ENCOUNTER WITH THE NEW HIV PATIENT: COMORBIDITIES

WEERAWAT MANOSUTHI, MD

BAMRASNARADURA INFECTOUS DISEASES INSTITUTE, MOPH

CASE PRESENTATION

- A 63-year-old man recently diagnosed with HIV infection presents to initiate ART.
- Baseline testing revealed a CD4 of 220 cells/mm^3, HIV-1 RNA of 155,000 copies/mL. Serum creatinine was 1.6 mg/dL (eGFR 49 mL/min), LDL cholesterol was 92 mg/dL, HDL was 38 mg/dL, and HbA1C was 7.2%.
- His BMI was 27, and he was hypertensive and receiving of enalapril 20 mg and amlodipine 10 mg . His diabetes was controlled by 1,000 mg of metformin. He experienced a MI 8 years ago and receiving beta-blocker, ASA, and atorvastatin 40 mg. He has reactive airways disease, which is controlled with the inhaled steroid fluticasone.

Q1: What backbone NRTI would you prescribe for this patient?

A. ABC/3TC
B. TDF/FTC
C. TAF/FTC
D. 3TC ONLY
E. I wouldn't use NRTI

CASE PRESENTATION

- A 63-year-old man recently diagnosed with HIV infection presents to initiate ART.
- Baseline testing revealed a CD4 of 220 cells/mm^3, HIV-1 RNA of 155,000 copies/mL. Serum creatinine was 1.6 mg/dL (eGFR 49 mL/min), LDL cholesterol was 92 mg/dL, HDL was 38 mg/dL, and HbA1C was 7.2%.
- His BMI was 27, and he was hypertensive and receiving of enalapril 20 mg and amlodipine 10 mg . His diabetes was controlled by 1,000 mg of metformin. He experienced a MI 8 years ago and receiving beta-blocker, ASA, and atorvastatin 40 mg. He has reactive airways disease, which is controlled with the inhaled steroid fluticasone.

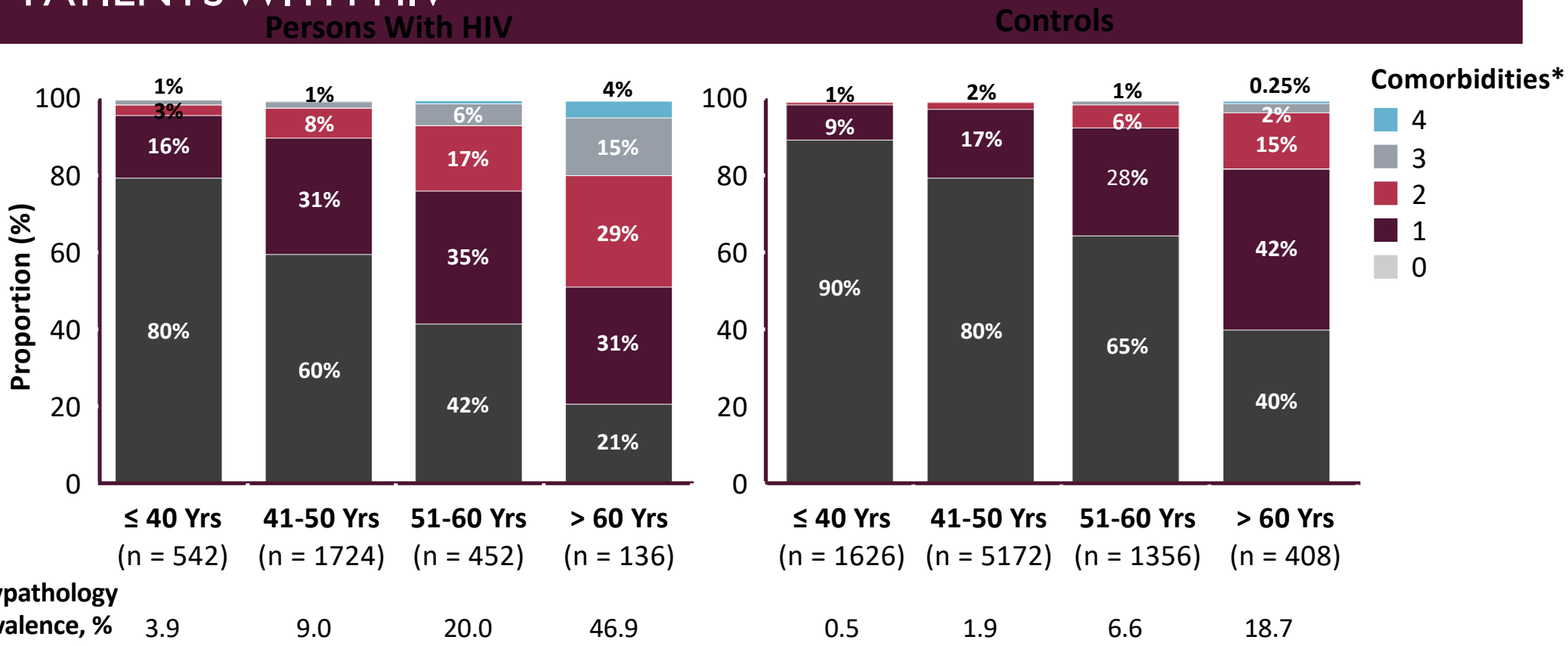
Q2: What anchor agent would you prescribe?

