BHIVA
British HIV Association

2023 Spring Conference

Mon 24th – Wed 26th April
Gateshead, UK

HIV and Resistance

Chair:
Nicola Mackie

This educational event is supported by

GILEAD Creating Possible
MSD
ViiV Healthcare

Highly Treatment Experienced: what it means & best management

Laura Waters

Mortimer Market Centre, London

Highly treatment experienced
Definition & management

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Consultant Physician Sexual Health & HIV
CNWL NHS Trust
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Conflicts of interest

Speaker/advisory fees
ViiV, MSD, Janssen, Gilead, Pfizer

Investigator on trials
Gilead, ViiV, MSD & Janssen

Geographic
I live and work in England

Content

1 Definition

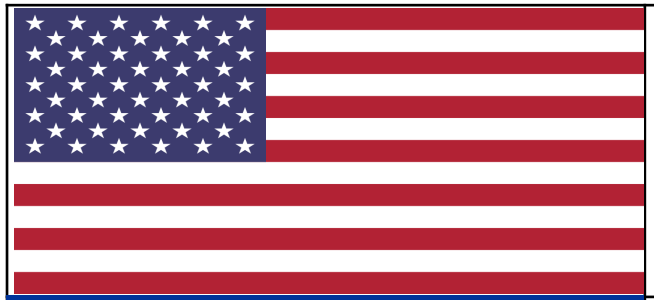
2 Challenges

3 Management

4 Closing thoughts

1 DEFINITION

