively studied.

The World Health Organization (WHO) recommends boosted protease inhibitor (PI) plus nucleos(t)ide reverse transcriptase inhibitors (NRTIs) as the preferred second-line ART and boosted PI plus raltegravir (RAL) as an alternative regimen if NRTI toxicity is limiting [18]. Exploring QoL changes in individuals on these two regimens is important to support future recommendations.

The aim of this study is to assess changes in the QoL after one year of second-line ART in RLS in individuals on lopinavir/ritonavir (LPV/r) + NTRI versus those on LPV/r + RAL. Associations of QoL with demographic and clinical variables at time of starting second-line ART (e.g. CD4 count and HIV-1 RNA viral load) were also assessed.

## Methods

A5273 study

The AIDS Clinical Trial Group (ACTG) A5273 study, entitled "Multicenter Study of Options for **SE**cond-**L**ine **E**ffective **C**ombination **T**herapy(SELECT)" was a phase III, open-label, randomized clinical trial comparing LPV/r + RAL with LPV/r + NRTIs in participants failing a non-nucleoside reverse transcriptase inhibitor (NNRTI)-containing regimen (clinicaltrials.gov NCT01352715). Details of the study design have previously been described [19].Participants were enrolled between March 2012 and

October 2013 at 15 sites in 9 countries: Brazil (1 site), India (3 sites), Kenya, Malawi (2 sites), Peru (2 sites), South Africa (3 sites), Tanzania (1 site), Thailand (1 site) and Zimbabwe (1 site). Eligible participants were HIV-infected men and women (≥18 years) who had virologic failure (VF) confirmed by two consecutive plasma HIV-1 RNA viral load(VL) ≥1000 copies/mL at least one week apart after at least 24 weeks on an NNRTI-containing first-line regimen. Participants were followed for at least 48 weeks at the end of study follow-up. The primary analysis of the trial showed no difference in virologic outcome between the two regimens [19]. The study was approved by the institutional review board at each participating site and written informed consent was obtained from all study participants.

Quality of life measures

Participants were interviewed at weeks 0, 4, 24 and 48 using a modified version of the SF-21 measure (ACTG SF-21) [3, 20]. The ACTG SF-21 tool was originally adapted from the Medical Outcomes Study HIV Health Survey (MOS-HIV), an instrument with well-established reliability and validity [21]. SF-21 and its short and long forms (SF-12, SF-36) have been widely used in HIV/AIDS research [3, 22-26]. The ACTG SF-21 questions form 8 domains: General Health Perceptions (GHP), Physical Functioning (PF), Role Functioning (RF), Social Functioning (SF), Cognitive Functioning (CF), Pain (P), Mental Health (MH), and Energy/Fatigue (E/F) (Table 1). A standardized score ranging from 0 (worst QoL) to 100 (best QoL) was calculated for each domain using standard methods [3]. High scores for Pain and Energy/Fatigue mean less

pain and less fatigue, respectively. The ACTG SF-21 tool was administered in a face-to-face interview by study staff in the participant's local language.

Demographic and Clinical Factors

The following study entry demographic and clinical factors at the time of starting second-line ART were assessed: sex, age (years), plasma HIV-1 RNA viral load (VL), CD4 cell count (CD4), body mass index (BMI), country of enrollment (country), history of AIDS-defining events (ADE), number of comorbidities, and years on first-line ART. History of AIDS was defined by a specified subset of diagnoses codes maintained by the ACTG (Appendix 60) [27] taking into account the WHO [28] and CDC [29] classifications of ADE. Number of comorbidities was defined as number of diagnoses (other than ADE) included in ACTG Appendix 60 (considering all ongoing and previous comorbidities).

**Statistical Analysis**

A regression model for baseline and week 48 QoL scores was fitted using the generalized estimating equations (GEE) method. Differences by randomized treatment arm (LPV/r + RAL vs. LPV/r +NRTI) in mean change in QoL, as well as QoL scores at week 48, were assessed.

In a previous cross-sectional analysis, participants with higher VL and lower CD4 at baseline (time of starting second-line ART) had lower QoL at this time-point for most domains. Additionally, we previously showed that lower BMI, 3 or more comorbidities, and history of AIDS were associated with lower QoL in some domains. No association

with age and sex was observed [17]. In order to evaluate the impact of second-line ART, linear regression models for baseline and week 48 QoL scores were fitted using the GEE method to assess the variables (VL, CD4, BMI, comorbidities, history of AIDS) by estimating the mean difference in QoL between groups at baseline, the QoL score change between baseline and week 48, and the QoL score at week 48. Furthermore, we fitted multivariable linear regression models for QoL scores at week 48 to assess if differences at week 48 remained after adjustment. These multivariable models included baseline VL, CD4, BMI, comorbidities and history of AIDS as well as country and study arm (LPV/r + RAL vs. LPV/r + NRTIs).

