Selected Treatment Highlights - CROI 2020 - Regional Relevance

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Regional Relevance

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Asia-Pacific HIV Clinical Forum 2020
12 October 2020

Disclosure

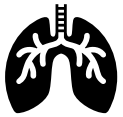
I have no confilct of interest in relation to this presentation.

Outlines

ARV strategies

Metabolic complication and Weight Gain

HIV in Pregnancy HIV and Tuberculosis

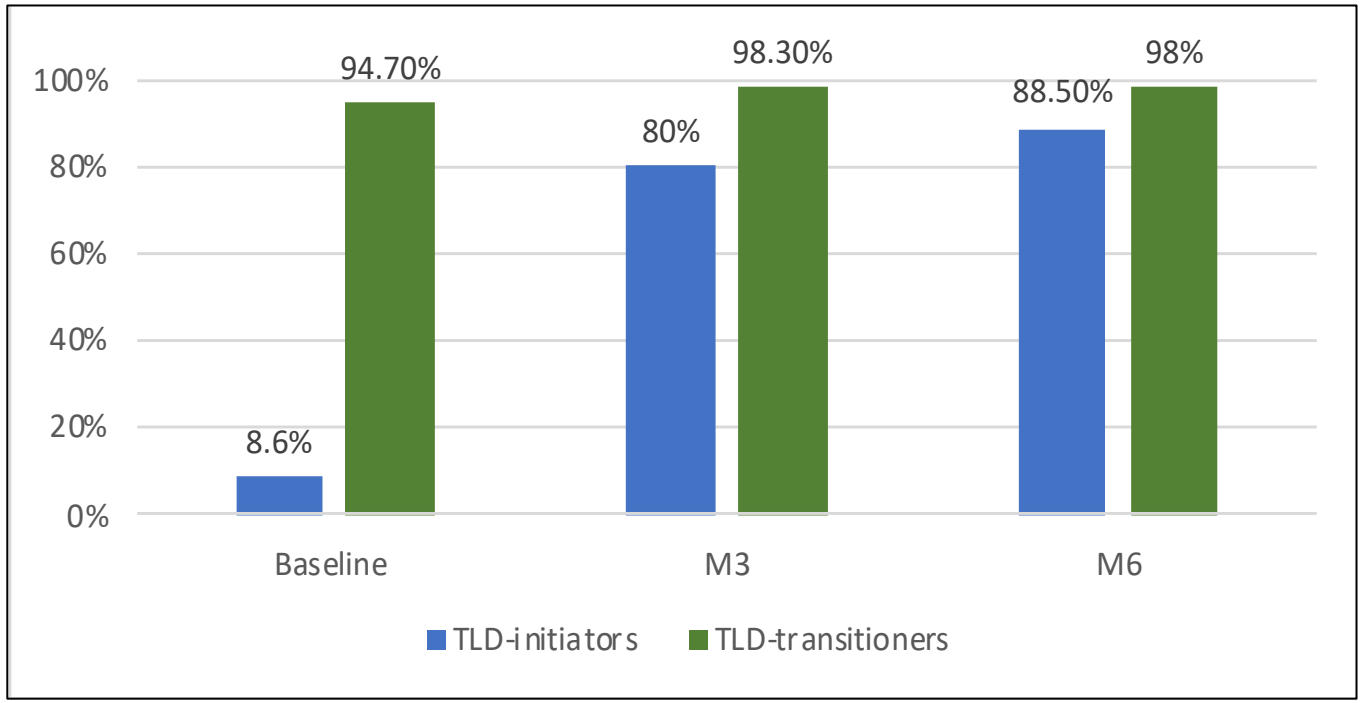


HIV and Tuberculosis

Transition to TLD in MALAWI

- To describe virological response to TLD
  - Transitioned from NNRTI (n= 1892)
  - Initiating ART with TLD (n=35)
- No HIV-1 viral load testing at baseline.
- Plasma viral load was assessed at 3, 6, 12- and 18-months post TLD-start.