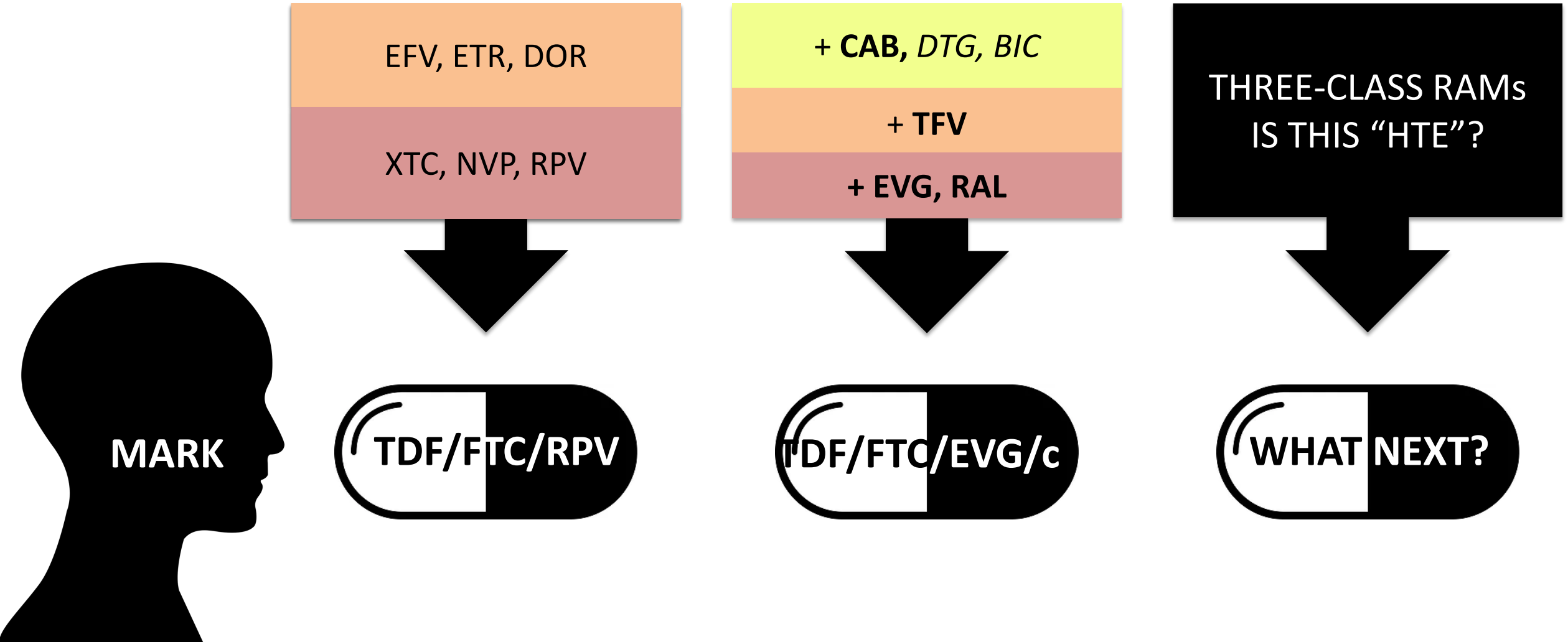
Guidelines

	No fixed definition
	Multiclass resistance = ≥ 2 classes A 2-3 drugs active regimen cannot be constructed with NRTI, NNRTI, PI/b & INSTI
BHIVA British HIV Association	“Individuals with limited or no therapeutic options when a suppressive regimen cannot be constructed”

Terminology

HIGHLY TREATMENT EXPERIENCED	HIGHLY TREATMENT EXPOSED?	LIMITED TREATMENT OPTIONS? CHOICE?
Implies failure & a long history of taking ART?	Implies failure & a long history of taking ART?	A more inclusive & accurate term?

An example….


EFV, ETR, DOR
XTC, NVP, RPV
+ CAB, DTG, BIC
+ TFV
+ EVG, RAL
THREE-CLASS RAMs
IS THIS "HTE"?
MARK
TDF/FTC/RPV
TDF/FTC/EVG/c
WHAT NEXT?

A reasonable definition?

LIMITED TREATMENT OPTIONS (LTO)

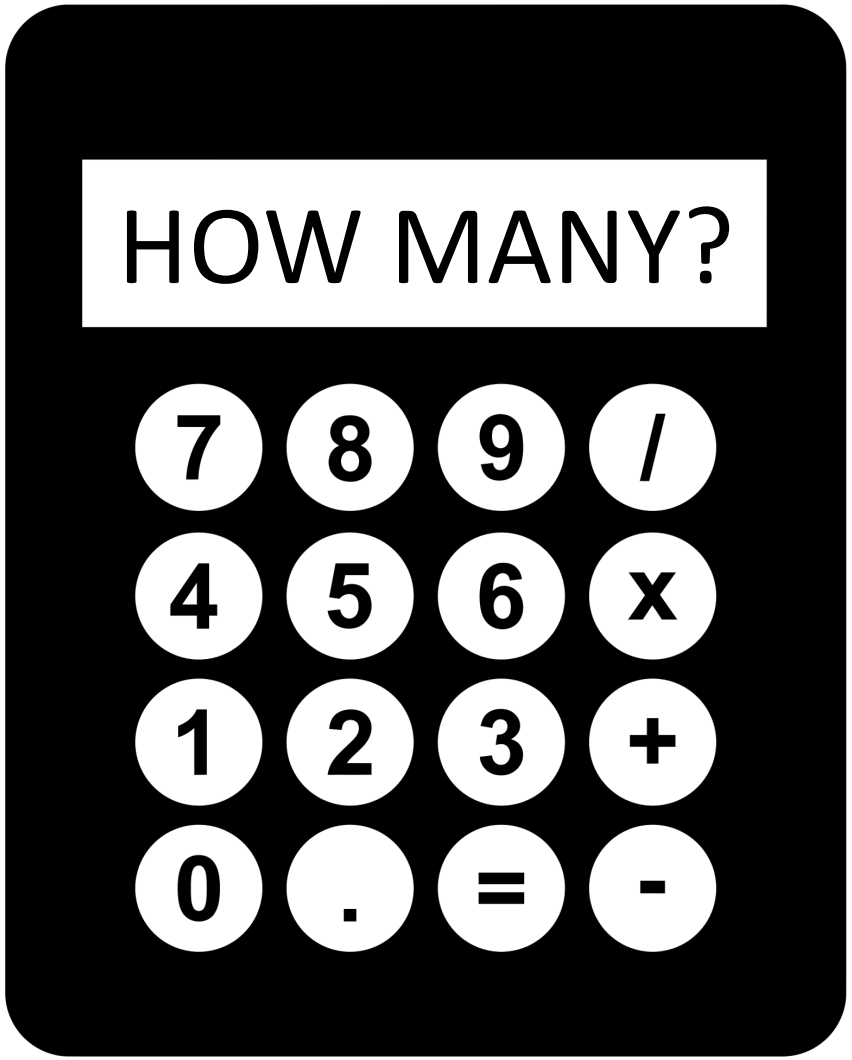
Resistance to 3 or more of:

