Efficacy and safety of switching from boosted protease inhibitors plus emtricitabine and tenofovir disoproxil fumarate regimens to single-tablet darunavir, cobicistat, emtricitabine, and tenofovir alafenamide at 48 weeks in adults with virologically suppressed HIV-1 (EMERALD): a phase 3, randomised, non-inferiority trial

Chloe Orkin, Jean-Michel Molina, Eugenia Negredo, José R Arribas, Joseph Gathe, Joseph J Eron, Erika Van Landuyt, Erkki Lathouwers, Veerle Hufkens, Romana Petrovic, Simon Vanveggel, Magda Opsomer, on behalf of the EMERALD study group

Summary

Background Simplified regimens with reduced pill burden and fewer side-effects are desirable for people living with HIV. We investigated the efficacy and safety of switching to a single-tablet regimen of darunavir, cobicistat, emtricitabine, and tenofovir alafenamide versus continuing a regimen of boosted protease inhibitor, emtricitabine, and tenofovir disoproxil fumarate.

Methods EMERALD was a phase-3, randomised, active-controlled, open-label, international, multicentre trial, done at 106 sites across nine countries in North America and Europe. HIV-1-infected adults were eligible to participate if they were treatment-experienced and virologically suppressed (viral load <50 copies per mL for ≥2 months; one viral load of 50–200 copies per mL was allowed within 12 months before screening), and patients with a history of virological failure on non-darunavir regimens were allowed. Randomisation was by computer-generated interactive web-response system and stratified by boosted protease inhibitor use at baseline. Patients were randomly assigned (2:1) to switch to the open-label study regimen or continue the control regimen. The study regimen consisted of a fixed-dose tablet containing darunavir 800 mg, cobicistat 150 mg, emtricitabine 200 mg, and tenofovir alafenamide 10 mg, which was taken once per day for 48 weeks. The primary outcome was the proportion of participants with virological rebound (confirmed viral load ≥50 copies per mL or premature discontinuations, with last viral load ≥50 copies per mL) cumulative through week 48; we tested non-inferiority (4% margin) of the study regimen versus the control regimen in the intention-to-treat population. This study is registered with ClinicalTrials.gov, number NCT02269917.

Findings The study began on April 1, 2015, and the cutoff date for the week 48 primary analysis was Feb 24, 2017. Of 1141 patients (763 in the study group and 378 in the control group), 664 (58%) had previously received five or more antiretrovirals, including screening antiretrovirals, and 169 (15%) had previous virological failure on non-darunavir regimens. The study regimen was non-inferior to the control for virological rebound cumulative through week 48 (19 [2.5%] of 763 patients in the study group vs eight [2.1%] of 378 patients in the control group; difference 0.4%, 95% CI –1.5 to 2.2; p=0.010) difference between the two groups in change from baseline in total cholesterol to HDL-cholesterol ratio. Only one serious adverse event (pancreatitis in the study group) was deemed as possibly related to the study regimen.

Interpretation Our findings show the safety and efficacy of single-tablet darunavir, cobicistat, emtricitabine, and tenofovir alafenamide as a potential switch option for the treatment of HIV-1 infection in adults with viral suppression.

Funding Janssen.

Introduction Since the advent of combination antiretroviral therapy (ART) for HIV, morbidity and mortality have significantly declined. However, incomplete adherence to ART and emergence of antiretroviral resistance can compromise the success of long-term treatment.

Single-tablet HIV-1 regimens that are taken once per day are preferred by patients and might improve treatment adherence and satisfaction and virological outcomes.

Treatment guidelines include darunavir and cobicistat combined with two nucleoside or nucleotide analogue...
Evidence before this study
We searched PubMed for clinical trials of darunavir or protease inhibitors and cobicistat and tenofovir alafenamide for the treatment of HIV-1 infection. Our search terms included (“tenofovir alafenamide” OR “TAF”) AND (“darunavir” OR “protease inhibitor”) AND “cobicistat” AND “HIV” and we looked for manuscripts on randomised controlled trials published in English up to Sept 1, 2017. The once per day regimen of darunavir, cobicistat, emtricitabine, and tenofovir alafenamide (the study regimen) has only been investigated in one exploratory phase 2 study in treatment-naive, HIV-1-infected adults. In that study the study regimen had virological efficacy similar to that of cobicistat-boosted darunavir given in combination with emtricitabine and tenofovir disoproxil fumarate at week 24 (US Food and Drug Administration [FDA]-snapshot analysis, primary endpoint), with improved bone and renal laboratory parameters and no resistance to any components of the regimen.

Added value of this study
The darunavir, cobicistat, emtricitabine, and tenofovir alafenamide regimen is the first and only single-tablet HIV-1 regimen in development that includes a protease inhibitor, darunavir. We report the first virological and safety outcomes in a phase 3 trial of switching to this regimen versus remaining on regimens of boosted protease inhibitor (darunavir or atazanavir boosted by either ritonavir or cobicistat or lopinavir) plus emtricitabine and tenofovir disoproxil fumarate (the control regimen) in adults with virologically suppressed HIV-1. In contrast with other switch studies, this study allowed enrolment of patients with a history of previous virological failure on non-darunavir-based regimens. Switching to the study regimen was non-inferior to continuing on the control regimen in terms of cumulative rebound rate through 48 weeks. Through 48 weeks no observed resistance was seen in either group, and both regimens were well tolerated. Patients who switched to the study regimen had improvements in measures of proteinuria and in bone mineral density. Overall, our findings show safety and efficacy of the study regimen as a potential switch option for the treatment of HIV-1.

Implications of all available evidence
The study regimen is a convenient and effective antiretroviral regimen that combines the high genetic barrier to resistance of darunavir with the renal and bone safety advantages of tenofovir alafenamide in virologically suppressed HIV-1-infected adults, including those with a history of virological failure on non-darunavir-based regimens.

