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AIDS (OCTOBER 2017- APRIL 2018)

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Articles

- 9 Short article reviews
  - 3- general
  - 3- women
  - 3- children
- 1 Main article review
Time from HIV infection to virological suppression: dramatic fall from 2007 to 2016

- Retrospective cohort.
- Date of infection -- Testing history or serological evidence (indeterminate/Mid point imputation) or baseline CD4⁺.
- Date of virological suppression -- VL (<200 copies/ml).
- Factors (demographic, clinical and behavioural) that were associated with the odds of diagnosis --- Logistic regression.
- Factors associated with time to suppression and duration of infectiousness --- Cox regression

Medland et al; AIDS Issue: Volume 31(17), 13 November 2017, p 2377–2385

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Time from HIV infection to virological suppression: dramatic fall from 2007 to 2016

- The median time from
  - Infection to diagnosis -- 6.8 to 4.3 months ($P = 0.001$)
  - Diagnosis to suppression -- 22.7 to 3.2 months ($P < 0.0001$)
  - Infection to suppression -- 49.0 to 9.6 months ($P < 0.0001$)
- Serological evidence of recent infection -- 15.6 to 34.3% ($P < 0.0001$) of diagnoses.
- Multivariate analyses-- age, being recently arrived from a non-English speaking country, H/O IDU, other STIs, and sexual risk were not associated with any of these measures.
- Positive milestone for the treatment as prevention paradigm.

Medland et al; AIDS Issue: Volume 31(17), 13 November 2017, p 2377–2385
Comparative effectiveness of dual vs. single-action antidepressants on HIV clinical outcomes in HIV-infected people with depression

- Depression highly prevalent among PLWHA
- To evaluate changes in depression symptoms, viral suppression, and CD4 cells who initiated antidepressant treatment during routine care and to compare the effectiveness of dual vs single action antidepressants.
- Identified new user treatment episodes with no antidepressant use in the preceding 90 days.

Primary outcomes were viral suppression (HIV viral load <200 copies/ml) and increase in CD4 count.

In a secondary analysis, Patient Health Questionnaire-9 (PHQ-9) to evaluate changes in depression symptoms and remission (PHQ <5).

Initiating antidepressant treatment was associated with improvements in depression, viral suppression, and CD4 cells, highlighting the health benefits of treating depression in PLWHA.

Dual and single-action antidepressants had comparable effectiveness.
Cancer burden attributable to cigarette smoking among HIV-infected people in North America

- High prevalence of smoking – HIV patients.
- North American AIDS Cohort Collaboration on Research and Design consortium
- Observational cohort -- 270,136 person-years of follow-up 52,441 participants, 2306 were diagnosed with cancer during 2000–2015
- Estimated hazard ratios and population-attributable fractions (PAF) associated with ever cigarette smoking for all cancers combined, smoking-related cancers, and cancers that were not attributed to smoking.

Cancer burden attributable to cigarette smoking among HIV-infected people in North America

- Adj.-- demographic and clinical factors, cigarette smoking and increased cancer risk--
  - Overall [hazard ratios = 1.33]
  - Smoking-related [HR= 2.31]; lung cancer [HR= 17.80]
  - But not nonsmoking-related [HR= 1.12]
- PAFs —
  - All cancers combined: 19%
  - Smoking-related, PAF = 50%; lung cancer, PAF = 94%
  - Nonsmoking-related, PAF = 9%
- Cigarette smoking could contribute to some cancers that were classified as nonsmoking-related cancers in this report.
Elevated ischemic stroke risk among women living with HIV infection

- To establish if in WLWH compared with HIV-uninfected women increased risk of stroke.
- Observational cohort study
- WLWH (n = 1214)
- Matched HIV-uninfected women (n = 12,041) seen between 1996 and 2011 at two tertiary care hospitals in Boston.
- Cox proportional hazards regression analyses, adjusting first for demographics and traditional stroke risk factors and then for sex-specific stroke risk factors.


Elevated ischemic stroke risk among women living with HIV infection

- Incidence of ischemic stroke was higher among WLWH compared with HIV-uninfected [Incidence rate ratio 2.39, 95% CI 1.62–3.43].
- Adjusting -- demographics and traditional risk factors, TWICE-(hazard ratio 1.93, 95% CI 1.31–2.85).
- Sex-specific risk factors (HR-1.89, 95% CI 1.28–2.81).
- Longer duration of ART--- lower risk (hazard ratio 0.86 per year, 95% CI 0.76–0.96).

Perceived and posttraumatic stress is associated with decreased learning, memory, and fluency in HIV-infected women

- Psychological risk factors --- impaired learning and memory in HIV+women.
- Multicenter, prospective cohort study.
  - 2009 and 2013
  - 646 HIV+ and 300 demographically similar HIV-
  - Women’s Interagency HIV Study
- Completed neuropsychological testing and questionnaires measuring PRFs [perceived stress, PTSD symptoms, depressive symptoms].

Rubin et al; AIDS Issue: Volume 31(17), 13 November 2017, p 2393–2401

Perceived and posttraumatic stress is associated with decreased learning, memory, and fluency in HIV-infected women

- Using mixed-effects regressions, they examined separate and interactive associations between HIV-serostatus and PRFs on performance.
- Results: HIV+ and HIV- women had similar rates of PRFs.
- In HIV, higher stress and PTSD were associated with a greater cognitive decline in performance (P < 0.05)
- Effects were pronounced without effective treatment or viral suppression.

Rubin et al; AIDS Issue: Volume 31(17), 13 November 2017, p 2393–2401
Perceived and posttraumatic stress is associated with decreased learning, memory, and fluency in HIV-infected women

- Regardless of time or HIV-serostatus, all PRFs were associated with lower speed, global neuropsychological, and executive function.
- More than depression, perceived stress and PTSD symptoms are treatment targets for improving cognitive function.

