22nd HIV/AIDS Workshop 2023

# Industrial Sponsored Symposium
# Obstacles in Real-life Management for PLWH

11.00 – 11.50 I 25 AUG 2023
Mandarin Grand Ballroom A B C, Mandarin Hotel Bangkok (Samyan)


**Prof. Sasisopin Kiertiburanakul, MD, MHS**
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# Agenda

5 Mins:

**Welcome and Introduction**

20 Mins:

**Obstacles in Real-life Management for PLWH**

20 Mins:

**Cases Sharing**

5 Mins:

**Q & A**

# Disclosure

- Speakers Bureau
  - Pfizer, Astellas, MSD, Janssen, AstraZeneca, GSK, DKSH, BMS, AbbVie, Meiji, Siam, Daiichi, Takeda, Sanofi, Mylan, DCH Auriga, Biopharm, BLHua, Roche, Berlin, Zuellig Pharma, Medtronic, Biogenetech, Celltrion, Novartis
- Congress Travel
  - Astellas, Pfizer, MSD, Janssen, BMS, AbbVie, Siam, Daiichi, Takeda, DKSH, AstraZeneca
- Research Grant
  - Gilead, MSD, BMS, Daiichi, Biopharm, Medicago

# Difficulties Faced by PLWH in the Disease Management

Intrafamilial prejudice and its impact on coping with the disease

Social prejudice: macro environment impacts

Difficulties in managing risk of HIV transmission and its implications on partnerships

Maintenance of high rates of HIV treatment adherence: qualifying the service

Quality of life promotion for PLWH

de Jesus GJ, et al. Acta Paul Enferm 2017;30. http://dx.doi.org/10.1590/1982-0194201700046

# HIV Treatment Goals

Maximally and durably suppress plasma HIV RNA

Restore and preserve immunologic function

Reduce HIV-associated morbidity and prolong the duration and quality of survival

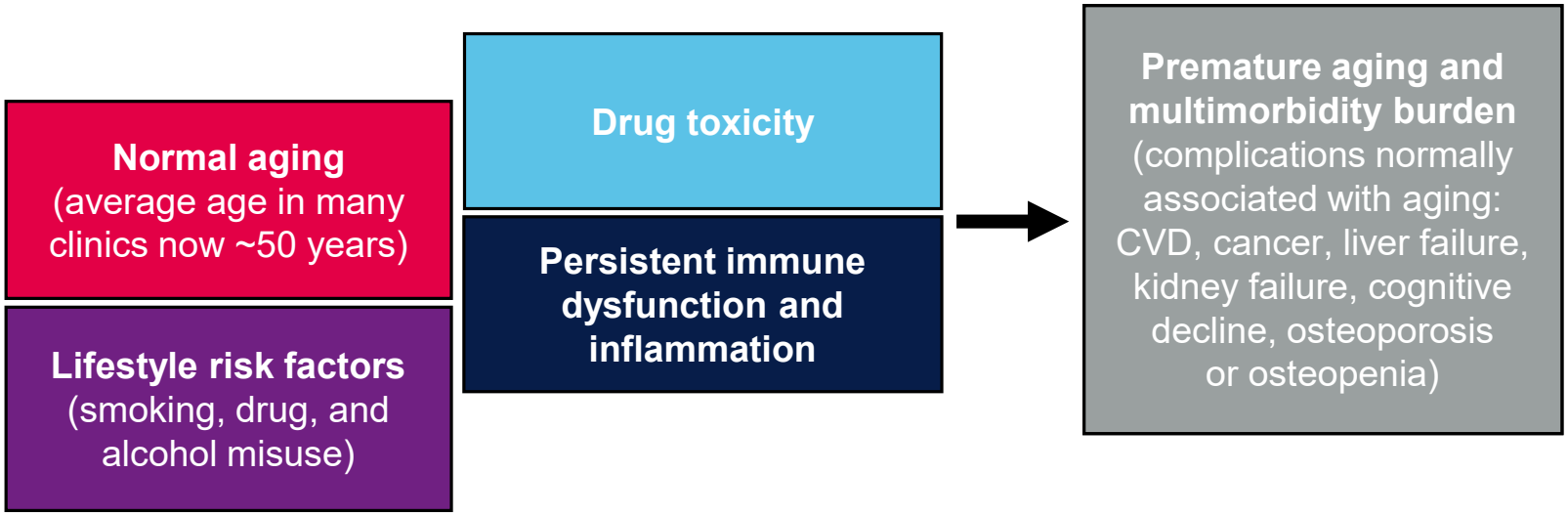

Prevent HIV transmission

- Predictors of virologic success:
  - Low baseline viremia
  - High potency of the ARV regimen
  - Tolerability of the regimen
  - Convenience of the regimen
  - Excellent adherence to the regimen

DHHS ART Guidelines. January 2016.

# Non-AIDS-related Comorbidities

## Factors causally associated with premature development of age-related comorbidities in PLWH




**In PLWH, drug-specific toxicity, lifestyle factors, persistent inflammation, and residual immunodeficiency are associated with premature development of age-related comorbidities**

Deeks SG, et al. BMJ 2009;338:288-92.

# ARVs Can Impact Several Conditions Which Are More Prevalent in Older Adults Living with HIV

**Neuropsychiatric impairment**

EFV

DTG

**Diabetes**

AZT

d4T

ddI

LPV

NFV

IDV

**Myocardial infarction**

ABC

**CV disease**

DRV

LPV

**Low BMD Osteoporotic fracture**

TDF

**Chronic kidney disease**

IDV

TDF

**Kidney stones**

IDV

ATV

**Weight gain**

DTG

BIC

TAF

AZT, zidovudine; BIC, bictegravir; d4T, stavudine; ddI, didanosine; DRV, darunavir; EFV, efavirenz; IDV, indinavir; LPV, lopinavir; NFV, nelfinavir

Eu B, et al. Aust J Gen Pract 2019;48:440-5. Richterman A, et al. Curr Opin HIV AIDS 2020;15:118-25.

# Polypharmacy

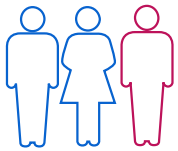
- Definition: use of ≥5 medications[1]
- Increased medication use is associated with[1]


- Polypharmacy is one of the strongest predictors of serious adverse drug events,[2] drug-drug interactions,[2] and fall risk[3]
- Dose-response association with all-cause and CVD mortality[4]

1. Back D, et al. J Int AIDS Soc 2020;23:e25449. 2. Sharp CN, et al. Crit Rev Clin Lab Sci 2019;1-20. 3. Edelman EJ, et al. Curr Opin HIV AIDS 2020;15:126-33.
4. Huang YT, et al. J Gerontol A Biol Sci Med Sci 2022;77:1002-8.

# PLWH Are Looking for More from Their ART

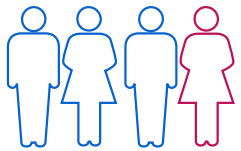
- Based on insights from Positive Perspectives, a study of 2389 PLWH currently receiving ART, many participants were not optimally served by their current regimens[1,2]



**2 in 3** people were worried about the **long-term side effects** of HIV medication (n=1406/2112)[2]

**~1/2**

switched therapies due to **severity or frequency of side effects** (n=702/1550)[2]



**~6 in 10** people believe there is room for **improving their overall HIV management** (n=1457/2389)[3]

## Comorbidities and Simplifying Treatment

**Willingness to switch to a regimen with fewer ARVs* significantly increased among those with comorbidities (n=2112, P <0.001)[2]**


*Willingness to switch was predicated on the understanding they would remain virologically suppressed

1. Okoli C, et al. AIDS Behav 2021;25:1384-95. 2. Okoli C, et al. Prev Chronic Dis 2020;17:E22. 3. Okoli C, et al. AIDS 2020. Poster PED0808.

# Why Consider Treatment Optimization?

- Prevent or mitigate drug–drug interactions
- Reduce pill burden and/or dosing frequency by simplifying a regimen
- Eliminate food or fluid requirements
- Reduce costs
- Allow for optimal use of ART during pregnancy or in cases where pregnancy may occur
- Enhance tolerability and/or decrease short- or long-term toxicity

**The fundamental principle of treatment optimization is to maintain virologic suppression without jeopardising future treatment options**

DHHS Guidelines. January 2022.

# Thailand National Guidelines: First-line Regimen

## Standard regimen (3 drugs) (prefer single tablet regimen)

| NRTIs (backbone) | | | INSTIs (recommend) |
|---|---|---|---|
| TAF / TDF | 3TC / FTC | + | DTG |

| NRTIs (alternative) | | | NNRTI (alternative) | | |
|---|---|---|---|---|---|
| ABC / AZT | 3TC | + | EFV | OR | RPV |

## Optional regimen (2 drugs)

| Regimen | Remarks |
|---|---|
| DTG + 3TC | ▪ Contraindication to TDF and TAF<br>▪ Considerations if<br>➢ HBsAg negative<br>➢ Baseline VL <500,000 copies/mL or CD4 count >200 cells/$mm^3$<br>➢ No 3TC resistance |

แนวทางการตรวจวินิจฉัย รักษาและป้องกันการติดเชื้อเอชไอวี ประเทศไทย ปี 2564/2565

# Selecting Initial ART: Factors to Consider

**Initial characteristics to consider in all persons with HIV**

- Pretreatment HIV RNA
- Pretreatment CD4 cell count
- History of prior exposure to CAB-LA as PrEP
- HIV genotype results
- HLA-B*5701 status
- Individual preferences
- Anticipated adherence
- ART timing postdiagnosis

**Regimen-specific considerations**

- Regimen's barrier to resistance
- Potential AEs and drug toxicities, including risk of development of comorbid diseases
- Known/potential DDIs
- Convenience
- Cost and access

**Presence of specific conditions/ factors**

- Comorbid conditions
- Pregnancy and potential for pregnancy
- Coinfections: HBV, HCV, TB

DHHS ART Guidelines. September 2022.