Additionally, we describe the temporal change in QoL by baseline VL (> versus ≤ 100,000 copies/mL) and baseline CD4 (< versus ≥ 50 cells/mm$^3$) over the first 48 weeks of second-line ART by plotting the mean (95% pointwise Wald CIs) of the QoL scores for each domain at baseline, week 4, 24 and 48.

Data were analyzed using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA).

**Results**

Five hundred and twelve eligible participants were enrolled into the A5273 study: 258 were randomized to the LPV/r+RAL arm and 254 to the LPV/r+NRTIs arm. Baseline demographic and clinical characteristics of participants by arm are depicted in Table 2. Median age was 39 years (inter-quartile range [IQR]: 34-44), approximately half were women and approximately two-thirds were black African. Median CD4 count was 135 cells/mm$^3$, VL 4.5 $\log_{10}$ copies/mL and BMI 22 kg/m$^2$. A total of 150 participants

(29%) had a history of AIDS. Median duration of first-line ART was 4.2 years (IQR: 2.3–6.2).

Among 512 participants who had QoL assessment at baseline, 492 also had at week 48. Mean QoL score at baseline was 67 for the General Health Perception (GHP), 91 for Physical Functioning (PF), 80 for Role Functioning (RF), 91 for Social Functioning (SF), 91for Cognitive Functioning (CF), 83 for Pain (P), 85 for Mental Health (MH) and 80 for Energy/Fatigue (E/F). QoL improved significantly by week 48 on second-line ART; mean improvements from baseline were 7 for GHP, 4 for PF, 9 for RF, 3 for SF, 4 for CF, 5 for P, 5 for MH and 4 for E/F ($p<.001$ for all domains).There was no significant difference in the mean increase in QoL scores at week 48 between randomized treatment arms (Table 3, $p\geq0.17$ for all domains).

Table 3 summarizes mean QoL scores for each domain at baseline and at week 48, as well as mean changes in QoL score between baseline and week 48 by selected stratification variables. Individuals with higher baseline VL had lower mean baseline QoL in all domains but larger improvements throughout follow-up, such that mean QoL by baseline VL was similar at week 48 (Figure 1).Similarly, the differences in mean QoL at baseline by baseline CD4 count had disappeared by week 48 for all domains except RF (Figure 2). For the RF domain, mean QoL was similar at week 0 for the two baseline CD4 count groups and improved over time in the baseline CD4 <50 cells/$mm^3$ group such that it was significantly higher in the baseline CD4 ≥ 50 cells/$mm^3$ group at week 48.

Participants with lower baseline BMI (<18kg/$m^2$) had lower QoL at baseline in all domains than those with higher BMI (≥18kg/$m^2$), but at week 48 both groups had similar QoL for all domains except for E/F. For E/F, mean QoL score was significantly lower at

week 48 for those with baseline BMI <18kg/$m^2$ (mean 76, versus 85 for BMI ≥18 kg/$m^2$, p=0.004). Individuals with ≥3 non-AIDS comorbidities had lower mean QoL score for some domains at baseline, notably RF, SF and P, in comparison with those with <3 comorbidities. At week 48, the differences in RF and P by number of baseline comorbidities persisted (p=0.001 for both). At baseline, there was significantly lower mean QoL score for the PF and E/F domains for individuals with versus without a history of AIDS; these differences were reduced and not significant at week 48.

In multivariable models, there was significant variation among countries in adjusted mean QoL score at week 48 for all domains (p<.001) except PF (p=0.10), but there were very few other significant associations. In particular, baseline VL, CD4 count, BMI and history of AIDS were not significantly associated with QoL at week 48 (p>0.17, for all domains), except that baseline CD4 count was significantly associated with mean E/F score (4 lower for <50 vs. ≥50 cells/$mm^3$, 95% CI: 0 to 8 lower; p=0.033]). In addition, higher number of comorbidities remained associated with lower mean RF score (6 lower for ≥3 vs. <3 comorbidities, 95% CI: 1 to 10 lower; p=0.031) and lower mean P score (7 lower for ≥3 vs. <3 comorbidities, 95% CI: 2 to 11 lower; p=0.004) at week 48.

**Discussion**

In RLS, effective second-line ART with successful virologic suppression was associated with improvements in QoL following failure of first-line ART. Improvements in QoL were similar after starting second-line ART with LPV/r + RAL or LPV/r + NRTIs. Mean QoL scores were worse at first-line failure among participants with higher VL, lower CD4, lower BMI and with a history of AIDS prior to starting second-line

regimen, but after one year of second-line ART similar QoL scores were achieved. Differences in mean QoL scores among countries and by number of comorbidities remained at week 48 for some domains, which likely reflects differences in QoL which are not directly impacted by ART.

In a study conducted in high and middle income countries comparing LPV/r + RAL versus LPV/r + NRTIs for second-line ART, QoL (physical and mental domains) also improved in both treatment arms after one year with no difference between arms [16]. Other observational studies in high income settings have described improvements in QoL after one year of PI-containing ART [14] and over a 24-month period of treatment with a RAL-containing regimen [15]. In a randomized clinical trial conducted in Spain evaluating the use of either a PI or EFV based second-line regimen among participants who failed a PI-containing first-line regimen, QoL increased in both arms although it increased more for those in an EFV-containing versus PI-containing second-line regimen [30].