A. Dolutegravir
B. Raltegravir
C. Evitegravir/c
D. Efavirenz
E. Rilpivirine
F. Boosted protease inhibitor
G. Something else

CONSIDERATIONS WHEN SELECTING ART IN AGING PATIENTS WITH COMORBIDITIES

- How to achieve or maintain undetectable viral load
  - How to minimize the effect on comorbidities
    - How to avoid drug-drug interactions
- How to modify ARV according to baseline kidney and liver function

COMORBIDITIES INCREASE WITH AGE BUT ARE MORE COMMON IN PATIENTS WITH HIV

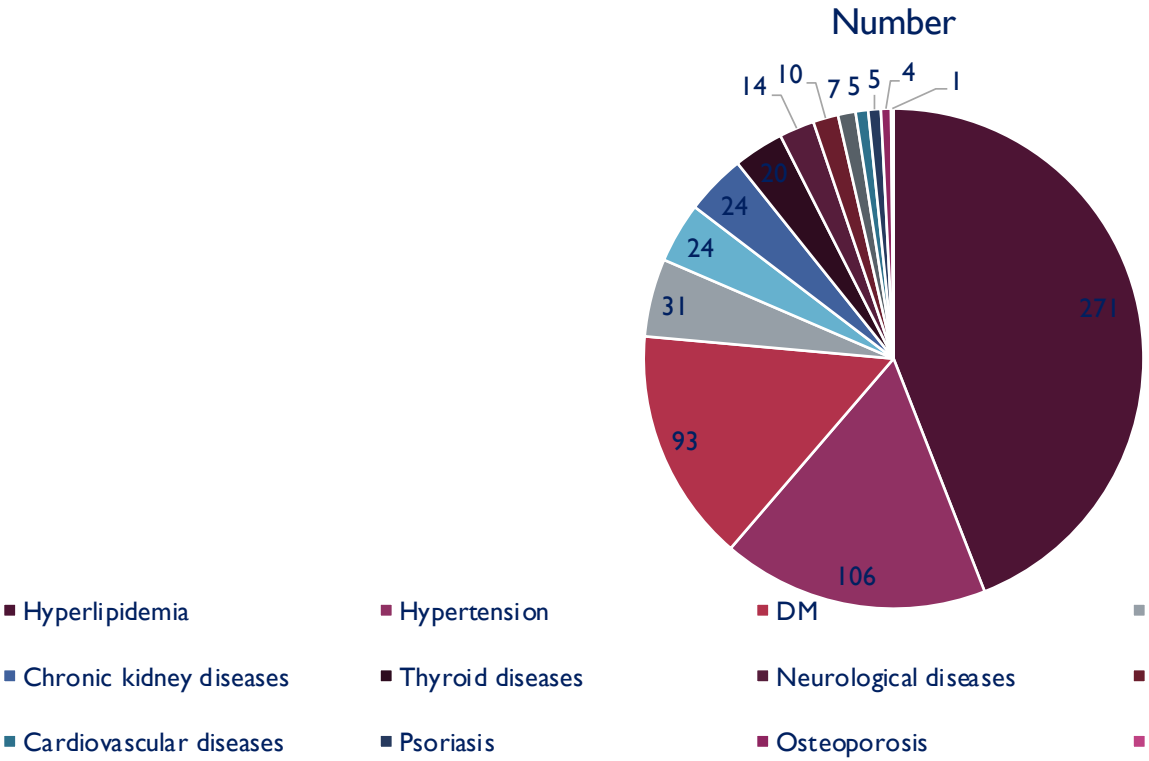


*Includes evaluation of HTN, diabetes, hypothyroidism, CVD, and bone fracture.

