BHIVA treatment guidelines:
interim statement on two-drug regimens

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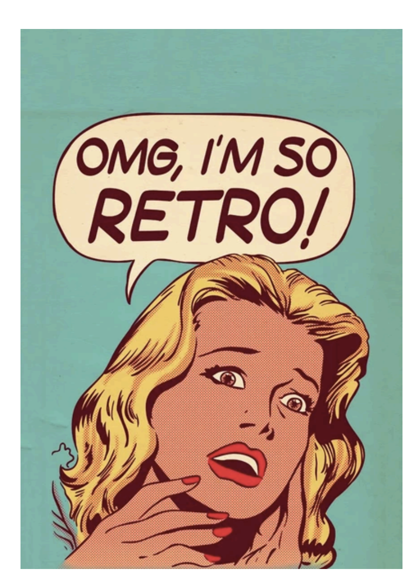
Disclosures

- Conference support, speaker/advisory fees from Gilead, ViiV, Janssen, Mylan, Cipla & MSD
- Investigator on Gilead & Janssen trials

Sorry, but….

- **It's only this year that has seen new products & strategies requiring a guidelines update**
  - Biktarvy
  - Dolutegravir-based 2DR
  - Doravirine
- **Following GRADE is not speedy**
- **Significant organisational change**



What do you think?

Does the lack of updated BHIVA guidance affect:

1. Your ability to prescribe new options?
2. Your confidence in prescribing new options?

WHAT DO OTHER GUIDELINES SAY ABOUT 2DR FOR INITIAL THERAPY?

DHHS guidelines: October 2018

Recommended in certain clinical situations

INSTI + 2 NRTI	
TAF/FTC/EVG/c or TDF/FTC/EVG/c (BI)	
ABC/3TC + RAL (CII)	If VL <100k
PI/b + 2 NRTI	
ATV/r or /c + TAF/FTC or TDF/FTC (BI)	In general DRV preferred to ATV
DRV/r or /c + TAF/FTC or TDF/FTC (AI)	
DRV/r or /c + ABC/3TC (BII)	
NNRTI + 2 NRTI	
DOR/TDF/3TC (BI) or DOR + TAF/FTC (BIII)	
EFV/TDF/FTC or EFV/TDF/3TC (BI) or EFV + TDF/FTC (BII)	EFV 600mg
RPV/TAF/FTC or RPV TDF/FTC	VL <100k and CD4 >200
Consider when ABC, TAF, & TDF Can't be Used or Aren't Optimal	
DTG + 3TC (BI) or DRV/r + 3TC (CI)	
DRV/r OD + RAL BD	If VL <100k and CD4 >200

EACS guidelines v9.1: October 2018

Alternative (when no preferred regimens feasible or available)

INSTI + 2 NRTI	
TAF/FTC/EVG/c or TDF/FTC/EVG/c	
ABC/3TC + RAL	If VL <100k
PI/b + 2 NRTI	
ATV/r or /c + TAF/FTC or TDF/FTC or ABC/3TC	
DRV/r or /c + ABC/3TC	
NNRTI + 2 NRTI	
ABC/3TC + EFV	If VL <100k
TDF/FTC/EFV	
Other	
DTG + 3TC	If VL <500k
DRV/r or DRV/c OD + RAL BD	If VL <100k and CD4 >200

What does BHIVA say about 2DR now?

5.5.2 Recommendation

- We suggest the use of DRV/r + RAL in treatment-naïve patients with CD4 >200 & VL <100,000 if need to avoid abacavir, tenofovir-DF or tenofovir-AF (2A)
- We recommend against the use of PI-based dual ART with a single NNRTI, NRTI or CCR5 receptor antagonist for treatment-naïve patients (1B)

What about switch?