Virological suppression (VL 50 < copies/mL)



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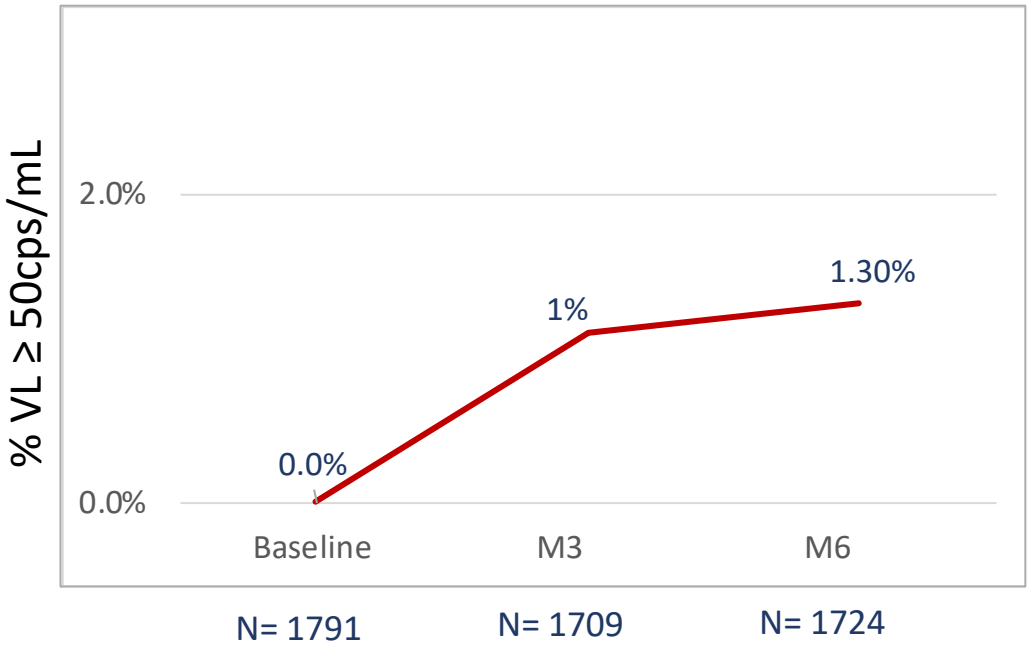
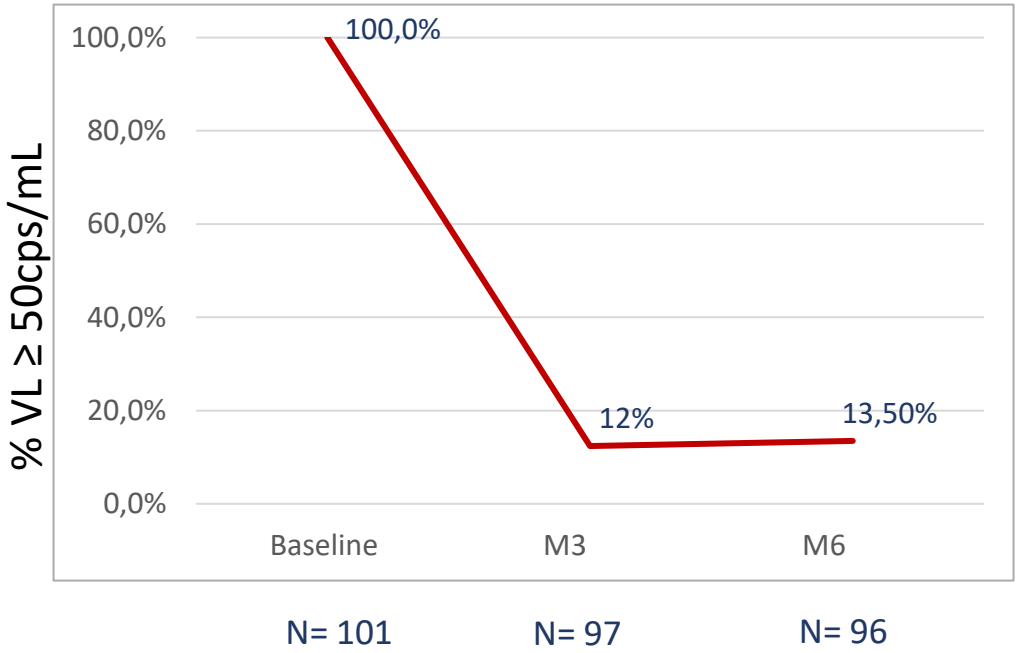
Transitioners with virological failure

VL ≥ 50 cps/mL
Transitioners suppresed at baseline



VL ≥ 50 cps/mL
Transitioners non- suppresed at baseline



Confrimed VF : 5 transitioners => 2/5 had DTG at M6 in combination with resistance to TDF.
Safety : 2 cases of severe psychosis leading to TLD discontinuation before M3

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GEMINI-1 and -2: Confirmed Virologic Withdrawals Through Wk 96

- DTG + 3TC non-inferior DTG + TDF/FTC in ART-naïve patients (N = 1974) at Weeks 48/96
- At W96, “confirmed virologic withdrawal”: 11 in DTG + 3TC arm vs 7 in the DTG + TDF/FTC arm
- No emergent genotypic/phenotypic resistance to INSTI/NRTIs was observed.