Methods
Study design and participants
EMERALD is a phase 3, randomised, active-controlled, open-label, international, multicentre, non-inferiority study. We did the trial in accordance with the International Conference on Harmonization guideline for Good Clinical Practice, principles of Good Clinical Practice, and the Declaration of Helsinki. The protocol was reviewed and approved by central or site-specific institutional review boards or independent ethics committees before the start of the study, and is available.
in the appendix. All participants provided written informed consent.

The trial was done at 106 hospitals and clinics across nine countries in North America (Canada and USA) and Europe (Belgium, France, Poland, Spain, Sweden, Switzerland, and UK).

Study investigators enrolled HIV-1-infected, treatment-experienced adults (≥18 years), with no history of virological failure on darunavir-based regimens, and if historical genotypes were available, absence of darunavir resistance-associated mutations. Participants had to be virologically suppressed, with at least one viral load less than 50 copies per mL within 2 months before screening while on a stable ART regimen consisting of a boosted protease inhibitor (darunavir and ritonavir or darunavir and cobicistat once per day, atazanavir and ritonavir or atazanavir and cobicistat once per day, or lopinavir and ritonavir twice per day) combined with emtricitabine and tenofovir disoproxil fumarate for at least 6 months before screening. One viral load greater than or equal to 50 copies per mL and less than 200 copies per mL was allowed within 12 months before screening. Participants needed to have an estimated glomerular filtration rate based on serum creatinine (eGFRcr; calculated with the Cockcroft–Gault formula) of at least 50 mL/min. Exclusion criteria included infection with hepatitis B or C, active clinically significant disease (e.g. malignancy or severe infections), and women who were pregnant or breastfeeding. Disallowed drugs included medications or herbal supplements known or suspected to have drug interactions with the investigational medication. A complete list of exclusion criteria is shown in the appendix.

Randomisation and masking

Randomisation was done with a computer-generated interactive web-response system. Patients were randomly assigned (2:1) to receive darunavir, cobicistat, emtricitabine, and tenofovir alafenamide (study regimen) or boosted protease inhibitor plus emtricitabine and tenofovir disoproxil fumarate (control regimen). We chose the randomisation ratio to increase the precision for the safety assessment of the study regimen. Patients were instructed to take all the medications in the study (pill count and patient log booklet), concomitant medications, and adverse events at each visit. Laboratory evaluations for efficacy (plasma viral load, CD4 cell count) and safety (biochemical and haematological parameters, renal function measures, urinalysis, and urine chemistry) were done at each visit, except at week 52. Renal function measures were serum cystatin C to calculate eGFRcr (calculated with the Chronic Kidney Disease Epidemiology Collaboration [CKD-EPI] formula) and serum creatinine to calculate eGFR, (Cockcroft-Gault and CKD-EPI formulas). The renal proteinuria biomarkers retinol binding protein and β-2-microglobulin in the fasted state were measured at baseline, weeks 2, 4, 12, 24, and 48. We assessed fasted metabolic profile (total, HDL and low-density lipoprotein LDL-cholesterol, triglycerides) at baseline, weeks 24 and 48.

We quantified plasma viral load with the COBAS AmpliPrep/COBAS TaqMan HIV-1 Test V2.0 (Roche Diagnostics, Basel, Switzerland). Post-baseline HIV-1 protease and reverse transcriptase genotype was established with the GenoSure MG (HIV-1 protease and reverse transcriptase genotype) assay (Monogram Biosciences, South San Francisco, CA, USA) for patients with virological rebound (confirmed viral load ≥50 copies per mL) and who had a viral load of 400 copies per mL or higher at failure or at later timepoints, including patients who discontinued with a last single viral load of 400 copies per mL or higher. No baseline genotypes were available because patients had to have suppressed viral load at study entry.

Bone assessments, including bone biomarkers and dual energy x-ray absorptiometry (DXA) scans, were done as part of a substudy at selected study sites in patients from both randomisation groups who provided

Control group drugs were supplied for the study. Patients in both groups could continue receiving the study regimen after week 48 in an extension phase. This extension phase was single arm, with all participants receiving the study regimen. Participants were to return every 12 weeks until week 96. After week 96 participants were given the opportunity to remain in the trial until the study drug becomes commercially available and reimbursed.

Study visits were scheduled for baseline, weeks 2, 4, 8, and 12, and then every 12 weeks until week 96, with a visit at week 52 for patients in the control group to switch to the study regimen. Patients who prematurely discontinued or changed study treatment were required to complete study assessments within 72 h of the decision. Any patient who had an ongoing or serious adverse event at their last study visit had a 30 day follow-up visit unless consent had been withdrawn.

We monitored treatment adherence (pill count and patient log booklet), concomitant medications, and adverse events at each visit. Laboratory evaluations for efficacy (plasma viral load, CD4 cell count) and safety (biochemical and haematological parameters, renal function measures, urinalysis, and urine chemistry) were done at each visit, except at week 52. Renal function measures were serum cystatin C to calculate eGFRcr (calculated with the Chronic Kidney Disease Epidemiology Collaboration [CKD-EPI] formula) and serum creatinine to calculate eGFR, (Cockcroft-Gault and CKD-EPI formulas). The renal proteinuria biomarkers retinol binding protein and β-2-microglobulin in the fasted state were measured at baseline, weeks 2, 4, 12, 24, and 48. We assessed fasted metabolic profile (total, HDL and low-density lipoprotein LDL-cholesterol, triglycerides) at baseline, weeks 24 and 48.