Rubin et al; AIDS Issue: Volume 31(17), 13 November 2017, p 2393–2401

Antiretroviral combination use during pregnancy and the risk of major congenital malformations

- Population-based prospective cohort study from Canada
- Inclusion C.- Age- 15-45; Singleton Pregnancy.
- ART- alone/combination were considered.
- Excluded – Known teratogen, Chromosomal abnormalities, minor malformations only.
- MCMs overall and organ-specific -- first year

Berard et al, AIDS Issue: Volume 31(16), 23 October 2017, p 2267–2277
### Antiretroviral combination use during pregnancy and the risk of major congenital malformations

- N = 214,240
- 0.09% (n = 198) - ART during the first trimester
- 169 HIV positive without ART.
- Comparing the prevalence of MCMs was significantly higher in unexposed HIV-positive women (14.8 vs. 8.6%, P = 0.004) but not in ART-exposed HIV-positive women (10.3%, P = 0.41).
- Adjusting for potential confounders, including maternal HIV status, ART use during the first trimester was not associated with the risk of MCMs (adjusted OR 0.59, 95% CI: 0.33–1.06).
- However, increased risk of defects of the small intestine (adjusted OR 10.32, 95% CI: 2.85–37.38, P = 0.0004).

Berard et al., AIDS Issue: Volume 31(16), 23 October 2017, p 2267–2277

### Stool Xpert MTB/RIF and urine lipoarabinomannan for the diagnosis of tuberculosis in hospitalized HIV-infected children

- TB -- morbidity and mortality in HIV children.
- Sample collection- sputum expectorate/gastric aspirates and the paucibacillary nature of TB in children makes diagnosis challenging.
- Hospitalized, HIV-infected children aged 12 years or less enrolled in a RCT.
- At enrollment, sputum or gastric aspirates were collected for TB culture or Xpert and stool for Xpert, and urine for lipoarabinomannan (LAM).
- Stool Xpert and urine LAM performance were compared to reference sputum/gastric aspirate culture.

Lacourse et al. AIDS Issue: Volume 32(1), 2 January 2018, p 69–78
165 HIV-infected children,
- Median age - 24 months
- Median CD4+ % - 14.3 (IQR 8.9–22.0%)
- Severe immunosuppression - 114(69.5%)
- Confirmed TB (positive culture and/or Xpert)- 13 (7.9%)

Sensitivity -
- Sputum/gastric aspirate Xpert – 60%
- Stool Xpert – 63%
- Urine LAM – 43%

Specificity -
- Sputum/gastric aspirate Xpert – 98%
- Stool Xpert – 99%
- Urine LAM – 91%

Stool Xpert MTB/RIF and urine lipoarabinomannan for the diagnosis of tuberculosis in hospitalized HIV-infected children

- Stool Xpert and urine LAM sensitivity increased among children with severe immunosuppression [80% and 60%]
- Stool Xpert had similar performance compared with sputum/gastric aspirate Xpert to detect TB.
- Urine LAM had lower sensitivity and specificity, but increased among children with severe immunosuppression.

Lacourse et al. AIDS Issue: Volume 32(1), 2 January 2018, p 69–78
Changes in insulin sensitivity over time and associated factors in HIV-infected adolescents

- To compare prevalence of insulin resistance between perinatally HIV-infected (PHIV+) and perinatally HIV-exposed, but uninfected adolescents (PHEU) - Cross-sectional design
- For incidence and resolution of insulin resistance among PHIV+ at risk – Longitudinal design
- Pediatric HIV clinics in the United States and Puerto Rico --- Pediatric HIV/AIDS Cohort Study, an ongoing prospective cohort study -- evaluate impact of HIV infection and its treatment on multiple domains in preadolescents and adolescents.


Changes in insulin sensitivity over time and associated factors in HIV-infected adolescents

- Assessed by homeostatic model assessment of insulin resistance.
- Unadjusted prevalence of IR in PHIV+ was 27.3 versus 34.1% in PHEU.
- After adjustment for Tanner stage, age, sex, and race/ethnicity, there was no significant difference between groups.
- Factors positively --- female sex, higher BMI, and higher waist circumference.
- Prevalence of IR in PHIV+ and PHEU was substantially higher than that reported in HIV-uninfected nonoverweight youth, but similar to that in HIV-uninfected obese youth.

Neuropsychological performance in African children with HIV enrolled in a multisite antiretroviral clinical trial

- Children with HIV infection (HIV+) are at neuropsychological risk.
- Compared neuropsychological outcomes at enrollment (>5 years age) among HIV+, HEU, and HUU -- four sub-Saharan countries.
- Study - children at 5–11 years of age -- neuropsychological performance over 2 years
  - Kaufman Assessment Battery for Children (KABC-II),
  - Tests of Variables of Attention (TOVA),
  - Bruininks–Oseretsky Test, 2nd edition (BOT-2), and
  - Parent-reported Behavior Rating Inventory of Executive Function (BRIEF).

- Compared and adjusted for site, child age and sex, and personal and social characteristics for child and caregiver.
- N= 611 (246 HIV+, 183 HEU, 182 HUU)
- Mean age -- 7.2 years, 48% male, 69% in school.
- Unadjusted and adjusted comparisons were consistent.
- HIV+ children performed significantly worse than HEU and HUU cohorts on KABC-II and on BOT-2 (P < 0.001), but not on the BRIEF Global Executive Indices.
Neuropsychological performance in African children with HIV enrolled in a multisite antiretroviral clinical trial

- HUU and HEU cohorts were comparable on cognitive outcomes.
- HIV+ children initiated on ART before 1 year of age had significantly better BRIEF evaluations ($P = 0.03$).
- Earlier HIV treatment, neuropsychological monitoring, and rehabilitative interventions are all needed.

Markers of chronic obstructive pulmonary disease are associated with mortality in people living with HIV

- Triplette et al
- University of Washington

- Issue: Volume 32(4), 20 February 2018, p 487–493
Markers of chronic obstructive pulmonary disease are associated with mortality in people living with HIV

**INTRODUCTION:**
- PLWH are surviving to older age.
- Increased burden of comorbidities, more mortality.
- The prevalence of COPD is greater in PLWH as well.
- Due to smoking, independent contribution related to HIV infection.