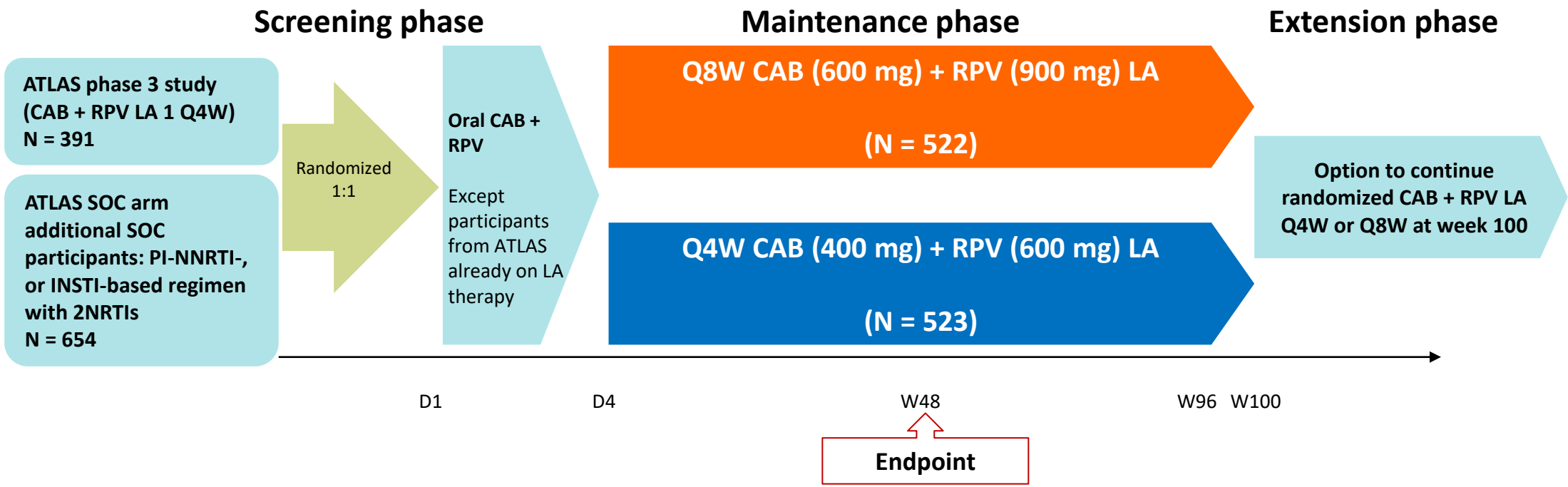
Table. Summary of CVWs in DTG + 3TC Arm

Sub#	BL VL (c/mL)	BL CD4 (cells/mm^3)	CVW Visit	SVW VL	CVW VL	WD VL	Non-adherence/Treatment interruption
1	368439	19	W24	212	376	362	Adherent
2	341818	317	W108	396	726	280	Non-adherence
3	124492	212	W16	6648	56435	95	Unknown
4	112812	74	W72	61076	87794	671	Non-adherence
5	101671	347	WK60	703	85556	ND	Treatment interruption
6	96277	213	W24	451	9602	67	Treatment interruption
7	63817	50	W72	422	2154	115	Non-adherence
8	50263	284	W24	348	206	96	Adherent
9	37701	414	W48	43908	38457	ND	Unknown; had concurrent SAE of psychosis
10	17232	529	W24	461	251	59	Unknown
11	7654	567	W60	3972	3131	1513	Non-adherence