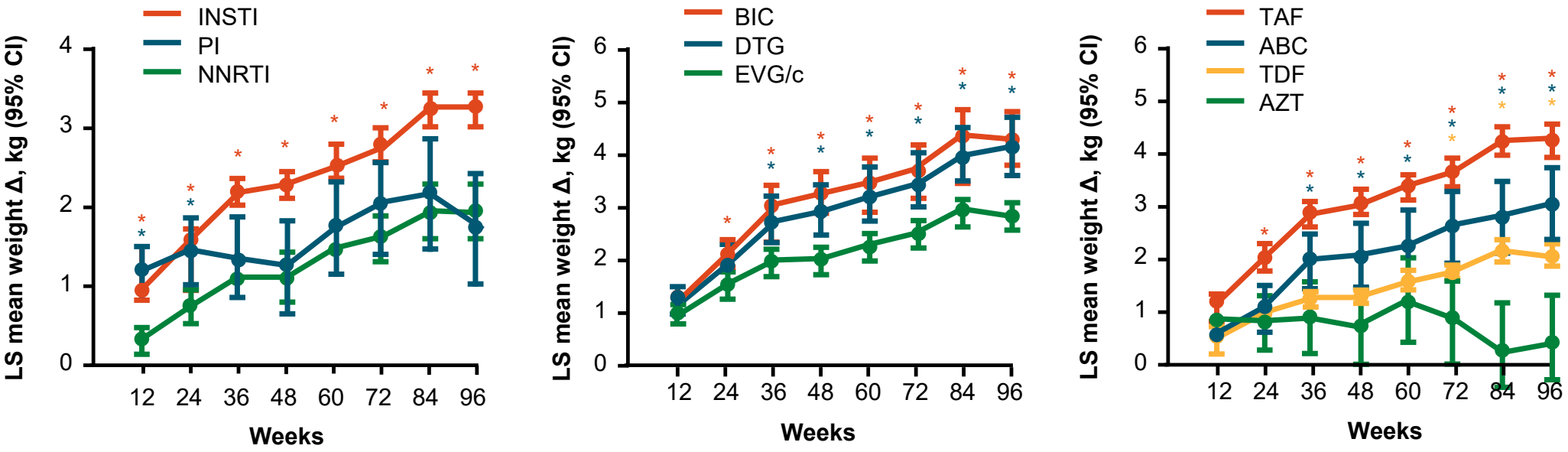
# Antiretroviral Regimen for Initial Therapy Based on Specific Clinical Scenarios 1

| Clinical scenario | Consideration(s) | Clinical scenario | Consideration(s) |
|---|---|---|---|
| **CD4 count <200 cells/mm$^3$** | Do not use<br>▪ RPV<br>▪ DRV/r + RAL | **Osteoporosis** | Avoid TDF |
| **HIV RNA >100,000 copies/mL** | Do not use<br>▪ RPV<br>▪ ABC/3TC with EFV or ATV/r<br>▪ DRV/r + RAL | **High cardiac risk** | ▪ Consider avoiding ABC<br>▪ ATV may have advantages over DRV |
| **HIV RNA >500,000 copies/mL** | Do not use<br>▪ RPV<br>▪ ABC/3TC with EFV or ATV/r<br>▪ DRV/r + RAL<br>▪ DTG/3TC | **Concern for excess weight gain** | ▪ BIC and DTG, has been associated with greater weight gain than NNRTI or boosted PI<br>▪ TAF > TDF |
| **HLA-B*5701 positive or result unknown** | Do not use ABC | **HIV-associated dementia** | Avoid EFV if possible |

DHHS ART Guidelines. September 2022.

# Multivariate Analysis of Weight Gain following ART Initiation in RCTs

- Pooled analysis of weight gain across 8 randomized phase III clinical trials of first-line ART initiation occurring in 2003-2015 (N = 5680)




*Color-coded to match respective comparators, denoting *P* ≤0.05 vs NNRTI (first panel), EVG/COBI (second panel) or AZT (last panel).

Sax PE, et al. Clin Infect Dis 2020;71:1379-89.

# Antiretroviral Regimen for Initial Therapy Based on Specific Clinical Scenarios 2

| Clinical scenario | Consideration(s) | Clinical scenario | Consideration(s) |
|---|---|---|---|
| **Hyperlipidemia** | ARV drugs have been associated with dyslipidemia:<br>▪ PI/r or PI/c<br>▪ EFV<br>▪ EVG/c<br>BIC, DOR, DTG, RAL, and RPV have fewer lipid effects<br>TDF lowers lipids | **Treating TB with rifamycin** | ▪ Rifamycin are inducers of CYP3A4 and UGT1A1 enzymes, causing significant decreases in concentrations of PIs, INSTIs, and RPV<br>▪ May require dose adjustment |
| **Patients with history of poor adherence** | Consider using regimens with boosted PI, BIC, or DTG | **Psychiatric illnesses** | ▪ Consider avoiding EFV and RPV<br>▪ Patients on INSTI who have pre-existing psychiatric conditions should be closely monitored |

DHHS ART Guidelines. September 2022.

# DTG: Advantage and Disadvantage

| Advantage(s) | Disadvantage(s) |
|---|---|
| ▪ Higher barrier to resistance than EVG or RAL<br>▪ Coformulated with TXF/XTC<br>▪ No food requirement<br>▪ Minimal CYP3A4 interactions<br>▪ Favorable lipid profile | ▪ Oral absorption of DTG can be reduced by simultaneous administration with drugs containing **polyvalent cations** (e.g., Al-, Ca-, or Mg-containing antacids or supplements or multivitamin tablets with minerals)<br>▪ **UGT1A1 substrate**; potential for drug-drug interactions<br>▪ Inhibits renal tubular secretion of Cr and can **increase serum Cr** without affecting glomerular function<br>▪ **Depression and suicidal ideation** (rare; usually in patients with preexisting psychiatric conditions)<br>▪ **Weight gain**<br>▪ DTG exposure during conception may be associated with a small risk of **NTDs** in the infant compared with non-DTG ARV drugs (1.9 per 1000 vs 1.1 per 1000), that was not statistically significant |

Modified from DHHS ART Guidelines. June 2021.

# EFV: Advantage and Disadvantage

| Advantage(s) | Disadvantage(s) |
|---|---|
| ▪ Coformulated with TDF/FTC<br>▪ Has long-term clinical experience<br>▪ EFV-based regimens (except for EFV + ABC/3TC) have well-documented efficacy in patients with high HIV RNA<br>▪ EFV 400 mg has fewer CNS side effects than EFV 600 mg<br>▪ EFV 600 mg can be given with rifamycin (rifampin, rifabutin, or rifapentine) | ▪ Short- and long-term **neuropsychiatric side effects**, including depression and, in some studies, suicidality and catatonia<br>- Late-onset ataxia and encephalopathy<br>▪ **Dyslipidemia**<br>▪ **Rash**<br>▪ **QTc interval prolongation**<br>▪ **Transmitted resistance** is more common than with PIs and INSTIs<br>▪ Greater **risk of resistance** at the time of treatment failure than with PIs<br>▪ Potential for **CYP450 drug interactions**<br>▪ Should be **taken on an empty stomach** (increases CNS toxicities) |

Modified from DHHS ART Guidelines. June 2021.

# NNRTIs vs INSTIs as First-line ART: Possible Role of NNRTIs Today

**Possible role for NNRTIs[1]**

- Patient experiencing AE(s) with INSTIs, including weight gain with INSTIs[2]
- Drug-drug interactions with DTG and BIC

**Challenges with NNRTI use**

- Low barrier to resistance at VF with EFV and RPV[3,4]
- Neuropsychiatric AEs with EFV[3]
- Higher rates of VF in RPV patients[5] with HIV RNA >100,000 copies/mL and CD4 counts <200 cells/mm³
- RPV must be taken with a meal[4]
- Lipid increases with EFV[3]
- Drug-drug interactions with EFV and RPV[3,4]

1. DHHS ART Guidelines. September 2022.
2. McCann K, et al. EACS 2019. Abstract PS3/3. 3. EFV PI. 4. RPV PI. 5 Cohen C, et al. AIDS 2014;28:989-97.

# ข้อบ่งชี้ในการเปลี่ยนสูตรยาต้านเอชไอวีในกรณีที่ไม่ดื้อยา

เกิดภาวะข้างเคียงยาจากยาต้านเอชไอวี

ป้องกันการเกิดผลข้างเคียงระยะยาว

Drug–drug interaction และ drug–food interaction

ตั้งครรภ์หรือวางแผนที่จะมีบุตร

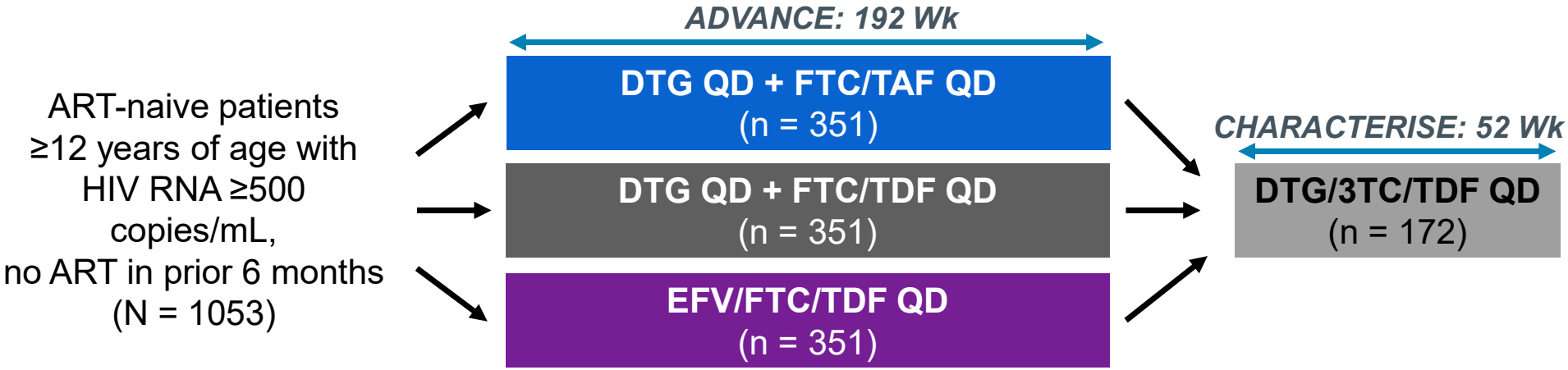
เพื่อให้กินยาง่ายขึ้น เช่น ปรับสูตรยาหลายเม็ดหรือสูตรยาที่กินหลายครั้งต่อวัน

เปลี่ยนเป็นสูตรแนะนำตามแนวทางการรักษาที่มีประสิทธิภาพดีขึ้น

แนวทางการตรวจวินิจฉัย รักษาและป้องกันการติดเชื้อเอชไอวี ประเทศไทย ปี 2564/2565

# CHARACTERISE: Switch to DTG/3TC/TDF After ADVANCE Trial Participation

- ADVANCE: randomized, open-label phase III noninferiority trial in South Africa
  - HIV RNA <50 copies/mL similar across treatment groups at Wk 48 (primary endpoint)[1] and through Wk 192,[2] but weight increases higher with DTG regimens: +8.9 kg with DTG + FTC/TAF, +5.8 kg with DTG + FTC/TDF, and +3.3 kg with EFV/FTC/TDF at Wk 192[2]
- CHARACTERISE: evaluation of weight and laboratory changes ≥52 wk after switch from ADVANCE trial to open-label DTG/3TC/TDF[3,4]