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informed consent. We did DXA scans for hip, lumbar spine (L1–L4), and femoral neck BMD at baseline and weeks 24 and 48. We measured bone biomarkers in the fasted state, including alkaline phosphatase and C-type collagen sequence (markers of bone resorption) and procollagen type N-terminal propeptide (a marker of bone formation) at baseline, weeks 2, 4, 12, 24, and 48, and parathyroid hormone and 25-hydroxy vitamin D at baseline and weeks 24 and 48.

Any adverse events and clinically significant laboratory abnormalities were graded according to the Division of AIDS grading table scale. Adverse events were coded with the Medical Dictionary for Regulatory Activities (version 19.1). All clinical laboratory testing was done at a central laboratory. If grade 3 or 4 laboratory abnormalities occurred, the investigators and sponsor were notified, and confirmatory tests were done.

Outcomes
The US FDA stipulated a novel primary efficacy endpoint for this study because patients were virologically suppressed at study entry: the proportion of patients with virological rebound (confirmed viral load ≥50 copies per mL or premature discontinuations irrespective of reason with last viral load ≥50 copies per mL) cumulative through week 48. The primary outcome was non-inferiority of the study regimen compared with the control regimen in terms of the proportion of virological rebounders in each group. Secondary endpoints analysed included antiviral activity (proportion of patients with viral load <20, <50, and <200 copies per mL at week 48, analysed with the FDA snapshot algorithm), time to virological rebound; changes from baseline in CD4 cell count, safety and tolerability, post-baseline HIV-1 genotypic resistance, adherence to treatment, the pharmacokinetics of darunavir in the study group (presented separately), and changes from baseline at week 48 in serum creatinine, eGFRcr, eGFRcor, and ratios of total urine protein, urine albumin, retinol binding protein, and β-2-microglobulin to creatinine.

Endpoints in the bone investigation substudy were percentage change from baseline in hip, lumbar spine, and femoral neck BMD, changes in associated T-score (normal BMD defined as a T-score ≥−1; osteopenia as a T-score from ≥−2.5 to <−1; and osteoporosis as a T-score <−2.5), and changes in bone biomarkers.

Statistical analysis
We did the primary week 48 analysis after the last active patient had reached week 48 in the study group or week 52 in the control group, whichever came last, or had prematurely discontinued from the study. We did the data analysis with SAS version 9.2.

The non-inferiority of the study regimen relative to the control regimen would be established if the upper bound of the two-sided 95% CI of the stratum-adjusted (boosted protease inhibitor used at screening) Mantel-Haenszel difference between groups (study minus control) in the cumulative rebounder rate through week 48 was less than 4%. Superiority would be shown if the upper bound of the 95% CI was less than 0.

For a cumulative virological rebound rate of 4% through week 48, 1100 participants would be needed to establish non-inferiority of the study regimen compared with control, with a maximum allowable difference of 4% at 89% power and one-sided significance of 0.025. Assuming a screening failure rate of 20%, 1375 patients needed to be screened. For the bone investigation substudy, 300 patients (200 in the study group vs 100 in the control group) were needed to detect a 2% difference between groups in the percentage change from baseline in spine BMD at 98% power, assuming an between-patient variability of 4%.

We did the primary analysis on the intention-to-treat population (all randomised patients who received at least one dose of study medication). We also did a per-protocol analysis, which included the intention-to-treat population minus patients with major protocol violations or other predefined criteria that potentially affected the efficacy outcome.

In our immunology analysis, we calculated the difference between groups in least square mean change from baseline at week 48 for CD4 cell count and associated 95% CIs with ANCOVA, including a term for boosted protease inhibitor used at screening and baseline CD4 count value as a covariate. For premature
discontinuations, we imputed data with baseline values (non-completer = failure). For other missing values, the last observation was carried forward.

We analysed post-baseline HIV-1 genotypes for protease mutations (including International Antiviral Society [IAS]-USA primary protease inhibitor resistance-associated mutations and IAS-USA non-nucleoside reverse transcriptase inhibitor [NNRTI] resistance-associated mutations), reverse transcriptase mutations (including IAS-USA NRTI resistance-associated mutations and IAS-USA non-nucleoside reverse transcriptase inhibitor [NNRTI] resistance-associated mutations), and specific mutations associated with resistance to the study drugs. We also assessed antiretroviral susceptibility, which was based on the genotype report.

We made within-treatment comparisons of renal and bone biomarkers and fasting lipids with the Wilcoxon signed-rank test. We made between-treatment comparisons of changes from baseline to week 48 with the van Elteren test, controlling for the boosted protease inhibitor used at screening. We tested between-treatment differences in change from baseline to weeks 24 and 48 in renal function (serum creatinine, eGFR, and BMD) as a covariate.

Baseline characteristics were balanced between the two groups (table I). Median age of patients was 46 years and most were male, white, and receiving boosted darunavir (with ritonavir or cobicistat) at screening. Median time since diagnosis was 9-26 years (IQR 4-22-18-12). 664 (58%) of 1141 patients had received at least five previous antiretrovirals, (including screening NRTIs).

Role of the funding source
The funder was involved in the study design, study conduct, data collection, and data analysis. All authors had access to the data, were involved in the development of the manuscript, interpretation of data, and have read and approved the final version. The corresponding author had final responsibility to submit the manuscript for publication.

Results
The study began on April 1, 2015, and the cutoff date for this week 48 primary analysis was February 24, 2017. Of the 1299 patients screened, 1141 underwent randomisation and were included in the intention-to-treat population, with 765 assigned to the study group and 376 assigned to the control group (figure I). Overall, 1087 (95%) of 1141 patients included in the intention-to-treat analysis completed week 48. During treatment, 34 participants discontinued from the study group and 20 discontinued from the control group. The discontinuations were mostly because of adverse events, withdrawn consent, and loss to follow-up (figure I).