Underwood M, CROI 2020, Abs. 483

ATLAS-2M : CAB LA + RPV LA IM Q4W vs Q8W

- **Phase 3, randomized, multicenter, noninferiority, open-label study**



- Primary endpoint: HIV-1 RNA ≥ 50 copies/mL at Wk 48 by FDA snapshot in ITT-E (NI margin 4%)
- Secondary endpoints: HIV-1 RNA < 50 copies/mL at Wk 48 by FDA snapshot in ITT-E, safety and tolerability, VF, resistance, and treatment preference

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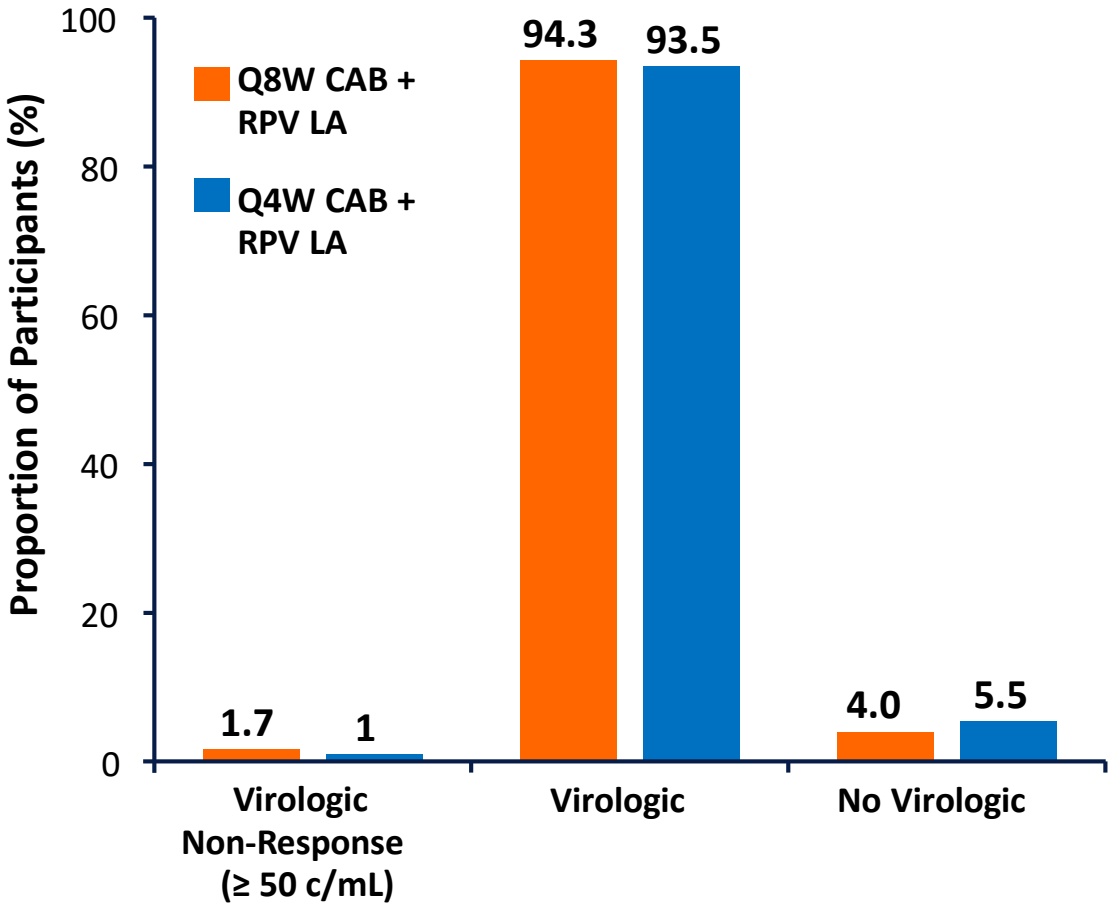
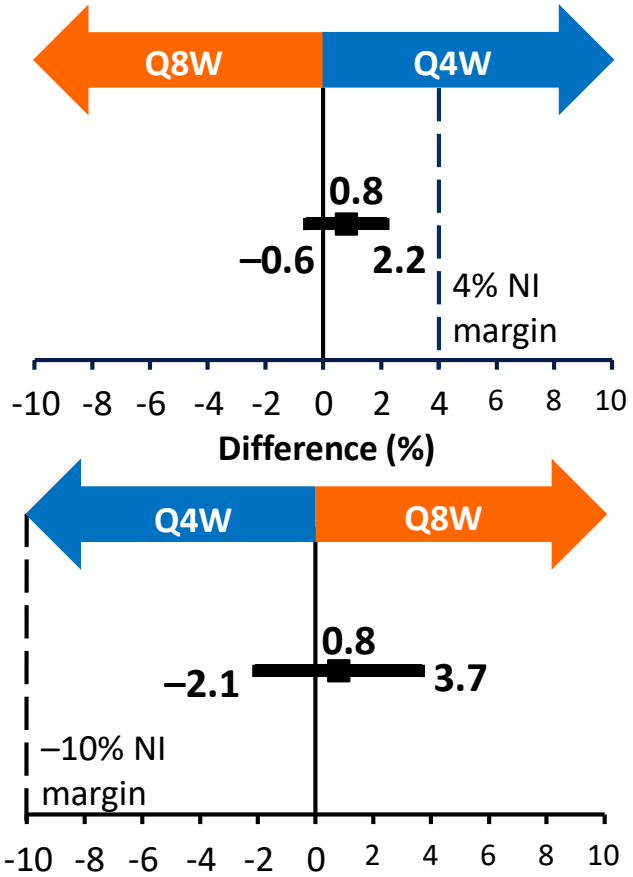
ATLAS-2M : Virologic Outcomes at Wk 48 for ITT-E