Markers of chronic obstructive pulmonary disease are associated with mortality in people living with HIV

**INTRODUCTION:**
- COPD is associated with increased morbidity in PLWH, but an association with mortality has not been determined.
- In this study-- whether physiologic and radiographic markers of COPD were associated with mortality in PLWH.
- And whether these markers of COPD were independent of the Veterans Aging Cohort Study (VACS) Index(https://medicine.yale.edu/intmed/vacs), a validated research and clinical tool that predicts mortality in PLWH.
Markers of chronic obstructive pulmonary disease are associated with mortality in people living with HIV

**METHODS:**

- The study utilizes the Examinations of HIV-Associated Lung Emphysema (EXHALE) study, a pulmonary substudy of VACS.
- VACS study participants were enrolled into EXHALE at four Veterans Affairs Medical Centers between 2009 and 2012.
- PLWH and uninfected study participants were recruited matched on smoking status.
- Study participants were ineligible if they had chronic pulmonary diseases other than COPD or asthma, and had experienced recent acute respiratory symptoms.

Markers of chronic obstructive pulmonary disease are associated with mortality in people living with HIV

**METHODS:**

- Study participants were followed from enrollment through March 2017, with deaths determined from the Veterans Affairs vital status file.
- 366 patients were enrolled and underwent any testing, with five patients excluded because of abnormalities precluding further testing (four with aortic aneurysms and one with a pulmonary mass).
- 342 -- pulmonary function testing (PFTs) and 323 -- CT analyses.
Markers of chronic obstructive pulmonary disease are associated with mortality in people living with HIV

**METHODS:**
- Demographic and smoking information - self-completed surveys at enrollment.
- Lab data - electronic medical record.
- The VACS Index was calculated at enrollment using electronic medical record data closest to EXHALE enrollment, no longer than 12 months prior.
- The VACS Index incorporates age, CD4+, VL, hepatitis C serostatus, hemoglobin, eGFR, and the fibrosis-4 index for liver fibrosis.

Markers of chronic obstructive pulmonary disease are associated with mortality in people living with HIV

**METHODS:**
- Pulmonary markers - PFTs and chest CT images.
- PFTs- Testing included postbronchodilator forced expiratory volume in 1 s (FEV1), forced vital capacity (FVC), and diffusion capacity (DLCO).
- COPD was defined as airflow obstruction (FEV1/FVC <0.7) and alternatively as FEV1/FVC below lower limit of normal (LLN, <5th percentile)
- CT scans-- at baseline- Thoracic radiologist and University of Pittsburgh software.
Markers of chronic obstructive pulmonary disease are associated with mortality in people living with HIV

**METHODS:**

- Baseline characteristics were compared by HIV status using \([\text{chi}]^2\) testing.
- We used Cox proportional hazards regression to examine variable associations with mortality, stratified by HIV status.
- Separate bivariate Cox models were created including the pulmonary markers: airflow obstruction (by both methods), FEV1%-predicted, FVC % predicted, DLCO %-predicted, more than 10% emphysema, %LAA.

In the models, sex was not included as there were no deaths among the 20 women.

All models had limited power to detect less than moderate associations with mortality: 80% power to detect a mortality hazard ratio of 2.2 for categorical variables of interest in the entire cohort.
Markers of chronic obstructive pulmonary disease are associated with mortality in people living with HIV

**RESULTS:**

- N = 361 study participants,
- 196—PLWH & 165 were uninfected.
- Median age was 54 [interquartile range (IQR) 50–59] and 94% were men.
- PLWH largely had well controlled disease:
  - 14% had CD4+ < 200 cells/µl
  - 17% had VL > 400 copies/ml.

- Median VACS Index
  - 29 (IQR 18–42) in PLWH
  - 18 (IQR 12–27) in the uninfected (P < 0.001).
- PLWH had higher pack-years of smoking (P = 0.06).
- PLWH had lower DLCO %-predicted (53 vs. 57, P = 0.005),
- Higher prevalence of emphysema > 10% (31 vs. 16%, P = 0.003).
- Median follow-up was 6.9 years and similar by HIV status.
Markers of chronic obstructive pulmonary disease are associated with mortality in people living with HIV

RESULTS:
- 93% of study participants alive at study end had Veterans Affairs follow-up within the last 12 months.
- The mortality rate:
  - 2.7/100 person-years- PLWH (33 deaths)
  - 1.7/100 person-years- uninfected. (18 deaths) \( P = 0.11 \).

Available cause of death data -59%,
- 23% - heart disease
- 37% - cancer
- 6.7% - respiratory causes.
- Only 9.5% of PLWH died from HIV/AIDS-related causes.
Table 1

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total cohort (n = 361)</th>
<th>PLWH (n = 196)</th>
<th>HIV-uninfected (n = 165)</th>
<th>P-value (PLWH vs. HIV-uninfected)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td>54 (20–39)</td>
<td>53 (21–39)</td>
<td>55 (19–39)</td>
<td>0.08</td>
</tr>
<tr>
<td><strong>Gender (male)</strong></td>
<td>94%</td>
<td>95%</td>
<td>93%</td>
<td>0.30</td>
</tr>
<tr>
<td><strong>Race/ethnicity</strong></td>
<td>White (%)</td>
<td>58%</td>
<td>63%</td>
<td>0.04</td>
</tr>
<tr>
<td></td>
<td>Hispanic (%)</td>
<td>21%</td>
<td>14%</td>
<td>0.01</td>
</tr>
<tr>
<td><strong>BMI</strong></td>
<td>28 (24–32)</td>
<td>26 (24–30)</td>
<td>30 (26–34)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Smoking status</strong></td>
<td>Current (%)</td>
<td>61%</td>
<td>54%</td>
<td>0.04</td>
</tr>
<tr>
<td></td>
<td>Former (%)</td>
<td>24%</td>
<td>25%</td>
<td>1.00</td>
</tr>
<tr>
<td></td>
<td>Never (%)</td>
<td>15%</td>
<td>16%</td>
<td>1.00</td>
</tr>
<tr>
<td><strong>Pack-years smoked (current or former smokers)</strong></td>
<td>24 (11–40)</td>
<td>26 (13–42)</td>
<td>20 (7–37)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>COHIDA (mL)</strong></td>
<td>36 (25–61)</td>
<td>36 (25–61)</td>
<td>53 (40–103)</td>
<td>0.25</td>
</tr>
<tr>
<td><strong>CD4 cell count (median)</strong></td>
<td>443 (259–631)</td>
<td>443 (259–631)</td>
<td>14 (1–14)</td>
<td>0.14</td>
</tr>
</tbody>
</table>