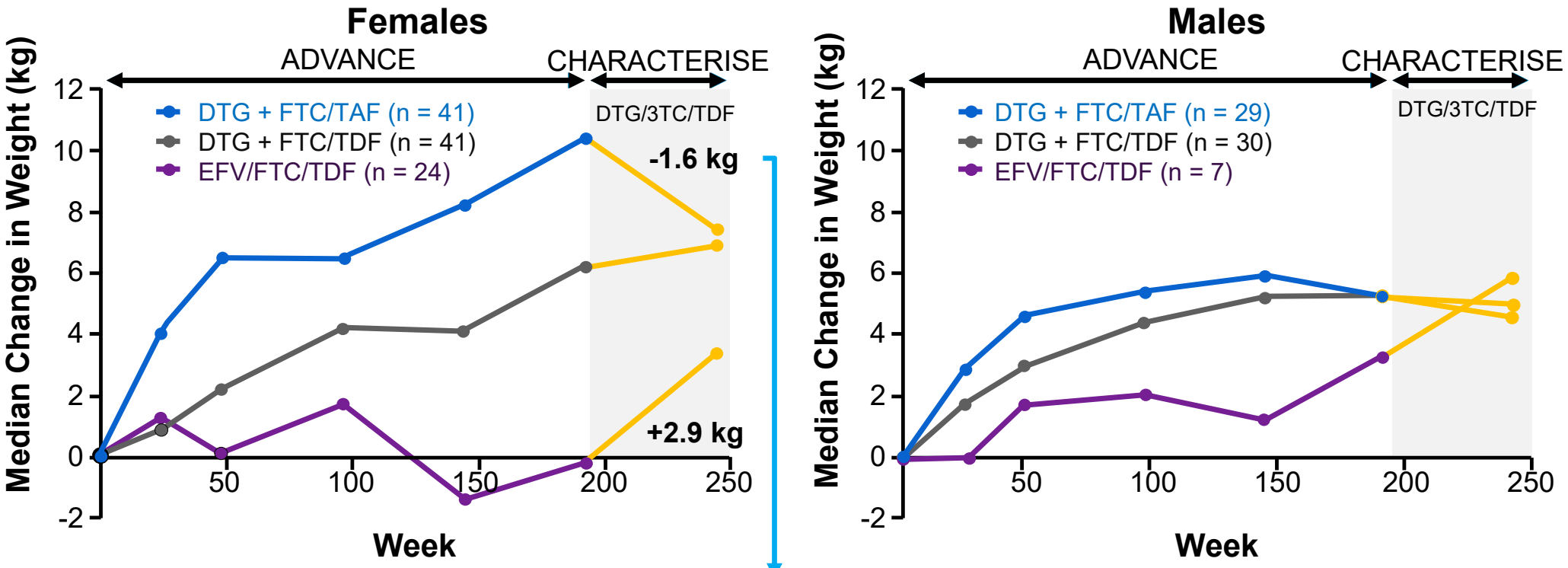

1. Venter WDF, et al. N Engl J Med 2019;381:803-15. 2. Venter WDF, et al. AIDS 2022. Abstract PELBB01. 3. Bosch BE, et al. CROI 2023. Abstract 167.
4. Bosch BE, et al. Clin Infect Dis 2022;ciac949.

# ADVANCE 96-Wk Analysis: Conclusions

- No significant differences in virologic suppression rates were observed in South African PLWH initiating treatment with DTG + FTC/TAF vs DTG + FTC/TDF vs EFV/FTC/TDF
  - HIV RNA <50 copies /mL in ITT population: 79% vs 78% vs 74%
- Rate of treatment-emergent NRTI and NNRTI resistance slightly higher in EFF/FTC/TDF arm (6%) [DTG + FTC/TAF 3% vs DTG + FTC/TDF 5%]
- Body weight increases were higher with DTG + FTC/TAF (+8.2 Kg)
  - Increases were most pronounced in women, driven by trunk fat gains, and continued after Wk 96
- Treatment-emergent metabolic syndrome was significantly higher with DTG + FTC/TAF vs EFV/FTC/TDF (8.4% vs 3.9%; P = 0.03)
- **Investigators concluded that 96-wk data support reserving DTG + FTC/TAF for patients with impaired renal function or osteoporosis**

Sokhela S, et al. AIDS 2020. Abstract OAXLB0104. Venter WDF, et al. Lancet HIV 2020;7:e666-e676.

# CHARACTERISE: Weight Change by Sex after Switch from ADVANCE Trial Regimens to DTG/3TC/TDF




In females, switch from **DTG + FTC/TAF** to **DTG/3TC/TDF** associated with median **1.6 kg weight loss**

Bosch BE, et al. CROI 2023. Abstract 167.

# CHARACTERISE: Laboratory Value Changes After Switch from ADVANCE Trial Regimens to DTG/3TC/TDF

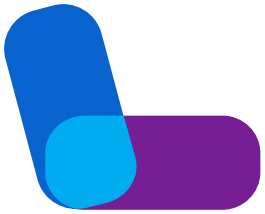
- HIV RNA <50 c/mL at/after Wk 52 of DTG/3TC/TDF by original regimen in ADVANCE: **100% (68/68) for switch from DTG + FTC/TAF**, **97% (68/70) for switch from DTG + FTC/TDF**, **89% (25/28) for switch from EFV/FTC/TDF**

| Median Change From Switch | Switch From DTG + FTC/TAF (n = 70) | | Switch From DTG + FTC/TDF (n = 71) | | Switch From EFV/FTC/TDF (n = 31) | |
|---|---|---|---|---|---|---|
| | Change | P-value | Change | P-value | Change | P-value |
| Total cholesterol, mmol/L | -0.2 | 0.002 | +0.2 | 0.001 | -0.3 | 0.011 |
| LDL cholesterol, mmol/L | -0.3 | <0.001 | -0.01 | NS | -0.3 | 0.001 |
| HDL cholesterol, mmol/L | -0.03 | NS | +0.04 | 0.021 | -0.1 | 0.049 |
| Total/HDL cholesterol ratio | -0.085 | NS | -0.004 | NS | +0.141 | NS |
| Triglycerides, mmol/L | -0.1 | 0.025 | -0.02 | NS | -0.1 | 0.057 |
| Fasting glucose, mmol/L | -0.2 | <0.001 | 0 | NS | -0.1 | NS |
| A1C, mmol/L | -0.1 | <0.001 | -0.1 | NS | -0.15 | 0.008 |

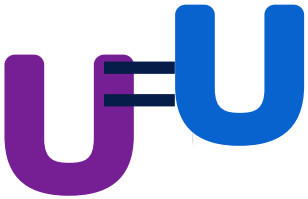
Bosch BE, et al. CROI 2023. Abstract 167.

# Conclusions: Obstacles in Real-life Management for PLWH

Preventing or managing comorbidities[1,2]



Minimizing drug–drug interactions[1,2]




Maintaining an undetectable VL long term[2]

Maintaining optimal mental health and overall health[1,2]

1. Okoli C, et al. Prev Chronic Dis 2020;17:E22. 2. de los Rios P, et al. Popul Med 2020;2:23.

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**Prof. Sasisopin Kiertiburanakul, MD, MHS**
Faculty of Medicine Ramathibodi Hospital
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**Warunyu Namsiripongpan, MD**
Faculty of Medicine Ramathibodi Hospital
Bangkok, Thailand

# Interesting cases

**Warunyu Namsiripongpun, MD**
Division of Infectious Disease, Department of Medicine,
Faculty of Medicine Ramathibodi Hospital, Mahidol University

Camber Symposium, The 22nd TAS HIV/AIDS Workshop, Mandarin Hotel Bangkok (25 August 2023)

# Case 1

# Case 1: 54-year-old man living  with HIV

June 2021

- First visit with new ID specialist
- Known case HIV infection F/U since ’2008
- Hx PCP ’2008, Hx secondary syphilis ’2011
- ART:
  - Switch from AZT/3TC (600/300) + EFV (600) to TDF/FTC (300/200) + EFV (600) ’2009
  - Switch from TDF/FTC (300/200) + EFV (600) to single-pill TDF/FTC/EFV (300/200/600) ’2015

CD4 302 cells/$mm^3$ (10%), HIV VL <40 copies/mL, Cr 0.95 mg/dL

# Case 1: 54-year-old man living with HIV

Dec 2021

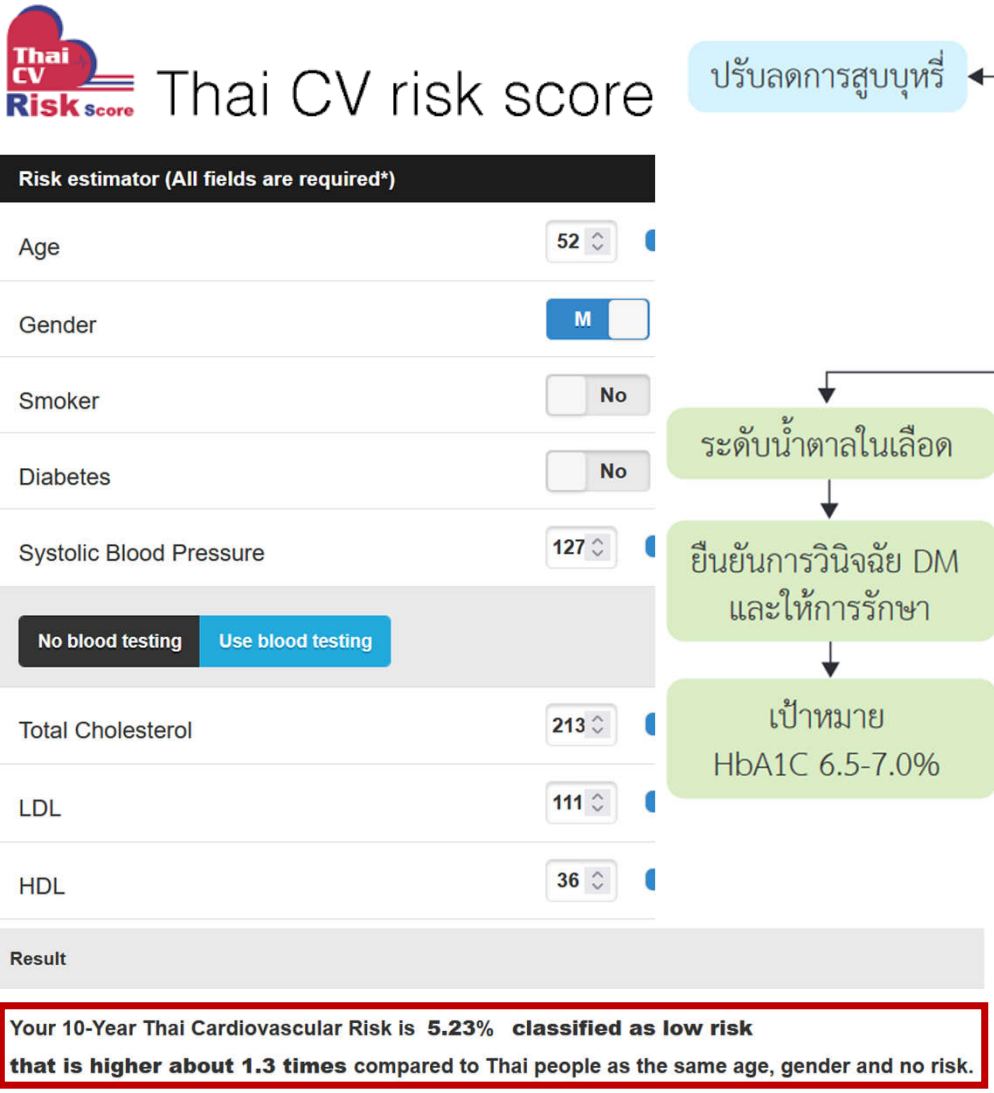
- CD4 285 cells/mm$^3$ (9%), HIV VL <40 copies/mL, Cr 1.12 mg/dL
- HyperTG: **TG 213 mg/dL**, TC 178 mg/dL, HDL 36 mg/dL, LDL-C 111 mg/dL
- Continue single-pill TDF/FTC/EFV (300/200/600)