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Asp67Asp/Asn; these mutations were not related to any rebound had an NRTI resistance-associated mutation, recombination 95% CI –1 to 2.2, with a corresponding one-sided antiretrovirals and 312 (27%) had received eight or more previous antiretrovirals; 472 (41%) had received at least two protease inhibitors (including screening protease inhibitors), 474 (42%) at least three NRTIs (including screening NRTIs), 340 (30%) at least one NNRTI, and 63 (6%) at least one integrase inhibitor. 169 (15%) patients had previous antiretroviral virological failure (80 [7%] patients on protease inhibitor, 130 [11%] on NNRTI, 74 [6%] on NNRTI, and ten [1%] on integrase inhibitor).

The virological rebound rate (confirmed viral load ≥50 copies per mL or premature discontinuations with last viral load ≥50 copies per mL) through 48 weeks was low and similar in both groups (19 [2.5%] of 763 patients in the study group and eight [2.1%] of 378 patients in the study group; figure 2). The treatment difference for the study group minus the control group was 0.4% (95% CI –0.7 to 1.2%), with a corresponding one-sided non-inferiority p value less than 0.0001, showing that the study regimen was non-inferior to the control regimen. Of the patients with virological rebound, most (12 [63%]) of 19 patients in the control group and four (50%) of eight patients in the control group achieved suppression again by week 48 (ie, they had viral load <50 copies per mL by the FDA-snapshot approach, without a change in therapy). There were three confirmed rebounds (viral load ≥200 copies per mL) in the study group and none in the control group. The per-protocol analysis supported the finding that the study regimen was non-inferior to the control regimen with respect to the cumulative virological rebound rate (14 [1.9%] of 721 patients in the study group vs three [0.8%] of 358 patients in the control group; difference 1.1%, 95% CI –0.3 to 2.5, p<0.0001). The results were consistent across baseline patient subgroups (figure 3). Up to week 48, there was no
difference in time to virological rebound (viral load ≥50 copies per mL) between both treatment groups (p=0.824) and the time to rebound was evenly spread out over 48 weeks. Product limit estimates at week 48 for virological rebound were 0.0245 for the study group and 0.0216 for the control group.

At week 48, virological response (viral load <50 copies per mL; FDA-snapshot analysis) was observed in 724 (94.9%) of 763 patients in the study group and 354 (93.7%) of 378 patients in the control group (difference 1.2%, 95% CI –1.7 to 4.1; figure 2 and appendix p 1). Viral load of 50 copies per mL or higher (FDA-snapshot analysis) occurred in six (0.8%) patients in the study group and two (0.5%) patients in the control group (difference 0.3%, 95% CI –0.7 to 1.2%). Of these patients, four in the study group and two in the control group had a last viral load in the week 48 window of 50 copies per mL or higher. No patients in either group discontinued because of efficacy-related reasons as assessed by the investigator. Two patients in the study group and no patients in the control group discontinued because of reasons other than efficacy, adverse events, or death, but had a last available viral load of 50 copies per mL or higher (appendix, p 1).

In the per-protocol FDA-snapshot analysis, responses were achieved by 694 (96.3%) of 721 patients in the study group versus 342 (95.5%) of 358 patients in the control group. In the intention-to-treat analysis, virological responses defined as a viral load less than 20 copies per mL occurred in 685 (89.8%) of 763 patients in the study group versus 334 (88.4%) of 378 patients in the control group; with a definition of a viral load less 200 copies per mL, responses occurred in 725 (95.0%) patients in the study group versus 356 (94.2%) in the control group. The least squares mean increases from baseline to week 48 in CD4 cell count (where non-completer equals failure) were 18.7 cells per µL (95% CI 4.5 to 32.9) in the study group versus 4.9 cells per µL (–12.9 to 22.7) in the control group (difference 13·8 cells per µL, 95% CI –4·9 to 32·7, p=0.0216 for the control group).

As few patients had virological rebound, most of whom had low viral load values throughout the study, not many samples were eligible for genotyping (rebounders with viral load ≥400 copies per mL at failure or at later timepoints or at discontinuation). Of the patients with virological rebound, one in the study group and three in the control group had genotypes sequenced. We detected no primary protease inhibitor mutations and no mutations associated with resistance to darunavir, tenofovir, or emtricitabine. One patient with rebound in the control group had an NNRTI resistance-associated mutation, Glu138Glu/Gly, which conferred resistance to rilpivirine, and one patient in the study group who had rebound had an NRTI resistance-associated mutation, Asp67Asp/Asn; these mutations were not related to any of the study drugs and were probably present before the patients entered the study.

Figure 2: Confirmed virological rebound cumulative through week 48 (A) and FDA-snapshot analysis at week 48 (B)
A

**Virological rebound rate**

<table>
<thead>
<tr>
<th>Study group</th>
<th>Control group</th>
<th>Difference in proportion of patients with virological rebound (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>140 (3.6)</td>
<td>65 (1.5)</td>
</tr>
<tr>
<td>Male</td>
<td>623 (2.2)</td>
<td>313 (2.2)</td>
</tr>
<tr>
<td><strong>Age (years)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤50</td>
<td>507 (2.6)</td>
<td>252 (2.8)</td>
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<tr>
<td>&gt;50</td>
<td>256 (2.9)</td>
<td>126 (0.8)</td>
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<tr>
<td><strong>Race</strong></td>
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<td></td>
</tr>
<tr>
<td>Black</td>
<td>155 (3.9)</td>
<td>82 (1.2)</td>
</tr>
<tr>
<td>Non-black</td>
<td>597 (2.2)</td>
<td>293 (2.4)</td>
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<tr>
<td><strong>Previous antiretrovirals (including screening regimen)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>316 (2.2)</td>
<td>160 (1.9)</td>
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<tr>
<td>5</td>
<td>98 (2.0)</td>
<td>56 (1.8)</td>
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<td>6</td>
<td>69 (7.2)</td>
<td>30 (1.3)</td>
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<tr>
<td>7</td>
<td>69 (0)</td>
<td>30 (1.3)</td>
</tr>
<tr>
<td>&gt;7</td>
<td>211 (2.4)</td>
<td>101 (2.0)</td>
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<tr>
<td><strong>Previous antiretroviral failure</strong></td>
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<tr>
<td>0</td>
<td>647 (2.5)</td>
<td>325 (2.5)</td>
</tr>
<tr>
<td>≥1</td>
<td>116 (2.6)</td>
<td>53 (0)</td>
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</tbody>
</table>

