BHIVA
British HIV Association

BASHH

Professor Chloe Orkin

Barts Health NHS Trust, London

Fourth Joint Conference *of the* **British HIV Association** *with the* **British Association for Sexual Health and HIV**
Edinburgh International Conference Centre ◆ 17–20 April 2018

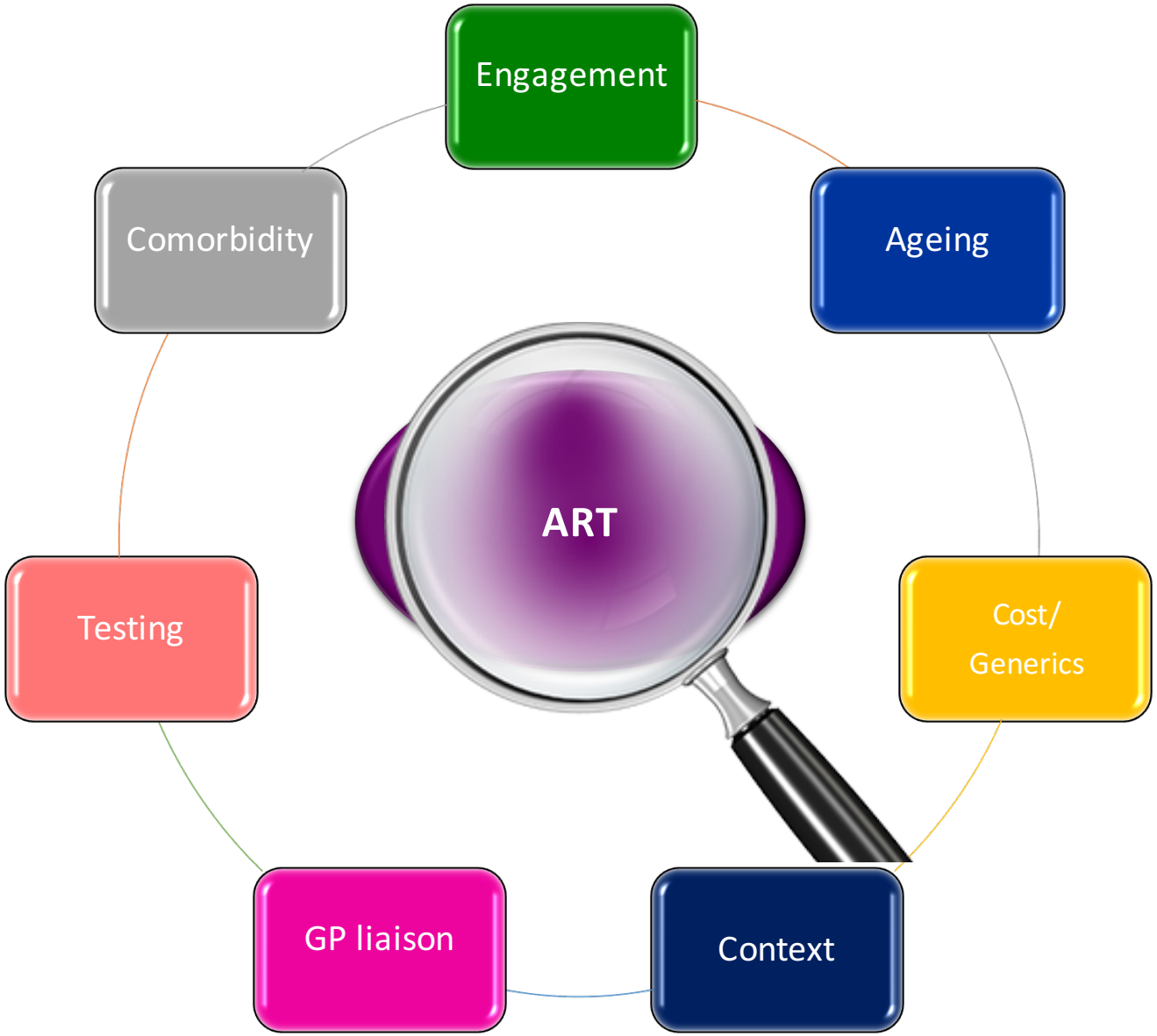
Advances in HIV Care for 2018

Professor Chloe Orkin
Barts Health NHS Trust

Disclosures

- Educational grants (HIV Unit): Merck Sharp & Dohme, Gilead Sciences, Janssen, ViiV Healthcare and Barts Charity
- Honoraria and travel sponsorship for lectures and advisory board contributions
- Member of the BHIVA Guidelines Subcommittee (2008–2017)
- Chair and executive trustee of BHIVA
- Not a patent holder or a shareholder
- No disclosures for spouse or family members

Advances in HIV Care



Advances in ART

Treatment and management strategies

Reducing ART exposure

- Drug dose
- Dosing frequency
- Number of drugs

New agents

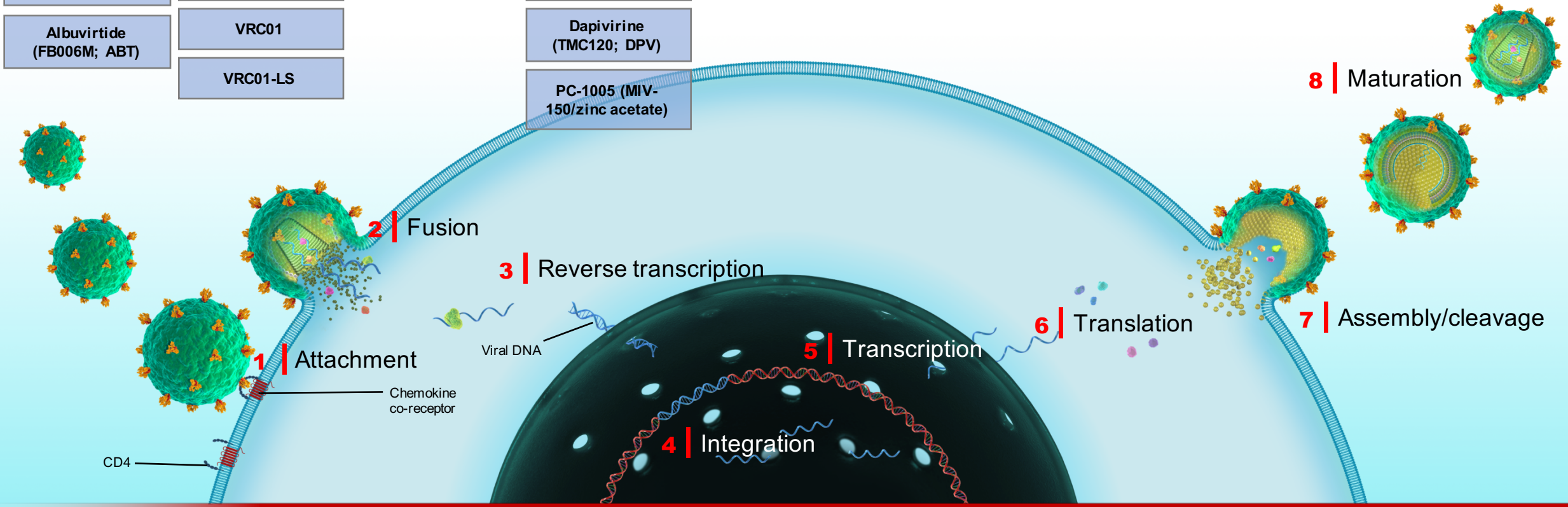
- Investigational ARTs
- Monoclonal antibodies

Different ART formulations

- Long-acting oral
- Implantable
- Long-acting injectable

HIV drug pipeline under clinical evaluation (Phase I–III)

Entry inhibitors	Monoclonal antibodies (mAb)	NRTIs/NtRTIs ('nukes')	NNRTIs ('non-nukes')	Integrase inhibitors	Protease inhibitors	Capsid inhibitors	Maturation inhibitors	Unique/ unknown MoA
Fostemsavir (GSK-934; FTR)	UB-421 (CD4 receptor)	EFdA (MK-8591)	Doravirine (MK-1439)	Bictegravir (GS-9883)	GS-PI1	GS-CA1	GSK2838232	MK-8507
Cenicriviroc (TBR-652; CVC)	PRO-140 (CCR5 receptor)	GS-9131	Elsulfavirine (VM1500)	Cabotegravir-LAI (GSK-744; CAB)				ABX464
Sifuvirtide (FS-0101)	Ibalizumab (TMB-355)		Rilpivirine-LAI (TMC278; RPV)	MK-2048				LEDGINs
Albuvirtide (FB006M; ABT)	VRC01		Dapivirine (TMC120; DPV)					
	VRC01-LS		PC-1005 (MIV-150/zinc acetate)					



H I V L I F E C Y C L E

Modes of delivery

ORAL

- ABX464
- Bictegravir (GS-9883)
- Cenicriviroc (TBR-652; CVC)
- Doravirine (MK-1439)
- Doravirine
- EFdA (MK-8591)
- Elsulfavirine (VM1500)
- Fostemsavir (GSK-934; FTR)
- GS-9131
- GS-PI1
- GS-CA1
- GSK2838232
- MK-8507

INJECTABLE

- Albuvirtide (FB006M; ABT)
- Ibalizumab (TMB-355)
- PRO-140 (CCR5 receptor)
- Sifuvirtide (FS-0101)
- UB-421 (CD4 receptor)
- VRC01
- VRC01-LS

OTHER (TOPICAL, IMPLANTABLE, GEL)

- Dapivirine (TMC120; DPV)
- MK-2048
- PC-1005 (MIV-150/zinc acetate)

LONG-ACTING INJECTABLE

- Cabotegravir-LAI (GSK-744; CAB)
- Rilpivirine-LAI (TMC278; RPV)

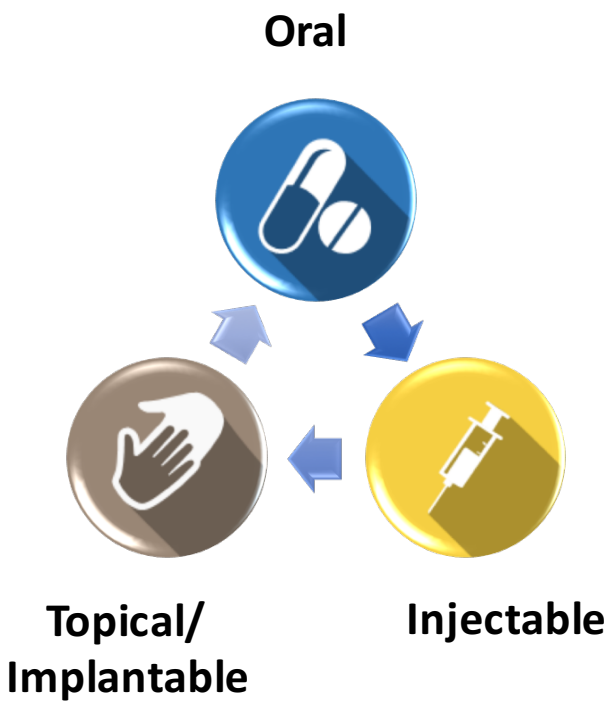
LEDGINs — Not currently under clinical investigation

Is there demand for long-acting injectable or implantable ART?

Patients in LATTE-2 trial preferred LA injectable CAB/RPV to taking pills[1,2]

Lessons from women using contraception:

- **multiple** modalities
- **different** modalities at **different** times
- **variety** makes it easier



CAB, cabotegravir; LA, long-acting; RPV, rilpivirine.
1. Margolis DA, *et al*. *Lancet* 2017;390:1499–1510; 2. Eron J, *et al*. IAS 2017, Paris, France; abstract #MOAX0205LB.