RESULTS:

Markers of chronic obstructive pulmonary disease are associated with mortality in people living with HIV

- In adjusted models, the following were associated with mortality in PLWH:
  - **Airflow obstruction**
    - FEV1/FVC <0.7: hazard ratio 3.1, 95% CI 1.4–7.1
    - FEV1/FVC <LLN: hazard ratio 4.3, 95% CI 1.9–9.8
    - FEV1%-predicted (HR 1.3, 95% CI 1.0–1.7)
    - DLCO % predicted (HR 1.8, 95% CI 1.3–2.5)
    - Emphysema as semiquantitative > 10% (HR 2.4, 95% CI 1.1–5.5)
    - %LAA (HR 1.3, 95% CI 1.1–1.7)
Markers of chronic obstructive pulmonary disease are associated with mortality in people living with HIV

**RESULTS:**

- Among the uninfected, there were no significant associations with mortality in adjusted models.
- Interaction between HIV status and airflow obstruction was significantly associated with mortality, using either definition of obstruction ($P = 0.04$ for both).
- There was no significant interaction between emphysema more than 10% and HIV status.

**DISCUSSION:**

- Finding - Markers that define COPD and emphysema are associated with mortality in PLWH, independent of smoking and the VACS Index.
- The impact of COPD is underrated and in general COPD is underdiagnosed.
- In the general population, FEV1 decline, the key measure grading COPD severity, is a well established predictor of death in patients with COPD.
- The association of markers of COPD with mortality in HIV has not been previously established.
DISCUSSION:

- Although the majority of cohort deaths were not directly related to respiratory causes, COPD is an important contributor or cofactor in other deaths from chronic disease (such as lung cancer and heart disease).
- Support increased attention to smoking cessation in PLHW to reduce COPD incidence and attenuate pulmonary decline.
- The importance of interventions to diagnose and manage COPD in PLWH.

Finally, markers of COPD may have a role in mortality prediction models in HIV, such as the VACS Index, though this will require further study.

No significant associations with mortality among uninfected study participants is reflective of limited power, cant imply that COPD is not associated with mortality in the general population.

There is significant interaction between airflow obstruction and HIV status, suggesting a potential differential impact of COPD on mortality in PLWH.
Markers of chronic obstructive pulmonary disease are associated with mortality in people living with HIV

**CRITICAL REVIEW:**
- Good Study design although not representative as majority are males. Well matched
- Detailed demographic and smoking history.
- Carefully characterization of physiologic and radiographic pulmonary data.
- Follow up - median almost 7 years.

**LIMITATIONS:**
- Male predominance, ?generalizable.
- The study power limited ability to detect associations.
- Cause of death details lacking.. especially important as main objective is to establish markers of COPD for mortality of PLWH.
- ? Adds value, but emphasizes on the importance of early diagnoses of COPD in PLWH, which can be missed.
The kidneys and HIV

Professor David Gracey
Royal Prince Alfred Hospital

Disclosure

• Gilead: Ad boards, speaker honoraria, travel grants
• MSD: Ad boards, honoraria
• ViiV Healthcare: speaker honoraria, Ad boards, research grant
The kidney PLWHIV: Key questions

- What are the current renal issues in PLWHIV?
- What is the new key clinical trial evidence on renal effects of ARV therapy?
- How does this affect management of PLWHIV and their outcomes?
- Are there PLWHIV populations who could benefit from therapy optimisation?

ARV, antiretroviral; PLWHIV, people living with HIV

**SURVIVAL OF HIV-POSITIVE PATIENTS STARTING ANTIRETROVIRAL THERAPY 1996–2013: A COLLABORATIVE ANALYSIS OF COHORT STUDIES**

Between 1996 and 2010, life expectancy increased:
- 9 years in women
- 10 years in men

Even in the late ART era, survival continues to improve, likely reflecting the transition to less toxic antiretroviral drugs, improved adherence, prophylactic measures, and management of comorbidity.
As HIV healthcare providers, we have to prevent all the comorbidities we can, as their burden will only increase in the future

- Common points:
  - Tobacco consumption
  - STIs
  - Relocation and mobility
- Heterogeneity and complexity
  - Each patient has a different life history
  - Each patient has a different history of virology and antiretroviral management
- Comorbidities:
  - Patients may have multiple comorbidities, early in their medical history

Today’s patient and comorbidities: the Aquitaine cohort

- Cohort objective:
  - Describe the evolution of chronic non-HIV related diseases
  - Describe the risk factors in patients included in the French ANRS CO3 Aquitaine prospective cohort, 10 years apart, observed both in 2004 and in 2014
- Patient demographics:
  - 2,138 patients
  - 71% men, 40% MSM
  - In 2014, 62.3% were aged ≥50 years (median age 52 years)
PLWHIV aged ≥50 years worldwide

ESTIMATED PERCENTAGE OF HIV-POSITIVE INDIVIDUALS AGED ≥50 YEARS IN 2012, BY REGION

The proportion of older HIV-positive individuals is increasing all around the world

Today’s patient and comorbidities:
Aquitaine Cohort

Outcomes of comorbidity monitoring:
- High rate of all comorbidities in 2004, and prevalence significantly increased to 2014
- Dyslipidaemia (+40.2%) and hypertension (+37.5%) had the highest increases, and are the most prevalent. Frequency of chronic kidney disease (+14.7%) and cardiovascular events (+10.4%) increased
- Frequency of tobacco consumption (~40%) is still important

Screening for comorbidity is now not just necessary but mandatory

Proportion of patients (%)

<table>
<thead>
<tr>
<th>Condition</th>
<th>2004 (n=2138)</th>
<th>2014 (n=2138)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>18.9</td>
<td>25.8</td>
</tr>
<tr>
<td>Dyslipidaemia</td>
<td>55.9</td>
<td>61.0</td>
</tr>
<tr>
<td>Diabetes</td>
<td>16.5</td>
<td>19.5</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>5.8</td>
<td>4.5</td>
</tr>
<tr>
<td>Chronic liver disease</td>
<td>35.6</td>
<td>35.5</td>
</tr>
<tr>
<td>Depression</td>
<td>2.7</td>
<td>2.8</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>8.4</td>
<td>7.0</td>
</tr>
<tr>
<td>Malignancy</td>
<td>0.4</td>
<td>0.4</td>
</tr>
</tbody>
</table>
Non-AIDS comorbidities: 1st cause of mortality in France in PLWHIV*

- Individuals with HIV are more susceptible to developing CV disease, bone fractures and renal failure than HIV-negative people.
- HIV infection and ART can have long-term effects on numerous aspects of health.