Our results and those of other studies provide reassurance that a switch to second-line ART is associated with improvements in QoL in settings where VL is less regularly monitored and HIV infected individuals may have experienced an extended period of time on a failing first-line ART. Although we found that QoL scores were worse among participants with higher VL on the failing first-line regimen, within a year after starting a WHO-recommended second-line regimen, these differences had been resolved and there was no association of QoL score with baseline viral load.

Associations of lower Role Functioning and Pain scores with higher number of comorbidities persisted even after one year of second-line ART. This might reflect the

burden of comorbidities beyond HIV infection on an individual's daily activities and resultant increased pain. Chronic diseases were strong independent risk factors for low QoL in a study conducted in Tanzania with HIV-infected individuals on any ART for at least 2 years [31]. This is consistent with our findings although the definition of comorbidities in our study was broader, including not only chronic diseases. Since the HIV population is aging the impact of comorbidities in QoL needs to be taken into account when a second line ART is being initiated.

The highly significant heterogeneity in mean QoL scores among countries for all domains, even after one year effective second-line ART, may be related to different cultural perceptions of QoL. It could also be affected by differences in characteristics of participants being enrolled in different countries beyond those characteristics that we had data for (e.g. socio-economic status, social support).

This study has limitations. Data were not collected on factors such as employment and educational status, depression or mental health disorders, sexual behavior and social stigma that might be associated with QoL. The population studied was from a clinical trial and so may differ from those in clinical practice. The improvements in QoL could reflect factors other than the initiation of second-line ART such as changes in care including participation in a clinical trial. Each clinical site may have selected participants for enrollment differently, with potential differences between countries and between sites. We do not have data on the length of time on first-line ART failure, which could have impacted QoL at baseline and its improvement. Caution should therefore be taken before generalizing our findings to other clinical and cultural settings.

In conclusion, QoL improved after second-line therapy initiation, with no difference between randomized treatments. These results are important to support the use of LPV/r with RAL or NRTIs in RLS as second-line regimens. QoL was poorer among participants with higher VL and lower CD4 at baseline but these differences disappeared after one year of second-line ART use. Optimization of QoL is particularly important now that treated HIV infection is a chronic disease and individuals have long-term survival and expectations for near-normal life expectancy. Our findings support the need for ongoing effective ART with successful virologic suppression and immunologic recovery, to support improvements in QoL. This study provides important data for RLS, where individuals may start or switch ART after longer periods of detectable viral load than in higher income settings.

**Contributors**

TST did the literature search. TST, LJH, MDH analyzed the data and generated the tables and figures. TST, LJH, LZ, MDH interpreted the data. TST, LJH, MDH drafted the manuscript. AMLR, SWC, LZ, MN, FS, UGL, TM, ACC revised the manuscript and contributed intellectually. The members of the study group were responsible for study oversight and played other important roles for the study at their sites, reviewed the study results, manuscript, and provided input and other intellectual contributions.

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Figure 1. Unadjusted Mean QoL from week 0 to week 48 by baseline VL (>100,000 cp/mL vs. VL ≤100,000 copies/mL) (bars are 95% confidence intervals)