PRESENT

Life Expectancy = near normal, UK CHIC Cohort

May M et al. AIDS (2014); 28: 1193-202.

Guidelines: Recommended and preferred regimens

GUIDELINES	NRTI BACKBONE	NNRTI	INSTI	PI
EACS (2017)[1]	TAF/FTC TDF/FTC ABC/3TC*	RPV*	DTG RAL EVG	DRV/c or /r
DHHS (2018)[2]	TAF/FTC TDF/FTC ABC/3TC*	–	BIC DTG RAL EVG/c	–
IAS USA (2016)[3]	TAF/FTC ABC/3TC*	–	DTG RAL EVG/c	–
BHIVA (2016)[4]	TAF/FTC TDF/FTC	RPV*	DTG RAL EVG/c	DRV/r ATV/r
WHO (2016)[5]	TDF/XTC	EFV	–	–

*Use recommended only if baseline viral load <100,000 copies/mL.
3TC, lamivudine; ABC, abacavir; ATV, atazanavir; AZT, zidovudine; BHIVA, British HIV Association; c, cobicistat; DHHS, Department of Health and Human Services; DRV, darunavir; DTG, dolutegravir; EACS, European AIDS Clinical Society; EFV, efavirenz; EVG, elvitegravir; FTC, emtricitabine; IAS USA, International Antiviral Society–USA; LPV, lopinavir; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; NVP, nevirapine; PI, protease inhibitor; r, ritonavir; RAL, raltegravir; RPV, rilpivirine; TAF, tenofovir alafenamide fumarate; TDF, tenofovir disoproxil fumarate; WHO, World Health Organization; XTC, FTC or 3TC.

1. EACS Guidelines Version 9.0. Available from: http://www.eacsociety.org/guidelines/eacs-guidelines/eacs-guidelines.html. Accessed January 2018;
2. DHHS Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Available from: https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv/0. Accessed April 2018;
3. Günthard HF, *et al*. *JAMA* 2016;316:191–210;
4. BHIVA Guidelines. Available from: http://www.bhiva.org/documents/Guidelines/Treatment/2016/treatment-guidelines-2016-interim-update.pdf. Accessed January 2018;
5. WHO. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Available from: http://apps.who.int/iris/bitstream/10665/208825/1/9789241549684_eng.pdf?ua=1. Accessed January 2018.

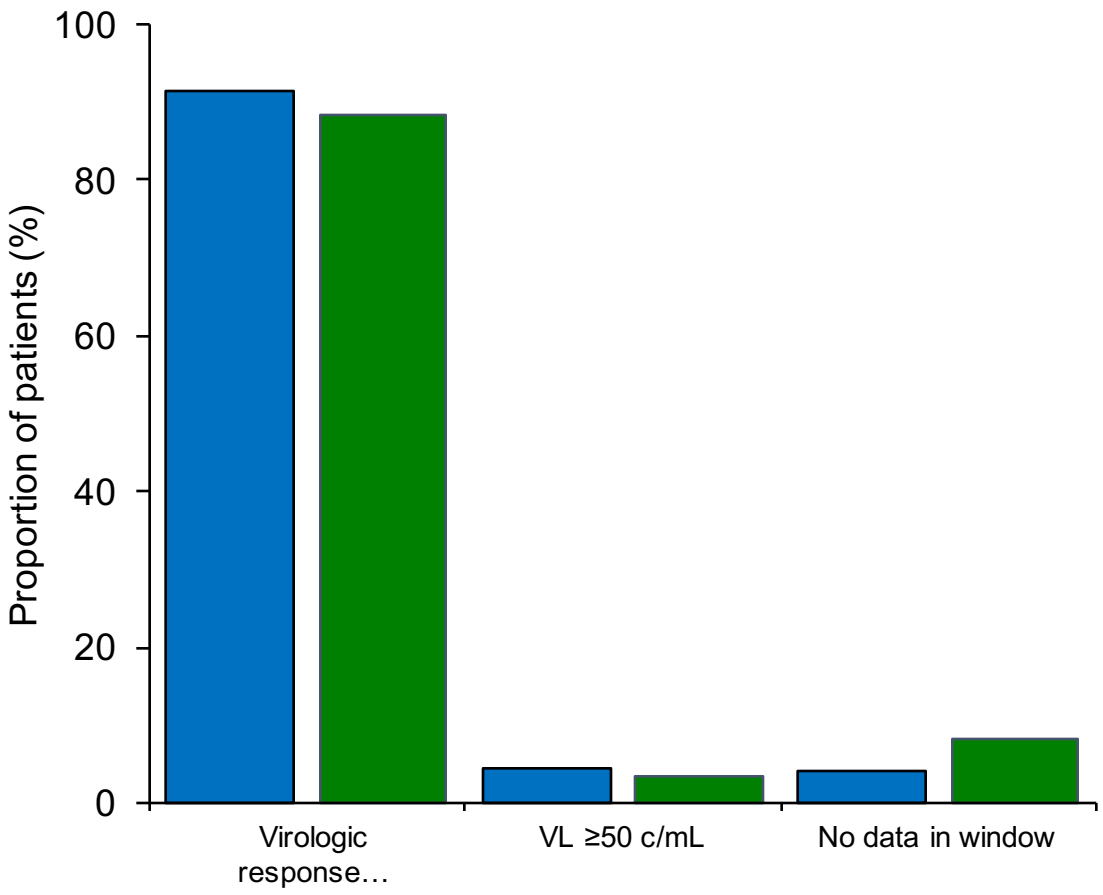
Recommended, preferred regimens + ALTERNATIVE

GUIDELINES	NRTI BACKBONE		NNRTI		INSTI		PI		NRTI-REDUCING
EACS (2017)[1]	TAF/FTC TDF/FTC ABC/3TC*	–	RPV*	EFV	DTG RAL EVG	–	DRV/c or /r	ATV/c or /r	DRV/c or /r + RAL LPV/r + XTC
DHHS (2018)[2]	TAF/FTC TDF/FTC ABC/3TC*	–	–	EFV RPV*	BIC DTG RAL EVG/c	–	–	ATV/c or /r DRV/c or /r	DRV/c or /r + RAL
IAS USA (2016)[3]	TAF/FTC ABC/3TC*	–	–	EFV RPV	DTG RAL EVG/c	–	–	DRV /c or /r	DRV/c or /r + RAL DRV/c or /r + DTG DRV/c or /r + XTC
BHIVA (2016)[4]	TAF/FTC TDF/FTC	ABC/3TC*	RPV*	EFV	DTG RAL EVG/c	–	DRV/r ATV/r	–	DRV/c or /r + RAL
WHO (2016)[5]	TDF/XTC	AZT/XTC	EFV	EFV 400 NVP	–	DTG	–	–	–

*Use recommended only if baseline viral load <100,000 copies/mL.
3TC, lamivudine; ABC, abacavir; ATV, atazanavir; AZT, zidovudine; BHIVA, British HIV Association; c, cobicistat; DHHS, Department of Health and Human Services; DRV, darunavir; DTG, dolutegravir; EACS, European AIDS Clinical Society; EFV, efavirenz; EVG, elvitegravir; FTC, emtricitabine; IAS USA, International Antiviral Society–USA; LPV, lopinavir; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; NVP, nevirapine; PI, protease inhibitor; r, ritonavir; RAL, raltegravir; RPV, rilpivirine; TAF, tenofovir alafenamide fumarate; TDF, tenofovir disoproxil fumarate; WHO, World Health Organization; XTC, FTC or 3TC.

1. EACS Guidelines Version 9.0. Available from: http://www.eacsociety.org/guidelines/eacs-guidelines/eacs-guidelines.html. Accessed January 2018;
2. DHHS Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Available from: https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv/0. Accessed January 2018;
3. Günthard HF, et al. JAMA 2016;316:191–210;
4. BHIVA Guidelines. Available from: http://www.bhiva.org/documents/Guidelines/Treatment/2016/treatment-guidelines-2016-interim-update.pdf. Accessed January 2018;
5. WHO. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Available from: http://apps.who.int/iris/bitstream/10665/208825/1/9789241549684_eng.pdf?ua=1. Accessed January 2018.

Describing efficacy outcomes (FDA snapshot)



3 categories:

VL < 50 c/mL

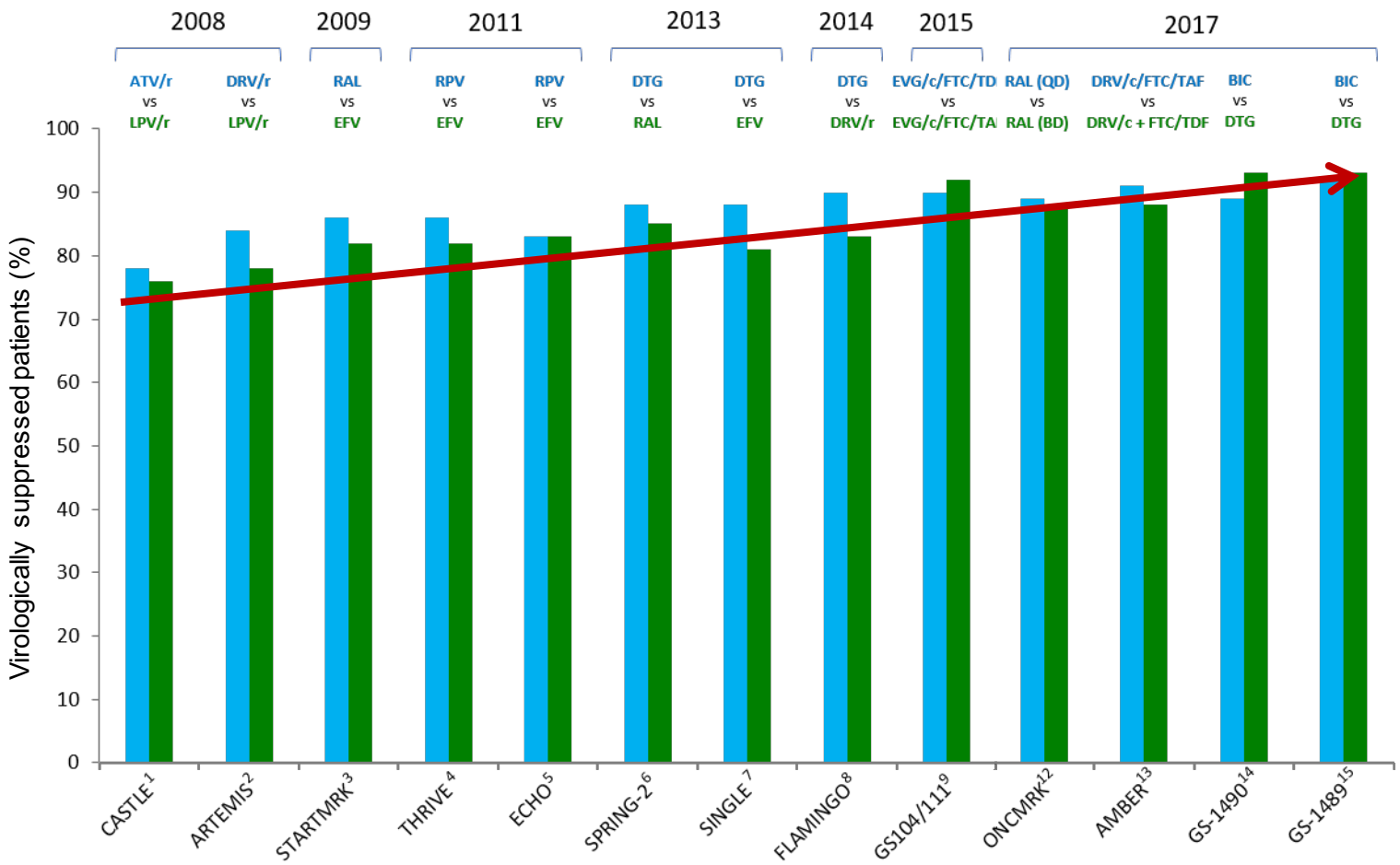
VL >50 c/mL driven by

No data in window = did not get to end

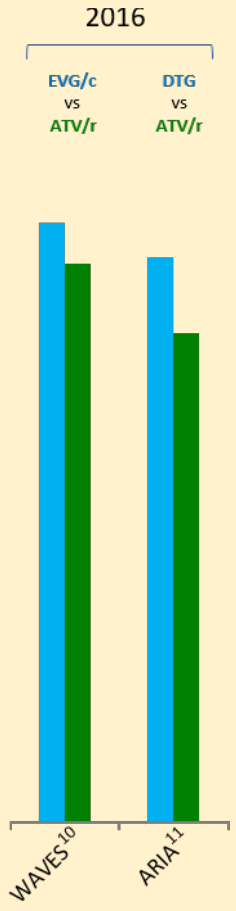
FDA, The Food and Drug Administration; VL, viral load.