Comorbidities associated with HIV: not only a problem of high-income countries

- PREVALENCE OF DIABETES AND HYPERCHOLESTEROLAEMIA AMONG ADULTS IN MALAWI (SUB-SAHARAN AFRICA)

  - Survey of HIV-positive individuals receiving ART for over 10 years
    - HIV-positive for over 10 years (n=379) and HIV-control group* (n=356), 73.2% were female

<table>
<thead>
<tr>
<th>Prevalence, %</th>
<th>HIV-positive</th>
<th>HIV-negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes by age, %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30–44 years</td>
<td>5.0</td>
<td>3.4</td>
</tr>
<tr>
<td>45–59 years</td>
<td>6.4</td>
<td>4.2</td>
</tr>
<tr>
<td>≥60 years</td>
<td>13.2</td>
<td>1.7</td>
</tr>
<tr>
<td>HyperChol by age, %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30–44 years</td>
<td>8.0</td>
<td>1.8</td>
</tr>
<tr>
<td>45–59 years</td>
<td>15.4</td>
<td>12.5</td>
</tr>
<tr>
<td>≥60 years</td>
<td>23.7</td>
<td>11.8</td>
</tr>
</tbody>
</table>

*Living around the selected health centres. **Defined in this study as HbA1c ≥6.0%.

HyperCT, hypercholesterolaemia.
comorbidities: Aquitaine Cohort

- Immunovirological and therapeutic results:

<table>
<thead>
<tr>
<th>Patients, %</th>
<th>2004 (n=2138)</th>
<th>2014 (n=2138)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD4 cell count ≥500 cells/mm³</td>
<td>44</td>
<td>72</td>
</tr>
<tr>
<td>Viral suppression (&lt;50 copies/mL)</td>
<td>51</td>
<td>92</td>
</tr>
</tbody>
</table>

In 2014, higher CD4 cell counts and rates of viral suppression (p<0.0001)

- Current ART regimen

<table>
<thead>
<tr>
<th>Current ART regimen</th>
<th>2004 (n=2138)</th>
<th>2014 (n=2138)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 NRTIs + 1 PI</td>
<td>24</td>
<td>32</td>
</tr>
<tr>
<td>2 NRTIs + 1 NNRTI</td>
<td>22</td>
<td>32</td>
</tr>
<tr>
<td>2 NRTIs + 1 INI</td>
<td>0</td>
<td>7</td>
</tr>
<tr>
<td>Other treatment</td>
<td>35</td>
<td>26</td>
</tr>
<tr>
<td>No treatment</td>
<td>19</td>
<td>3</td>
</tr>
</tbody>
</table>

No marked difference in ART regimens, except for use of INIs (p<0.0001)

Today’s patient: Aquitaine Cohort

- POLYPHARMACY: COMORBIDITY-RELATED MEDICATION INCREASED SIGNIFICANTLY FROM 2004 TO 2014 (P<0.0001), EXCEPT FOR ANTIDEPRESSANT DRUGS

Prescription of comorbidity-related medication, in 2004 and 2014

<table>
<thead>
<tr>
<th>Antidiabetics, n (%)</th>
<th>2004 (n=2138)</th>
<th>2014 (n=2138)</th>
</tr>
</thead>
<tbody>
<tr>
<td>51 (2.4)</td>
<td>125 (5.8)</td>
<td></td>
</tr>
</tbody>
</table>

Blood-pressure and lipid-lowering drugs had the highest increase

<table>
<thead>
<tr>
<th>Blood-pressure lowering treatment, n (%)</th>
<th>2004 (n=2138)</th>
<th>2014 (n=2138)</th>
</tr>
</thead>
<tbody>
<tr>
<td>128 (6.0)</td>
<td>486 (22.7)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Lipid-lowering treatment, n (%)</th>
<th>2004 (n=2138)</th>
<th>2014 (n=2138)</th>
</tr>
</thead>
<tbody>
<tr>
<td>331 (15.5)</td>
<td>626 (29.3)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Medication related to a risk of CV disease, n (%)</th>
<th>2004 (n=2138)</th>
<th>2014 (n=2138)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin</td>
<td>19 (0.9)</td>
<td>170 (8.0)</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>18 (0.8)</td>
<td>87 (4.1)</td>
</tr>
</tbody>
</table>

Increased frequency in prescription of drugs for renal conditions and CV prevention

<table>
<thead>
<tr>
<th>Treatment associated with a renal conditions, n (%)</th>
<th>2004 (n=2138)</th>
<th>2014 (n=2138)</th>
</tr>
</thead>
<tbody>
<tr>
<td>51 (2.4)</td>
<td>308 (14.4)</td>
<td></td>
</tr>
</tbody>
</table>

Blood-pressure and lipid-lowering drugs had the highest increase

<table>
<thead>
<tr>
<th>Psychotropic drugs, n (%)</th>
<th>2004 (n=2138)</th>
<th>2014 (n=2138)</th>
</tr>
</thead>
<tbody>
<tr>
<td>31 (1.4)</td>
<td>85 (4.0)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Antidepressant drugs, n (%)</th>
<th>2004 (n=2138)</th>
<th>2014 (n=2138)</th>
</tr>
</thead>
<tbody>
<tr>
<td>197 (9.2)</td>
<td>215 (10.1)</td>
<td></td>
</tr>
</tbody>
</table>

p<0.001 for all comparisons (except antidepressant drugs)

*Drugs for renal conditions (ACEi and ARB) and CV prevention (aspirin and clopidogrel): p=0.2872

Blood-pressure and lipid-lowering drugs had the highest increase

Increased frequency in prescription of drugs for renal conditions and CV prevention
A diabetes incidence of 17% among PLWHIV by 2030?