B

**Virological response rate**

<table>
<thead>
<tr>
<th>Study group</th>
<th>Control group</th>
<th>Difference in proportion of patients with virological response (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>140 (93.6)</td>
<td>65 (93.8)</td>
</tr>
<tr>
<td>Male</td>
<td>623 (95.2)</td>
<td>313 (93.6)</td>
</tr>
<tr>
<td><strong>Age (years)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤50</td>
<td>507 (95.5)</td>
<td>252 (93.7)</td>
</tr>
<tr>
<td>&gt;50</td>
<td>256 (93.8)</td>
<td>126 (93.7)</td>
</tr>
<tr>
<td><strong>Race</strong></td>
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<tr>
<td>Black</td>
<td>155 (92.3)</td>
<td>82 (96.3)</td>
</tr>
<tr>
<td>Non-black</td>
<td>597 (95.6)</td>
<td>293 (92.8)</td>
</tr>
<tr>
<td><strong>Previous antiretrovirals (including screening regimen)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
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<td>316 (95.9)</td>
<td>160 (96.3)</td>
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<tr>
<td>5</td>
<td>98 (94.9)</td>
<td>56 (90.3)</td>
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<tr>
<td>6</td>
<td>69 (92.8)</td>
<td>30 (96.7)</td>
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<tr>
<td>7</td>
<td>69 (95.7)</td>
<td>30 (90.0)</td>
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<tr>
<td>&gt;7</td>
<td>211 (93.8)</td>
<td>101 (92.1)</td>
</tr>
<tr>
<td><strong>Previous antiretroviral failure</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>647 (94.7)</td>
<td>325 (93.8)</td>
</tr>
<tr>
<td>≥1</td>
<td>116 (95.7)</td>
<td>53 (92.5)</td>
</tr>
</tbody>
</table>

Figure 3: Subgroup analyses of virological responses at week 48

Differences are the study group minus the control group. (A) Virological rebound (≥50 copies per mL) was assessed cumulatively through week 48 and (B) virological response (<50 copies per mL) was assessed at week 48 (FDA-snapshot analysis). Arrowheads show that the limits of the 95% CIs lie beyond the x-axis. Study regimen=darunavir, cobicistat, emtricitabine, and tenofovir alafenamide. Control regimen=boosted protease inhibitor plus emtricitabine and tenofovir disoproxil fumarate. FDA=US Food and Drug Administration.

*Data not reported for one patient who had previously used three antiretrovirals.
Another two patients in the study group who discontinued at week 12 but did not have rebound (assessed as no viral load data in the week 48 window by the FDA-snapshot analysis) had a genotype test at a post-treatment follow-up visit. One of these patients had a Lys80Ile/Asn NNRTI resistance-associated mutation that conferred resistance to efavirenz, which was related to previous use of efavirenz, emtricitabine, and tenofovir disoproxil fumarate. To the end of week 48, median cumulative adherence as measured by pill count was 99·7% (IQR 98·5–100·3) in the study group and 99·3% (97·4–100·0) in the control group. Safety was similar between groups, except for the higher incidence of study drug-related adverse events of any grade in the study group. Most adverse events, irrespective of causality, were grade 1 or 2, there were few grade 3 and 4 adverse events, serious adverse events, discontinuations related to adverse events (table 2). The most common adverse events were nasopharyngitis (81 [11%] patients in the study group vs 39 [10%] patients in the control group), upper respiratory tract infection (81 [11%] patients vs 39 [10%] patients), and diarrhoea (60 [8%] patients vs 16 [4%] patients).

No patients died, and only one serious adverse event (pancreatitis in the study group) was deemed as possibly related to a study drug by the investigator. The most common grade 3 adverse event was pneumonia in the study group, which was reported for three (<1%) patients. No grade 4 adverse events were reported in two or more patients in either group.

Renal adverse events occurred in 30 (4%) of 763 participants in the study group and 18 (5%) of 378 participants in the study group. Three renal adverse events led to discontinuation of the study medication, one in the study group (grade 2, non-serious worsening of pre-existing chronic kidney disease) and two in the control group (one grade 4, non-serious adverse event of toxic nephropathy and one grade 1, non-serious renal tubular disorder related to tenofovir disoproxil fumarate). No renal adverse events suggested treatment-emergent proximal renal tubulopathy in the study group.

Most laboratory abnormalities were grade 1 or 2, with only LDL-cholesterol grade 3–4 events occurring in more than 5% of study group and bilirubin grade 3–4 events in more than 5% of control patients (table 2). The incidences of the grade 3 or 4 laboratory abnormalities were similar in both groups.