Guaraldi. Clin Infect Dis. 2011;53:1120.

PREVALENCE OF NON-AIDS COMORBIDITIES AMONG HIV-INFECTED PATIENTS AT BAMRASNARADURA INSTITUTE (N=874)

- 388 patients had comorbidities, Metabolic complications (Lipid, HT, DM , Impair glucose) 89.4%

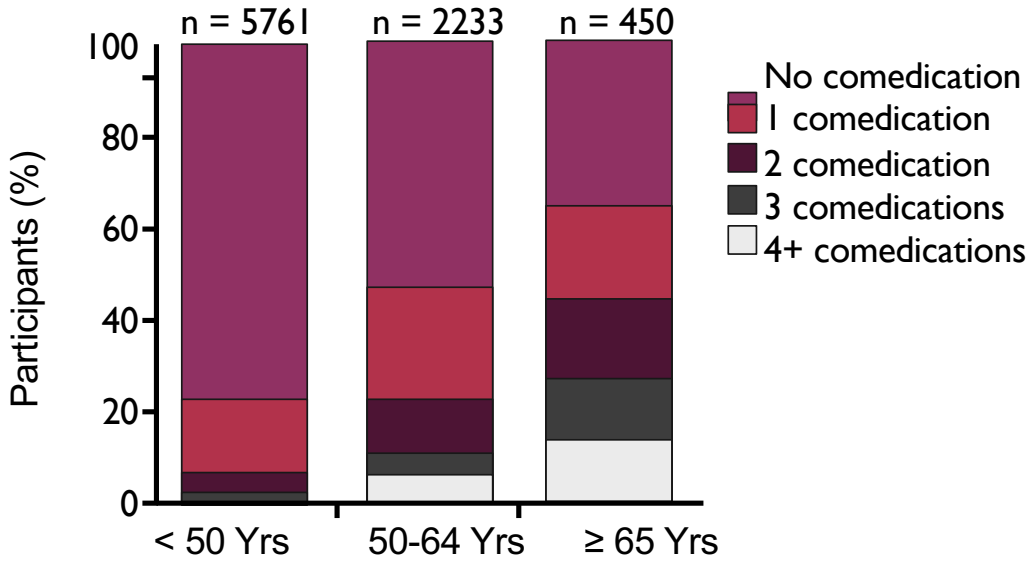


- Hyperlipidemia 69.8%
- HT 27.3%
- DM 23.9%
- Impair fasting glucose 7.9%
- Viral Hepatitis 6.2%
- CKD 6.2%
- Cardiovascular disease 1.3%

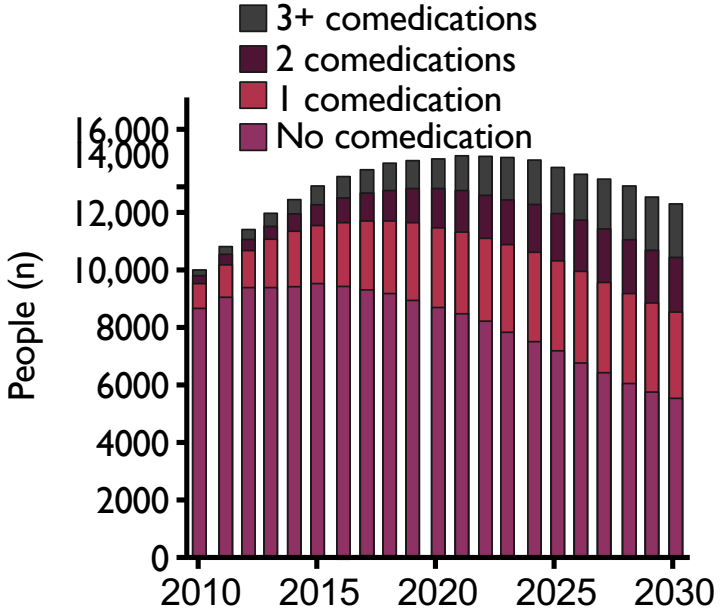
Nakaranurack C, Manosuthi W. et al. J Int Assoc Provid AIDS Care. 2018 17 1-6.