Incidence of newly diagnosed diabetes among PLWHIV (ATHENA cohort, 2011)

Incidence per 1,000 PY

Proportion of PLWHIV with diabetes predicted to increase*
• 2010: 4%
• 2030: predicted 17%

Chronic kidney disease: Key causes in HIV infected patients

- Diabetes mellitus
- Hypertension and vascular disease (smoking as a risk factor)
- Medication (ART or others + illicit drugs)
- HIV-associated (HIVAN, HIVICK)
- Glomerulonephritis
- PCKD
- Chronic pyelonephritis and obstructive nephropathy
  (History of AKI places patient at increased risk of CKD)
Prevention of CVD in HIV-positive individuals – EACS Guidelines

Assess CVD risk in next 10 years
Advise on diet and lifestyle in all persons
Consider ART modification if 10-year CVD risk ≥20%

Smoking
Blood pressure
Coagulation
Glucose
Lipids

Drug treatment if:
SBP ≥140 or DBP ≥90 mmHg (especially if 10-year CVD risk ≥20%)

Target: SBP <140 mmHg
DBP <90 mmHg

Treatment

Drug treatment if:
established CVD risk or age ≥50 years and 10-year CVD risk ≥20%

Target: N/A

Consider treating with acetylsalicylic acid 75–150 mg

Treatment

Drug treatment if:
established CVD or type 2 diabetes, or 10-year CVD risk ≥10%

Target: mmol/L (mg/dL)
Optimal Standard

TC ≤4 (155) ≤5 (190)
LDL ≤2 (80) ≤3 (115)

Renal disease in the guidelines: prevention

Prevention of progressive renal disease

Start ACE inhibitors or angiotensin II receptor antagonists if:
a) Hypertension &/or Proteinuria
b) Proteinuria

Monitor eGFR and K+ level closely on starting treatment or increasing dose
Blood-pressure target: <130/80 mmHg

CKD and proteinuria and independent risk factors for CVD

General measures:
a) Avoid nephrotoxic drugs
b) Lifestyle measures (smoking, weight, diet)
c) Treat dyslipidaemia and diabetes
d) Adjust drug doses where necessary
Modelling: Monitoring and treatment is important for patients with CVD risk

- INTENSIFIED MONITORING AND DRUG TREATMENT OF HYPERTENSION AND DYSLIPIDAEMIA WILL PREVENT 17–20% OF CVD CASES ANNUALLY

### Graph

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Average Annual Percentage Reduction in CVD Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Earlier HIV diagnosis and treatment</td>
<td>50% successful</td>
</tr>
<tr>
<td>Avoiding cART with increased cardiovascular risk</td>
<td>10% successful</td>
</tr>
<tr>
<td>Smoking cessation</td>
<td>15% successful</td>
</tr>
<tr>
<td>Monitoring/treatment of hypertension and dyslipidaemia</td>
<td>20% successful</td>
</tr>
</tbody>
</table>

### Chart

- 50% successful
- 100% successful

### Chart Explanation

- **Early HIV diagnosis and treatment**: 50% successful reduction in CVD cases.
- **Avoiding cART with increased cardiovascular risk**: 10% successful reduction in CVD cases.
- **Smoking cessation**: 15% successful reduction in CVD cases.
- **Monitoring/treatment of hypertension and dyslipidaemia**: 20% successful reduction in CVD cases.
Tenofovir (TDF) and renal risk

- TDF-containing regimens are not recommended if eGFR is <70 mL/min per 1.73 m$^2$.
- TDF is associated with low rates of PRT, around 1%, and requires additional monitoring (blood and urine tests).
- Increasing exposure to TDF is associated with higher incidence of CKD.
  - IRR per year 1.16, 95% CI 1.06–1.25, p<0.0001.

CKD, chronic kidney disease; IRR, incidence rate ratio; NRTI, nucleoside reverse transcriptase inhibitors; PRT, proximal renal tubulopathy.


GENVOYA (TAF) and the kidney: Key clinical trial results

- GENVOYA was not associated with development of PRT in clinical trials.
- GENVOYA can be used in suitable patients with a CrCl >30 mL/min.
- GENVOYA was not associated with changes in aGFR (actual glomerular filtration rate) in clinical trials.
- Cobicistat action on creatinine secretion causes a small reproducible early increase in serum creatinine.

CrCl, creatinine clearance; Cobicistat action on creatinine secretion causes a small reproducible early increase in serum creatinine.
Studies 104 and 111: comparison of E/C/F/TAF vs E/C/F/TDF regimens

- TWO PHASE III, INTERNATIONAL, RANDOMISED, DOUBLE-BLIND, ACTIVE-CONTROLLED STUDIES OF UP TO 144 WEEKS TREATMENT

Baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>E/C/F/TAF (n=866)</th>
<th>E/C/F/TDF (n=867)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age, years (range)</td>
<td>38 (18–74)</td>
<td>35 (18–76)</td>
</tr>
<tr>
<td>Female, %</td>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td>Median CD4 count, cells/μL</td>
<td>404</td>
<td>406</td>
</tr>
<tr>
<td>HIV-1 RNA &gt;100,000 copies/mL, %</td>
<td>23</td>
<td>22</td>
</tr>
</tbody>
</table>

Efficacy of E/C/F/TAF vs E/C/F/TDF up to week 144

- STUDIES 104 AND 111: RANDOMISED, DOUBLE-BLIND COMPARISON OF VIROLOGICAL EFFICACY OF E/C/F/TAF COMPARED WITH E/C/F/TDF IN NAÏVE ADULTS

Week 144: E/C/F/TAF vs E/C/F/TDF difference in response

- <50 copies/mL 4.2% [95% CI 0.6%, 7.8%; p=0.02]
Adverse events leading to discontinuation with FTC/TAF and FTC/TDF regimens