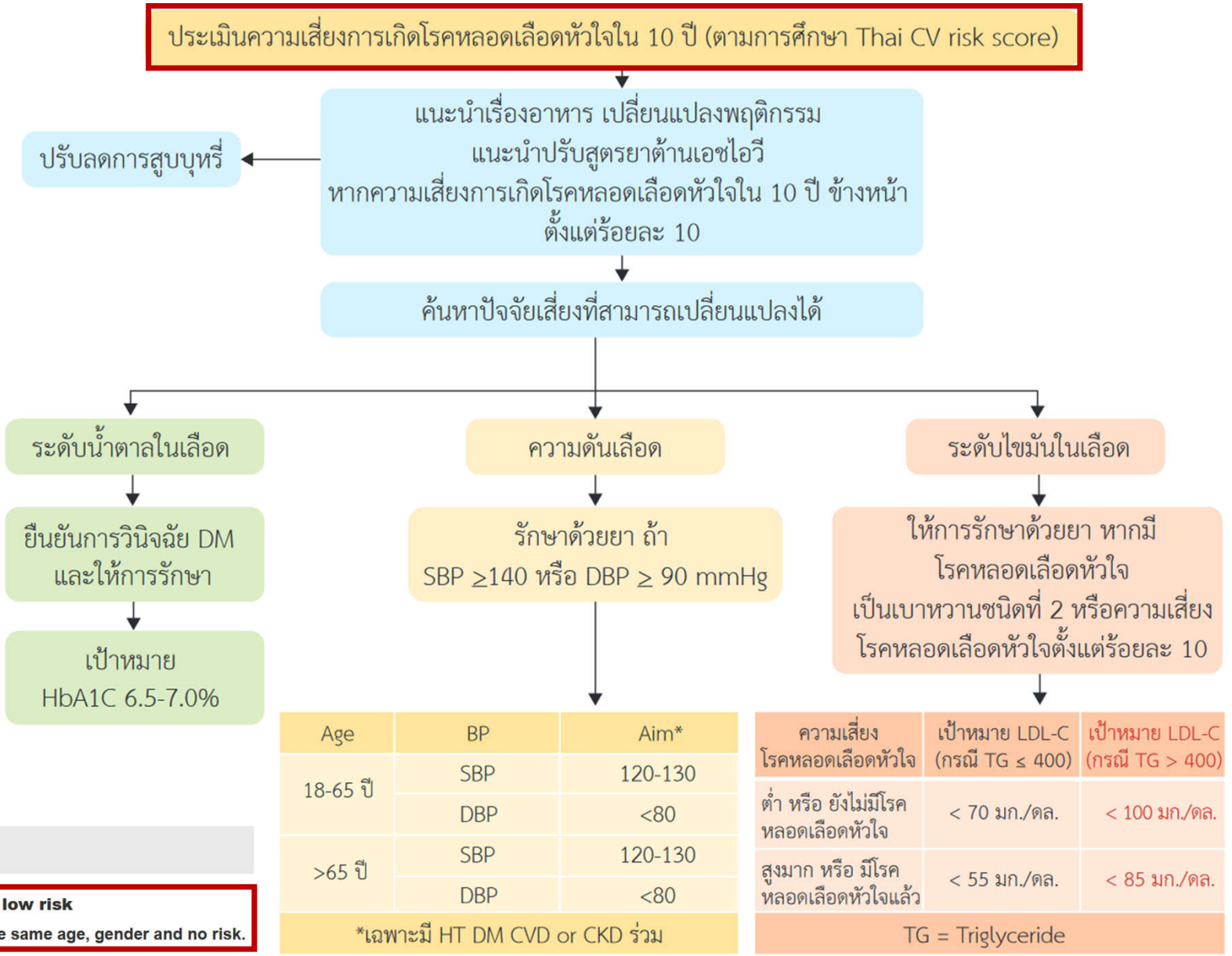
June 2022

- HIV VL <40 copies/mL, Cr 1.13 mg/dL
- HyperTG: **TG 299 mg/dL**, TC 186 mg/dL
- How would you manage hypertriglyceridemia?

# How would you manage hypertriglyceridemia?

A. Continue TDF/FTC/EFV, diet control
B. Continue TDF/FTC/EFV, add atorvastatin
C. Continue TDF/FTC/EFV, add gemfibrozil
D. Switch to TDF/3TC/DTG




Thailand National Guidelines on HIV/AIDS Treatment and Prevention 2021/2022.

# Prevention of Cardiovascular Disease in PLWHA

1. ประเมินความเสี่ยงการเกิดโรคหลอดเลือดหัวใจใน 10 ปีของผู้ติดเชื้อเอชไอวีตามการศึกษา Thai CV risk score
2. แนะนำปรับสูตรยาต้านเอชไอวี ดังนี้

| ผลข้างเคียง | ยาต้านเอชไอวีเดิม | ยาต้านเอชไอวีใหม่ |
|---|---|---|
| **โรคหัวใจและหลอดเลือด**<br>• กล้ามเนื้อหัวใจขาดเลือดและหลอดเลือดสมองตีบ | • ABC | • TDF หรือ TAF |
| | • RTV หรือ COBI boosted-PIs<br>• EFV | • BIC, DTG, RAL หรือ RPV |
| **ไขมันในเลือดสูง**<br>• ไตรกลีเซอไรด์สูง (มีหรือไม่มี LDL-C สูง) | • RTV หรือ COBI boosted-PIs<br>• EFV | • BIC, DTG, RAL หรือ RPV |

3. เป้าหมายการรักษากำหนดไว้เป็นแนวทาง ไม่จำเป็นต้องรักษาให้ได้ตามเป้าหมายเสมอ ต้องพิจารณาปัจจัยต่าง ๆ ร่วมด้วย กรณีที่ใช้วิธีคำนวณ LDL ต้องระวังในภาวะที่มีระดับไตรกลีเซอไรด์สูงมากกว่า 400 มก./ดล. จะทำให้ผลการตรวจ LDL จากการคำนวณผิดพลาดได้ [คำนวณจาก LDL = TC - HDL - (TG/5)] ในกลุ่มนี้ควรพิจารณาเพิ่มระดับเป้าหมายระดับไขมัน LDL ไปอีก 30 มก./ดล.
4. ไม่มีการกำหนดเป้าหมายระดับไตรกลีเซอไรด์ในการรักษาไว้ชัดเจน เนื่องจากระดับไตรกลีเซอไรด์สูงยังเป็นความเสี่ยงของการเกิดโรคหัวใจที่ไม่ชัดเจน อย่างไรก็ตามหากมีระดับไตรกลีเซอไรด์สูงมากกว่า 500 มก./ดล. พิจารณาปรับสูตรยาต้านเอชไอวีที่เหมาะสมและพิจารณาให้ยาลดระดับไตรกลีเซอไรด์ เพราะระดับไตรกลีเซอไรด์ที่สูงมากอาจก่อให้เกิดตับอ่อนอักเสบได้

Thailand National Guidelines on HIV/AIDS Treatment and Prevention 2021/2022.

# How would you manage hypertriglyceridemia?

A. Continue TDF/FTC/EFV, diet control

B. Continue TDF/FTC/EFV, add atorvastatin

C. Continue TDF/FTC/EFV, add gemfibrozil

D. Switch to TDF/3TC/DTG

RESEARCH ARTICLE Open Access

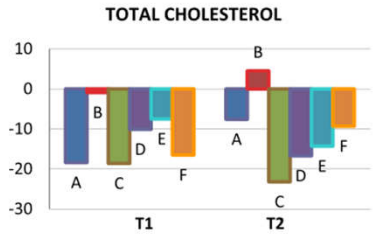
# Improvement of lipid profile after switching from efavirenz or ritonavir-boosted protease inhibitors to rilpivirine or once-daily integrase inhibitors: results from a large observational cohort study (SCOLTA)

Lucia Taramasso[1,2,16*†], Paola Tatarelli[1,3†], Elena Ricci[4], Giordano Madeddu[5], Barbara Menzaghi[6], Nicola Squillace[7], Giuseppe Vittorio De Socio[8], Canio Martinelli[9], Roberto Gulminetti[10], Paolo Maggi[11], Giancarlo Orofino[12], Francesca Vichi[13], Antonio Di Biagio[14], Paolo Bonfanti[15], on behalf of CISAI Study Group

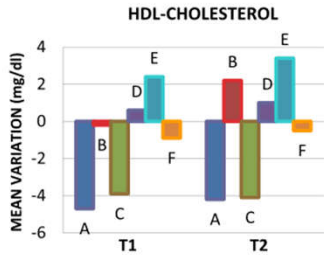
| Switch | | TC T2 - TC T0 (mg/dl) | | LDL T2 - LDL T0 (mg/dl) | | HDL T2 - HDL T0 (mg/dl) | |
|---|---|---|---|---|---|---|---|
| From | To | mean (±SE) | p* | mean (±SE) | p* | mean (±SE) | p* |
| 2 NRTI + EFV | DTG | −15.0 ± 6.5 | **.0210** | − 10.9 ± 6.2 | .0771 | −1.4 ± 1.8 | .4222 |
| | EVG | 1.7 ± 8.6 | .8401 | − 5.9 ± 8.0 | .4623 | 2.8 ± 2.4 | .2350 |
| | RPV | −31.6 ± 5.3 | **<.0001** | −21.0 ± 5.0 | **<.0001** | − 2.9 ± 1.4 | **.0421** |

| | | TC/HDL T2 - TC/HDL T0 (mg/dl) | | TG T2 - TG T0 (mg/dl) | | FRS T2 - FRS T0 | |
|---|---|---|---|---|---|---|---|
| | | mean (±SE) | p* | mean (±SE) | p* | mean (±SE) | p§ |
| 2 NRTI + EFV | DTG | − 0.21 ± 0.21 | .3242 | − 19.6 ± 15.2 | .1992 | 0.67 ± 0.71 | 0.35 |
| | EVG | − 0.32 ± 0.27 | .2488 | 27.2 ± 20.5 | .1853 | 0.74 ± 0.92 | 0.42 |
| | RPV | − 0.52 ± 0.17 | **.0021** | −31.5 ± 12.4 | **.0116** | 0.03 ± 0.38 | 0.93 |

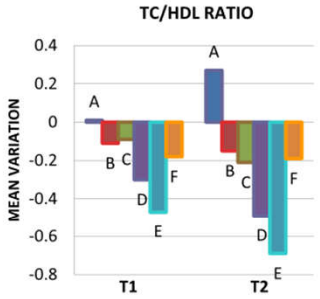
Taramasso L, Tatarelli P, Ricci E, et al. BMC Infect Dis. 2018;18(1):357. Published 2018 Jul 31.