BHIVA

- We suggest a PI/r + 3TC as an alternative to three-drug ART in individuals with viral suppression (2A)

EACS: strategies not associated with virological rebound vs 2DR

- DTG + RPV
- 3TC + (DRV/r or DRV/c) or
- 3TC + (ATV/r or ATV/c)

DHHS successful suppressed 2DR to 3DR switch strategies

- DTG + RPV
- Boosted PI + 3TC

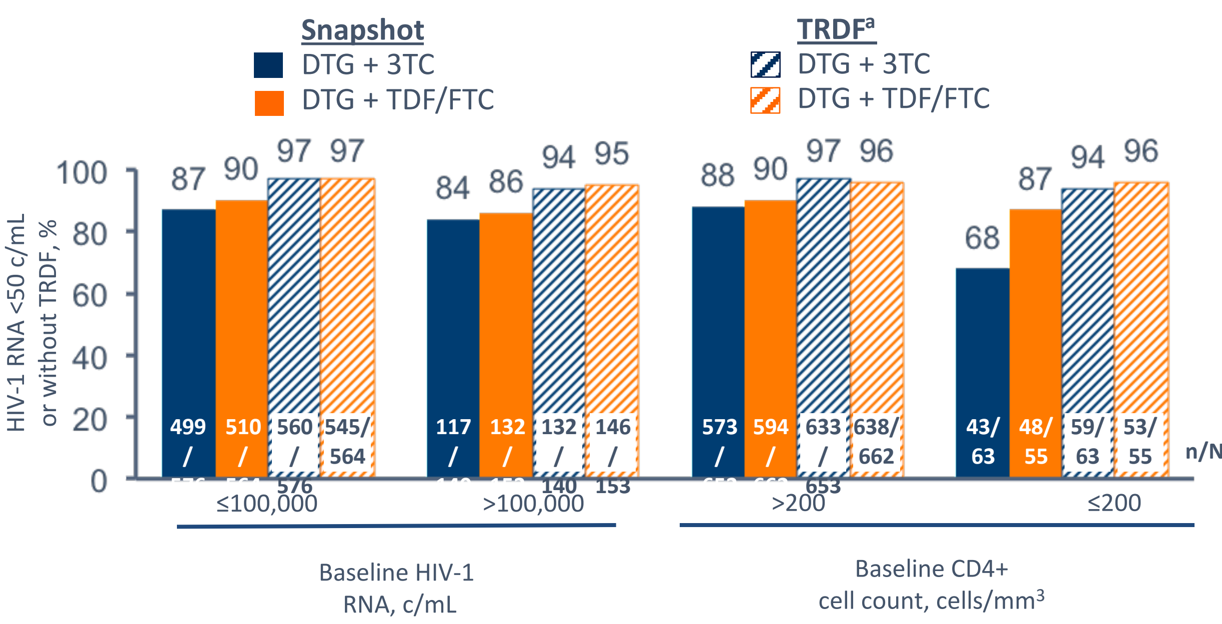
INTERIM ADVICE ON DTG-BASED 2DR

Initial therapy

- **Based on end-points & analyses used previously, DTG + 3TC will be an option for initial therapy with**
- **caveats**
  - Hepatitis B (infection or lack of immunity)
  - Genotype
  - VL >500,000 and/or CD4 <200
  - Special populations

GEMINI W96 suppression by CD4 & VL:

snapshot and TRDF analyses



At Week 96, there were 3 confirmed virologic withdrawals in the DTG + 3TC group and 2 in the DTG + TDF/FTC group in the CD4 ≤ 200 stratum

Cahn et al. IAS 2019; Mexico City, Mexico. Slides WEAB0404LB.

Do people with low CD4 in trials represent people with advanced HIV?

- Most CDC-C diagnoses excluded
- Complex DDI excluded
- Some with low CD4 have very early HIV, not late

Special populations

- **Lack of data in special populations**
- **Caution renal impairment**
  - Dose over-adjustment of 3TC (DTG creatinine effect)
  - Supportive data from Bristol (n=52) but all suppressed switch, only 46% on 3TC 150mg OD & 2% on 3TC 50mg OD

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SHORT COMMUNICATION

Dual therapy with renally adjusted lamivudine and dolutegravir: a switch strategy to manage comorbidity and toxicity in older, suppressed patients?

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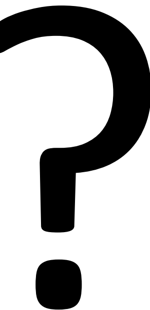
Suppressed switch

- **Based on TANGO DTG/3TC will be ‘recommended’**
  - Avoid if known/suspected M184V/I
- **Based on SWORD DTG/RPV will be ‘recommended’**
  - Caution, prior virological failure and/or NNRTI resistance were exclusions

Thank you

- **ART guidelines writing committee, particularly:**
  - Alan Winston (vice-chair)
  - Iain Reeves (what to start lead)
  - Nicky Mackie
  - Nick Larbalestier

Thank you!



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