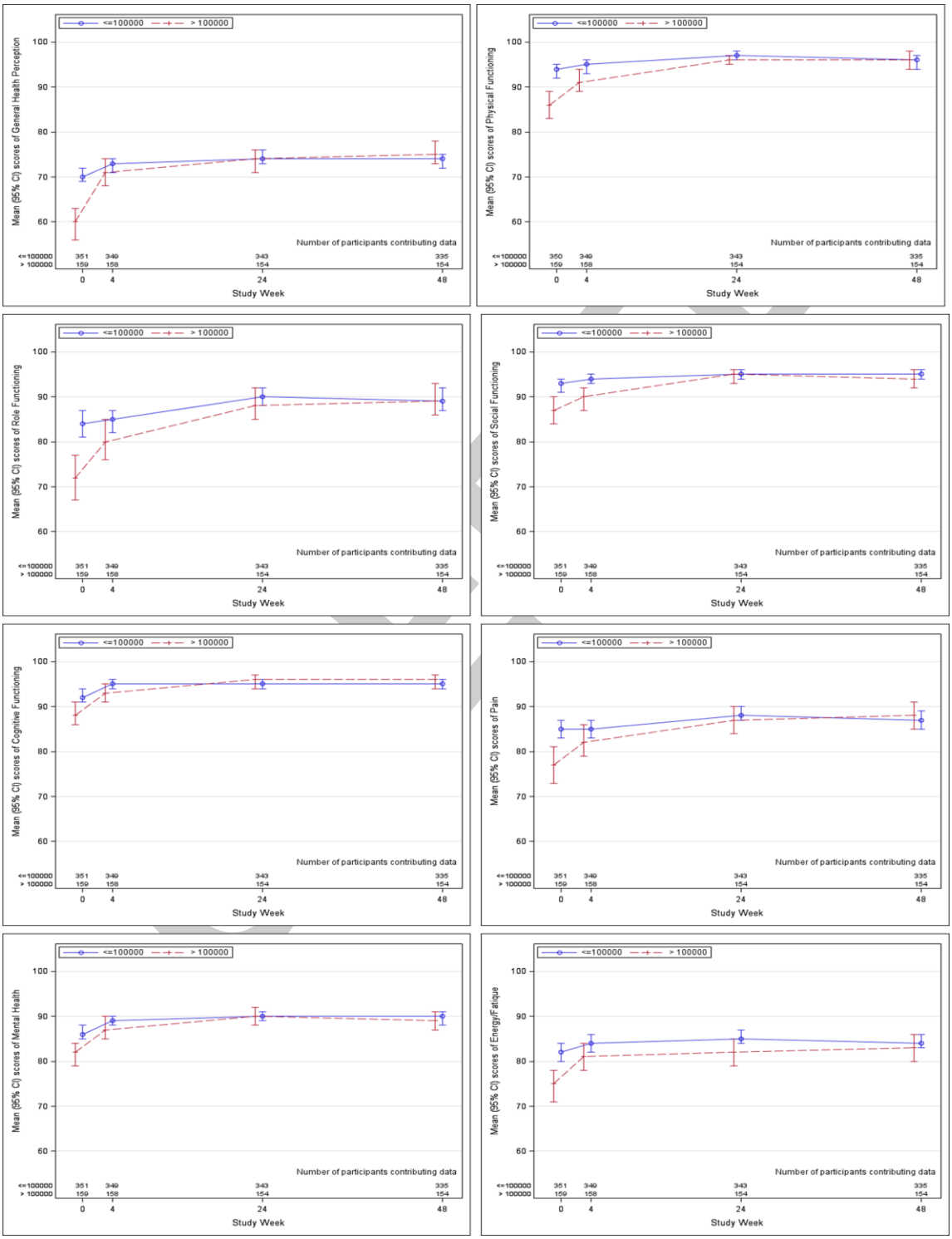

Figure 2. Unadjusted mean QoL from week 0 to week 48 by baseline CD4 count (<50 vs.≥50 cells/mm$^3$) (bars are 95% confidence intervals)