Median changes from baseline to week 48 are shown in the appendix (p 3) for fasting total cholesterol (19·7 mg/dL in the study group vs 1·3 mg/dL in the control group, p=0·0001), LDL-cholesterol (15·7 mg/dL vs 1·9 mg/dL, p=0·0001), and the ratio of total cholesterol to HDL-cholesterol (0·2 vs 0·1; p=0·010). During treatment, lipid-lowering drugs were started by 20 (3%) of 763 patients in the study group versus seven (2%) of 378 patients in the control group (between group p=0·54).

eGFRcr from baseline to week 48 was stable in the study group (mean change −0·4 mL/min per 1·73m² [SD 9·6], p=0·24 for ANCOVA vs baseline) and decreased in the control group (mean change −1·9 mL/min per 1·73m² [10·7]; p=0·0007 vs baseline; p=0·034 for between-treatment comparison at week 48 by ANCOVA; figure 4A). Differences between groups in terms of serum creatinine and eGFRcr at week 48 were not significant, although larger increases in serum creatinine (1·3 µmol/L) and larger decreases in eGFRcr (−1·9 mL/min per 1·73m²) occurred in patients switching to the study regimen compared with the control regimen (serum creatinine increase 0·6 µmol/L and eGFRcr decrease −0·9 mL/min per 1·73m²), possibly because of the effect of cobicistat on inhibition of creatinine tubular secretion (figure 4B).

Subgroup analyses showed consistent and more pronounced effects than in the overall analyses, but these between-group differences were not significant. In patients who received darunavir and cobicistat plus emtricitabine and tenofovir disoproxil fumarate

### Table 2: Adverse events and week 48 laboratory abnormalities

<table>
<thead>
<tr>
<th>Study regimen (n=763)</th>
<th>Control regimen (n=378)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any adverse event</td>
<td>625 (82%)</td>
</tr>
<tr>
<td>Any study drug-related adverse event</td>
<td>128 (18%)*</td>
</tr>
<tr>
<td>Any grade 3 or 4 adverse event</td>
<td>52 (7%)</td>
</tr>
<tr>
<td>Any serious adverse event</td>
<td>25 (5%)</td>
</tr>
<tr>
<td>Adverse event leading to permanent discontinuation</td>
<td>11 (1%)</td>
</tr>
<tr>
<td>Death</td>
<td>0</td>
</tr>
</tbody>
</table>

### Most common adverse events (≥5% in either group)

- Nasopharyngitis: 81 (11%) study group, 39 (10%) control group
- Upper respiratory tract infection: 81 (11%) study group, 39 (10%) control group
- Diarrhoea: 60 (8%) study group, 16 (4%) control group
- Headache: 58 (8%) study group, 16 (4%) control group
- Back pain: 54 (7%) study group, 21 (6%) control group
- Vitamin D deficiency: 50 (7%) study group, 27 (7%) control group
- Osteopenia: 38 (5%) study group, 21 (6%) control group

### Most common study drug-related adverse events (≥2% in either group)

- Diarrhoea: 16 (2%) study group, 3 (1%) control group
- Osteopenia: 5 (1%) study group, 8 (2%) control group

### Worst grade treatment-emergent grade 3 or 4 laboratory abnormalities (≥3% in either group)

- Fasting LDL-cholesterol (≥4·90 mol/L; ≥190 mg/dL): 48 (7%) study group, 6 (2%) control group
- Fasting total cholesterol (≥7·77 mol/L; ≥300 mg/dL): 28 (4%) study group, 5 (1%) control group
- Phosphate (≥0·65 mmol/L; ≥1·4 mg/dL): 25 (3%) study group, 19 (5%) control group
- Total bilirubin (≥0·6 x ULN): 1 (1%) study group, 22 (6%) control group

### Laboratory abnormalities

- Median changes from baseline to week 48 are shown in the appendix (p 3).
- eGFRcr from baseline to week 48 was stable in the study group (mean change −0·4 mL/min per 1·73m² [SD 9·6], p=0·24 for ANCOVA vs baseline) and decreased in the control group (mean change −1·9 mL/min per 1·73m² [10·7]; p=0·0007 vs baseline; p=0·034 for between-treatment comparison at week 48 by ANCOVA; figure 4A).
- Differences between groups in terms of serum creatinine and eGFRcr at week 48 were not significant, although larger increases in serum creatinine (1·3 µmol/L) and larger decreases in eGFRcr (−1·9 mL/min per 1·73m²) occurred in patients switching to the study regimen compared with the control regimen (serum creatinine increase 0·6 µmol/L and eGFRcr decrease −0·9 mL/min per 1·73m²), possibly because of the effect of cobicistat on inhibition of creatinine tubular secretion (figure 4B).

Subgroup analyses showed consistent and more pronounced effects than in the overall analyses, but these between-group differences were not significant. In patients who received darunavir and cobicistat plus emtricitabine and tenofovir disoproxil fumarate...
(64 in the control group and 98 in the study group who had this as the screening regimen), serum creatinine decreased in the study group and increased for the control group, eGFR<sub>cr</sub> increased in the study group and decreased in the control group, and eGFR<sub>cyst</sub> increased in the study group and decreased in the control group (data not shown). In patients who started with darunavir and ritonavir plus emtricitabine and tenofovir disoproxil fumarate (202 in the control group and 439 in the study group), patients in the study group had larger increases in serum creatinine and decreases in eGFR<sub>cr</sub> and fewer decreases in eGFR<sub>cyst</sub> than those in the control group (data not shown).