- STUDY 104 AND 111: RENAL AND BONE AEs LEADING TO DISCONTINUATION WITH E/C/F/TAF COMPARED WITH E/C/F/TDF UP TO WEEK 144

<table>
<thead>
<tr>
<th>AEs leading to discontinuation, n</th>
<th>E/C/F/TAF (n=866)</th>
<th>E/C/F/TDF (n=867)</th>
<th>p-value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>11 (1.3)</td>
<td>29 (3.3)</td>
<td>0.01</td>
</tr>
<tr>
<td>Bone AEs total</td>
<td>–</td>
<td>6 (&lt;1)</td>
<td>0.03</td>
</tr>
<tr>
<td>Renal/urinary AEs total*</td>
<td>–</td>
<td>12 (1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Proximal renal tubulopathy‡</td>
<td>–</td>
<td>4 (&lt;1)</td>
<td></td>
</tr>
<tr>
<td>Increased Cr/decreased eGFR</td>
<td>–</td>
<td>3 (&lt;1)</td>
<td></td>
</tr>
<tr>
<td>Renal failure</td>
<td>–</td>
<td>2 (&lt;1)</td>
<td></td>
</tr>
<tr>
<td>Nephropathy</td>
<td>–</td>
<td>1 (&lt;1)</td>
<td></td>
</tr>
<tr>
<td>Proteinuria</td>
<td>–</td>
<td>1 (&lt;1)</td>
<td></td>
</tr>
<tr>
<td>Bladder spasm</td>
<td>–</td>
<td>1 (&lt;1)</td>
<td></td>
</tr>
</tbody>
</table>

*AEs coded as renal and urinary disorders (MedDRA 19.0)
‡Calculated using Fisher’s exact test

STUDY 112: SUPPRESSED ADULTS WITH RENAL IMPAIRMENT SWITCHED TO GENVOYA

- Phase 3, 144-week, multicentered, single-arm, open label study

<table>
<thead>
<tr>
<th>Key inclusion criteria</th>
<th>N = 242</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV Suppressed Adults</td>
<td></td>
</tr>
<tr>
<td>Renal Impairment</td>
<td></td>
</tr>
<tr>
<td>eGFR 30-69 mL/min</td>
<td></td>
</tr>
</tbody>
</table>

- Primary Endpoint
  - Change from baseline in glomerular filtration rate* at Week 24

- Secondary Endpoints
  - Efficacy, safety, and tolerability observed through Week 144
  - Proportion of subjects with HIV-1 RNA <50 c/mL by FDA Snapshot analysis

Sub-analyses (Week 48)

- Safety of Genvoya in subjects who switched from a TDF or non-TDF-containing regimen
- Safety of Genvoya in subjects with baseline eGFR 30-49 mL/min compared to 50-69 mL/min

---

*GFR was measured using the Cockcroft-Gault formula (eGFRCG) in all patients.
†eGFR was measured at three timepoints (baseline, Week 2, 4 or 8 and Week 24) in a subset of patients.
SWITCH STUDY 112: CHANGES IN eGFR BY BASELINE eGFR STRATA

Changes in eGFR from baseline to Week 96

<table>
<thead>
<tr>
<th>Baseline eGFR</th>
<th>Median eGFR (mL/min/1.73 m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;60</td>
<td>n=76</td>
</tr>
<tr>
<td>51–60</td>
<td>n=78</td>
</tr>
<tr>
<td>41–50</td>
<td>n=54</td>
</tr>
<tr>
<td>31–40</td>
<td>n=78</td>
</tr>
<tr>
<td>≤30</td>
<td>n=76</td>
</tr>
</tbody>
</table>

One patient was excluded due to missing cysC data at baseline.

cysC, cystatin C; sCr, serum creatinine

- No clinically significant change in eGFR was seen with Genvoya in patients with mild-to-moderate renal impairment switching from other regimens.
- No patient developed renal tubulopathy or Fanconi syndrome.


STUDY 112: WEEK 48
SUB-GROUP ANALYSIS BY PRE-SWITCH ARV REGIMEN
PROTEINURIA: CHANGE FROM BASELINE TO WEEK 48

*UPCR* changes statistically significant (Week 48 vs. Baseline)

UPCR=Urine Protein:Creatinine Ratio; UACR= Urine Albumin: Creatinine Ratio; BL= Baseline


Patients (%)

Proteinuria (UPCR) Albuminuria (UACR)

<table>
<thead>
<tr>
<th></th>
<th>TDF*</th>
<th>Non-TDF</th>
<th>TDF*</th>
<th>Non-TDF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wk 48BL BL Wk 48</td>
<td>47</td>
<td>13</td>
<td>29</td>
<td>22</td>
</tr>
<tr>
<td></td>
<td>53</td>
<td>87</td>
<td>71</td>
<td>78</td>
</tr>
</tbody>
</table>

* Significant improvements from baseline in clinically significant proteinuria and albuminuria following switch to GENVOYA from a TDF-based regimen.

*TDF changes statistically significant (Week 48 vs. Baseline)
### STUDY 112 (WEEK 48):
ADVERSE EVENTS IN ≥5% OF PATIENTS

<table>
<thead>
<tr>
<th>Condition</th>
<th>eGFR 30-49 mL/min n=80</th>
<th>eGFR 50-69 mL/min n=162</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhea</td>
<td>13</td>
<td>11</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>8</td>
<td>10</td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>3</td>
<td>12</td>
</tr>
<tr>
<td>Bronchitis</td>
<td>9</td>
<td>8</td>
</tr>
<tr>
<td>Osteopenia*</td>
<td>11</td>
<td>7</td>
</tr>
<tr>
<td>Nausea</td>
<td>6</td>
<td>9</td>
</tr>
<tr>
<td>Headache</td>
<td>3</td>
<td>9</td>
</tr>
<tr>
<td>Pain in extremity</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>Back pain</td>
<td>4</td>
<td>8</td>
</tr>
<tr>
<td>Dizziness</td>
<td>10</td>
<td>4</td>
</tr>
<tr>
<td>Fatigue</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Renal cyst</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Cough</td>
<td>5</td>
<td>6</td>
</tr>
</tbody>
</table>

*Of 18 participants, 16 had baseline osteopenia, 2 had AE reported within 12 days of baseline.

Note: Similar rates of SAEs (11% vs 11%), grades 2, 3 or 4 AEs (9% vs 8%), and potential FTC adverse reactions (46% vs 52%) between eGFR categories.