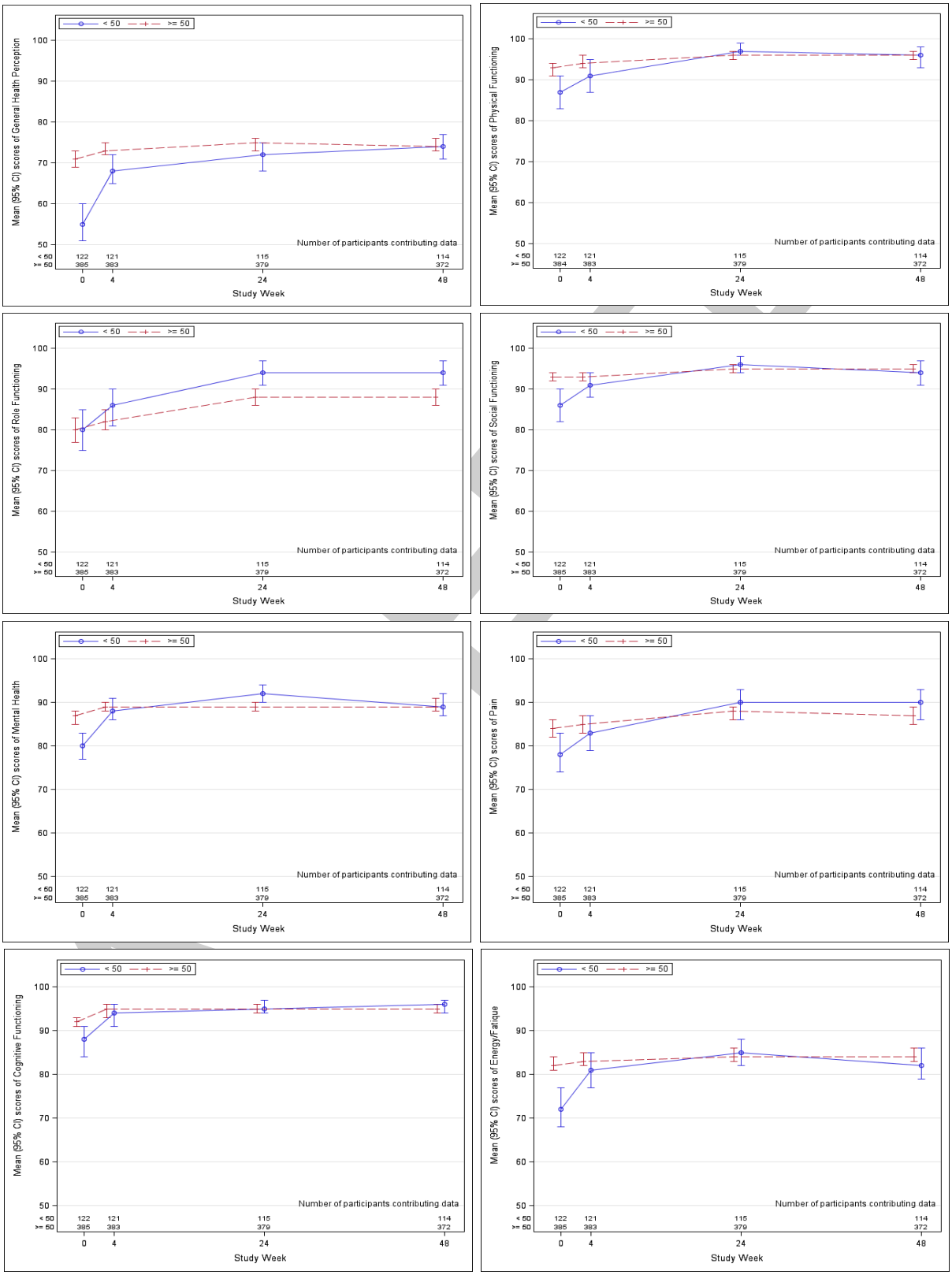

Table 1. Information obtained using the Short Form 21-item (SF-21) Quality of Life (QoL) Questionnaire

| Domains | Number of items | Summary of contents |
|---|---|---|
| General Health Perceptions (GHP) | 3 | Participants rate their general health, resistance to illnesses, and health outlook. It has been validated by Davies and Ware [32] and Stewart and Ware [33]. Two questions are reverse coded to control for response set effects. |
| Physical Functioning (PF) | 4 | It inquired about physical limitations ranging from severe to minor, including lifting heavy objects or running, walking uphill or climbing a few flights of stairs, and being able to eat, dress, bathe and use the toilet by oneself. |
| Role Functioning (RF) | 2 | Participants are asked if their health negatively impacts their ability to perform at a job/school or to work around the house in the past 4 weeks. |
| Social Functioning (SF) | 2 | Participants are asked to what extent their health in the past 4 weeks has limited their social activities [34]; one item is reverse coded to control for response set effects. |

| | | |
|---|---|---|
| Cognitive Functioning (CF) | 3 | This domain measures the degree of difficulty participants have experienced in the past four weeks with respect to their cognitive abilities. It assesses a participant's level of difficulty with reasoning/solving problems, being attentive, and remembering. |
| Pain (P) | 2 | This domain assess intensity of physical pain (e.g., headache, muscle pain, back pain, stomach ache) and degree of interference with daily activities in the past four weeks [35]; one item is reverse coded to control for response set effects. |
| Mental health (MH) | 3 | This domain assesses anxiety, depression, and overall psychological wellbeing in the past 4 weeks [36]. One item is reverse coded to control for response set effects. |
| Energy/ Fatigue (E/F) | 2 | This domain assesses vitality (feeling tired or fatigued and energy to do things the person wanted to); one item is reverse coded to control for response set effects. |

Table 2. Baseline demographic and clinical characteristics of participants included in the analysis by arm

| Characteristic | LPV/r + RAL (N=258) | LPV/r + NRTIs (N=254) | Total (N=512) |
|---|---|---|---|
| **Sex** | | | |
| Male | 124(48%) | 128(50%) | 252 (49%) |
| Female | 134(52%) | 126(50%) | 260 (51%) |
| **Age (years)** | | | |
| Median (IQR) | 39 (34; 44) | 38 (33; 43) | 39 (34; 44) |
| 18-29 | 22(9%) | 29(11%) | 51 (10%) |
| 30-39 | 111(43%) | 116(46%) | 227 (44%) |
| 40-49 | 92(36%) | 86(34%) | 178 (35%) |
| 50+ | 33(13%) | 23(9%) | 56 (11%) |
| **Race** | | | |
| Black African | 163(63%) | 162(64%) | 325 (63%) |
| Others | 95(37%) | 92(36%) | 187 (37%) |

| | | | |
|---|---|---|---|
| **Country** | | | |
| India | 80(31%) | 78(31%) | 158 (31%) |
| Malawi | 56(22%) | 55(22%) | 111 (22%) |
| South Africa | 52(20%) | 51(20%) | 103 (20%) |
| Kenya | 24(9%) | 24(9%) | 48 (9%) |
| Zimbabwe | 24(9%) | 23(9%) | 47 (9%) |
| Tanzania | 8(3%) | 9(3%) | 17 (3%) |
| Brazil | 6(2%) | 6(2%) | 12 (2%) |
| Peru | 5(2%) | 4(2%) | 9 (2%) |
| Thailand | 3(1%) | 4(2%) | 7 (1%) |
| **BMI ($kg/m^2$)** | | | |
| Median (IQR) | 23 (20; 27) | 22 (19; 25) | 22 (19; 26) |
| <18 | 24(9%) | 31(12%) | 55 (11%) |
| 18-<25 | 145(56%) | 150(59%) | 295 (58%) |
| 25-<30 | 56(22%) | 54(21%) | 110 (21%) |
| ≥30 | 33(13%) | 19(7%) | 52 (10%) |
| **Viral Load (HIV-1 RNA** | **N=257** | **N=253** | **n=510** |