Adjusted Treatment Difference at Week 48 (95% CI)*



Primary endpoint (≥ 50 c/mL):

Q8W is noninferior to Q4W (Week 48)

Key secondary endpoint (< 50 c/mL):

Q8W is noninferior to Q4W (Week 48)

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Slide credit: clinicaloptions.com

ATLAS-2M: Virologic Failure, ISRs, Patient Preferences

Outcome	CAB LA + RPV LA Q8W (n = 522)	CAB LA + RPV LA Q4W (n = 523)
CVF, n (%)	8 (1.5)	2 (0.4)
CVF with RPV RAMs,* n/N	6/8	1/2
Treatment-emergent RPV RAMs	K101E, E138E/K, E138A, Y188L	K101E, M230L
CVF with INSTI RAMs,* n/N	5/8	2/2
Treatment-emergent INSTI RAMs	Q148R, N155H†	E138E/K,Q148R, N155N/H

- CAB LA + RPV LA well tolerated
  - 98% of ISRs were grade 1/2; median duration was 3 days
- Patients preferred CAB LA + RPV LA over oral therapy
- Patients previously receiving CAB LA + RPV LA preferred Q8W dosing over Q4W dosing

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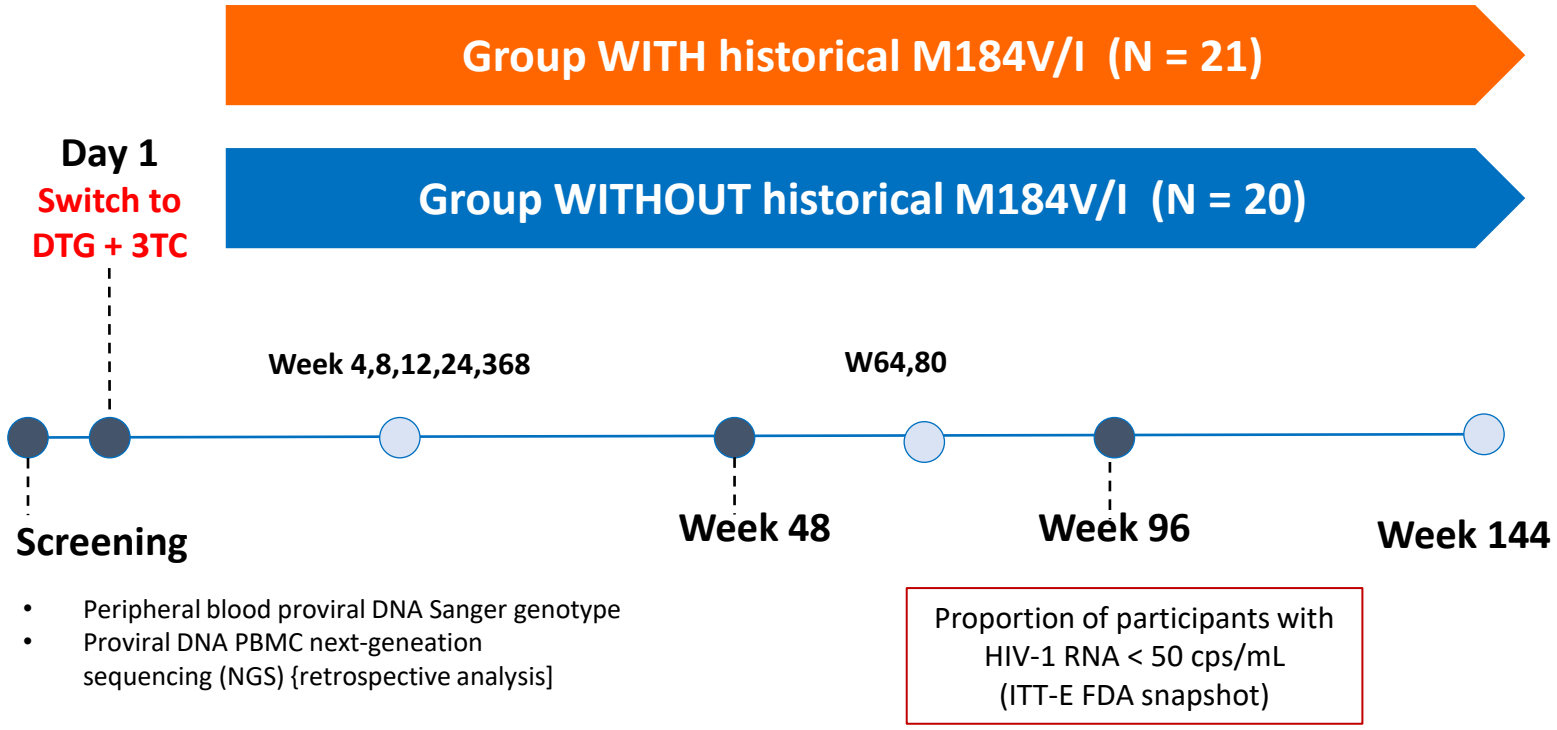
ART-PRO Trial: DTG + 3TC in patients with archived 3TC resistance

- Open, single-arm, pilot trial including HIV-1 infected adults

Inclusion
- CD4 > 350 cell/µL and VL < 50 c/mL for 12 months (1 blip allowed)
- Stable ART for 3 months
- FTC or 3TC in past/present treatment
- INSTI naive

Exclusion
- M184V/I or K65R in baseline proviral DNA Sanger genotype