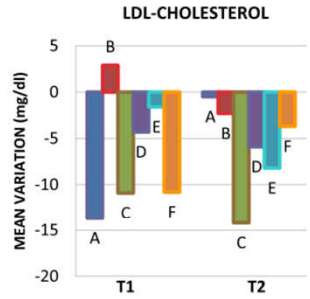

| TC | BL | T1 | T2 |
|---|---|---|---|
| Number of observations | 482 | 456 | 342 |



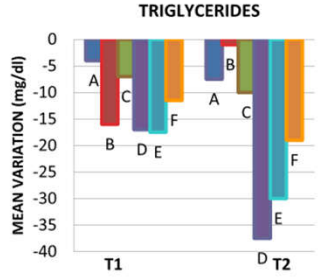

| HDL | BL | T1 | T2 |
|---|---|---|---|
| Number of observations | 474 | 448 | 332 |




| TC/HDL | BL | T1 | T2 |
|---|---|---|---|
| Number of observations | 474 | 447 | 329 |



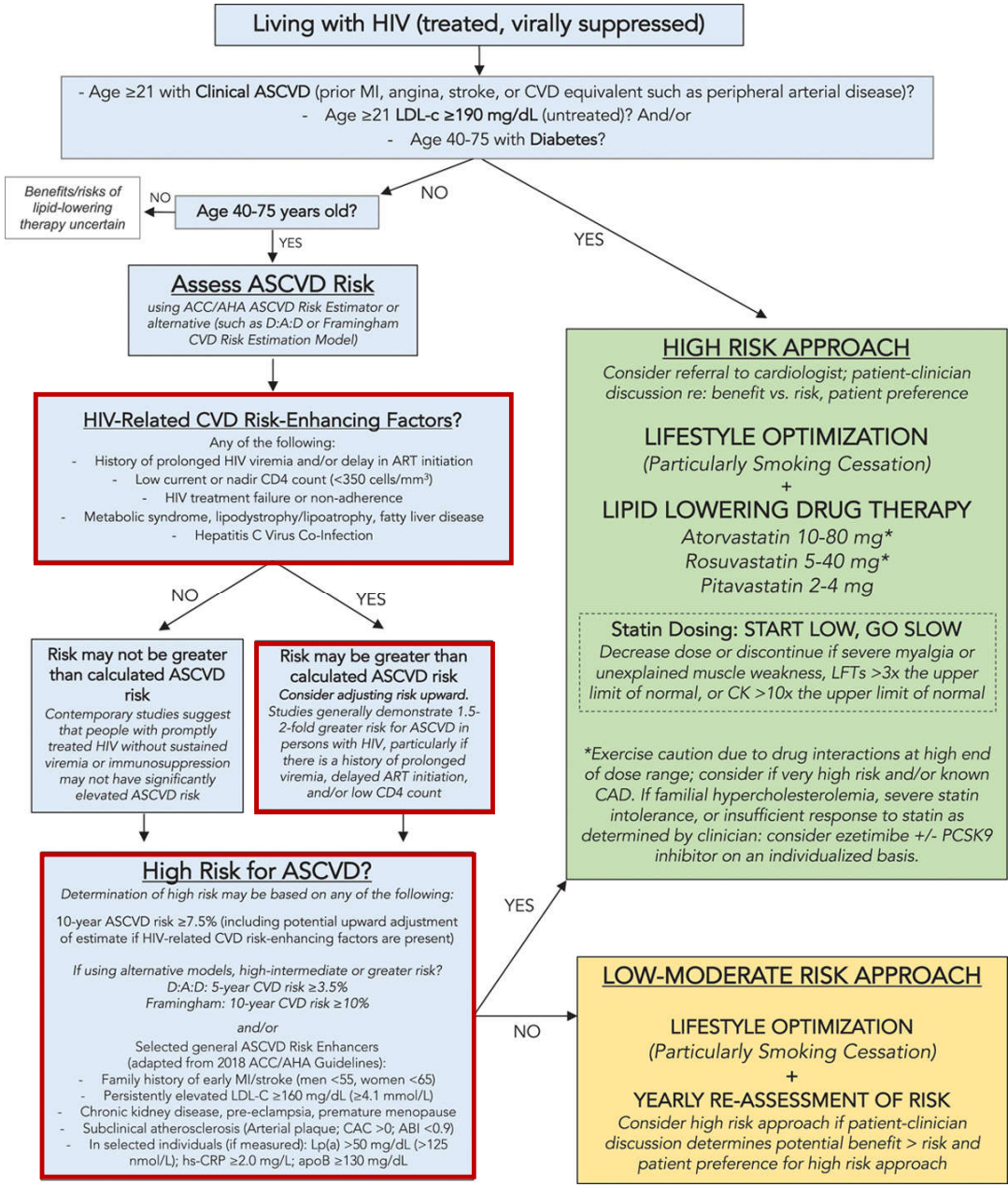

| LDL | BL | T1 | T2 |
|---|---|---|---|
| Number of observations | 466 | 440 | 324 |




| TG | BL | T1 | T2 |
|---|---|---|---|
| Number of observations | 478 | 454 | 341 |

# AHA Prevention of Cardiovascular Disease in PLWHA

- HIV-related CVD risk-enhancing factors
  - History of prolonged HIV viremia and/or delay in ART initiation
  - Low current or nadir CD4 count (<350 cells/mm$^3$)
  - HIV treatment failure or non-adherence
  - Metabolic syndrome, lipodystrophy/ lipoatrophy, fatty liver disease
  - Hepatitis C virus co-infection
- Studies generally demonstrate 1.5-2-fold greater risk for ASCVD in persons with HIV




Feinstein MJ, Hsue PY, Benjamin LA, et al. Circulation. 2019;140(2):e98-e124.

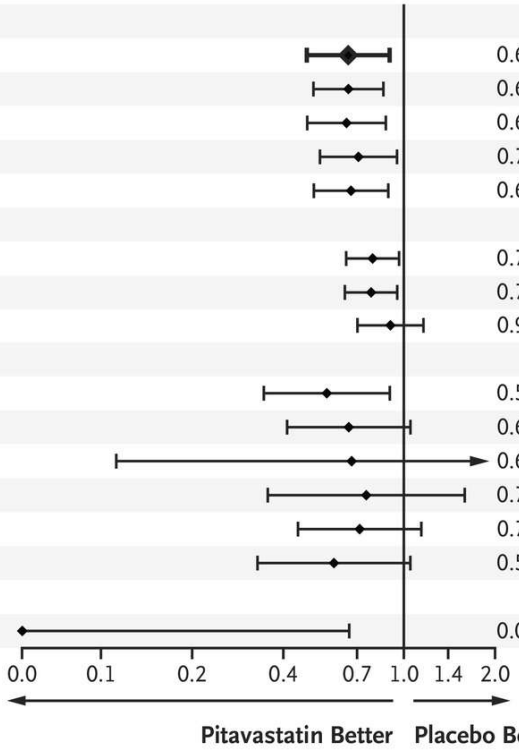
ORIGINAL ARTICLE

# Pitavastatin to Prevent Cardiovascular Disease in HIV Infection

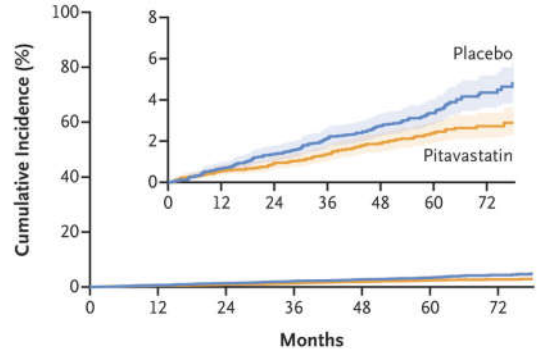
Steven K. Grinspoon, M.D., Kathleen V. Fitch, M.S.N., Markella V. Zanni, M.D., Carl J. Fichtenbaum, M.D., Triin Umbleja, M.S., Judith A. Aberg, M.D., Edgar T. Overton, M.D., Carlos D. Malvestutto, M.D., M.P.H., Gerald S. Bloomfield, M.D., M.P.H., Judith S. Currier, M.D., Esteban Martinez, M.D., Ph.D., Jhoanna C. Roa, M.D., et al., for the REPRIEVE Investigators*

**A Estimated Treatment Effect**

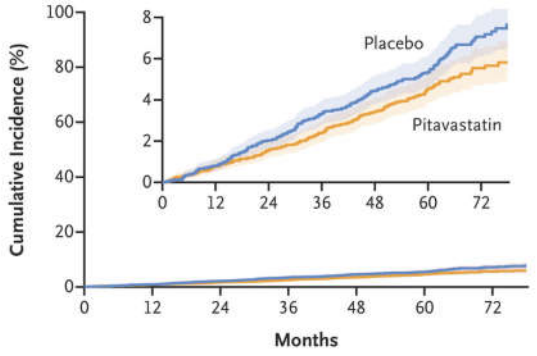
| Subgroup | Pitavastatin (N=3888) no./1000 person-yr (no. of events) | Placebo (N=3881) no./1000 person-yr (no. of events) | Hazard Ratio (95% CI) |
|---|---|---|---|
| Primary outcome and supporting analyses | | | |
| First MACE | 4.81 (89) | 7.32 (136) | 0.65 (0.48 to 0.90) |
| First MACE including vital status follow-up | 4.75 (90) | 7.22 (137) | 0.66 (0.50 to 0.86) |
| First confirmed MACE | 3.83 (71) | 5.92 (110) | 0.65 (0.48 to 0.87) |
| First MACE (as-treated analysis) | 4.44 (77) | 6.25 (107) | 0.71 (0.53 to 0.95) |
| First MACE (per-protocol analysis) | 4.54 (80) | 6.77 (120) | 0.67 (0.50 to 0.89) |
| Secondary outcomes and supporting analyses | | | |
| First MACE or death | 9.18 (170) | 11.63 (216) | 0.79 (0.65 to 0.96) |
| First MACE or death including vital status follow-up | 9.13 (173) | 11.70 (222) | 0.78 (0.64 to 0.95) |
| Death from any cause | 6.17 (116) | 6.83 (129) | 0.90 (0.70 to 1.16) |
| Individual components of MACE | | | |
| First cardiac ischemia or myocardial infarction | 1.40 (26) | 2.51 (47) | 0.56 (0.34 to 0.90) |
| First cerebrovascular event (stroke or TIA) | 1.56 (29) | 2.36 (44) | 0.66 (0.41 to 1.05) |
| First peripheral arterial ischemia | 0.11 (2) | 0.16 (3) | 0.67 (0.11 to 4.02) |
| Death from cardiovascular causes | 0.64 (12) | 0.85 (16) | 0.75 (0.36 to 1.59) |
| Death from cardiovascular or undetermined causes | 1.60 (30) | 2.24 (42) | 0.71 (0.45 to 1.14) |
| First cardiac catheterization or revascularization | 0.97 (18) | 1.66 (31) | 0.59 (0.33 to 1.05) |
| First carotid or cerebrovascular revascularization | 0.00 (0) | 0.00 (0) | — |
| First peripheral arterial revascularization | 0.00 (0) | 0.32 (6) | 0.00 (0.00 to 0.66) |