| | | | |
|---|---|---|---|
| **copies/mL)** | | | |
| Median (IQR) ($log_{10}$) | 4.6(4.0; 5.2) | 4.5(3.9; 5.1) | 4.5(3.9; 5.1) |
| <10,000 | 68(26%) | 77(31%) | 145 (29%) |
| 10,000-100,000 | 105(41%) | 101(40%) | 206 (40%) |
| >100,000 | 84(33%) | 75(30%) | 159 (31%) |
| **CD4 count (cells/mm³)** | **N=255** | **N=252** | **n=507** |
| Median (IQR) | 138(49; 268) | 133(56; 274) | 135 (53; 271) |
| <50 | 65(25%) | 57(23%) | 122 (24%) |
| 50-199 | 92(36%) | 102(40%) | 194 (38%) |
| 200-349 | 67(26%) | 54(21%) | 121 (24%) |
| ≥350 | 31(12%) | 39(16%) | 70 (14%) |
| **History of AIDS** | | | |
| Yes | 70(27%) | 80(31%) | 150 (29%) |
| No | 188(73%) | 174(69%) | 362 (71%) |
| **Number of comorbidities** | | | |
| 0 | 83(32.2%) | 97(38.2%) | 180 (35%) |

| | | | |
|---|---|---|---|
| 1 | 76(29.5%) | 72(38.4%) | 148 (29%) |
| 2 | 45(17.4%) | 35(13.8%) | 80 (16%) |
| ≥3 | 54(20.9%) | 50(19.7%) | 104 (20%) |
| **Time on 1st-line ART (years)** | | | |
| Median (IQR) | 4.2(2.2; 6.5) | 4.1(2.3; 6.0) | 4.2 (2.3; 6.2) |
| <4 | 121(46.9%) | 124(48.8%) | 245 (48%) |
| 4-<7 | 82(31.8%) | 95(37.4%) | 177 (34%) |
| ≥7 | 55(21.3%) | 35(13.8%) | 90 (18%) |

Table 3. QoL at Baseline (first-line failure) and Mean Increases (univariable model) at Week 48 of Second-line Therapy by Randomized Treatment and Baseline Variables