NRTI, NNRTI, PI & INSTI

Not possible to construct a reasonable regimen equivalent to at least 2 active agents where at least 1 is high barrier

CHALLENGES

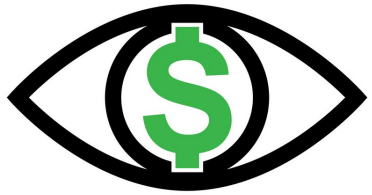
1. Identifying & quantifying people with LTO



2. Interpreting trial findings

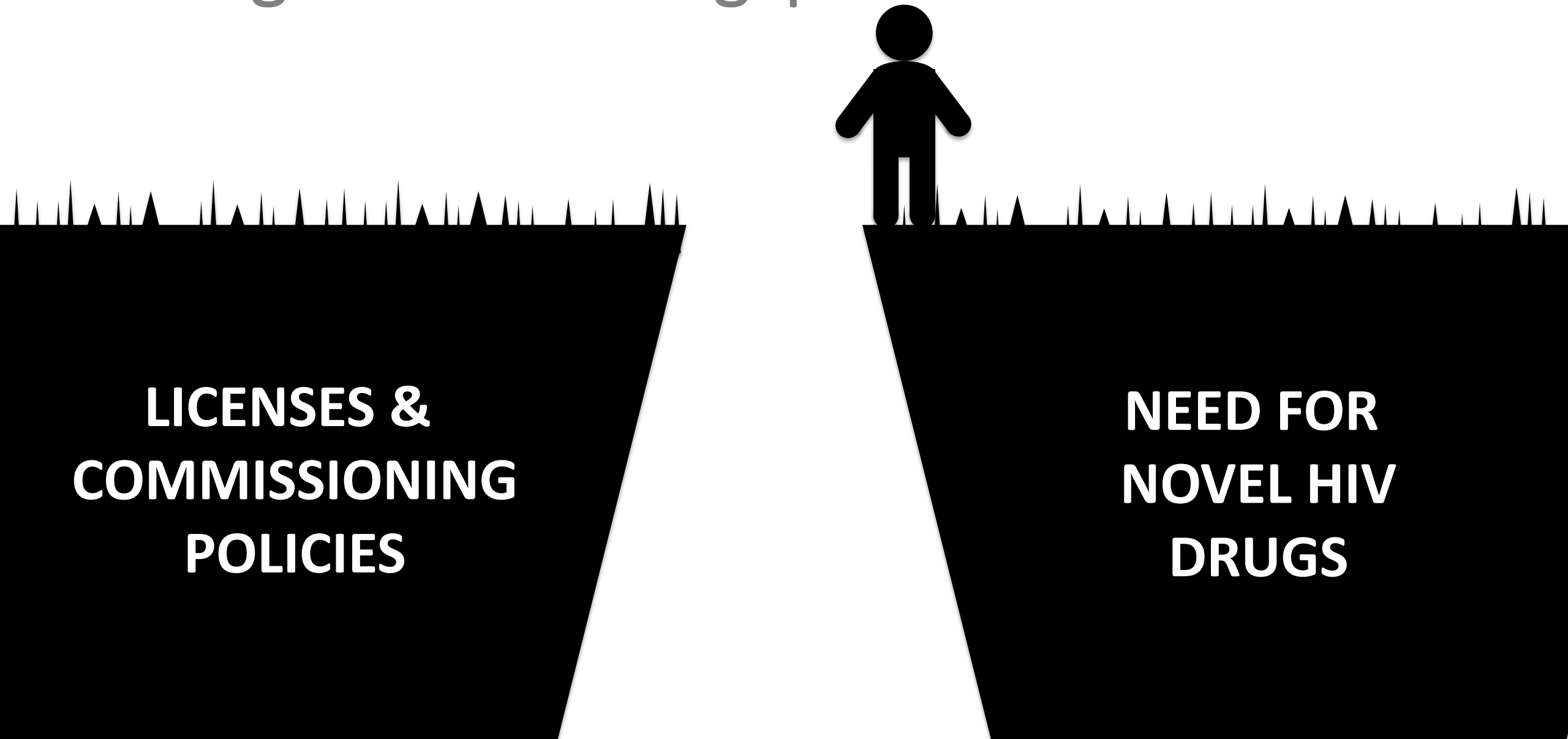
3. (Un)compassionate access schemes

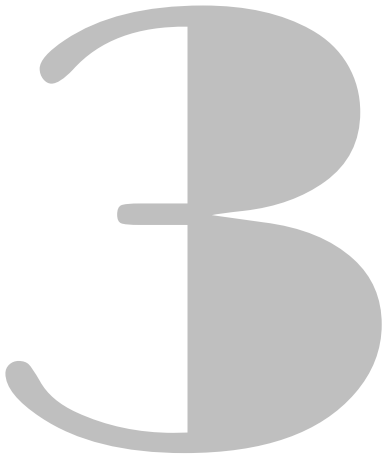
Pharma Company X



Product X will be provided until such time that it is commissioned routinely.

Falling between the gaps





MANAGEMENT & EVIDENCE

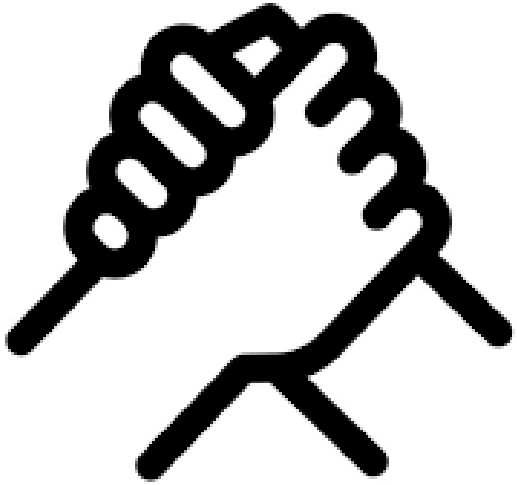
Basic principles

WHY?

LISTENING, TIME & KINDNESS

ADHERENCE & UNDERSTANDING

MDT & PEER SUPPORT



Language

POORLY ADHERENT

People are not "treatment failures"

Treatments fail people

Basic principles

RESISTANCE TESTING	"AVOID ADDING 1 DRUG TO A FAILING REGIMEN"	AVOID DRUGS THAT ADD LITTLE IF RAMs PRESENT
On failing therapy or within 4 weeks of drug cessation Consider all historical resistance	NADIA challenges this mantra! TDF/XTC superior to ZDV/3TC….	NNRTI: particularly EFV, NVP, RPV 1st generation INSTI T-20

Continue ART in presence of viraemia

✓

ACCUMULATING RESISTANCE, TOXICITY

REDUCED DISEASE PROGRESSION

BHIVA: “we recommend against discontinuing or interrupting ART”

