Improvements in patient reported outcomes of dolutegravir (DTG) based second-line treatment compared to lopinavir/ritonavir (LPV/r) based treatment: Results from the DAWNING study

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Introduction

- The DAWNING study compared dolutegravir (DTG) + 2 nucleoside reverse transcriptase inhibitors (NRTIs) to ritonavir-boosted lopinavir (LPV/r) + 2 NRTIs in HIV-1 infected adults failing first-line therapy (HIV-1 RNA ≥400 copies [c]/mL on 2 occasions) of a non-nucleoside reverse transcriptase inhibitor + 2 NRTIs (ClinicalTrials.gov: NCT02227238)
- Results showed DTG + 2 NRTIs to be superior in viral suppression (Plasma HIV-1 RNA <50 c/mL) at week 48 compared to LPV/r + 2 NRTIs[1]
- Here we present results of patient reported outcome (PRO) measures used in the DAWNING study

Methods

HIV Treatment Satisfaction Questionnaire (HIVTSQ)

- The HIVTSQ, now referred to as status version (HIVTSQs), was designed specifically to measure satisfaction with medication for people infected with HIV (Woodcock and Bradley, 2001; 2006). The change version (HIVTSQc) is used to overcome potential ceiling effects of HIVTSQs. Both versions were used in the DAWNING study
- HIVTSQ is a 12-item scale which results in total score calculated using items 1-6, 7a, 8, 9b, 10 & 11. The total score ranges from 0 to 66. Higher scores represent greater treatment satisfaction
- Change from baseline in the two treatment arms was compared at weeks 4, 24, and 48 using Wilcoxon rank sum test

Morisky Medication Adherence Scale (MMAS-8)

- The 8-item MMAS-8 is a self-reported measure of medication-taking behavior and addresses barriers to medication-taking
- Total score with a possible range of 0 to 8.0. High adherence=8, Medium from 6 to 7.75, Low from 0 to 5.75
- The two treatment arms were compared at weeks 4, 24, and 48 using Fisher's exact test

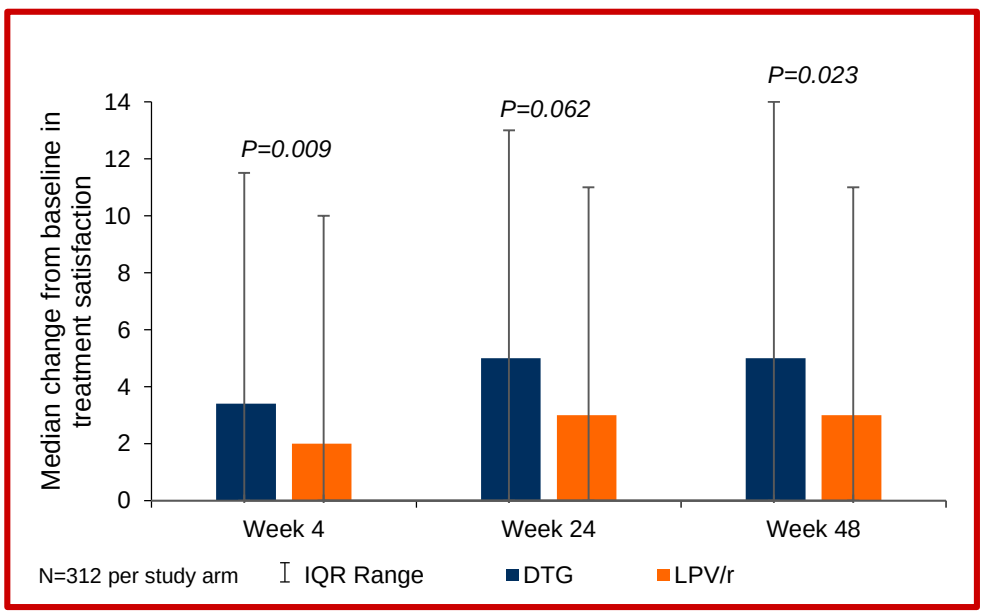
Gastrointestinal Symptom Rating Scale (GSRS)

- The GSRS is a disease-specific instrument of 15 items combined into five symptom clusters depicting Reflux, Abdominal pain, Indigestion, Diarrhoea, and Constipation. Each symptom is rated from 1 to 7 with higher scores representing more discomfort
- Change from baseline in the two treatment arms was compared at weeks 4, 24, and 48 using Wilcoxon rank sum test
- Observed case was the prespecified method for handling missing data for all PRO measures; a post hoc analysis using last observation carried forward (LOCF) was performed to ensure consistency with other studies