- HBAgS +
- Pregnant/women wishing to conceive



De Miguel R, CROI 2020, Abs. 485

ART-PRO Trial: DTG + 3TC in patients with archived 3TC resistance

Baseline characteristic	Historical M184V/I (N = 21)	No historical M184V/I (N = 20)
CD4/mm³ nadir/current, median	160 / 705	259 / 647
Duration of suppressed HIV RNA, median years	9.8	7.5
Baseline ART including 3TC or FTC, %	42.9 (N = 9)	95 (N = 19)
M184V in proviral DNA Sanger genotype, %	9,5 (N = 2)	0
M184V/I detected by NGS in proviral DNA, % **> 1%** **> 5%** **> 20%**	 95.2 66.7 33%	 35 15 5

Week 96 Results (FDA-SNAPSHOT)	Historical M184V/I (N = 21)	No historical M184V/I (N = 20)
HIV-1 RNA < 50 cps/mL	**18 (85.7)**	**19(95)**
Virologic failure or HIV-RNA ≥ 50 cps/mL	**0(0)**	**0(0)**
No virologic data at Wk 96	**3(14.3)**	**1(5)**
• Discontinuation due to an adverse event	1(4.8)	0(0)
• Discontinuation for other reasons and last available HIV-1 RNA < 50 cps/mL	2(9.5) *(Protocol violation)*	1(5) *(Declined to continue study)*

* 12 participants with 14 blips (6 pts. In Hx M184V)

De Miguel R, CROI 2020, Abs. 485

ADVANCE trial : Predicted 10-Yr risks of DM and CVD

- **Phase 3, randomized, open-label study in South Africa**

Treatment-naïve
HIV-1 RNA > 500 c/mL
no TB or pregnancy
no baseline genotyping
N= 1053