Fostemsavir, ibalizumab & lenacapavir

R = randomized; NR = non-randomised

	FOS: BRIGHTE	IBA: TMB-301	LEN: CAPELLA
Mechanism	gp120 inhibitor	CD4 mAb	Capsid inhibitor
Sample size	371 (272 R, 99 NR)	40 W24; 25 in EAP to W48	72 W24 (36 R, 36 non-R)
Inclusion	Exhaustion* all ARVs ≥4/6 classes; R = 1-2 active ARVs; VL >400 on ART	Resistant to ≥1 ARV in 3 classes; ≥1 active OBR ARV; VL >1000 on ART	Resistant ≥2 ARVs in 3/4 & ≤2 active ARVs 4 main classes: VL >400 on ART
New OBR ARVs	15% NR, 4% total IBA	43% FOS	24% IBA, 11% FOS
VL <40-50	R **54%**; NR 38% at W48	43% W25; **59%** (M=F) W48	**81%** W24 (all); **78%** W52 (R only)
CD4 change	+ 139 cells/mm^3 at W48	+ 62 cells/mm^3 at W25	+ 84 cells/mm^3 at W52
PDVF & RAMs	R 18%; 43% gp120 RAMs	10 CVF, 90% lower IBA susc	Total: 29% W24; 38% LEN RAMs Nil W24-W48 (R cohort only)

BRIGHTE: NEJM 2020 382:1232-1243; *including resistance, toxicity, side effects, contraindications, reluctance to use T20; NR = zero options
TMB-301: NEJM 2018 379:645-654 + HIV Glasgow 2022; **CAPELLA**:

Comparative-Effectiveness Research/HTA

Indirect Treatment Comparisons of Lenacapavir Plus Optimized Background Regimen Versus Other Treatments for Multidrug-Resistant Human Immunodeficiency Virus