Compared with staying on the control regimen, switching to study regimen resulted in significant improvements at 48 weeks in all measures of quantitative proteinuria (both glomerular proteinuria and proximal tubular proteins; p<0.0001 for all measures), including mean changes in the urine protein to creatinine ratio (−33.90 mg/g [SD 80.59] in the study group vs −6.43 mg/g [75.74] in the control group), urine albumin to creatinine ratio (−3.20 mg/g [31.64] vs 1.25 mg/g [21.12]), urine retinol binding protein to creatinine ratio (−630.45 µg/g [3659.52] vs 1037.06 µg/g [5958.90]), and urine β-2-microglobulin to creatinine ratio (−1454.70 µg/g [6343.24] vs 1371.29 µg/g [10090.06]).
In the bone investigation substudy, baseline patient characteristics were well balanced between the 209 patients in the study group and 108 patients in the control group and similar to those in the overall study (appendix, p 2). At week 48, BMD increased at the hip (1.43% [SD 2.34]; figure 4C), lumbar spine (1.49% [3.34]; figure 4D), and femoral neck (0.66% [3.20]) in the study group (p<0.0001 for the ANCOVA within-treatment comparison at hip and lumbar spine and p=0.029 for femoral neck). In the control group at week 48, hip BMD was stable (–0.26% [2.00]) whereas lumbar spine (–0.63% [2.86]) and femoral neck BMD (–0.54% [3.35]) decreased (p=0.78 for the ANCOVA within-treatment comparison at the hip, p=0.98 for lumbar spine, and p=0.34 for femoral neck). In the ANCOVA between-treatment comparison, p was less than 0.0001 for the hip and lumbar spine and p=0.004 for the femoral neck. Fewer patients had a decrease of 3% or more in hip BMD (four [2.1%] of 188 patients in the control group vs eight [8.2%] of 97 patients in the control group), lumbar spine BMD (15 [7.8%] of 192 patients vs 20 [19.8%] of 101 patients), or femoral neck BMD (19 [10.1%] of 188 patients vs 18 [18.6%] of 97 patients) in the study group than in the control group, and more patients had increases of 3% or more in the study group (38 [20.2%] of 188 patients vs four [4.1%] of 97 patients for hip BMD, 61 [31.8%] of 192 patients vs nine [8.9%] of 101 patients for lumbar spine BMD, and 43 [22.9%] of 188 patients vs 11 [11.3%] of 97 patients for femoral neck BMD). Conclusions were similar for increases or decreases of at least 5% or 7% from baseline (figure 4C and 4D). More patients in the study group than in the control group had improvements in BMD clinical status (osteopenia to normal or osteoporosis to osteopenia or osteoporosis) at week 48 at the hip (6 [3.2%] of 188 patients in the study group vs one [1.0%] of 97 patients in the control group), lumbar spine (16 [8.3%] of 192 patients vs four [4.0%] of 101 patients), and femoral neck (ten [5.3%] of 188 patients vs three [3.1%] of 97 patients). Fewer patients in the study group than in the control group had a decline in BMD status (normal to osteopenia or normal to osteopenia or osteoporosis) at week 48 at the hip (6 [3.2%] of 188 patients in the study group vs two [2.1%] of 97 patients in the control group at the hip, seven [3.6%] of 192 patients vs four [4.0%] of 101 patients at the lumbar spine, and five [2.7%] of 188 patients vs five [5.2%] of 97 patients at the femoral neck). Fractures were uncommon in both groups (nine [1.2%] of 763 patients in the study group vs two [0.5%] of 378 patients in the control group); all were trauma-related and none were suspected to be osteoporotic. Changes from baseline in bone biomarkers (alkaline phosphatase, C-type collagen sequence, procollagen type N-terminal propeptide, and parathyroid hormone) at week 48 suggested that patients in the study group had less bone turnover than patients in the control group, with decreases for all markers in the study group and stable values in the control group (appendix, p 4; between-treatment comparisons, p<0.0001 for alkaline phosphatase and procollagen type N-terminal propeptide, p=0.0003 for C-type collagen sequence, and p=0.0074 for parathyroid hormone). Increases from baseline in 25-hydroxy vitamin D levels occurred in both groups.

Discussion

In this phase 3, randomised, open-label trial, switching to the once-daily single-tablet regimen of darunavir, cobicistat, emtricitabine, and tenofovir alafenamide was non-inferior to remaining on a regimen of a boosted protease inhibitor combined with emtricitabine and tenofovir disoproxil fumarate in virologically suppressed, treatment-experienced HIV-1-infected adults, with respect to the proportion of patients with virological rebound cumulative through week 48.

The entry criteria for EMERALD were much less restrictive than is typical for a switch study, with 58% of patients having received five or more previous antiretroviral agents including screening antiretrovirals and 15% having had previous virological failure. The only exclusion criteria were history of virological failure on darunavir-based regimens, and if historical genotypes were available, presence of darunavir resistance-associated mutations. We had no exclusion on the basis of other protease inhibitor or NRTI resistance-associated mutations and emtricitabine or tenofovir alafenamide and tenofovir disoproxil fumarate resistance-associated mutations. In bictegravir switch studies (NCT02603107 and NCT02603120), exclusion criteria included previous resistance to emtricitabine, tenofovir, abacavir, and lamivudine. In the phase 3 SWORD-1 and SWORD-2 trials and STRIVIVING dolutegravir switch studies, the presence of any major protease inhibitor, integrase inhibitor, NRTI, or NNRTI resistance-associated mutations was an exclusion criterion. The ATLAS-M atazanavir switch study restricted patient enrolment to those who had not previously failed on a lamivudine-containing or protease inhibitor-containing regimen or who had not been previously exposed to lamivudine-containing or suboptimal antiretroviral regimens.

Although patients were treatment experienced and some had previous virological failure, this did not affect virological rebound and response rates. Incidents of virological rebound mainly consisted of low-level and transient viraemia, with very few confirmed rebounds to 200 copies per mL or higher (three in the study group vs none in the control group). Most patients with rebound had resuppression at week 48. At week 48, the FDA-snapshot analysis showed a high proportion of patients with virological suppression (viral load <50 copies per mL) within the study group. Responses were similar to those in SWORD-1 and SWORD-2 and higher than those in ATLAS-M, both of which recruited fewer treatment-experienced patients than in EMERALD. Switching to the study regimen resulted in few patients having a viral load of 50 copies per mL or higher, and no patients discontinued because of a viral load of 50 copies
per mL or higher. We detected no resistance to any of the study drugs. These findings are consistent with those of other studies of darunavir\(^ {27}\) and the study regimen,\(^ {28}\) and further support the efficacy and high genetic resistance barrier of darunavir.