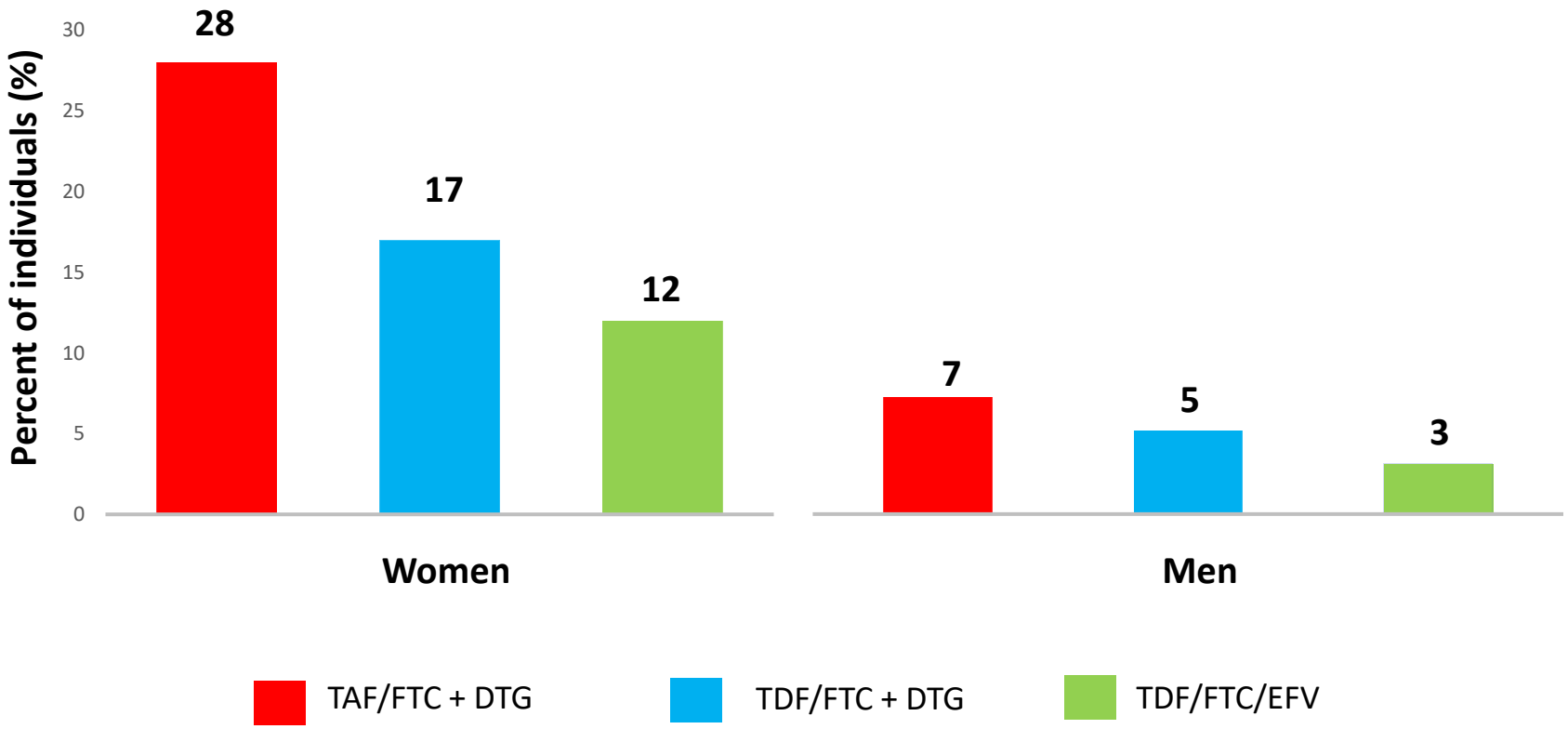
TAF/FTC + DTG
(n = 351)

TDF/FTC+ DTG
(n = 351)

TDF /FTC/EFV
(n = 351)

96 Weeks

Treatment emergent obesity to Wk 96



Hill A, CROI 2020, Abs. 81

ADVANCE trial : Predicted 10-Yr risks of DM and CVD

Summary of change in risk of cardiovascular disease and diabetes between baseline and W96