Efficacy outcomes excellent, improving year on year

Efficacy outcomes at week 48



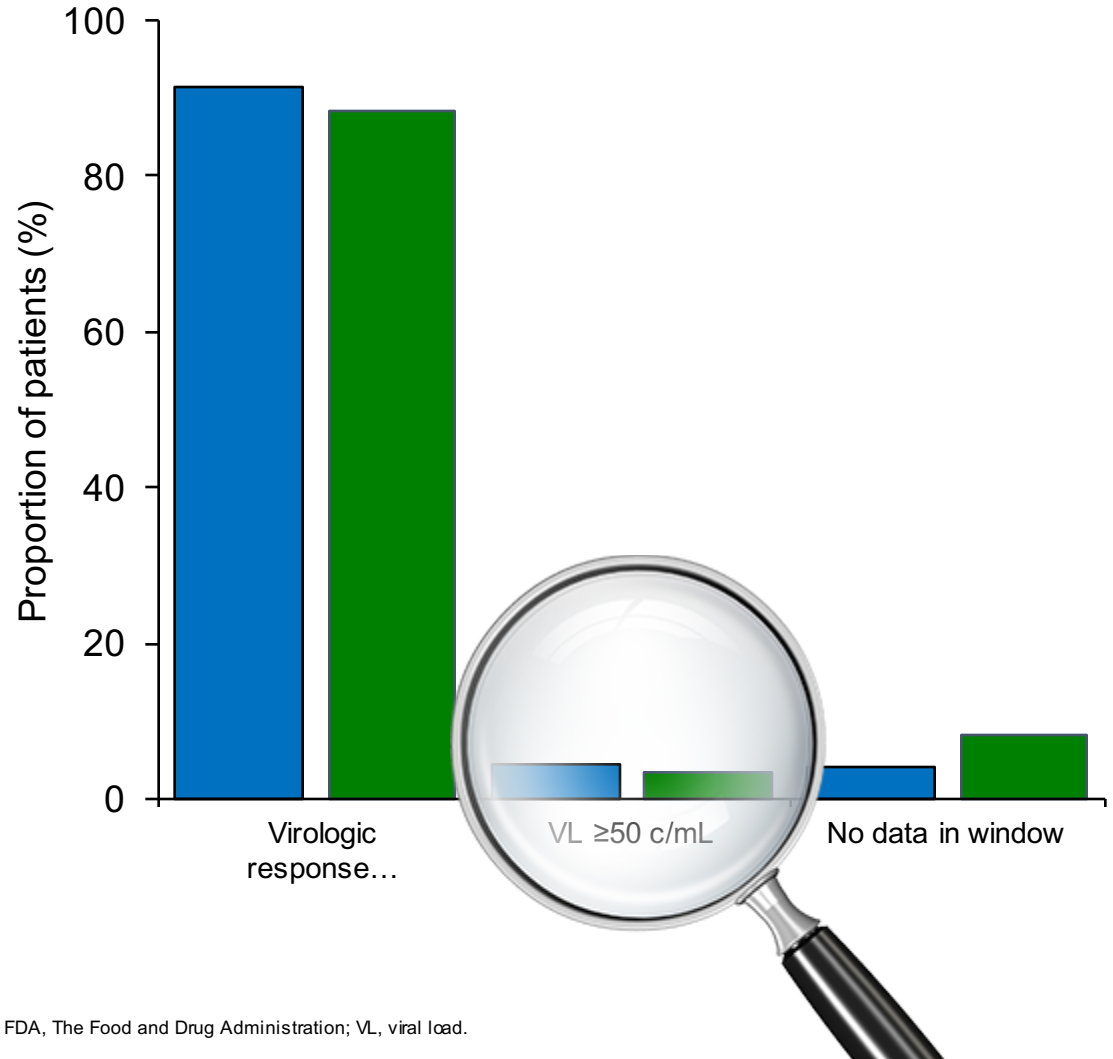
Women-only studies



ATV, atazanavir; BD, twice daily; BIC, bictegravir; c, cobicistat; DRV, darunavir; DTG, dolutegravir; EFV, efavirenz; EVG, elvitegravir; FTC, emtricitabine; LPV, lopinavir; QD, once daily; r, ritonavir; RAL, raltegravir; RPV, rilpivirine; TAF, tenofovir alafenamide fumarate; TDF, tenofovir disoproxil fumarate.

1. Molina JM, *et al*. *Lancet* 2008;372:646–55; 2. Ortiz R, *et al. AIDS* 2008;22:1389–97; 3. Lennox JL, *et al. Lancet* 2009;374:796–806; 4. Cohen CJ, *et al*. *Lancet* 2011;378:229–37;
5. Molina JM, *et al*. *Lancet* 2011;378:238–46; 6. Raffi F, *et al. Lancet* 2013;381:735–43; 7. Walmsley SL, *et al. N Engl J Med* 2013;369:1807–18;
8. Clotet B, *et al*. *Lancet* 2014;383:2222–31; 9. Sax PE, *et al*. *Lancet* 2015;385:2606–15; 10. Squires K, *et al. Lancet HIV* 2016;3:e410–20;
11. Orrell C, *et al*. *Lancet HIV* 2017;4:e536–46; 12. Cahn P, *et al*. *Lancet HIV* 2017;4:e486–94; 13. TBA; 14. Sax PE, *et al. Lancet* 2017;390:2073–82;
15. Gallant J, *et al*. *Lancet* 2017;390:2063–72.

Describing efficacy (FDA snapshot)

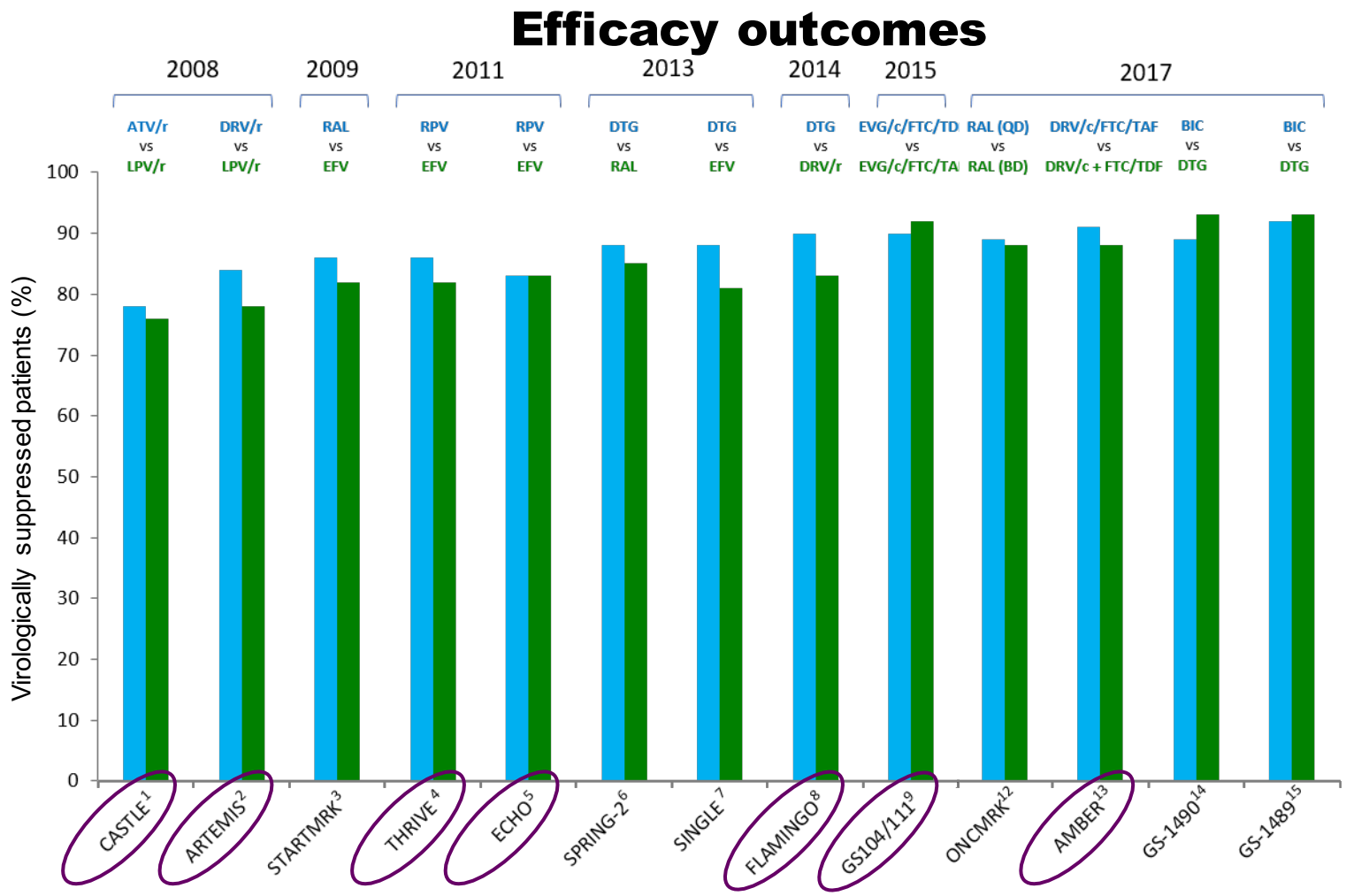


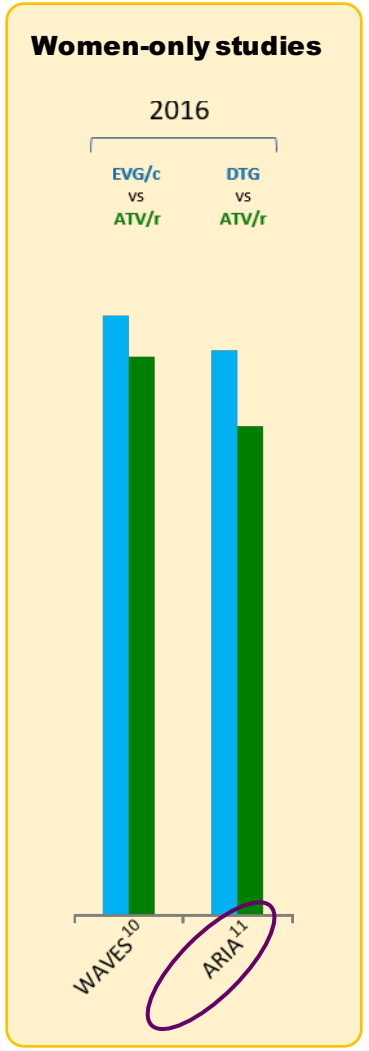
VL >50 c/mL driven by:

- **Baseline VL**
- **Barrier to resistance**

FDA, The Food and Drug Administration; VL, viral load.