BEWARE OF INTERACTIONS: POLYPHARMACY AMONG HIV-INFECTED PATIENTS ON ART

Swiss HIV Cohort Study (N = 8444)[1]
Prospective Observational Study



ATHENA Modeling Study[2]

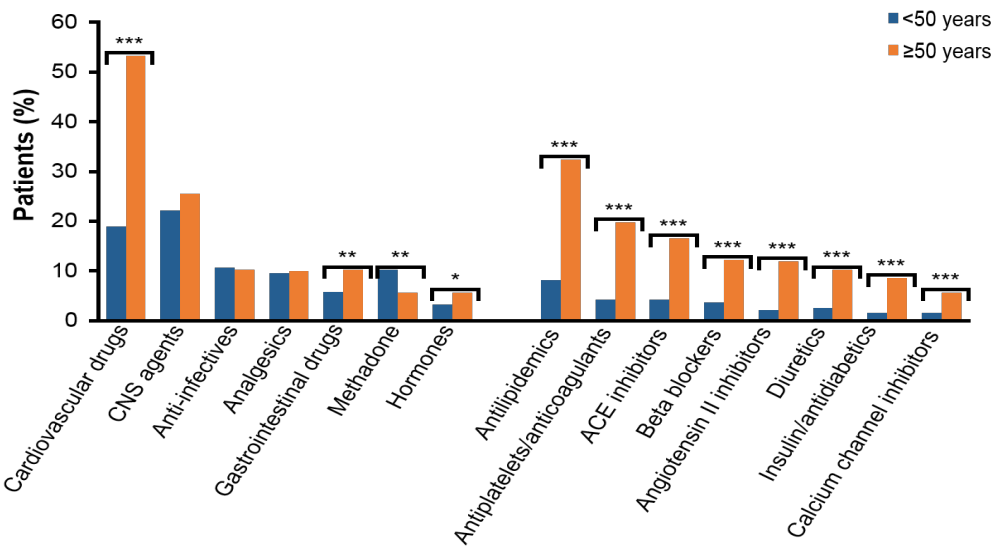


- 5.2% of patients 50-64 yrs of age and 14.2% of patients ≥ 65 yrs of age received ≥ 4 meds other than ART
- Predicts that 20% of patients will be receiving ≥ 3 meds other than ART in 2030

1. Hasse B, et al. Clin Infect Dis. 2011;53:1130-1139. 2. Smit M, et al. Lancet Infect Dis. 2015;15:810-818.

THE RISK OF POTENTIAL DDI INCREASES IN OLDER HIV+ PATIENTS

- Drug prescriptions were analysed for 1,497 HIV-infected individuals
- The risk for potential DDIs with ART* increased in older patients relative to younger patients with HIV
- Potential DDIs with ART occurred mainly with cardiovascular drugs (27%), CNS agents (22%) and methadone (6%) in older patients[1†]



* Patients were classified as receiving a PI, NNRTI, PI+NNRTI or other-based regimen. † Detailed use of cardiovascular drugs is presented on the right-hand side. CNS agents included anxiolytics/sedatives, antidepressants, antipsychotics and anticonvulsants. Anti-infectives included antibacterials, antivirals, antifungals and antimycobacterials. Analgesics included anti-inflammatory drugs, paracetamol and narcotic analgesics. Gastrointestinal drugs included proton pump inhibitors, antidiarrhoea drugs and H2 blockers.

ACE, angiotensin-converting-enzyme; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor.

[1] Marzolini C, *et al. J Antimicrob Chemother* 2011; **66**:2107–2111.