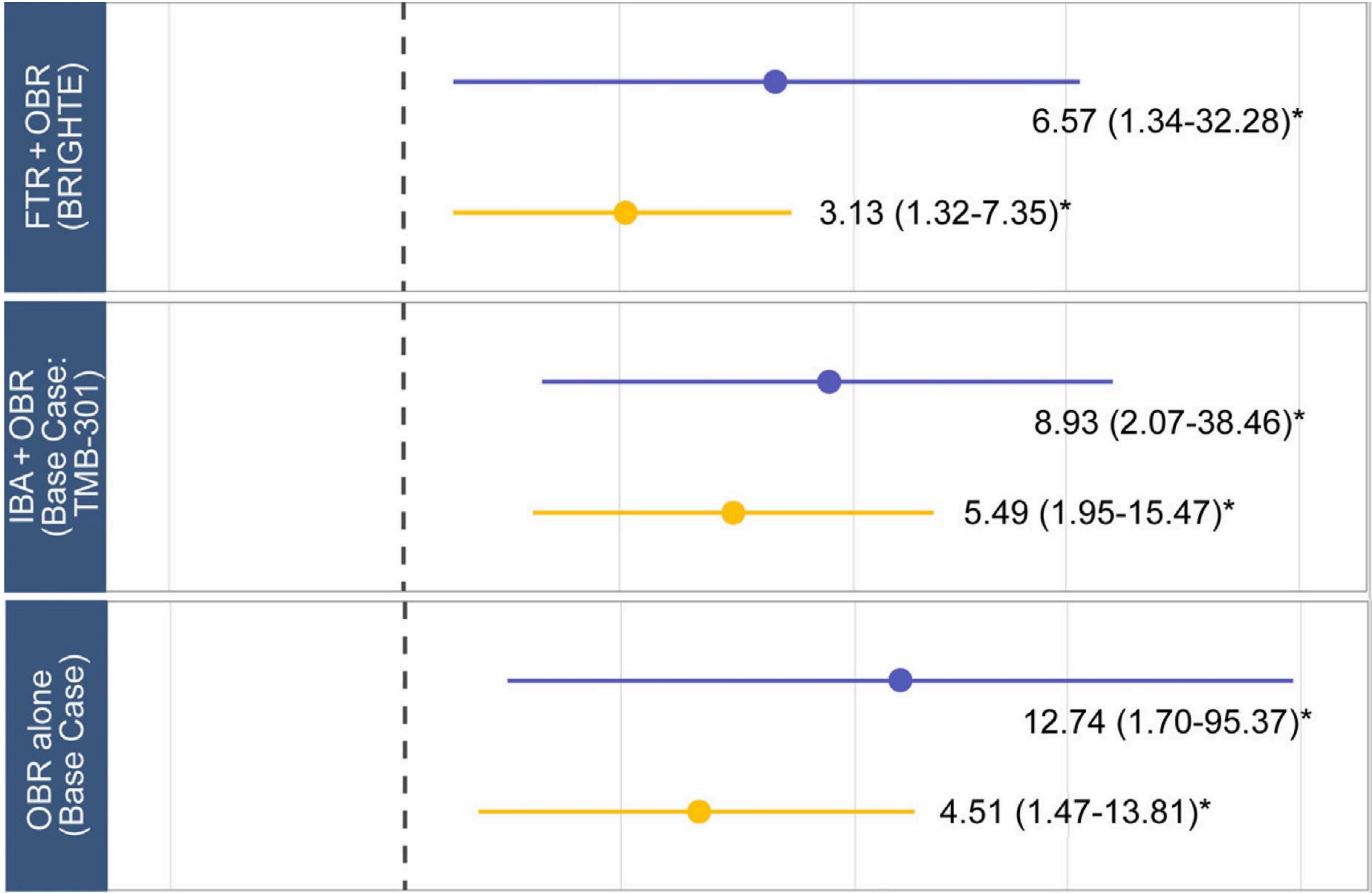
Iro Chatzidaki, MSc, Tristan Curteis, MSc, Hannah Luedke, MRes, Dylan J. Mezzio, PharmD, MS, Martin S. Rhee, MD, Eve McArthur, BSc, Lucy A. Eddowes, PhD