Not all regimens work well if baseline VL >100,000 c/mL





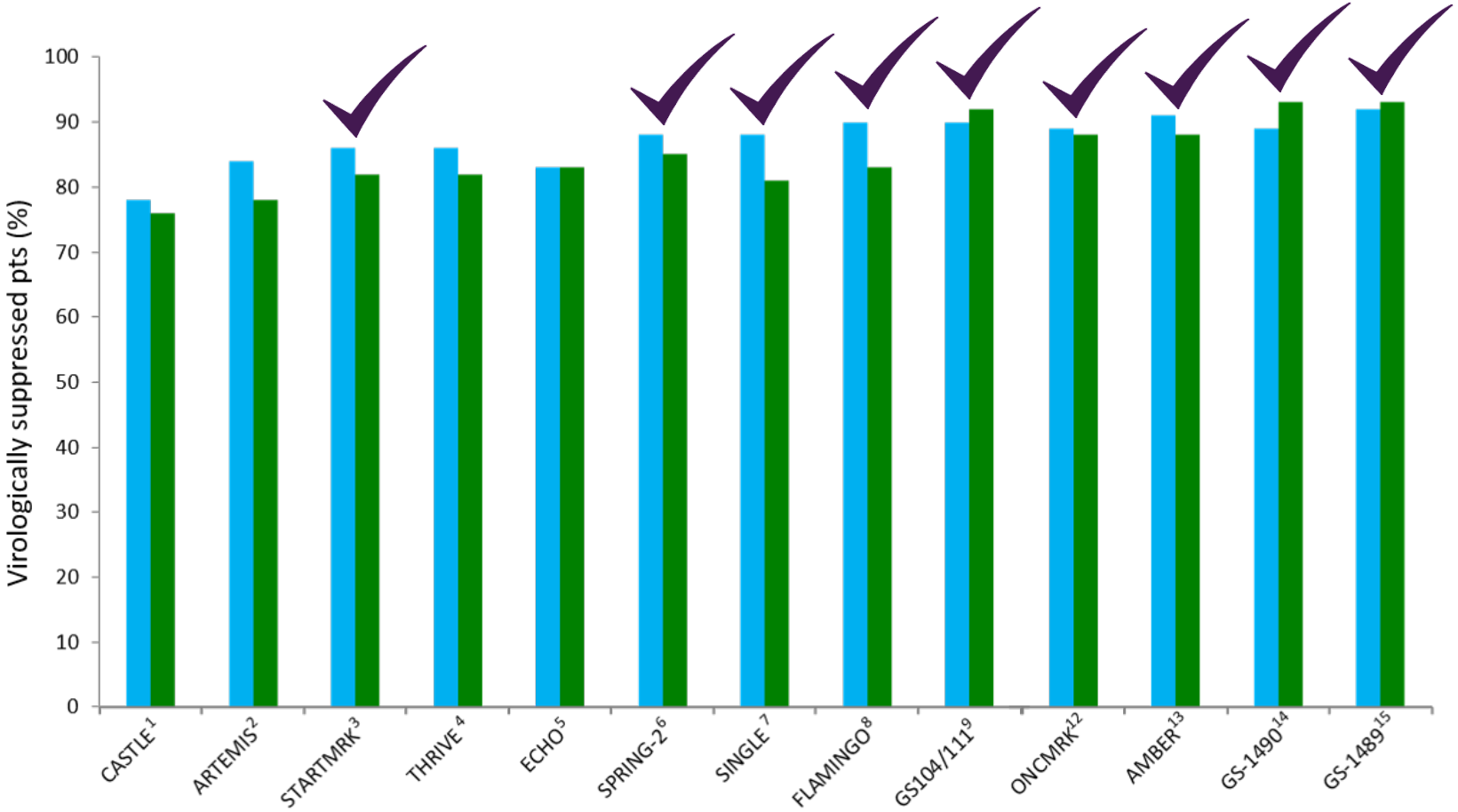
ATV, atazanavir; BD, twice daily; BIC, bictegravir; c, cobicistat; DRV, darunavir; DTG, dolutegravir; EFV, efavirenz; EVG, elvitegravir; FTC, emtricitabine; LPV, lopinavir; QD, once daily; r, ritonavir; RAL, raltegravir; RPV, rilpivirine; TAF, tenofovir alafenamide fumarate; TDF, tenofovir disoproxil fumarate.

1. Molina JM, *et al*. *Lancet* 2008;372:646–55; 2. Ortiz R, *et al. AIDS* 2008;22:1389–97; 3. Lennox JL, *et al. Lancet* 2009;374:796–806; 4. Cohen CJ, *et al*. *Lancet* 2011;378:229–37; 5. Molina JM, *et al*. *Lancet* 2011;378:238–46; 6. Raffi F, *et al. Lancet* 2013;381:735–43; 7. Walmsley SL, *et al. N Engl J Med* 2013;369:1807–18; 8. Clotet B, *et al*. *Lancet* 2014;383:2222–31; 9. Sax PE, *et al*. *Lancet* 2015;385:2606–15; 10. Squires K, *et al. Lancet HIV* 2016;3:e410–20; 11. Orrell C, *et al*. *Lancet HIV* 2017;4:e536–46; 12. Cahn P, *et al*. *Lancet* HIV 2017;4:e486–94; 13. TBA; 14. Sax PE, *et al. Lancet* 2017;390:2073–82; 15. Gallant J, *et al*. *Lancet* 2017;390:2063–72.

Who is represented in these studies?

Trials where participants are:

- ✓ 50% white
- ✓ >70% male
- ✓ 100% CD4 >300
- ✓ >75% VL <100,000



1. Molina JM, *et al*. *Lancet* 2008;372:646–55;
2. Ortiz R, *et al*. *AIDS* 2008;22:1389–97;
3. Lennox JL, *et al*. *Lancet* 2009;374:796–806;
4. Cohen CJ, *et al*. *Lancet* 2011;378:229–37;
5. Molina JM, *et al*. *Lancet* 2011;378:238–46;
6. Raffi F, *et al*. *Lancet* 2013;381:735-43;
7. Walmsley SL, *et al*. *N Engl J Med* 2013;369:1807–18;
8. Clotet B, *et al*. *Lancet* 2014;383:2222–31;
9. Sax PE, *et al*. *Lancet* 2015;385:2606–15;
10. Squires K, *et al*. *Lancet HIV* 2016;3:e410–20;
11. Orrell C, *et al*. *Lancet HIV* 2017;4:e536–46;
12. Cahn P, *et al*. *Lancet HIV* 2017;4:e486–94;
13. TBA;
14. Sax PE, *et al*. *Lancet* 2017;390:2073–82;
15. Gallant J, *et al*. *Lancet* 2017;390:2063–72.

We need longer term data AND…

Trials enrolling:

- ✓ Older adults
- ✓ Women
- ✓ Trans and non-binary
- ✓ Ethnically diverse
- ✓ Adolescents
- ✓ People who inject drugs
- ✓ HCV and HBV co-infected
- ✓ CDC C diagnoses
- ✓ Comorbidities allowed

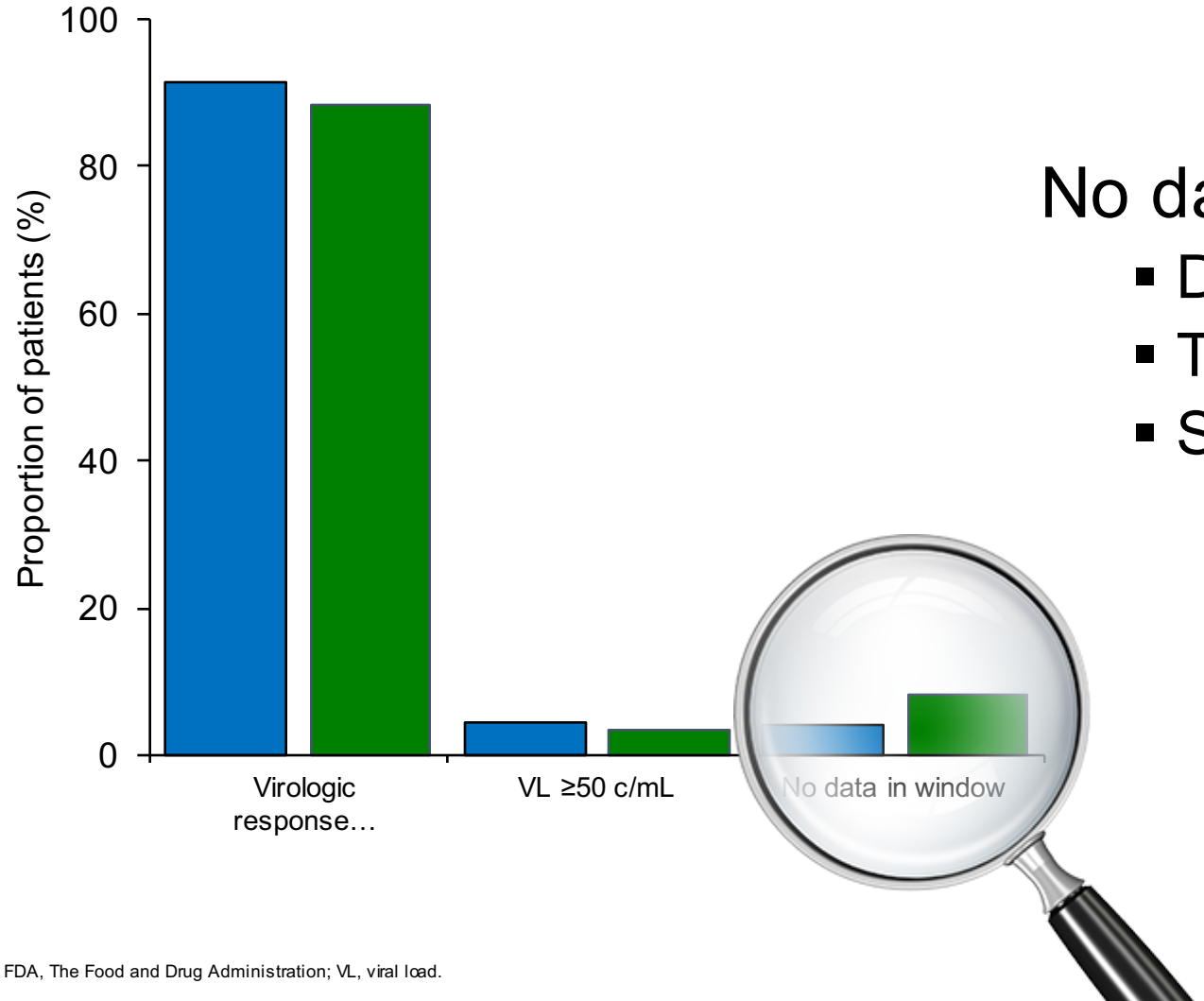
Toward zero resistance when failing INSTIs Wk 48

STUDY	FLAMINGO[1]	ARIA[2]	SINGLE[3]	GS-1489 (ABC)[4]		GS-1490 (TDF)[5]	
Drug	DTG	DTG	DTG	BIC	DTG	BIC	DTG
NRTI	0	0	0	0	0	0	0
INSTI	0	0	0	0	0	0	0

INSTI, Integrase strand transfer inhibitors DTG, dolutegravir; BIC, Bictegravir

1. BIC, bictegravir.
2. Clotet B, *et al*. *Lancet* 2014;383:2222–31; 2. Orrell C *et al*. *Lancet HIV* 2017;4:e536–46; 3. Walmsley SL, *et al*. *N Engl J Med* 2013;369:1807–18; 4. Gallant J, *et al*. *Lancet* 2017;390:2063–72; 5. Sax PE, *et al*. *Lancet* 2017;390:2073–82.