CASE PRESENTATION

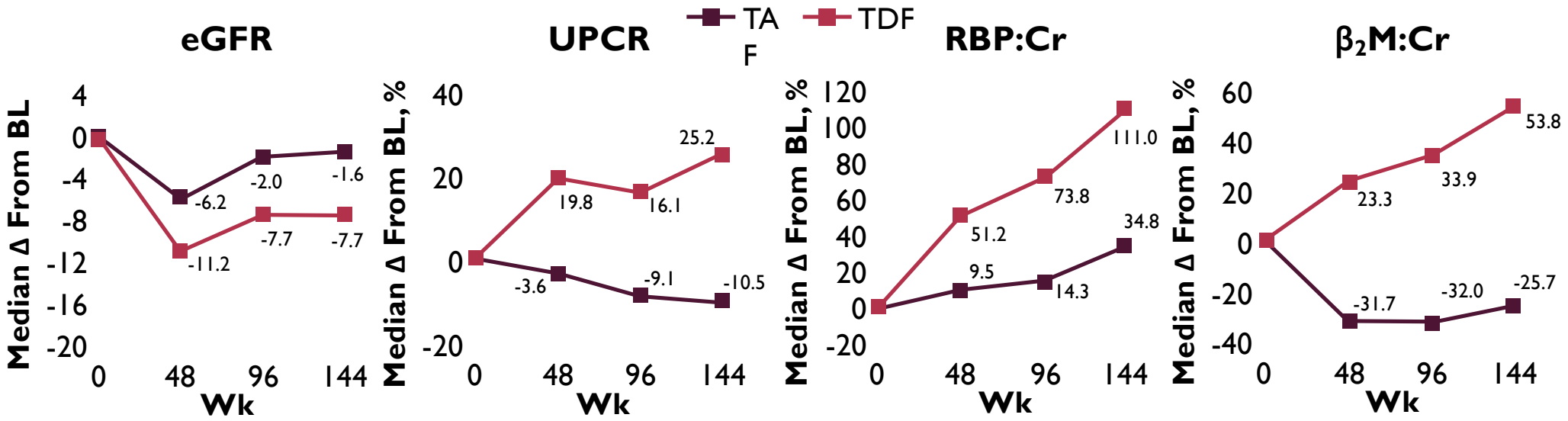
- A 63-year-old man recently diagnosed with HIV infection presents to initiate ART.
- Baseline testing revealed a CD4 of 220 cells/mm^3, HIV-1 RNA of 155,000 copies/mL. Serum creatinine was 1.6 mg/dL (eGFR 49 mL/min), LDL cholesterol was 92 mg/dL, HDL was 38 mg/dL, and HbA1C was 7.2%.
- His BMI was 27, and he was hypertensive and receiving of enalapril 20 mg and amlodipine 10 mg . His diabetes was controlled by 1,000 mg of metformin. He experienced a MI 8 years ago and receiving beta-blocker, ASA, and atorvastatin 40 mg. He has reactive airways disease, which is controlled with the inhaled steroid fluticasone.

Q1: What backbone NRTI would you prescribe for this patient?

A. ABC/3TC
B. TDF/FTC
C. TAF/FTC
D. 3TC ONLY
E. I wouldn't use NRTI

RENAL SAFETY OF FIRST-LINE TAF VS TDF

- Superior virologic efficacy, less renal toxicity at Wk 144 with TAF-based vs TDF-based ART