**B First MACE**




**C First MACE or Death**




| Cumulative Incidence of Event (%) | | | | | | | |
|---|---|---|---|---|---|---|---|
| Placebo | 0.00 | 0.80 | 2.03 | 3.34 | 4.44 | 5.35 | 7.06 |
| Pitavastatin | 0.00 | 0.77 | 1.58 | 2.39 | 3.40 | 4.54 | 5.54 |

Grinspoon SK, Fitch KV, Zanni MV, et al. Pitavastatin to Prevent Cardiovascular Disease in HIV Infection. N Engl J Med. 2023;10.1056/NEJMoa2304146.

# Case 1: 54-year-old man living with HIV

Dec 2021

- CD4 285 cells/mm$^3$ (9%), HIV VL <40 copies/mL, Cr 1.12 mg/dL
- HyperTG: **TG 213 mg/dL**, TC 178 mg/dL, HDL 36 mg/dL, LDL-C 111 mg/dL
- Continue single-pill TDF/FTC/EFV (300/200/600)

June 2022

- HIV VL <40 copies/mL, Cr 1.13 mg/dL
- HyperTG: **TG 299 mg/dL**, TC 186 mg/dL
- Continue single-pill TDF/FTC/EFV (300/200/600) and diet control

# Case 1: 54-year-old man living with HIV

Dec 2022

- CD4 331 cells/mm$^3$ (10%), HIV VL <40 copies/mL,
- Cr 1.10 mg/dL (eGFR 76.2 ml/min/1.73 m$^2$)
- HyperTG**: TG 299 → 170 mg/dL**, TC 209 mg/dL, HDL 51 mg/dL, LDL-C 128 mg/dL
- Switch from TDF/FTC/EFV (300/200/600) to TDF/3TC/DTG (300/300/50)

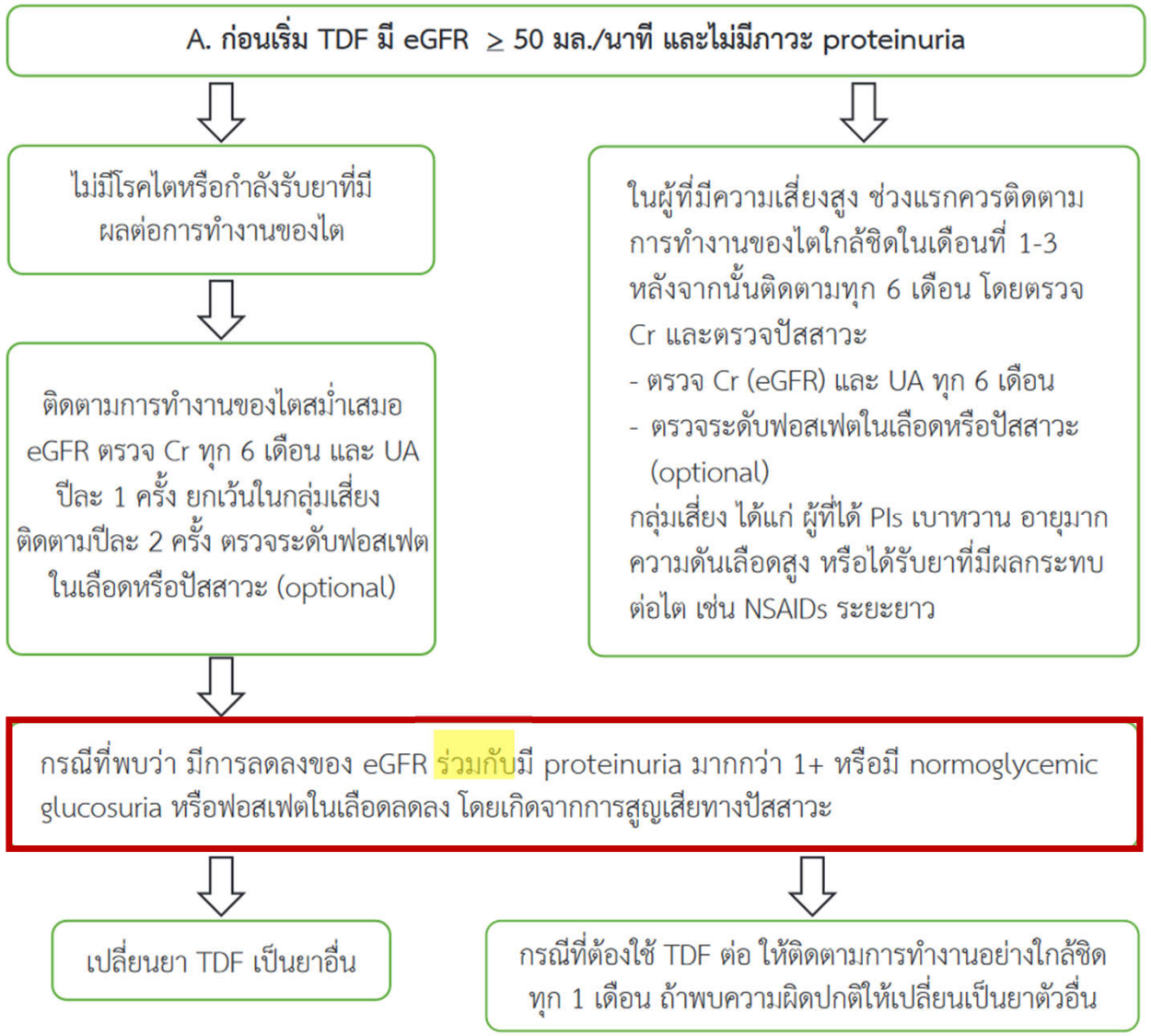
June 2023

- CD4 276 cells/mm$^3$ (11%), HIV VL not detected
- Cr **1.36** mg/dL (eGFR **58.6** ml/min/1.73 m$^2$, ↓**23**%)
- UA: Sp.gr. 1.019, pH 6.0, protein neg, glucose neg, WBC neg, RBC neg
- TG 105 mg/dL, TC 158 mg/dL, HDL 43 mg/dL, LDL-C 101 mg/dL
- Which ART regimen would you choose?

# Which ART regimen would you choose?

A. Continue TDF/3TC/DTG
B. Switch to ABC/3TC + DTG
C. Switch to 3TC + DTG
D. Switch back to TDF/FTC/EFV

# Thailand National Guidelines on HIV/AIDS Treatment and Prevention 2021/2022

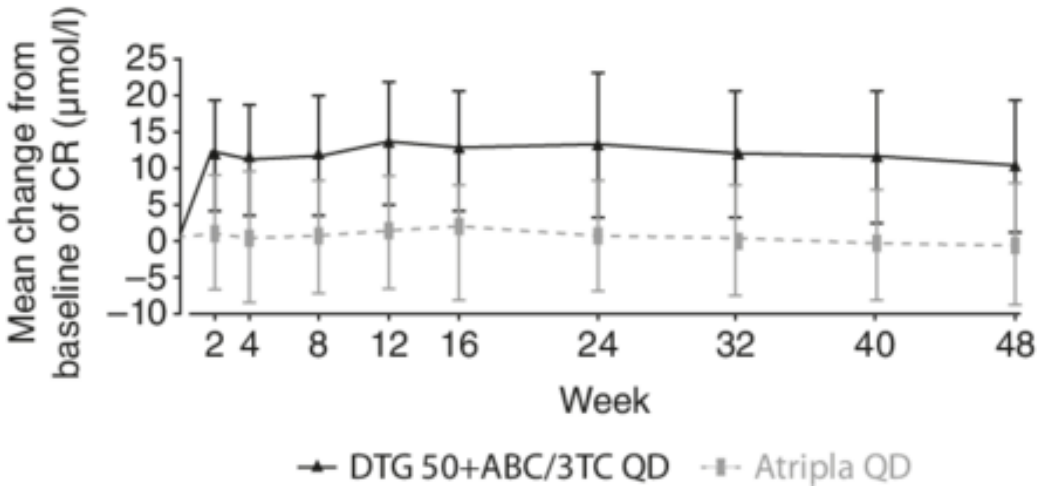


# IDSA and EASC Guidelines

- Avoid use in patients with preexisting CKD[1]
  - GFR <60 mL/minute/1.73 $m^2$
  - CrCl <50 mL/minute
  - Especially if the patient has any proximal tubular impairment
- Use of DTG, BIC, RPV, COBI and PI/b is associated with an increase in serum creatinine/reduction of eGFR (10-15 mL/min or up to 25%)[2]
  - Inhibition of proximal tubular creatinine transporters without impairing actual glomerular filtration
  - Consider new set point after 1-2 months

Clinical Practice Guideline for the Management of Chronic Kidney Disease in Patients Infected With HIV: 2014 Update by the HIV Medicine Association of the Infectious Diseases Society of America