Very few fail virologically, 'no data' group important



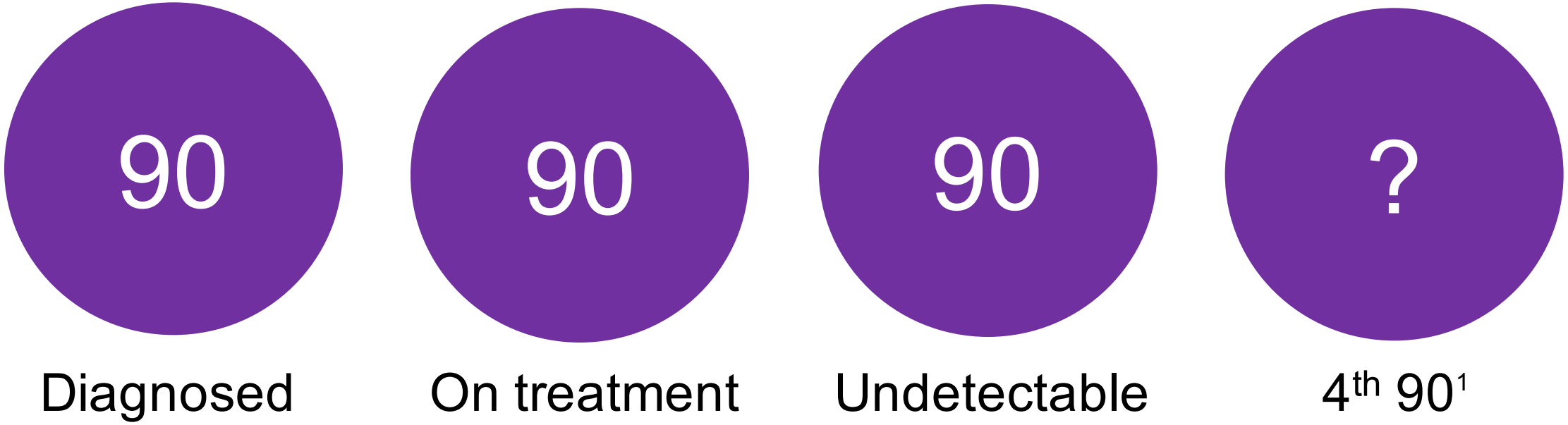
No data in window=did not get to end:

- Disengagement from care
- Tolerability (discontinuations)
- Safety (withdrawals)

FDA, The Food and Drug Administration; VL, viral load.

We can reduce this category by Improving quality of life : The 4th 90

Keeping people engaged with their care
Avoiding side effects and comorbidity



Enhancing engagement = make meds convenient

TRIPLE

DRUG	ATRIPLA[1]	EVIPLERA[2]	STRIBILD[3]	TRIUMEQ[4]	GENVOYA[5]	ODEFSEY[6]	SYMTUZA[7]	BIKTARVY[8]
COMPONENTS	Generic FDC TDF/XTC/EFV	TDF/FTC/RPV	TDF/FTC/EVG/c	ABC/3TC/DTG	TAF/FTC/EVG/c	TAF/FTC/RPV	TAF/FTC/DRV/c	TAF/BIC/FTC
CONSIDERATIONS	Premorbid Psychiatric	VL <100,000	Drug–drug interactions	HLAB*5701 co-infection	Drug–drug interactions	VL <100,000	Drug–drug interactions	Long-term data

Licensed once-daily fixed-dose combinations. Pill sizes are not to scale.

Filed for licensing: TDF/3TC/DOR (1439A)

1. Atripla SmPC. Available from: https://www.medicines.org.uk/emc/medicine/20505. Updated May 2017. Accessed October 2017;
2. Eviplera SmPC. Available from: https://www.medicines.org.uk/emc/medicine/25518. Updated June 2017. Accessed October 2017;
3. Stribild SmPC. Available from: https://www.medicines.org.uk/emc/medicine/27810. Updated June 2017. Accessed October 2017;
4. Triumeq SmPC. Available from: https://www.medicines.org.uk/emc/medicine/29178. Updated January 2017. Accessed October 2017;
5. Genvoya SmPC. Available from: https://www.medicines.org.uk/emc/medicine/31225. Updated September 2017. Accessed October 2017;
6. Odefsey SmPC. Available from: https://www.medicines.org.uk/emc/medicine/32117. Updated September 2017. Accessed October 2017;
7. Symtuza SmPC. Available from: http://www.medicines.org.uk/emc/medicine/34148. Updated September 2017. Accessed October 2017;
8. Biktarvy PI. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/210251s000lbl.pdf. Accessed February 2018;
9. Juluca SmPC. Available from: https://www.viivhealthcare.com/our-medicines/juluca.aspx. Updated November 2017. Accessed December 2017.

What else could we do to stop disengagement from care?

Address stigma and societal barriers

Different modalities (longer acting)

More peer mentoring and navigation

Behavioural interventions:

- App and SMS-based reminders
- Behavioural prompts

Toxicity and tolerability drives efficacy: ACTG 5257

Equivalent in terms of virologic failure endpoint but…

	RAL (N=603)	ATV/r (N=605)	DRV/r (N=601)
Any toxicity discontinuation	8 (1%)	95 (16%)	32 (5%)

Cumulative failure*		
ATV/r vs RAL	RAL superior	15% (10%, 20%)
DRV/r vs RAL	RAL superior	7.5% (3.2%, 12%)
ATV/r vs DRV/r	DRV/r superior	7.5% (2.3%, 13%)

*Difference in 96-week cumulative incidence (97.5% CI)

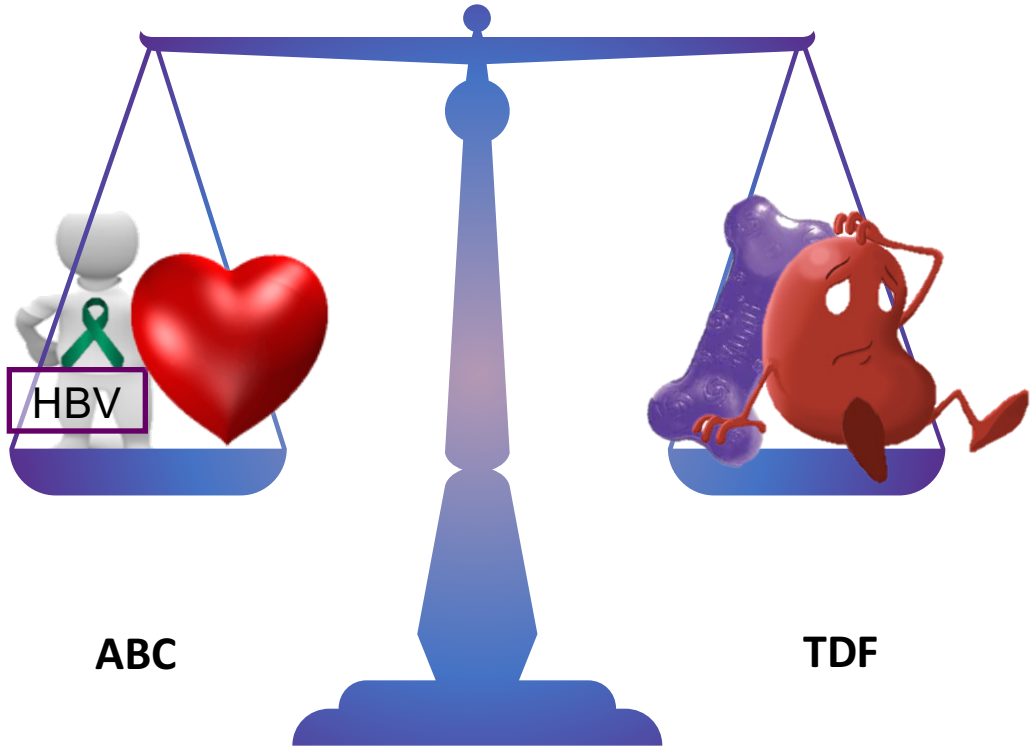
ACTG, AIDS Clinical Trials Group; ATV, atazanavir; CI, confidence interval; DRV, darunavir; r, ritonavir; RAL, raltegravir.
Landovitz RJ, *et al*. CROI 2014, Boston, MA, United States; abstract #85.

Safety outcomes in RCTs vs cohort studies

RCT: Surrogate markers	Cohort: Serious non-AIDS events
Renal = GFR, tubular biomarkers	Renal events e.g. CKD
Bone = DEXA & bone biomarkers	Fractures
CVS = lipids	CVS outcomes
CNS = side effects; questionnaires	Neurocognitive/psychiatric events
AEs	Hepatic events
	Non-AIDS malignancy
	Unexpected AEs: ▪ ABC hypersensitivity

ABC, abacavir; AE, adverse event; CKD, chronic kidney disease; CNS, central nervous system; CVS, cardiovascular; DEXA, dual-energy X-ray absorptiometry; GFR, glomerular filtration rate; RCT, randomized controlled trial.

Ways to avoid the safety concerns of the NRTI 'backbone'



Options:

- TAF backbone in triple ART
  - TAF and ABC similar for renal and bone
- Two-drug regimens (2DR)

1.Sax PE, *et al*. *Lancet* 2015;385:2606–15; 2. Arribas JR, *et al*. CROI 2017, Seattle, WA, United States; poster #453; 3. Molina J. et al. CROI 2018. Boston, MA. Oral #22

2DR, two-drug regimen; ART, antiretroviral therapy; HBV, hepatitis B; NRTI, nucleoside reverse transcriptase inhibitor; TAF, tenofovir alafenamide fumarate.

TAF and ABC -similar outcomes for bone and renal biomarkers

GS-104/111[1,2]

- EVG/c + TAF/FTC vs TDF/FTC
- TAF: favorable renal biomarkers and BMD
- No renal or bone discontinuations to Week 144

GS-1844[3]

- Switch from ABC/3TC/DTG to TAF/FTC/BIC
- No differences in renal or bone biomarkers at Week 48

3TC, lamivudine; ABC, abacavir; BIC, bictegravir; BMD, bone mineral density; c, cobicistat; DTG, dolutegravir; EVG, elvitegravir; FTC, emtricitabine; TAF, tenofovir alafenamide fumarate; TDF tenofovir disoproxil fumarate.