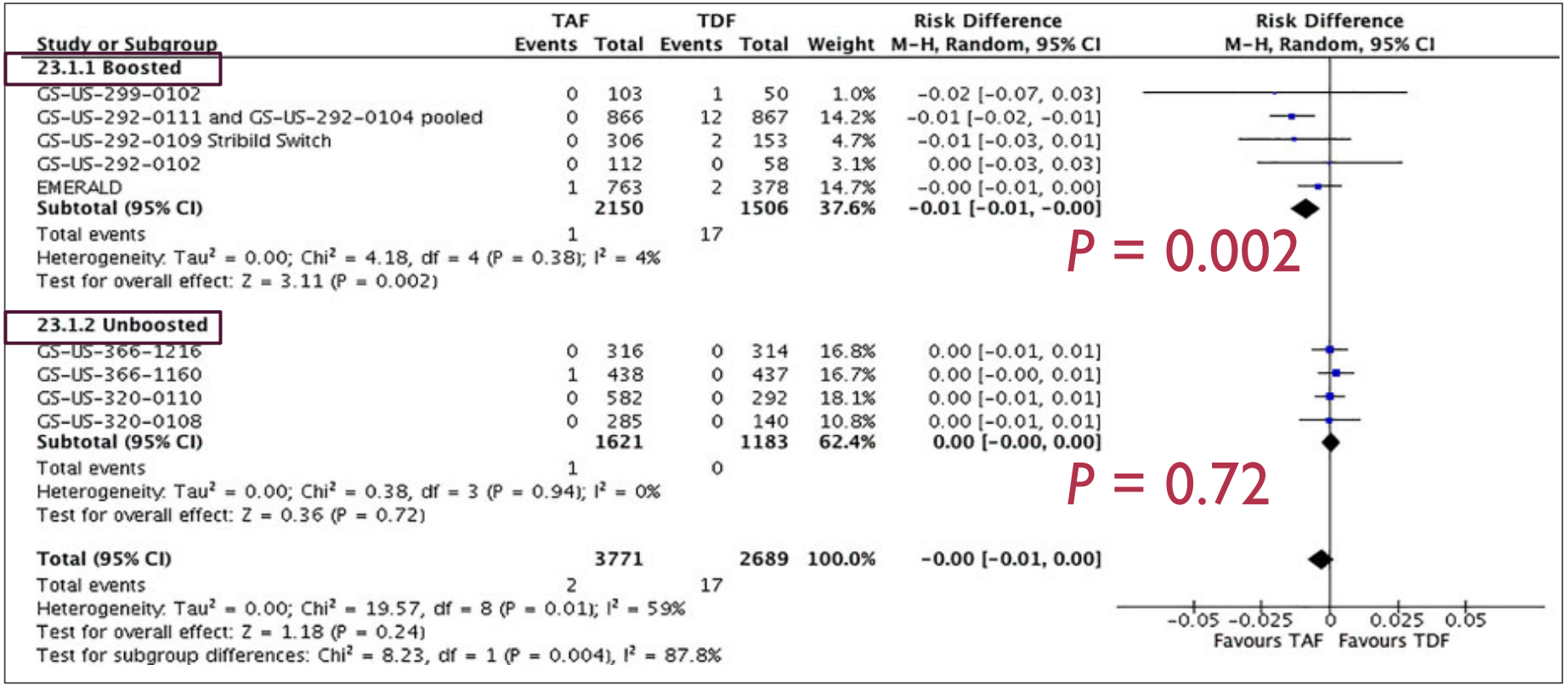
Patients at Risk,

n	821	771	740		866	819	768	740		855	812	769	728		848	803	761	722
866	806	756	707		866	801	751	699		855	800	746	687		848	789	737	681
867																		

P < .001 at all timepoints for all parameters.

Arribas J, et al. J Acquir Immune Defic Syndr 2017;75:211–218.

RENAL IMPACT OF TDF DEPENDS ON CONCOMITANT BOOSTING



Hill A, et al. Journal of Virus Eradication 2018; 4: 72–79.

ABC USE AND CVD EVENT RISK

- Multiple studies have identified increased risk of MI or overall CVD events with ABC use, including large cohort studies, RCTs, and case-control studies[1-10]
  - Range of risk estimates across studies: **1.3- to 4.3-fold** increase
- Other studies have demonstrated a lack of increased CVD risk with ABC use, including large cohort studies, a meta-analysis of RCTs, and a case-control study[10-14]

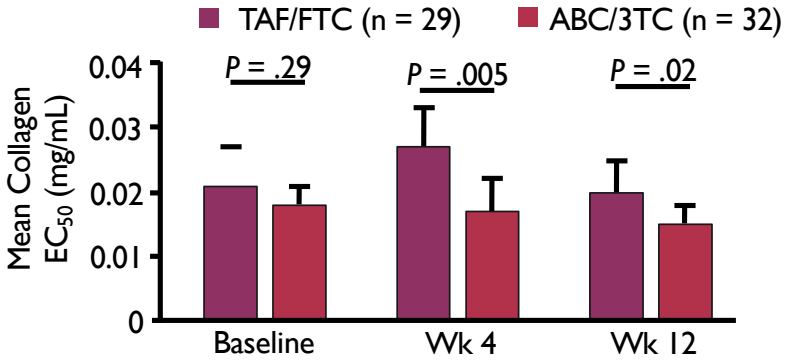
References:

1. Friis-Moller N, et al. Eur J Cardiovasc Prev Rehabil. 2010;17:491-501. 2. Friis-Moller N, et al. Eur J Prev Cardiol. 2016;23:214-223.
3. SMART/INSIGHT Study Group. AIDS. 2008;22:F17-F24. 4. Martin A, et al. Clin Infect Dis. 2009;49:1591-1601.
5. Durand M, et al. J Acquir Immune Defic Syndr. 2011;57:245-253. 6. Obel N, et al. HIV Med. 2010;11:130-136.
7. Choi AI, et al. AIDS. 2011;25:1289-1298. 8. Young J, et al. J Acquir Immune Defic Syndr. 2015;69:413-421.
9. Rotger M, et al. Clin Infect Dis. 2013;57:112-121. 10. Palella F, et al. CROI 2015. Abstract 749LB.
11. Lang S, et al. Arch Intern Med. 2010;170:1228-1238. 12. Ribaudo HJ, et al. Clin Infect Dis. 2011;52:929-940.
13. Bedimo RJ, et al. Clin Infect Dis. 2011;53:84-91. 14. Ding X, et al. J Acquir Immune Defic Syndr. 2012;61:441-447.

NA-ACCORD: RECENT ABC USE ASSOCIATED WITH RISK OF MI

- Analysis of 8265 ART recipients with 29,077 PYFU and 123 MI events in NA-ACCORD[1]
  - MI risk increased with recent ABC use (ie, in previous 6 mos)
  - Adjusted HR: 1.84 (95% CI: 1.17-2.91)
- Potential mechanism: enhanced platelet activation?

- PLT substudy of randomized, phase III Study 1717 (n = 61)[2]
  - Lower collagen EC_{50} (ie, more reactive PLTs) with ABC/3TC vs TAF/FTC at Wks 4 and 12



1. Elion RA, et al. J Acquir Immune Defic Syndr. 2018;[Epub ahead of print]. 2. Mallon PW, et al. CROI 2018. Abstract 80.

CHARACTERISTICS OF RECOMMENDED DUAL-NRTI OPTIONS IN THAILAND

	ABC/3TC	TAF/FTC	TDF/FTC	TDF+3TC
Adverse Effects	ABC: - HSR to ABC is associated with the presence of HLA- B*5701 - Increase in CV events is associated with ABC use in some, but not all, cohort studies	TAF: - Renal insufficiency, proximal renal tubulopathy (less frequent than with TDF) - Decrease in BMD (less than with TDF)	TDF: - Renal insufficiency, proximal renal tubulopathy - Decrease in BMD - Renal and bone toxicity are exacerbated by pharmacologic boosters	TDF: - Renal insufficiency, proximal renal tubulopathy - Decrease in BMD - Renal and bone toxicity are exacerbated by pharmacologic boosters
Other Considerations	- Perform HLA-B*5701 testing before initiating ABC; if result is positive, do not start ABC and add ABC to allergy list - If HIV RNA >100,000 copies/ mL, use only with DTG	- Also used for HBV treatment - Discontinuation may precipitate flair of HBV		

CASE PRESENTATION

- A 63-year-old man recently diagnosed with HIV infection presents to initiate ART.
- Baseline testing revealed a CD4 of 220 cells/mm^3, HIV-1 RNA of 155,000 copies/mL. Serum creatinine was 1.6 mg/dL (eGFR 49 mL/min), LDL cholesterol was 92 mg/dL, HDL was 38 mg/dL, and HbA1C was 7.2%.
- His BMI was 27, and he was hypertensive and receiving of enalapril 20 mg and amlodipine 10 mg . His diabetes was controlled by 1,000 mg of metformin. He experienced a MI 8 years ago and receiving beta-blocker, ASA, and atorvastatin 40 mg. He has reactive airways disease, which is controlled with the inhaled steroid fluticasone.

Q2: What anchor agent would you prescribe?