Similarly, low numbers of serious adverse events and adverse events leading to treatment discontinuation occurred in both treatment groups, and the incidences of overall adverse events and the most commonly reported adverse events of all grades were also similar. The open-label study design, in which participants on stable regimens switched multiple drugs might account for the higher frequency of treatment-related adverse events in the study group, as reported in SWORD-1 and SWORD-2.\(^ {24}\)

The most commonly reported adverse events were non-specific and have been reported previously with darunavir and cobicistat: nasopharyngitis, upper respiratory infection, diarrhea, and headache.\(^ {9–10,13,21,22,27}\)

The renal laboratory results were consistent with the established effects of cobicistat and tenofovir alafenamide mainly the preservation of GFR and less tubular proteinuria than with tenofovir disoproxil fumarate. Small increases in serum creatinine concentrations and accompanying decreases in eGFR, in both groups were within normal limits and not clinically significant. In the renal subgroup analysis, switching to the study regimen versus continuing on darunavir with cobicistat plus emtricitabine with tenofovir disoproxil fumarate resulted in a lowering of serum creatinine concentrations, as reported in other studies of switching from tenofovir disoproxil fumarate to tenofovir alafenamide.\(^ {28,29}\) However, in patients switching to the study regimen from darunavir and ritonavir plus emtricitabine and tenofovir disoproxil fumarate, the inclusion of cobicistat in the study regimen seems to have offset any serum creatinine-lowering effect of tenofovir alafenamide, possibly because of the reported effect of cobicistat on the inhibition of tubular secretion of creatinine without reducing measured GFR.\(^ {21–23}\) When we measured GFR with cystatin C, which is not affected by bone turnover at week 48 compared with patients who remained on the control regimen. These findings were consistent with those from previous phase 3 studies of virologically suppressed patients who switched from a tenofovir disoproxil fumarate to a regimen containing tenofovir alafenamide.\(^ {24,25}\)

In conclusion, in virologically suppressed, treatment-experienced, HIV-infected adults who switched to a single-tablet regimen of darunavir, cobicistat, emtricitabine, and tenofovir alafenamide, virological rebound rates were low cumulative through 48 weeks, and the regimen was non-inferior compared with regimens of boosted protease inhibitor plus emtricitabine and tenofovir disoproxil fumarate. Virological suppression was high, no patients discontinued because of a viral load greater than or equal to 50 copies per mL, and no drug resistance developed. The improved bone and renal biomarker safety of the study regimen compared with the control regimen and the similar lipid safety of the two regimens was consistent with the known profiles of tenofovir alafenamide and tenofovir disoproxil fumarate. The new regimen combines the known efficacy and high genetic barrier to resistance of darunavir with the safety advantages of tenofovir alafenamide in a single-tablet HIV-1 regimen.

**Contributors**

CO, J-MM, JG, EN, JRA, and JJE were investigators in the trial and reported data for those patients. EVL, EL, VH, RP, SV, and MO were involved in the data analyses. All authors were involved in the development of the primary manuscript, interpretation of data, and have read and approved the final version, and have met the criteria for authorship as established by the ICMJE.

**EMERALD Principal Investigators**


**Declaration of interests**

This study was sponsored by Janssen. CO has received speaker honoraria or consulting fees for attending speakers’ boards or advisory boards and research grants from Janssen, Merck, ViV Healthcare, and
Gilead Sciences; J-MM has participated in advisory boards for Merck, Gilead Sciences, Janssen, ViVi Healthcare, Bristol-Myers Squibb (BMS), and Teva, and a speaker’s bureau for Gilead; and has received research grants from Merck and Gilead Sciences. EN has received speaker honoraria or consulting fees from ViVi Healthcare, Merck, Janssen Cilag, BMS, Gilead Sciences, and AbbVie. JRA has received personal fees from Gilead Sciences, ViVi, Janssen Therapeutics, and Merck. JG has been a consultant or speaker in conferences supported by AbbVie, BMS, GlassSmithKline (GSK), ViVi Healthcare, Janssen, Merck, and Gilead Sciences; is affiliated with an institution that received research grants from AbbVie, BMS, GSK, ViVi Healthcare, Boehringer Ingelheim, Pfizer, Janssen, Merck, Gilead, and Janssen Therapeutics; has served as an investigator for Abbott Laboratories, AveXa, Boehringer Ingelheim, Gilead Sciences, GSK, Merck, Pfizer, Roche Laboratories, Parexel, Hiespe, and Janssen Therapeutics; and his institution has received honoraria for speaking or chairing engagements from AbbVie, BMS, GSK, Gilead Sciences, Merck, Pfizer, and Janssen Therapeutics. JJE has received research grants from Janssen, Gilead Sciences and ViVi Healthcare and has served as a consultant to BMS, Merck, Janssen, Gilead Sciences and ViVi Healthcare. E VL, EL, VH, SV, and MO are all full-time employees of Janssen and potential stockholders of Johnson and Johnson. RP is a contractor for Janssen.

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Liibre JM, Hung C-C, Brinson C, et al. Phase III SWORD 1&2: switch to DTG+RPV maintains virologic suppression through 48 weeks. Conference on Retroviruses and Opportunistic Infections (CROI); Seattle, WA, USA; Feb 13–16, 2017. Abstract 44LB.