1.Sax PE, *et al*. *Lancet* 2015;385:2606–15; 2. Arribas JR, *et al*. CROI 2017, Seattle, WA, United States; poster #453; 3. Molina J. et al. CROI 2018. Boston, MA. Oral #22

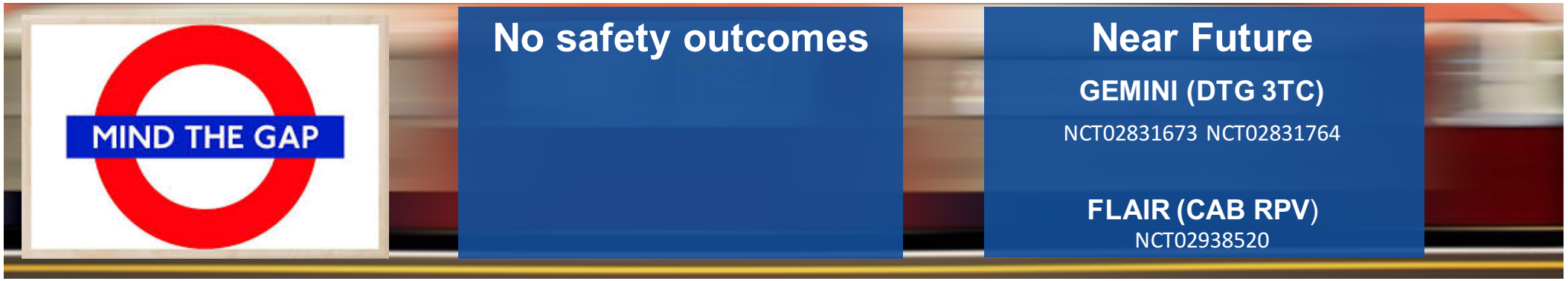
2 Drug Regimes (2DR)-naïve studies: Efficacy data only

WK 48 ANDES[1] (N=145)

- FDC DRV/r + 3TC vs DRV/r + TDF/3TC
- Non-inferior 93% DT, 94% TT

ACTG 5353[2] (N=120)

- Single-arm study DTG + 3TC
- 3 PDVF
- n=1 [emergent M184V, R263R/K]



2DR, two-drug regimen; 3TC, lamuvidine; ACTG, AIDS Clinical Trials Group; CAB, cabotegravir; DRV, darunavir; DTG, dolutegravir; PDVF, protocol-defined virologic failure; RPV, rilpivirine; RTV, ritonavir; TDF, tenofovir disoproxil fumarate.

1. Sued O, *et al*. IAS 2017, Paris, France; abstract #MOAB0106LB;
2. 2. Taiwo BO, *et al*. IAS 2017, Paris, France; abstract #MOAB0107LB.
3. Figueroa M CROI 2018 Poster 489

Adapted from clinicaloptions.com

Current challenges of the INSTI as third agent

CNS AEs

Phase III FDA trials DTG[1]

- Only insomnia reported

Six cohorts[3–8]: CNS discontinuations

- More DTG discontinuations than other INSTIs

Opera cohort[6]

- Similar CNS incidents

Wohl series[9]

- Depression and sleep disturbances were significantly higher in DTG

Resistance

First-generation INSTI

- RAL and EVG more resistance than PI

DDIs

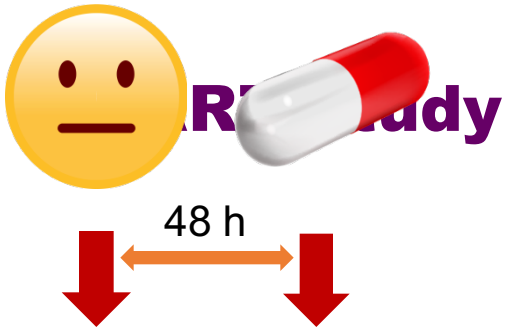
INSTI drug–drug interactions

- RAL/DTG chelation
- EVG/c booster, so DDIs

AE, adverse event; ART, antiretroviral therapy; BIC, bictegravir; CNS, central nervous system; DDI, dideoxyinosine; DRV, darunavir; DTG, dolutegravir; EVG, elvitegravir; FDA, The Food and Drug Administration; INI, integrase inhibitor; PI, protease inhibitor; r, ritonavir; RAL, raltegravir.

1. Viswanathan P, *et al*. CROI 2017, Seattle, WA, United States; poster #372; 2. Quercia R, *et al.* HIV Glasgow 2016, Glasgow, United Kingdom; poster #210; 3. Hoffmann C, *et al*. *HIV Med* 2017;18:56–63;
4. Padilla M, *et al*. International Workshop on Comorbidities and ADRs in HIV 2016, New York, NY, United States; 5. Lepik KJ, *et al.* IAS 2015, Vancouver, Canada; abstract #TUPEB256; 6. Hsu R, *et al*. CROI 2017, Seattle, WA, United States; poster #664;
7. Llibre JM, *et al*. CROI 2017, Seattle, WA, United States; poster #651; 8. Baldin G, *et al.* HIV Glasgow 2016, Glasgow, United Kingdom; poster # P106; 9. Wohl D, *et al.* ID Week 2017; San Diego, CA, United States; abstract #664.

When to start



- Engagement with care
- Infrastructure
- Resistance
- Virologic outcomes
- Safety

INSIGHT START Study Group, *et al. N Engl J Med* 2015;373:795–807 093:
Rosen et al Plos medicine 2016
Koenig et al PLOS medicine 2017
Bacon et al.CRO! 2018

RAPID ART in San Francisco: Accelerated ART Initiation for newly diagnosed HIV

- Getting to Zero Consortium's Citywide RAPID programme:
  - Time to first VL <50 decreased by 50% (from 134 to 61 days)
  - Time from care linkage to starting ART decreased by 96% (from 27 days to 1 day)

Bacon O, et al. CROI 2018. Abstract O93.

Principles of Switch: 2017-18 Guidelines

- Switch safely and for a good reason
  - Review ART history, genotype, interactions, co-infection
- Consider efficacy-based triple-therapy switch
- Consider efficacy-based 2DR switch

EACS European AIDS Clinical Society

3TC + PI/r-based[1]:
▪ DRV/r or /c + 3TC ▪ ATV/r or /c + 3TC
INSTI + NNRTI[1]:
▪ DTG + RPV

DHHS Guidelines

3TC + PI/r-based[2]:
▪ DRV/r + 3TC ▪ ATV/r + 3TC ▪ LPV/r + 3TC
INSTI + NNRTI[2]:
▪ DTG + RPV

2DR, two-drug regimen; 3TC, lamivudine; ART, antiretroviral therapy; ATV, atazanavir; c, cobicistat; DHHS, Department of Health and Human Services; DRV, darunavir; DTG, dolutegravir; EACS, European AIDS Clinical Society; LPV, lopinavir; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; r, ritonavir; RPV, rilpivirine; VL, viral load.

1. EACS Guidelines Version 9.0. Available from: http://www.eacsociety.org/guidelines/eacs-guidelines/eacs-guidelines.html. Accessed January 2018;
2. DHHS Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Available from: https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv/0. Accessed January 2018.

Safety data studies of 2DR 'n=100'

2DR

bPI + MVC

MARCH[2]

- bPI + MVC vs bPI + 2 NRTIs
- N=395
- –17.4%

bPI + INSTI

HARNESS[3]

% difference >12%

2DR

bPI + 3TC

SALT, ATLAS[4,5]

- ATV/r + 3TC vs ATV/r + 2 NRTIs
- N=286; 266
- +6%, +9.8%

OLE[6]

DUAL[7]

NNRTI + INSTI

SWORD 1 & 2[8]

- DTG + RPV vs CAR (NRTI + other)
- N=1024
- –0.2%

LATTE[9]

LATTE-2[10]

% difference <12%

Difference = % of virologically suppressed patients in triple ART compared with 2DR at Week 48. Minus value is in favor of triple therapy; positive value is in favor of 2DR

1. Orkin C, *et al*. *HIV Med* 2018;19:18–32;
2. Pett SL, *et al*. *Clin Infect Dis* 2016;63:122–32;
3. van Lunzen J, *et al*. *J Acquir Immune Defic Syndr* 2016;71:538–43;
4. Perez-Molina JA, *et al*. *Lancet Infect Dis* 2015;15:775–84;
5. Di Giambenedetto S, *et al*. *J Antimicrob Chemother* 2017;72:1163–71;
6. Arribas JR, *et al*. *Lancet Infect Dis* 2015;15:785–92;
7. Pulido F, *et al*. HIV Glasgow 2016, Glasgow, United Kingdom; abstract #0331;
8. Llibre JM, *et al*. CROI 2017, Seattle, WA, United States; abstract #44LB;
9. Margolis DA, *et al*. *Lancet Infect Dis* 2015;15:1145–55;
10. Margolis DA, *et al*. AIDS 2016, Durban, South Africa; abstract #THAB0206LB.

Safety data studies of 2DR ‘n=100’

2DR ✗

bPI + MVC

MARCH[2]

- bPI + MVC vs bPI + 2 NRTIs
- N=395
- –17.4%

bPI + INSTI

HARNESS[3]

- ATV/r + RAL vs ATV/r + TDF/FTC
- N=109
- -17.1%

2DR ✓

bPI + 3TC

SALT, ATLAS[4,5]

- ATV/r + 3TC vs ATV/r + 2 NRTIs
- N=286; 266
- +6%, +9.8%

NNRTI + INSTI

SWORD 1 & 2[8]

- DTG + RPV vs CAR (NRTI + other)
- N=1024
- –0.2%

More studies awaited

DTG+ 3TC or FTC	DTG/DRV/r	LA CAB + RPV
TANGO SIMPL’ HIV	DUALIS (NCT02486133)	ATLAS (NCT02951052) ATLAS-2M (NCT03299049)

Adapted from clinicaloptions.com

1. Orkin C, *et al*. *HIV Med* 2018;19:18–32;
2. Pett SL, *et al*. *Clin Infect Dis* 2016;63:122–32;
3. van Lunzen J, *et al*. *J Acquir Immune Defic Syndr* 2016;71:538–43;
4. Perez-Molina JA, *et al*. *Lancet Infect Dis* 2015;15:775–84;
5. Di Giambenedetto S, *et al*. *J Antimicrob Chemother* 2017;72:1163–71;
6. Arribas JR, *et al*. *Lancet Infect Dis* 2015;15:785–92;
7. Pulido F, *et al*. HIV Glasgow 2016, Glasgow, United Kingdom; abstract #0331;
8. Llibre JM, *et al*. CROI 2017, Seattle, WA, United States; abstract #44LB;
9. Margolis DA, *et al*. *Lancet Infect Dis* 2015;15:1145–55;
10. Margolis DA, *et al*. AIDS 2016, Durban, South Africa; abstract #THAB0206LB;

2DR…questions for the future

Data gaps

- Hep B an exclusion
- Long-term data
- VL > 500,000 c/ml; Low CD4
- Resistance*
- Reservoir/ inflammation

*Gagliardini R, et al. CROI 2018. Abstract 498.

2DR…questions for the future

Data gaps

- Hep B an exclusion
- Long-term data
- VL > 500,000 c/ml; Low CD4
- Resistance
- Pregnancy
- Inflammation
- Sanctuary site penetration
- Viral reservoir
- Immune senescence

Questions that occur in clinic

- How much adherence is enough?
- Is it ok to monitor VL for 2DR twice or once a year?
- Can it be used for those with unclear history of suppression/unknown genotype at failure?
- How does one salvage a failure on 2DR?

Studies done in resource-deprived settings - despite NRTI resistance, excellent outcomes:

- Using LPV/r + recycled NRTI was non-inferior to using LPV/r + RAL
- Using DTG+ NRTIs superior to NRTI+LPV/r

ACTG, AIDs Clinical Trials Group; DTG, dolutegravir; LPV, lopinavir; NRTI, nucleoside reverse transcriptase inhibitor; r, ritonavir; RAL, raltegravir.

1. Paton NI, *et al*. *N Engl J Med* 2014;371:234–47; 2. La Rosa AM, *et al*. *Lancet HIV* 2016;3:e247–58; 3. Aboud *et al*. IAS 2017, Paris, France; oral #TUAB0105LB
2. Aboud M CROI 2018 P508.

Triple-class experience

- Drug dose varies for triple-experienced vs triple-class resistance (QD vs BID)
- INSTI naïve pts can dose drugs OD
- INSTI –resistant pts need to dose BD

*(ABC/3TC or TDF/FTC); †Minus EVG or RAL.
3TC, lamivudine; ABC, abacavir; BID, twice daily; DTG, dolutegravir; EVG, elvitegravir; FTC, emtricitabine; OBR, optimized background regimen; PI, protease inhibitor; QD, once daily; r, ritonavir; RAL, raltegravir; TDF, tenofovir disoproxil fumarate.
1. Cahn P, *et al*. *Lancet* 2013;382:700–8; 2. Castagna A, *et al*. *J Infect Dis* 2014;210:354–62.