Results

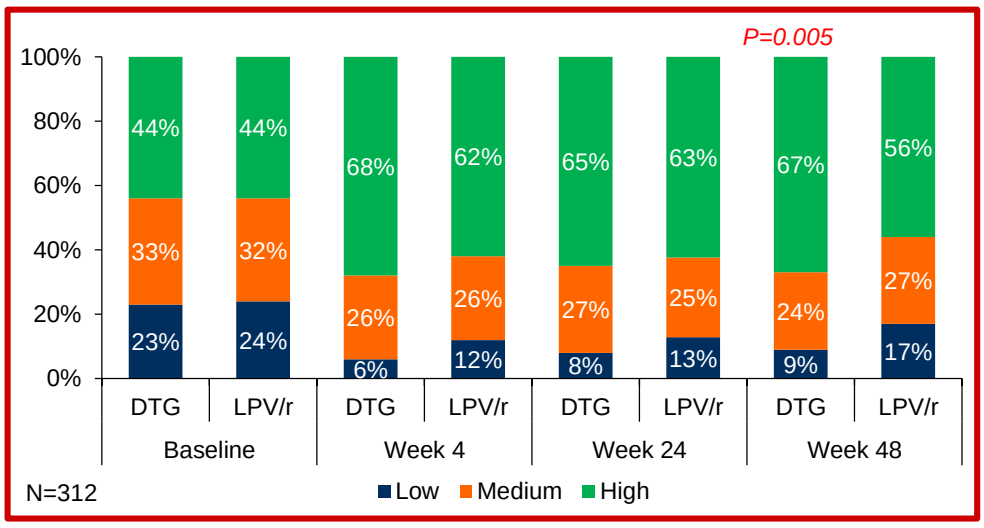
- HIVTSQ Total Score increased from baseline in both arms with greater increase in the DTG arm compared to LPV/r. This difference was statistically significant at week 4 and week 48 (Figure 1)

Figure 1. Satisfaction with treatment (HIVTSQ) during study duration



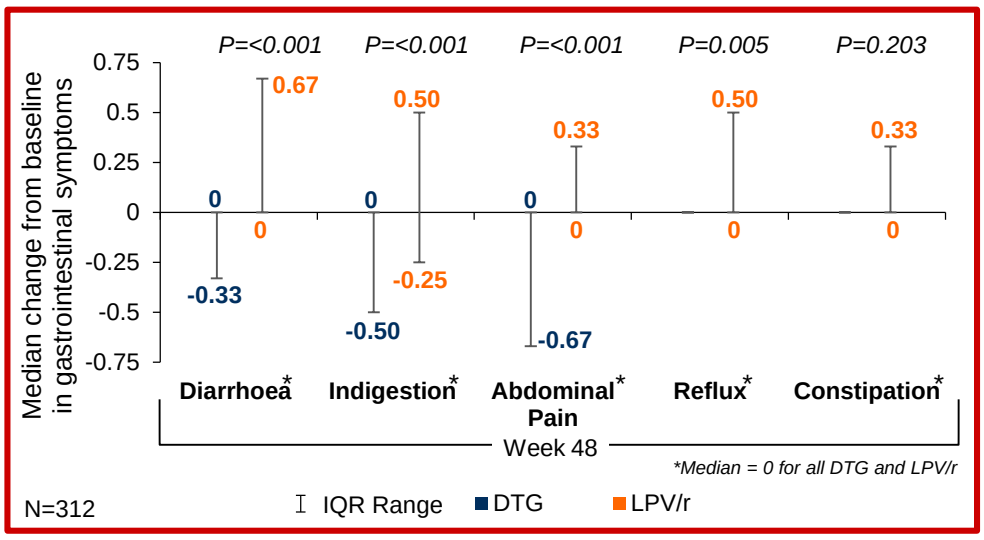
- In both arms, % low adherence decreased from baseline and % high adherence increased from baseline (Figure 2)
- % low adherence was lower in the DTG arm, while % high adherence was higher in the DTG arm compared with the LPV/r arm with a statistically significant difference at week 48 (high adherence: 67% [n=205] vs 56% [n=173], medium adherence: 24% [n=74] vs 27% [n=82], low adherence: 9% [n=28] vs 17% [n=52]; *P*=0.005)

Figure 2. Adherence with treatment (MMAS-8) during study duration



- Diarrhoea and indigestion scores decreased from baseline (improvement) in the DTG arm and increased from baseline (worsening) in the LPV/r arm, consistent with GI AEs observed for LPV/r. This difference was statistically significant at weeks 4, 24, and 48 (Figure 3)
- Abdominal Pain and Reflux scores decreased from baseline (improvement) in DTG arm and increased from baseline (worsening) in LPV/r arm with statistically significant difference between the DTG and LPV/r arms at weeks 4, 24, and 48
- The change in constipation scores was small in both arms with no statistically significant difference between DTG and LPV/r at any time point

Figure 3. Gastrointestinal symptoms with treatment (GSRS) during study duration



Conclusions

- Patient reported outcomes were maintained or slightly improved after starting DTG compared to LPV/r, with improvements in gastrointestinal symptoms which may have lead to improved adherence
- These results support DTG as a treatment option with improved tolerability after first-line treatment failure in resource constrained settings
- In its recently published interim guidance, the WHO recommends DTG + 2 NRTIs as a preferred second-line regimen for patients whose non-DTG-based first-line regimen is failing

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Reference:
1. Aboud et al. IAC 2018; Amsterdam, the Netherlands. Poster THPEB040.