Value Health 2022; S1098-3015(22)04785-4

SIMULATED TREATMENT COMPARISON

Study								
CAPELLA,[32,33] randomized cohort							umber of evious agents,	OSS ≥ 2, n (%)
								7 (29)
								3 (25)
BRIGHTE,[10] all randomized participants								NR
TMB-301[7]	IBA 800 mg Q2W + OBR	40	51 (11)	4.5 (0.8)	150 (182)	20 (8)	11 (5)	23 (58)
TMB-202[41]	IBA 800 mg Q2W + OBR	59	48	5.1	106 (91)	17 (4)	NR	NR

+15 OBR studies e.g. DUET, MOTIVATE, VIKING


FTR + OBR (BRIGHTE)
6.57 (1.34-32.28)*
3.13 (1.32-7.35)*
IBA + OBR (Base Case: TMB-301)
8.93 (2.07-38.46)*
5.49 (1.95-15.47)*
OBR alone (Base Case)
12.74 (1.70-95.37)*
4.51 (1.47-13.81)*

Basic principles

BHIVA	DHHS
Include at least 2, preferably 3, fully active agents At least 1 active PI/b (preferably DRV) + an agent with a novel mechanism of action e.g. INSTI, MVC, FOS, IBA, LEN, other Ix agents	Is one fully active high barrier drug available? Consider combining partially active NRTI, 2nd generation INSTI, PI with new classes. BD DTG or DRV if RAMs.

OFFICIAL

NHS England

Clinical Commissioning Policy
Fostemsavir for multi-drug resistant HIV-1 infection (adult) (URN 2108) [201008P]

Publication date: October 2022 version number: v1.0

Needs assessment

2016: 2,400 people with viraemia, 3% with PI RAMs = 70 in need

Eligibility

Not suppressed on existing ART **OR** Suppressed on highly complex ART where FOS could simplify regimen + optimise patient outcome & experience

ALL of….

1. Discussed/agreed with person + MDT
2. Adult with HIV
3. FOS added to an OBR
4. MDR HIV-1*
5. Limited/no therapeutic options

*limited options: RAMs, tolerability, safety etc.

Ibalizumab


£
£822 per 200mg vial
200mg loading dose
800mg fortnightly

Lenacapavir

GILEAD

Reactive individual patient access (Early access) programme in UK&I

Capella

Key eligibility criteria

- HIV-1 RNA ≥ 400 c/mL
- Resistance to ≥ 2 agents from 3 of 4 main ARV classes

om 4 main ARV

NICE National Institute for Health and Care Excellence

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Lenacapavir for treating multidrug resistant HIV-1 ID6196

In development [GID-TA11125] Expected publication date: TBC

N IRELAND

No IBA, LEN or FOS use
No off-license CAB/RPV
IBA NPP funding: TBC

ROI

No IBA, LEN or FOS use
No FOS access yet
No off-license CAB/RPV
possible if consensus
IBA NPP funding: local then seek national reimbursement

SCOTLAND

No IBA, LEN or FOS use
No off-license CAB/RPV but possible if MDT agreed
IBA NPP funding: national budget?

WALES

No IBA, LEN or FOS use
No off-license CAB/RPV
possible if best interest
IBA NPP funding: IFR to local Health Board

CLOSING THOUGHTS

NICE National Institute for Health and Care Excellence

Cabotegravir with rilpivirine would be beneficial for people who find daily tablets challenging or who would prefer an injectable regir

But not so challenging to have a detectable viral load or a history of virological failure?

EQUITY

Acknowledgements

Northern Ireland

Melissa Parry, John White

Scotland

Kathryn Brown, Dan Clutterbuck, Rebecca Metcalfe

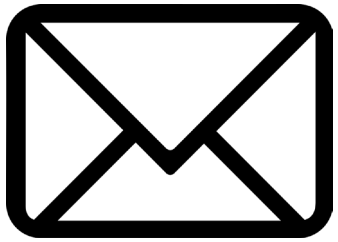
Republic of Ireland

Emma Devitt, Fiona Lyons

Wales

Fiona Clark, Jane Nicholls

Thank you for listening



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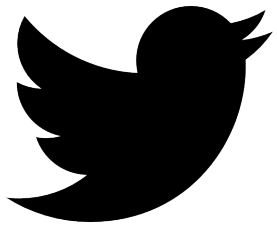

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