Investigational agents for treatment-experienced patients

FOSTEMSAVIR[1]

- Fostemsavir is an attachment inhibitor to gp120
- HIV VL decline of 0.79 $\log_{10}$ in 8 days functional monotherapy

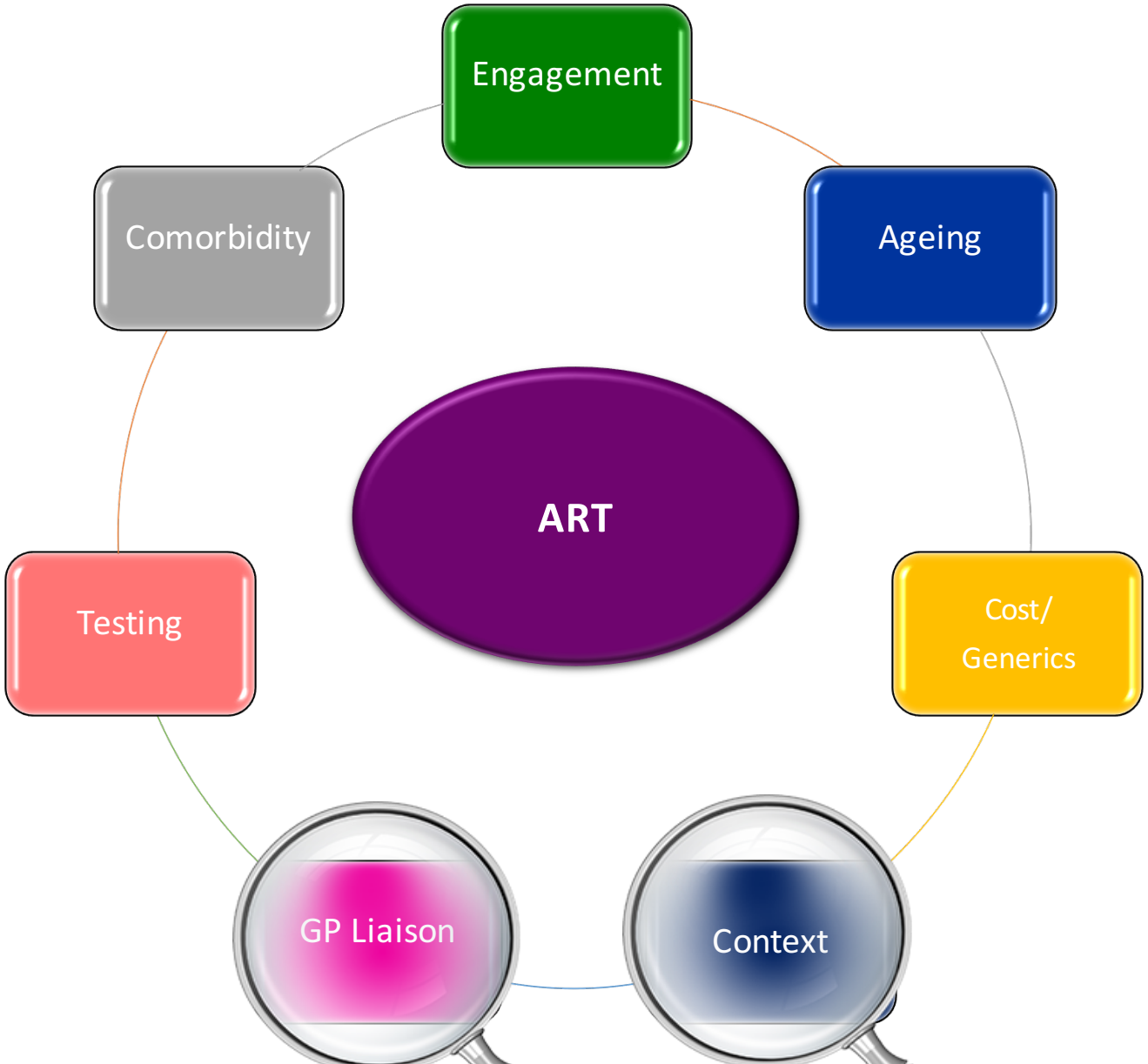
IBALIZUMAB[2,3] & PRO-140 [4]

- Ibalizumab is a humanised monoclonal antibody to CD4 receptor (FDA licensed)
- PRO-140: is a humanised monoclonal antibody to CCR5 receptor-subcutaneous weekly
- 83% achieved ≥0.5 $\log_{10}$ drop at Day 14

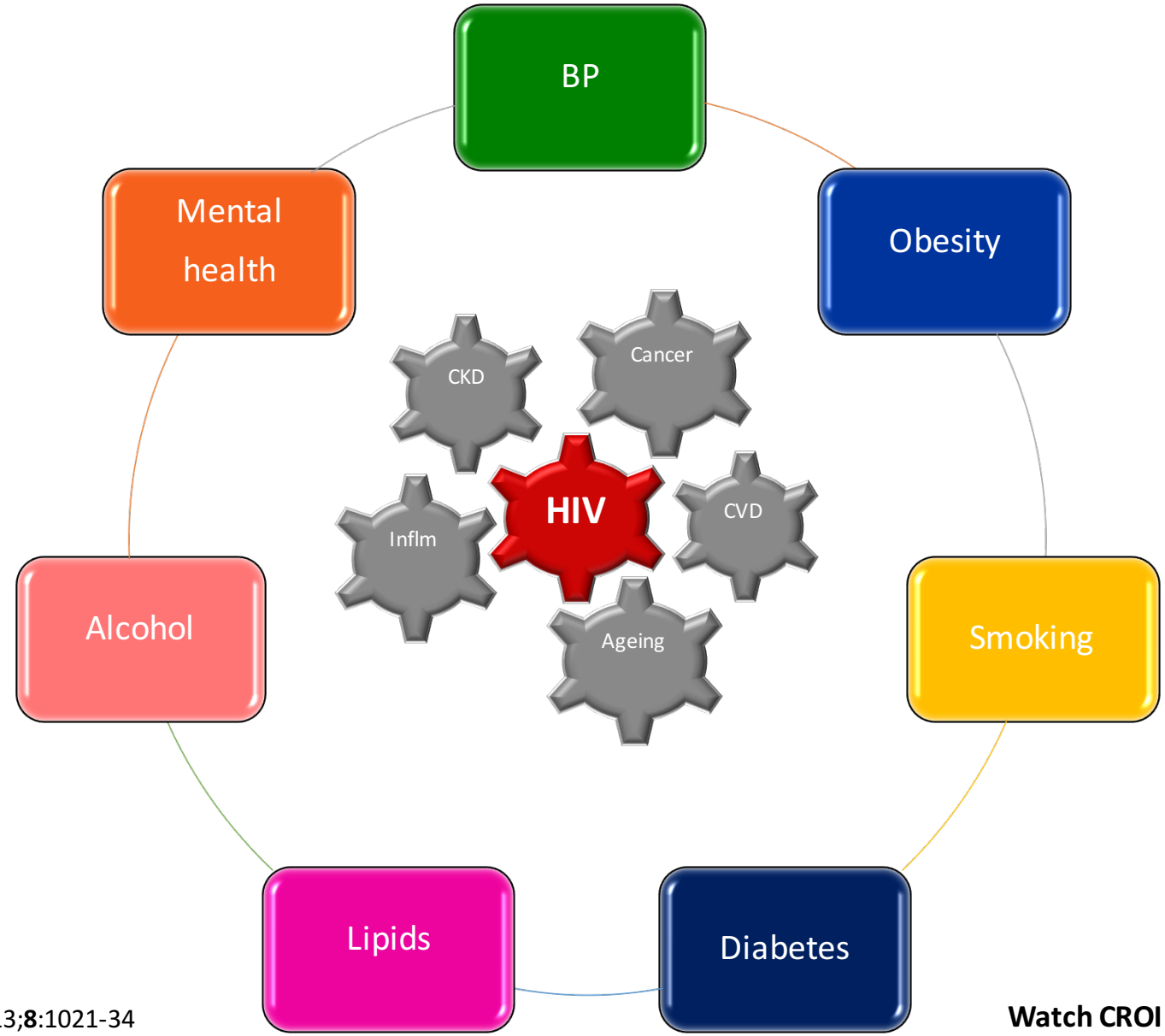
ATV/r, atazanavir/ritonavir; RAL, raltegravir; TDF, tenofovir disoproxil fumarate; VL, viral load.

1. M Kozal et al. EACS 2017; Milan, Italy. Oral PS8/5; 2.Lalexari J, *et al* IDWeek 2016. Abstract LB-6; 3. Lewis S, *et al.* CROI 2017. Abstract 449LB. 4. Lalezari et al CROI 2017 , Seattle

Advances in HIV Care



Comorbidity and traditional risk factors interact to cause mortality



Adapted from O'Halloran J, et al. *Fut Virol* 2013;**8**:1021-34

Watch CROI 2018 Symposium on life expectancy

OUR Role: Communicate with GPs
Ensure modifiable traditional factors are addressed

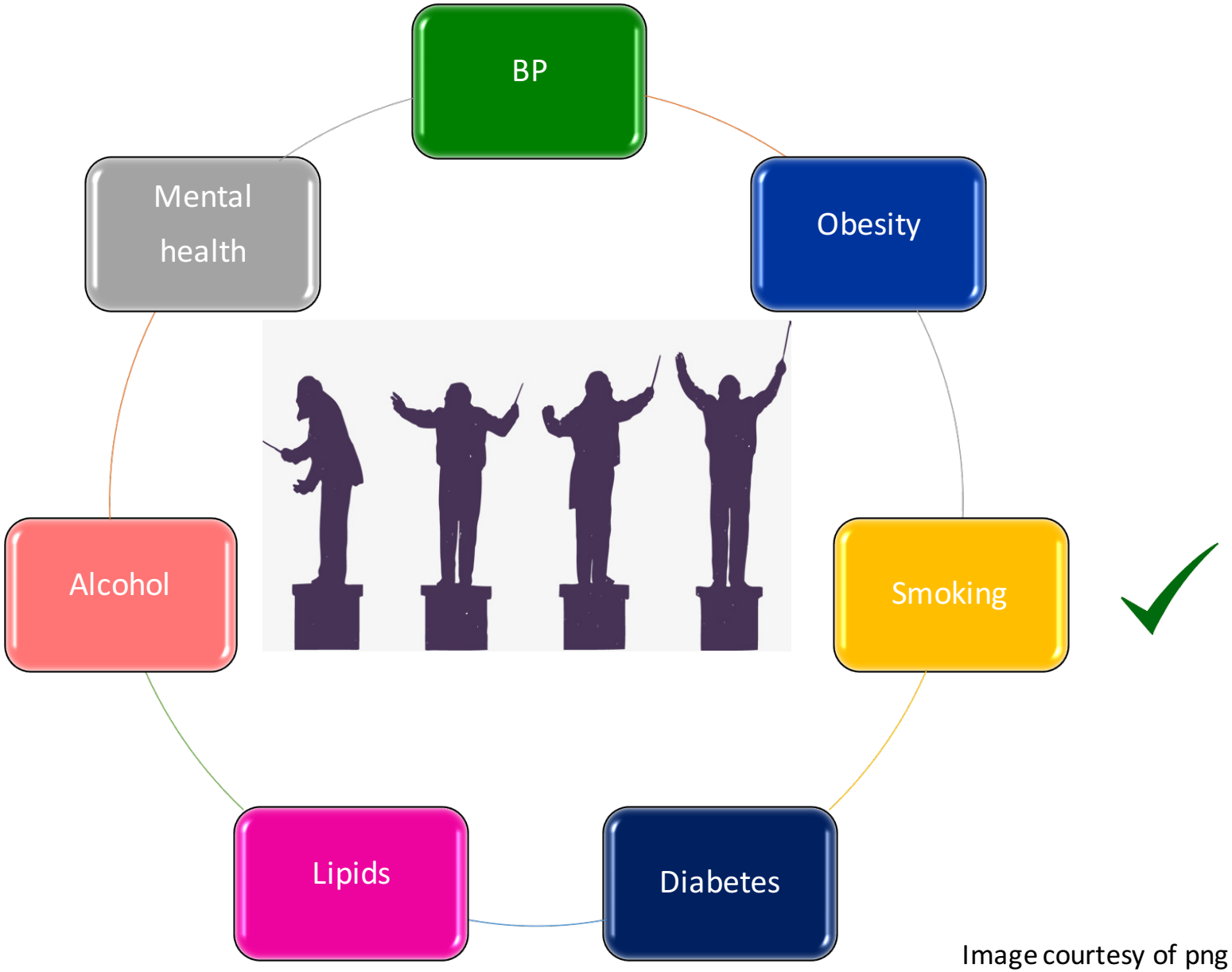


Image courtesy of png images

Advances in HIV Care for 2018

- Caring for people living with HIV is more than just tablets and GP referrals
- Societal and political difficulties arise can challenge our ability to provide care