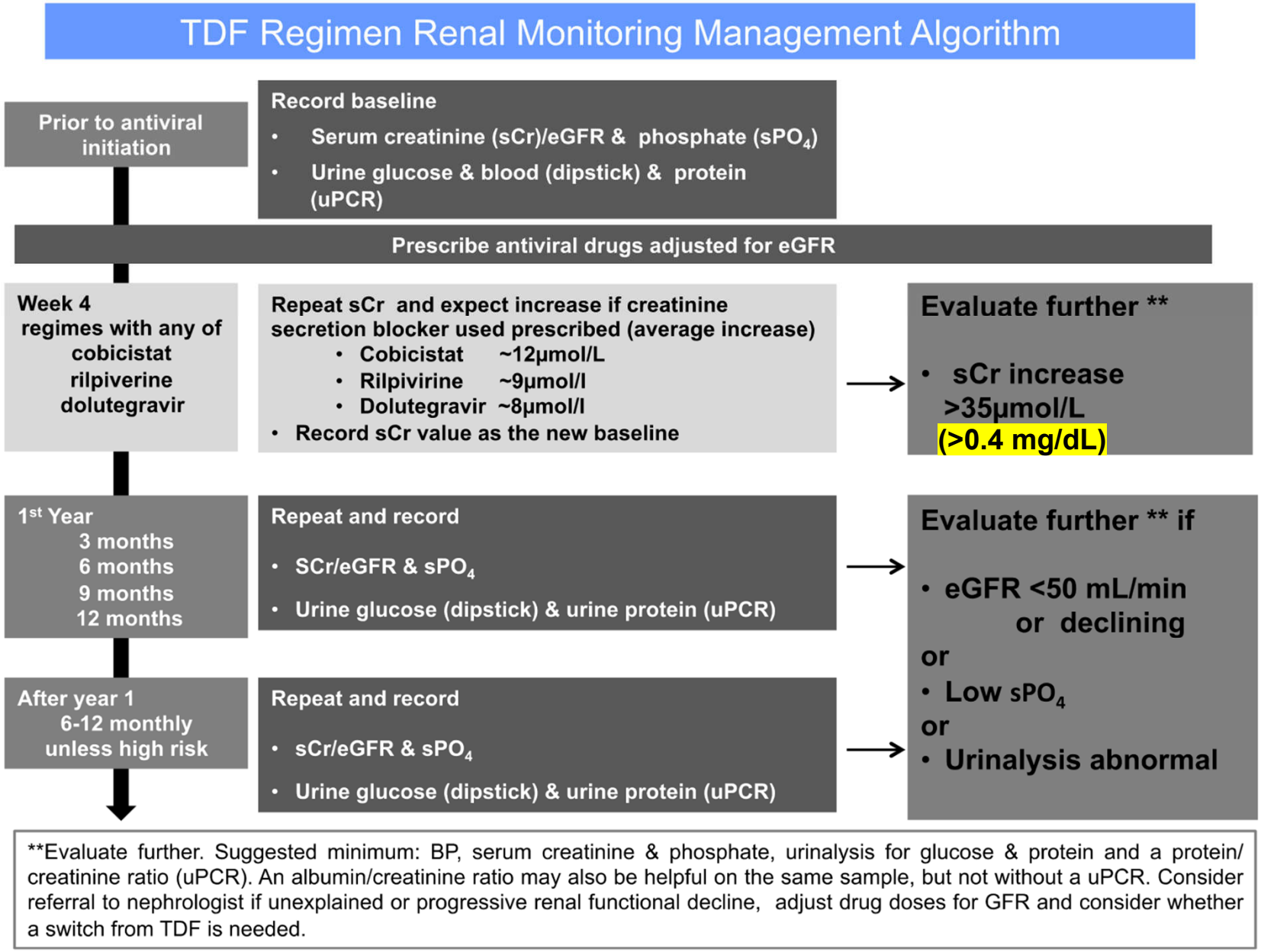
10. In patients infected with HIV who have a GFR <60 mL/minute/1.73 $m^2$, we recommend avoiding tenofovir and other potential nephrotoxic drugs (eg, nonsteroidal anti-inflammatory drugs) when feasible (strong, low).
11. In tenofovir-treated patients who experience a confirmed GFR decline by >25% from baseline and to a level <60 mL/minute/1.73 $m^2$, we recommend substituting alternative antiretroviral drug(s) for tenofovir, particularly in those with evidence of proximal tubular dysfunction (strong, low).




[1]Lucas GM, Ross MJ, Stock PG, et al. Clin Infect Dis. 2014;59(9):e96-e138.
[2]EACS Guidelines V11.1 October 2022

Koteff J, Borland J, Chen S, et al. Br J Clin Pharmacol. 2013;75(4):990-996.

# Suggested Approach for Renal Monitoring




Holt SG, Gracey DM, Levy MT, et al.
AIDS Res Ther. 2014;11:35.

# Which ART regimen would you choose?

A. Continue TDF/3TC/DTG

B. Switch to ABC/3TC + DTG

C. Switch to 3TC + DTG

D. Switch back to TDF/FTC/EFV

# Case 2

# Case 2: 58-year-old woman living with HIV

- Known case HIV infection, GERD, DLP F/U since ’2011
- First visit with new ID specialist
- ART:
  - Switch from AZT/3TC/NVP to d4T/3TC/NVP 27/7/2012
  - Switch from d4T/3TC/NVP to TDF+3TC+NVP 19/9/2014

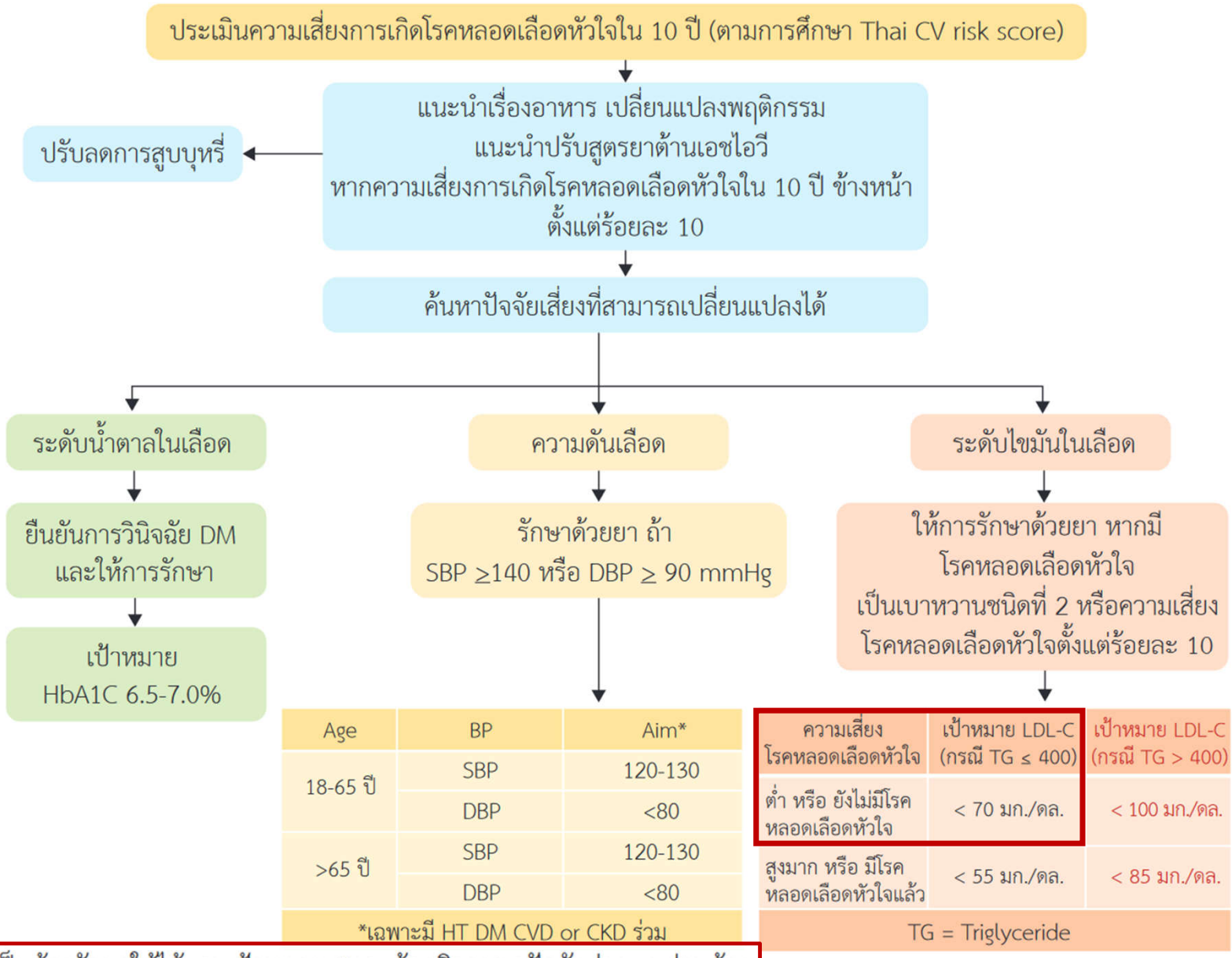
  CD4 1,203 cells/$mm^3$ (39%), HIV VL <40 copies/mL, Cr 0.84 mg/dL
- Medications
  - GERD: self-medication
  - DLP: atorvastatin 40 mg/day

  TG 148 mg/dL, TC 208 mg/dL, HDL 44 mg/dL, LDL-C 140 mg/dL
  - NVP shortage! Which ART regimen would you choose?

# Which ART regimen would you choose?

A. 3TC + DTG
B. TDF/FTC + RPV
C. TDF/FTC/EFV
D. TDF/3TC/DTG

# Thailand National Guidelines on HIV/AIDS Treatment and Prevention 2021/2022



| ยาลดกรดในกระเพาะอาหาร | | |
|---|---|---|
| DTG | Antacid | ให้ DTG ก่อน antacid อย่างน้อย 2 ชม. หรือ ให้หลังอย่างน้อย 6 ชม. หรือพิจารณาใช้ยาลดกรดกลุ่มอื่น |
| ATV, ATV/r | Antacid | ให้ ATV ก่อน Antacid หรือ buffered medicine อย่างน้อย 2 ชม. หรือให้หลังอย่างน้อย 1-2 ชม. |
| | H2 blocker | ให้ boosted ATV พร้อมกับ และ/หรือห่างจากการให้ HRAs อย่างน้อย 10 ชม. |
| | PPI | - ไม่แนะนำให้ใช้ร่วมกับ ATV ในผู้ที่เคยได้ PIs มาก่อน<br>- ในผู้ที่ไม่เคยได้ PIs มาก่อน ให้ PPIs ก่อนการให้ ATV อย่างน้อย 12 ชม. และต้องใช้ boosted ATV เท่านั้น |
| RPV | Antacid | ให้ antacid ก่อน RPV อย่างน้อย 2 ชม. หรือหลังอย่างน้อย 4 ชม. |
| | H2 blocker | ให้ HRAs ก่อน RPV อย่างน้อย 12 ชม. หรือให้หลังอย่างน้อย 4 ชม. |
| | PPI | ไม่แนะนำให้ใช้ร่วมกับ RPV |
| RAL | Antacid | - ห้ามให้ RAL คู่กับ Al-มก. hydroxide antacids พิจารณาให้ยาลดกรดตัวอื่นแทน<br>- ไม่มีความจำเป็นต้องแยกการให้ยาระหว่าง RAL กับ CaCO3 antacid |

Thailand National Guidelines on HIV/AIDS Treatment and Prevention 2021/2022.