- Similar rates and types of AEs between low and high BL eGFR categories

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Switching From TDF to TAF Improves Bone and Renal Safety Independent of Age, Sex, Race, or 3rd Agent: Results From Pooled Analysis (N=3816) of Virologically Suppressed HIV-1 Infected Adults

Jürgen Rockstroh,1 Chiho Okano,2 Yazdan Yazdanpanah,3 Giovanni Di Perri,4 Paolo E. Sari,5 Jose R. Arribas,6 Keen Brinkman,7 David A. Wohl,7 Andrew Cheng,8 Li-jie Zhang,5 Scott McCallister,9 Mounelli Dey10

1. University Hospital Bonn, Germany. 2. The Royal London Hospital, Barts Health NHS Trust, London, UK. 3. Hospital Bichat-Claude Bernard, Paris, France. 4. Clinique Armoise di Savoia, Torino, Italy. 5. Brigham and Women’s Hospital, Boston, Massachusetts, USA. 6. Hospital Universitario La Paz, Madrid, Spain. 7. Casa de Lava, Hospital Gerrius, Amsterdam, the Netherlands. 8. University of North Carolina at Chapel Hill School of Medicine, USA. 9. Gilead Sciences, Inc., Foster City, California, USA. 10. IMPEZ0289

99th IAS Conference on HIV Science (IAS 2017)
23-26 July 2017 | Paris, France
**Study Design**

![Diagram showing study design]

- **Primary Endpoint**
  - HIV-1 RNA <50 copies/mL

- **Week 0**
  - Switch to TAF

- **48 weeks**
  - Continue TDF-Based Regimen

*Includes ritonavir (RTV)-boosted atazanavir (ATV), RTV-boosted darunavir (DRV), darunavir (GT), efavirenz (EFV), RTV-boosted lopinavir (LPV), maraviroc (MVC), nevirapine (NVP), raltegravir (RAL), and ritonavir (RTV). COB, coformulated, EVO, efavirenz, FTC, emtricitabine.

- Phase 3, international, multicenter, switch studies (N=3816: TAF, n=2205; TDF, n=1611)
- Virologically suppressed (HIV-1 RNA <50 copies/mL) adults with stable estimated glomerular filtration rate by Cockcroft-Gault equation (eGFR_{CR,2} ≥ 250 mL/min) switched from TDF-containing regimens to E/C/F/TAF
- We report efficacy (HIV-1 RNA <50 copies/mL; US Food and Drug administration snapshot algorithm), and renal and bone safety endpoints

---

**Results**

**Baseline Characteristics**

<table>
<thead>
<tr>
<th></th>
<th>TAF n=2205</th>
<th>TDF n=1611</th>
<th>Total n=3816</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age, y</td>
<td>44</td>
<td>45</td>
<td>45</td>
</tr>
<tr>
<td>Male, %</td>
<td>81</td>
<td>86</td>
<td>83</td>
</tr>
<tr>
<td>Race/ethnicity, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>68</td>
<td>69</td>
<td>68</td>
</tr>
<tr>
<td>Black or African descent</td>
<td>22</td>
<td>23</td>
<td>23</td>
</tr>
<tr>
<td>Asian</td>
<td>4</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Latin/Hispanic</td>
<td>20</td>
<td>18</td>
<td>18</td>
</tr>
<tr>
<td>Mean BMI, kg/m² (SD)</td>
<td>26.8 (3.3)</td>
<td>26.7 (3.1)</td>
<td>26.7 (3.3)</td>
</tr>
<tr>
<td>HIV-1 RNA &lt;50 copies/mL, %</td>
<td>98</td>
<td>99</td>
<td>98</td>
</tr>
<tr>
<td>Median CD4 count, cell/µl</td>
<td>665</td>
<td>659</td>
<td>662</td>
</tr>
<tr>
<td>Median eGFR_{CR,2} ml/min (Q1, Q3)</td>
<td>105.3 (68.7, 124.8)</td>
<td>105.1 (67.8, 125.7)</td>
<td>105.2 (68.2, 125.2)</td>
</tr>
<tr>
<td>Diabetes mellitus, %</td>
<td>4</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>22</td>
<td>25</td>
<td>23</td>
</tr>
<tr>
<td>Cardiovascular disease, %</td>
<td>5</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Hyperlipidemia, %</td>
<td>31</td>
<td>32</td>
<td>31</td>
</tr>
</tbody>
</table>

*No participants had Grade 3 proteinuria at baseline. BMI, body mass index; Q, quartile; SD, standard deviation.*
Bone and Renal Safety by 3rd Agent

- Improvements in BMD and renal safety parameters were independent of 3rd agent, with \( p < 0.001 \) for treatment differences at Week 48.

*For BMD, p-values were from analysis of variance (ANOVA) model including study and treatment as fixed effects; *For renal safety parameters, p-values were from van Elteren test including study as stratification factor.

Renal Safety Parameters in Participants at Increased Renal Risk*

*For all at Week 48 from van Elteren test including study as stratification factor. UACR, urine albumin/creatinine ratio; BL, baseline; BDM, body mass index; Cr, creatinine; GFR, glomerular filtration rate; RBP, retinal-binding protein; UACR, urine albumin/creatinine ratio.
Conclusions

• Pooling data showed continued high rates of virologic suppression, and significant improvement in median measures of bone and renal safety in 2205 participants who switched to TAF vs 1611 who stayed on TDF, confirming results of individual studies
  - Improvements in bone and renal safety were independent of 3rd agent
• Pooling data also confirmed that subpopulations at greater bone and renal risk had clinically meaningful and significant improvements
• Women and older adults had greater improvements in spine BMD vs the overall population
• Participants with renal impairment (eGFR<90 mL/min) had greater improvements in albuminuria and tubular proteinuria vs the overall population
• These data support that switching from TDF to TAF is associated with continued virologic suppression and improvements in bone and renal safety, which is particularly notable in individuals at greater bone and renal risk

• Careful HIV management, including regular monitoring and screening of major comorbidities, and adequate selection of ART, could lead to:
  • Early management and prevention of comorbidities
  • Continuous improvement of HIV-positive individuals’ health status and quality of life

• In this context:
  • Effective ART that balances HIV outcomes (potency, genetic barrier) with less toxicity (long-term impact on CV, bone, and renal events) will be beneficial for patients’ care and treatment
  • Additionally, a good control of risk factors, particularly through an improved lifestyle to prevent comorbidities