Affect testing/engagement

- Charging to Overseas Visitors
- Data-sharing between the NHS and Immigration

Life free from stigma

- Bill considering prosecuting people who refuse testing for BBVs when they spit/bite emergency workers
- Civil Aviation Authority preventing HIV + pilots from flying
- Use of spit-hoods by emergency services

1. Health and Social Care Bill 2012

Health care professionals not policy specialists

- BUT we can provide medical evidence to support the work of policy specialists
- Engage with social media, traditional media, MPs, the police, the crown prosecution service, the Home Office

Health care professionals not policy specialists

- BUT we can provide medical evidence to support policy specialists
- Actions: position statements, challenge medical evidence, petitions, review articles, repond to consultations

BASHH

BHIVA British HIV Association

RESPONSE TO FORMAL REVIEW OF 'THE NATIONAL HEALTH SERVICE (CHARGES TO OVERSEAS VISITORS) (AMENDMENT) REGULATIONS 2017*

Summary

The British Association for Sexual Health and HIV (BASHH) and the British HIV Association (BHIVA) welcomes this consultation on the formal review of the National Health Service (Charges to Overseas Visitors Amendment) Regulations 2017 (Amendment Regulations) and appreciates the opportunity to respond jointly.

As the Amendment Regulations have only been in place for several months, with these extended to include non-NHS providers of relevant services from 23rd October 2017 onwards, it is difficult for respondents to provide clear evidence on the impact that the legislative changes have had thus far. Despite this, BASHH and BHIVA have serious concerns around the negative long-term impact we believe the Amendment Regulations and the requirement to charge upfront for certain services will have on public health outcomes as a whole in this country. We also have specific concerns around the impact the Regulations will likely have on overseas visitors who are HIV positive - an already marginalised group that face a particularly complex and challenging set of health requirements.

With this in mind, and as supported by the evidence set out below, BASHH and BHIVA strongly believe that overseas visitors who are HIV positive should be excluded from these Amendment Regulations due to the detrimental impact they will likely have on access to care and public health outcomes more broadly. Ultimately, we believe that the Amendment Regulations should be withdrawn until a comprehensive assessment has been carried out on the full impact that they will likely have.

Pinned Tweet

BASHH @BASHH_UK · 01/12/2017

We are proud to be supporting the petition to reverse the #publichealth #cuts and save our #sexualhealth services – join us and sign up here you.38degrees.org.uk/p/Save-our-sex...

#sexualhealthSOS #NHS

Literature reviews

Risk of transmission via biting /spitting

HIV[1] P66

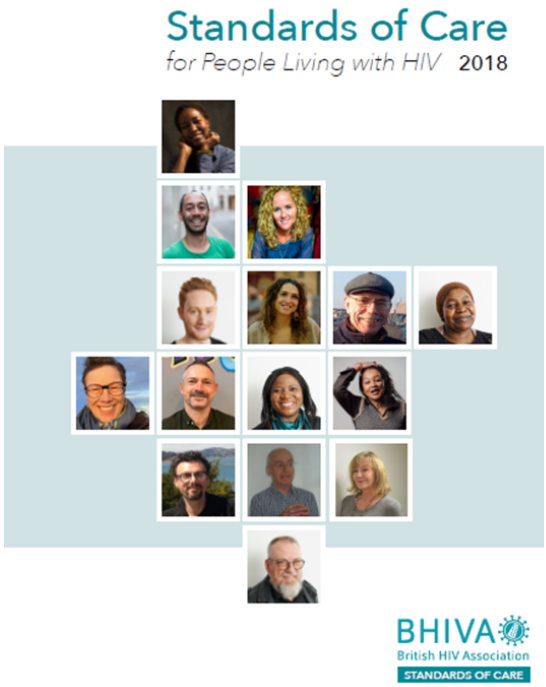
Hepatitis[2] P140

Working to improve standards of care beyond the UK

EACS Invited symposium October 2017

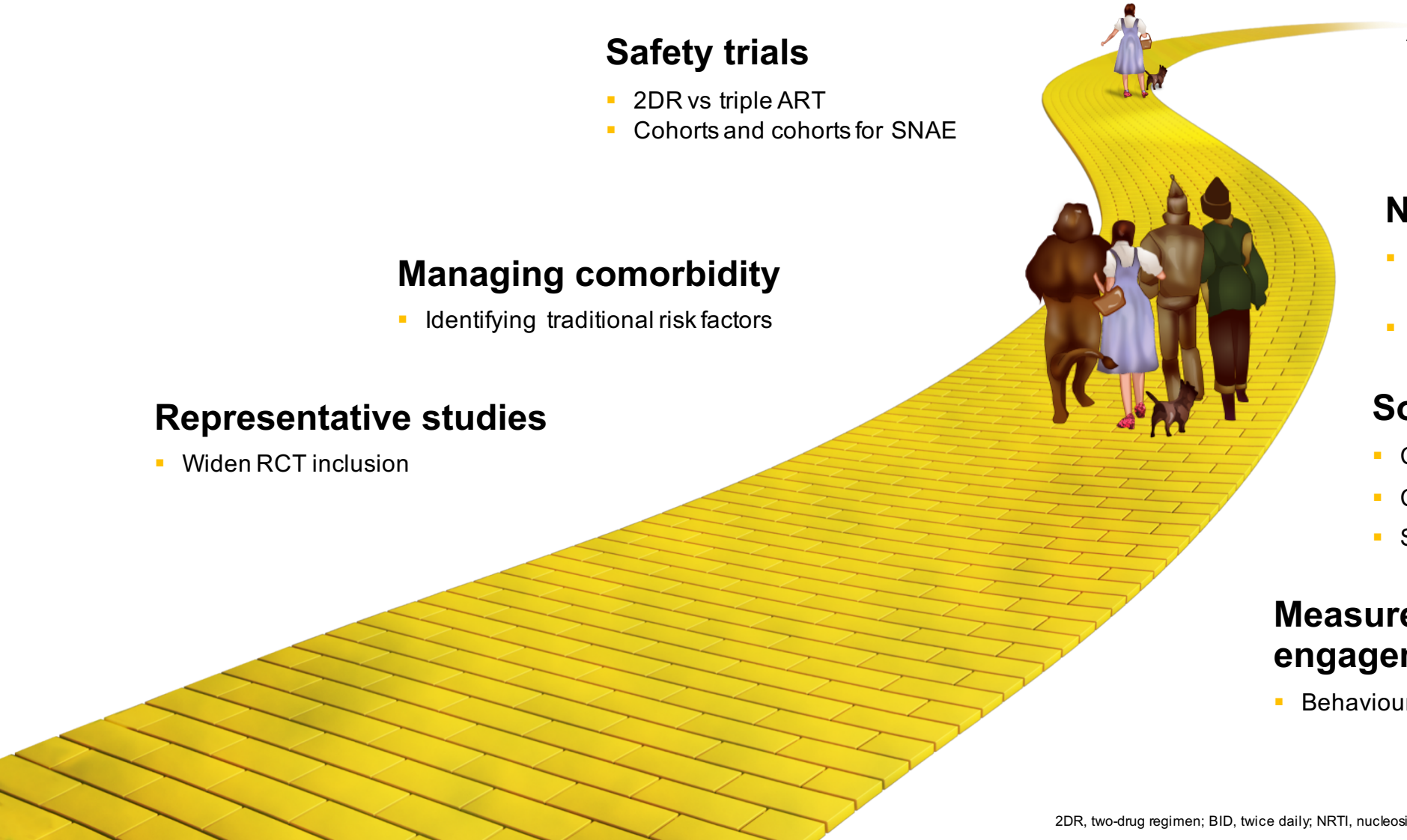
BHIVA-EACS

Inaugural 'Standards of Care' symposium



Advancing standards of care AIDS 2018

The next 25 years…… how will you advance HIV Care?



Safety trials

- 2DR vs triple ART
- Cohorts and cohorts for SNAE

Managing comorbidity

- Identifying traditional risk factors

Representative studies

- Widen RCT inclusion

Access

- Negotiating health policy / drug access
- Access to generics
- Infrastructure investment

New compounds

- Supporting pipeline research
- Long-acting fomulations

Social justice, standards

- Challenge stigma
- Challenge discriminatory legislation
- Standards of care

Measures to improve engagement

- Behavioural measures

2DR, two-drug regimen; BID, twice daily; NRTI, nucleoside reverse transcriptase inhibitor; RCT, randomized controlled trial.

Thank you

Royal London Hospital

Vanessa Apea

Rageshri Dhairyawan

James Hand

Jane Deayton

Nashaba Matin

Maurice Murphy

Simon Rackstraw

Liat Sarner

Sadna Ullah

Andy Williams

Mentor

Jane Anderson

Slides

Michael Aboud

Marta Boffito

Andrew Carr

Annemiek de Ruiter

Bojana Dragovic

Joe Eron

Clifford Leen

Nneka Nwokolo

Adrian Palfreeman

Erin Quirk

Jürgen Rockstroh

Caroline Sabin

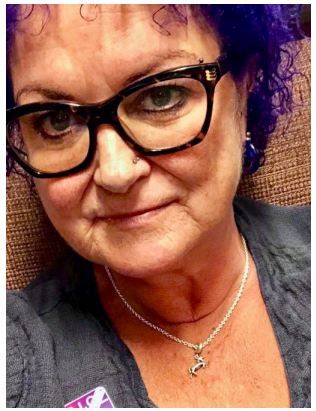
Laura Waters

Gary Whitlock

Graphics by John Wong
Nucleus Central

Wonderful Wife

Flick Thorley



NHS
Barts Health
NHS Trust

QUEEN MARY
UNIVERSITY OF LONDON

Impact of M184V on Virologic Efficacy of Switch to 3TC-Based 2DR

- Retrospective Antiretroviral Resistance Cohort Analysis database
- Conclusions:
  - Risk of virological failure similar (P=0.323)
  - Higher rates of virological blips in 2DR regimes (P = .016)
  - More likely be blip free and suppressed if on ART > 6 years

Gagliardini R, et al. CROI 2018. Abstract 498.