| | Mean QoL at baseline (95% CI) | | Difference in mean QoL at baseline | Mean increase in QoL from baseline to week 48 (95% CI) | | Difference in mean increase | Mean QoL at week 48 (95% CI) | | Difference in mean QoLat week 48 |
|---|---|---|---|---|---|---|---|---|---|
| **Randomized Treatment** | **LPV/r+NRTIs** | **LPV/r+RAL** | **p-value** | **LPV/r+NRTIs** | **LPV/r+RAL** | **p-value** | **LPV/r+NRTIs** | **LPV/r+RAL** | **p-value** |
| General Heath Perceptions (GHP) | 68 (66, 71) | 66 (63, 69) | N/A | 6 (4, 9) | 8 (5, 11) | 0.38 | 74 (72, 76) | 74 (72, 76) | 0.76 |
| Physical Functioning (PF) | 93 (91, 95) | 90 (88, 92) | N/A | 4 (1, 6) | 5 (2, 8) | 0.42 | 96 (95, 98) | 95 (93, 97) | 0.33 |
| Role Functioning (RF) | 82 (78, 86) | 79 (75, 83) | N/A | 9 (5, 12) | 9 (5, 13) | 0.85 | 91 (88, 93) | 88 (85, 91) | 0.19 |
| Social Functioning (SF) | 92 (90, 94) | 91 (89, 93) | N/A | 4 (2, 6) | 3 (1, 5) | 0.40 | 96 (94, 97) | 94 (92, 95) | 0.03 |
| Cognitive Functioning (CF) | 92 (90, 94) | 90 (88, 92) | N/A | 3 (1, 5) | 5 (3, 8) | 0.17 | 95 (94, 96) | 95 (94, 97) | 0.42 |
| Pain (P) | 85 (82, 87) | 81 (78, 84) | N/A | 4 (1, 7) | 5 (2, 8) | 0.51 | 89 (86, 91) | 86 (84, 89) | 0.35 |
| Mental Health (MH) | 86 (84, 87) | 84 (82, 86) | N/A | 4 (2, 6) | 5 (3, 8) | 0.28 | 89 (88, 91) | 90 (88, 91) | 0.66 |
| Energy / Fatigue (E/F) | 81 (79, 83) | 79 (76, 81) | N/A | 3 (1, 6) | 5 (2, 8) | 0.51 | 84 (82, 86) | 84 (82, 86) | 0.63 |
| | | | | | | | | | |
| **Baseline Viral Load (c/mL)** | **≤100,000** | **>100,000** | **p-value** | **≤100,000** | **>100,000** | **p-value** | **≤100,000** | **>100,000** | **p-value** |
| General Heath Perceptions (GHP) | 70 (69, 72) | 60 (56, 63) | <.001 | 3 (1, 5) | 16 (12, 19) | <.001 | 73 (72, 75) | 75 (73, 77) | 0.25 |
| Physical Functioning (PF) | 94 (92, 95) | 86 (83, 89) | <.001 | 2 (0, 4) | 10 (6, 14) | 0.001 | 96 (94, 97) | 96 (94, 98) | 0.83 |
| Role Functioning (RF) | 84 (81, 87) | 72 (67, 77) | <.001 | 5 (2, 8) | 17 (12, 23) | <.001 | 89 (87, 92) | 89 (86, 93) | 0.94 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Social Functioning (SF) | 93 (90, 94) | 87 (84, 90) | 0.001 | 2 (0, 4) | 7 (3, 10) | 0.015 | 95 (94, 96) | 94 (92, 96) | 0.45 |
| Cognitive Functioning (CF) | 92 (91, 94) | 88 (86, 91) | 0.022 | 3 (1, 5) | 7 (4, 10) | 0.010 | 95 (94, 96) | 96 (94, 97) | 0.41 |
| Pain (P) | 85 (83, 87) | 77 (73, 81) | 0.001 | 2 (-1, 4) | 11 (7, 15) | <.001 | 87 (85, 89) | 88 (85, 91) | 0.58 |
| Mental Health (MH) | 86 (85, 88) | 82 (79, 84) | 0.002 | 3 (2, 5) | 8 (4, 11) | 0.020 | 90 (88, 91) | 89 (87, 91) | 0.82 |
| Energy / Fatigue (E/F) | 82 (80, 84) | 75 (71, 78) | 0.001 | 2 (0, 5) | 8 (5, 12) | 0.006 | 84 (82, 86) | 83 (80, 86) | 0.42 |
| | | | | | | | | | |
| **Baseline CD4 (cells/mm$^3$)** | **<50** | **≥50** | **p-value** | **<50** | **≥50** | **p-value** | **<50** | **≥50** | **p-value** |
| General Heath Perceptions (GHP) | 55 (51, 59) | 71 (69, 73) | <.001 | 19 (15, 23) | 3 (1, 5) | <.001 | 74 (71, 77) | 74 (73, 76) | 0.99 |
| Physical Functioning (PF) | 87 (83, 91) | 93 (91, 94) | 0.005 | 8 (4, 13) | 3 (1, 5) | 0.027 | 95 (93, 98) | 96 (95, 97) | 0.79 |
| Role Functioning (RF) | 80 (75, 85) | 80 (77, 83) | 0.96 | 14 (9, 19) | 7 (4, 11) | 0.041 | 94 (91, 97) | 88 (85, 90) | 0.002 |
| Social Functioning (SF) | 86 (82, 90) | 93 (92, 94) | 0.001 | 9 (4, 13) | 2 (0, 3) | 0.005 | 94 (91, 97) | 95 (94, 96) | 0.68 |
| Cognitive Functioning (CF) | 88 (84, 91) | 92 (90, 93) | 0.016 | 8 (5, 12) | 3 (1, 5) | 0.007 | 96 (94, 97) | 95 (94, 96) | 0.33 |
| Pain (P) | 78 (74, 83) | 84 (82, 86) | 0.016 | 12 (7, 17) | 2 (0, 5) | 0.001 | 90 (86, 93) | 87 (85, 89) | 0.10 |
| Mental Health (MH) | 80 (77, 83) | 87 (85, 88) | 0.001 | 9 (6, 13) | 3 (1, 5) | 0.002 | 89 (86, 92) | 89 (88, 91) | 0.87 |