A. Dolutegravir
B. Raltegravir
C. Evitegravir/c
D. Efavirenz
E. Rilpivirine
F. Boosted protease inhibitor
G. Something else

DHHS: CONSIDERATIONS FOR INITIAL ART BASED ON AGE-RELATED COMORBIDITY

Scenario	Consider Avoiding	Options for Consideration*	
		Agent	Caveat
CKD (eGFR < 60 mL/min)	▪ TDF, especially in RTV-containing regimens	▪ FTC/TAF ▪ ABC/3TC ▪ DRV/RTV + RAL ▪ DRV/RTV + 3TC ▪ DTG + 3TC	▪ If eGFR > 30 mL/min ▪ If HLA-B*5701 negative; 3TC requires dose adjustment if CrCl < 50 mL/min ▪ If TAF or ABC cannot be used; if HIV-1 RNA < 100,000 copies/mL and CD4+ cell count > 200 cells/mm^3 ▪ If TAF or ABC cannot be used; 3TC dose adjustment if CrCl < 50 mL/min
Osteoporosis	▪ TDF	▪ FTC/TAF ▪ ABC/3TC	▪ If HLA-B*5701 negative
CVD risk	▪ ABC	▪ DTG-, RAL-, or RPV-based regimens	▪ If choosing boosted PI, ATV may be preferable to DRV, but further study needed
Hyperlipidemia	▪ PI/RTV or PI/COBI ▪ EVG/COBI	▪ DTG-, RAL-, or RPV-based regimens ▪ TDF associated with lower lipid levels vs ABC or TAF	

*This section of the guidelines has not yet been updated to reflect February 2018 FDA approval of BIC/FTC/TAF.

DHHS Guidelines. July 2019.

ART AND EFFECTS ON LIPIDS

TDF

TAF
RAL
DTG
BIC

RPV
ETV

ABC

EFV

ATV/RTV or ATV/COBI
DRV/RTV or DRV/COBI
EVG/COBI

SELECTING INSTI-BASED MAINTENANCE REGIMENS: SPECIAL CONSIDERATIONS

Agent(s)	Backbone	Key DDIs*	Food Requirement?
All regimens		Polyvalent cation–containing supplements/ medications (including antacids), rifampin	
BIC	FTC/TAF	Metformin	
DTG	ABC/3TC	Metformin	
	FTC/TAF	Metformin	
	FTC/TDF	Metformin	
	RPV	Metformin, PPIs	✓
EVG/ COBI	FTC/TAF	Statins, inhaled/injected/systemic steroids	✓
	FTC/TDF	Statins, inhaled/injected/systemic steroids	✓
RAL	FTC/TAF		
	FTC/TDF		

*Consider **www.hiv-druginteractions.org** to assist with identifying potential interactions for all regimens.

SELECTING PI- OR NNRTI-BASED MAINTENANCE REGIMENS: SPECIAL CONSIDERATIONS

Agent	Backbone	STR?	Key DDIs*	Food Requirement?
Boosted ATV or DRV	NRTI backbone		Statins, inhaled/injected/systemic steroids, PPIs	✓
				✓
				✓
RPV	FTC/TAF	✓	PPIs	✓
	FTC/TDF	✓		✓

*Consider **www.hiv-druginteractions.org** to assist with identifying potential interactions for all regimens.

DHHS AND IAS-USA RECOMMENDATIONS ON 1ST LINE 2 DRUG REGIMENS

DHHS 2019

- Consider when TAF, TDF, and ABC are not desirable or optimal
  - DR V/r + RAL (VL <100K, CD4 >200)
  - DRV/r + 3TC
  - DTG + 3TC

IAS-USA 2018

- Only when TAF, TDF, and ABC can not be used
  - DR V/r + RAL (VL <100K, CD4 >200)
  - DRV/r + 3TC

CASE PRESENTATION

- A 63-year-old man recently diagnosed with HIV infection presents to initiate ART.
- Baseline testing revealed a CD4 of 220 cells/mm^3, HIV-1 RNA of 155,000 copies/mL. Serum creatinine was 1.6 mg/dL (eGFR 49 mL/min), LDL cholesterol was 92 mg/dL, HDL was 38 mg/dL, and HbA1C was 7.2%.
- His BMI was 27, and he was hypertensive and receiving of enalapril 20 mg and amlodipine 10 mg . His diabetes was controlled by 1,000 mg of metformin. He experienced a MI 8 years ago and receiving beta-blocker, ASA, and atorvastatin 40 mg. He has reactive airways disease, which is controlled with the inhaled steroid fluticasone.

The recommended ARV regimen would be…….
1. TAF/FTC + RAL
2. TAF/FTC + DTG (lower MFM dosage)
3. TXF/FTC + EFV

THANK YOU