# Which ART regimen would you choose?

A. 3TC + DTG

B. TDF/FTC + RPV

C. TDF/FTC/EFV

D. TDF/3TC/DTG

# Case 2: 58-year-old woman living with HIV

- Known case HIV infection, GERD, DLP F/U since ’2011
- First visit with new ID specialist
- ART:
  - Switch from AZT/3TC/NVP to d4T/3TC/NVP 27/7/2012
  - Switch from d4T/3TC/NVP to TDF+3TC+NVP 19/9/2014

  CD4 1,203 cells/$mm^3$ (39%), HIV VL <40 copies/mL, Cr 0.84 mg/dL
- Medications
  - GERD: self-medication
  - DLP: atorvastatin 40 mg/day

  TG 148 mg/dL, TC 208 mg/dL, HDL 44 mg/dL, LDL-C 140 mg/dL
  - Switch to TDF/3TC/DTG (NVP shortage and single-pill)

# Case 2: 58-year-old woman living with HIV

- Second visit (next 6 months)
  - HIV: CD4 819 cells/mm$^3$ (40%), HIV VL <40 copies/mL
  - BW 54.7 → 57.8 kg (↑**3.1** kg)
  - Cr 0.84 → **1.06** mg/dL (eGFR 78.8 → 59.1 ml/min/1.73 m$^2$, ↓**25**%)
  - FBS 94 mg/dL
  - DLP: TG 182 mg/dL, TC **208** → **304** mg/dL, HDL 46 mg/dL, LDL-C **140** → **213** mg/dL
- Management
  - HIV: TDF/3TC/DTG (300/300/50)
  - DLP: atorvastatin 40 mg/day
  - How would you manage ART/dyslipidemia/weight gain?

# How would you manage ART/dyslipidemia/weight gain?

A. Continue TDF/3TC/DTG, diet control, exercise

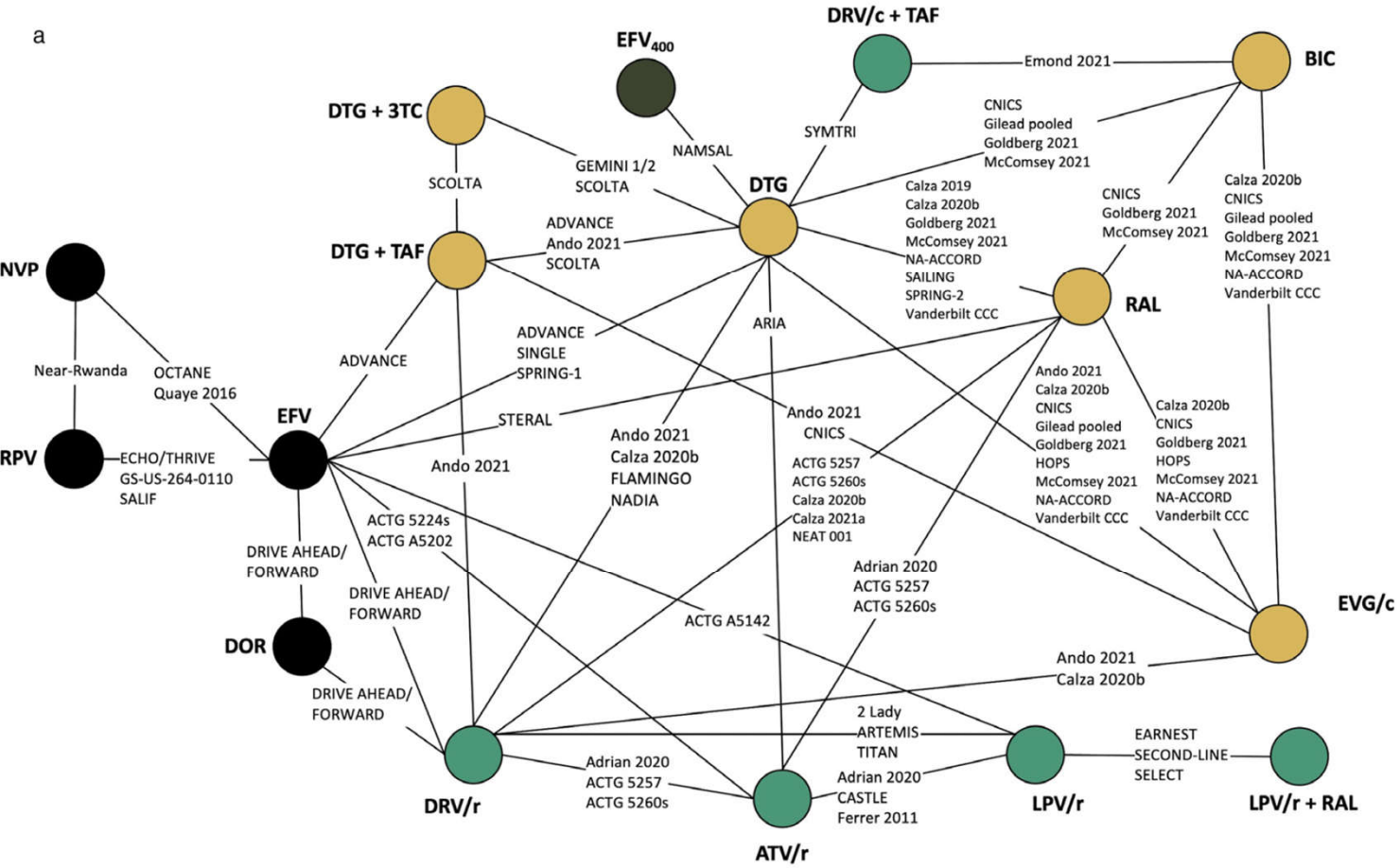
B. Continue TDF/3TC/DTG, diet control, exercise, ↑atorvastatin 80 mg/day

C. Switch to TDF/FTC/EFV

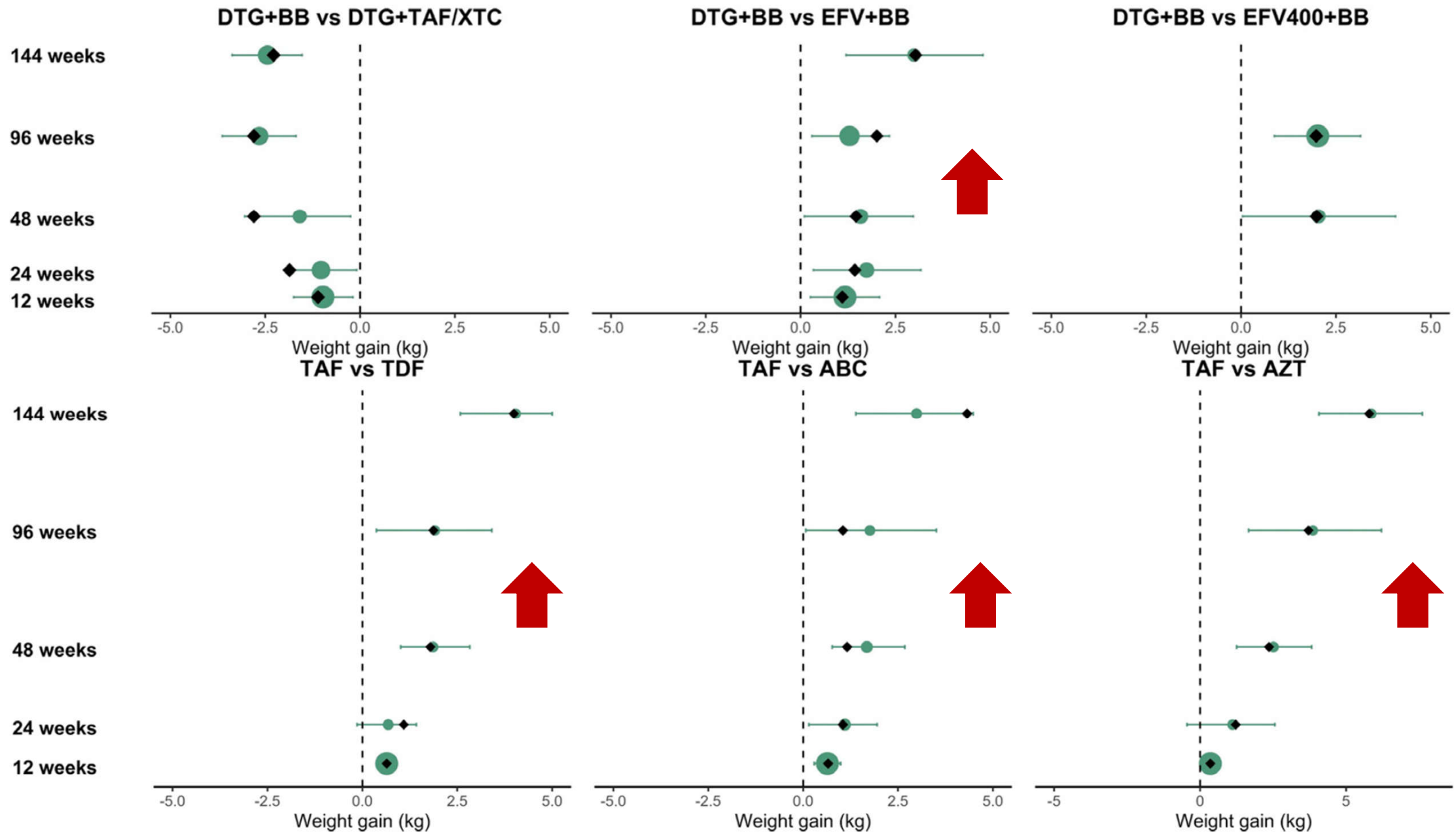
D. Switch to TAF/FTC/DTG

# Evidence synthesis evaluating body weight gain among people treating HIV with antiretroviral therapy - a systematic literature review and network meta-analysis

*Steve Kanters,[a,b,*] Francoise Renaud,[c] Ajay Rangaraj,[c] Kenneth Zhang,[b] Eve Limbrick-Oldfield,[b] Monica Hughes,[d] Nathan Ford,[c] and Marco Vitoria[c]*




Kanters S, Renaud F, Rangaraj A, et al. EClinicalMedicine. 2022;48:101412. Published 2022 May 12.


DTG+BB vs DTG+TAF/XTC
DTG+BB vs EFV+BB
DTG+BB vs EFV400+BB
144 weeks
96 weeks
48 weeks
24 weeks
12 weeks
-5.0
-2.5
0.0
2.5
5.0
Weight gain (kg)
TAF vs TDF
TAF vs ABC
TAF vs AZT
144 weeks
96 weeks
48 weeks
24 weeks
12 weeks
-5.0
-2.5
0.0
2.5
5.0
-5
0
5
Weight gain (kg)

# How would you manage ART/dyslipidemia/weight gain?

A. Continue TDF/3TC/DTG, diet control, exercise

B. Continue TDF/3TC/DTG, diet control, exercise, ↑atorvastatin 80 mg/day

C. Switch to TDF/FTC/EFV

~~D. Switch to TAF/FTC/DTG~~

# Q & A