| Energy / Fatigue (E/F) | 72 (68, 76) | 82 (81, 84) | <.001 | 10 (5, 15) | 2 (0, 4) | 0.005 | 82 (78, 86) | 84 (83, 86) | 0.29 |
| | | | | | | | | | |
| **BMI (kg/m$^2$)** | **<18** | **≥18** | **p-value** | **<18** | **≥18** | **p-value** | **<18** | **≥18** | **p-value** |
| General Heath Perceptions (GHP) | 59 (52, 65) | 68 (66, 70) | 0.007 | 15 (9, 22) | 6 (4, 8) | 0.007 | 74 (71, 77) | 74 (73, 76) | 0.96 |
| Physical Functioning (PF) | 80 (73, 86) | 93 (91, 94) | <.001 | 15 (7, 22) | 3 (1, 5) | 0.002 | 95 (91, 98) | 96 (95, 97) | 0.52 |
| Role Functioning (RF) | 63 (54, 71) | 82 (80, 85) | <.001 | 21 (10, 31) | 7 (5, 10) | 0.015 | 83 (76, 90) | 90 (88, 92) | 0.072 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Social Functioning (SF) | 82 (76, 87) | 92 (91, 94) | 0.001 | 11 (4, 18) | 3 (1, 4) | 0.024 | 92 (88, 96) | 95 (94, 96) | 0.22 |
| Cognitive Functioning (CF) | 85 (80, 90) | 92 (90, 93) | 0.008 | 9 (3, 15) | 4 (2, 5) | 0.07 | 94 (91, 97) | 95 (94, 96) | 0.53 |
| Pain (P) | 71 (64, 78) | 84 (82, 86) | 0.001 | 15 (8, 22) | 3 (1, 5) | 0.001 | 86 (80, 92) | 87 (86, 89) | 0.62 |
| Mental Health (MH) | 80 (76, 84) | 85 (84, 87) | 0.009 | 7 (2, 12) | 4 (3, 6) | 0.22 | 87 (83, 91) | 90 (88, 91) | 0.24 |
| Energy / Fatigue (E/F) | 72 (66, 78) | 81 (79, 83) | 0.008 | 4 (-5, 12) | 4 (2, 6) | 0.92 | 76 (70, 82) | 85 (83, 86) | 0.004 |
| | | | | | | | | | |
| **Number of comorbidities** | **<3** | **≥3** | **p-value** | **<3** | **≥3** | **p-value** | **<3** | **≥3** | **p-value** |
| General Heath Perceptions (GHP) | 68 (65, 70) | 65 (62, 69) | 0.25 | 7 (5, 10) | 6 (2, 9) | 0.40 | 75 (73, 76) | 71 (68, 74) | 0.024 |
| Physical Functioning (PF) | 92 (91, 94) | 88 (85, 91) | 0.026 | 4 (2, 6) | 6 (3, 10) | 0.29 | 96 (95, 97) | 94 (92, 96) | 0.15 |
| Role Functioning (RF) | 84 (81, 87) | 67 (60, 73) | <.001 | 7 (4, 10) | 15 (8, 21) | 0.051 | 91 (89, 93) | 81 (76, 86) | 0.001 |
| Social Functioning (SF) | 92 (91, 94) | 87 (84, 91) | 0.006 | 3 (1, 5) | 6 (2, 9) | 0.22 | 95 (94, 96) | 93 (90, 95) | 0.10 |
| Cognitive Functioning (CF) | 91 (89, 92) | 92 (90, 94) | 0.29 | 5 (3, 7) | 2 (-1, 4) | 0.020 | 96 (95, 97) | 94 (92, 96) | 0.08 |
| Pain (P) | 85 (83, 87) | 74 (70, 78) | <.001 | 4 (2, 6) | 7 (1, 12) | 0.39 | 89 (87, 91) | 81 (76, 84) | 0.001 |
| Mental Health (MH) | 85 (83, 86) | 85 (82, 87) | 0.90 | 5 (3, 7) | 2 (-1, 6) | 0.17 | 90 (89, 91) | 87 (85, 90) | 0.048 |
| Energy / Fatigue (E/F) | 80 (78, 82) | 79 (76, 83) | 0.66 | 4 (1, 6) | 5 (1, 9) | 0.50 | 84 (82, 86) | 85 (82, 87) | 0.68 |
| | | | | | | | | | |
| **History of AIDS** | **No** | **Yes** | **p-value** | **No** | **Yes** | **p-value** | **No** | **Yes** | **p-value** |
| General Heath Perceptions (GHP) | 68 (66, 70) | 65 (61, 69) | 0.17 | 6 (4, 8) | 10 (6, 13) | 0.12 | 74 (72, 75) | 75 (71, 77) | 0.72 |
| Physical Functioning (PF) | 93 (92, 95) | 87 (84, 91) | 0.004 | 3 (1, 5) | 8 (4, 12) | 0.029 | 96 (95, 97) | 95 (93, 98) | 0.64 |
| Role Functioning (RF) | 80 (77, 83) | 81 (76, 85) | 0.90 | 8 (5, 12) | 10 (5, 15) | 0.60 | 89 (86, 91) | 91 (87, 94) | 0.36 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Social Functioning (SF) | 92 (90, 93) | 90 (87, 93) | 0.37 | 3 (1, 5) | 4 (1, 8) | 0.54 | 95 (94, 96) | 94 (92, 97) | 0.81 |
| Cognitive Functioning (CF) | 91 (89, 93) | 91 (88, 93) | 0.96 | 4 (2, 6) | 5 (2, 7) | 0.77 | 95 (94, 96) | 95 (94, 97) | 0.66 |
| Pain (P) | 82 (80, 85) | 84 (80, 87) | 0.64 | 4 (2, 7) | 6 (2, 10) | 0.47 | 86 (84, 88) | 89 (86, 92) | 0.14 |
| Mental Health (MH) | 85 (84, 87) | 84 (81, 86) | 0.25 | 4 (2, 5) | 7 (4, 10) | 0.063 | 89 (88, 90) | 90 (88, 93) | 0.23 |
| Energy / Fatigue (E/F) | 82 (80, 84) | 75 (72, 79) | 0.002 | 3 (1, 5) | 6 (2, 11) | 0.24 | 85 (83, 87) | 81 (78, 85) | 0.07 |