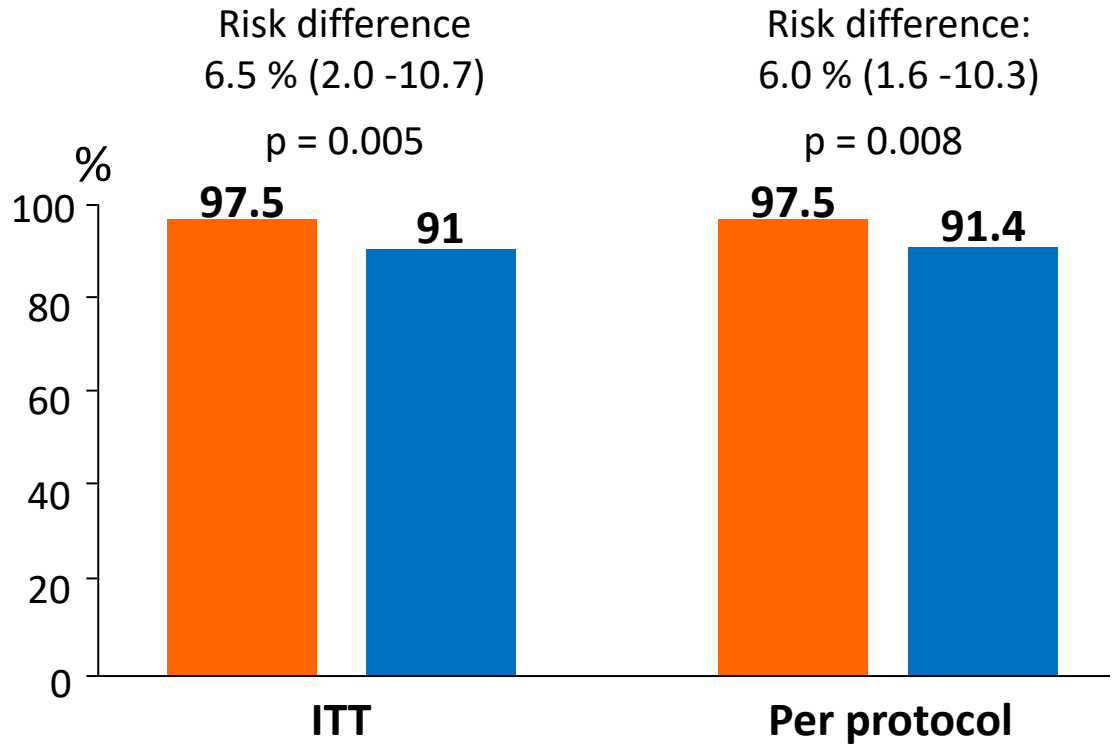
	TAF/FTC + DTG (N = 351)	TDF/FTC + DTG (N = 351)	TDF/FTC/EFV (N = 351)	Inter-arm comparison
Metabolic syndrome				
Baseline	5 %	6 %	4 %	
Emergent during treatment	8 % *	6 %	4 % *	* p = 0.031
Framingham CV risk Equation				
Baseline	2.37 %	2.53 %	2.24 %	
Median change at W96	+ 0.43 %	+ 0. 22 %	+ 0.28 %	ns
QRISK Equation				
Baseline	0.60 %	0.60 %	0.50 %	
Median change at W96	+ 0.20 %* †	+ 0.20 %	+ 0.10 %*	*p = 0.027
QDIABETES Equation				
Baseline	0.30 %	0.40 %	0.30 %	
Median change at W96	+ 0.90 %*	+ 0.50 % *,**	+ 0.70 %**	* p = 0.004 ** p = 0.005

Hill A, CROI 2020, Abs. 81

IMPAACT 2010 : DTG vs EFV & TDF vs TAF in pregnancy

- **Phase III, randomized, open-label, pregnant WLHIV at 14-28 wks of gestational age**
  - Up to 14 days' pre-entry ART was permitted.
- **Randomized (1:1:1)**
  - DTG + TAF/FTC (n = 217)
  - DTG + TDF/FTC (n = 215)
  - TDF/FTC/EFV (n = 211)
- **Primary efficacy analysis**
  - Compared the combined DTG-containing arms to the EFV arm, with regard to delivery HIV RNA <200 cps/mL.
- **Conclusions:**
  - DTG-containing regimens had superior virologic efficacy at delivery to EFV/FTC/TDF.
  - DTG+FTC/TAF had the lowest composite frequency of adverse pregnancy outcomes.
  - More weight gain in DTG + FTC/TAF.

HIV RNA < 200 cps/mL at delivery
Pooled DTG vs EFV/FTC/TDF



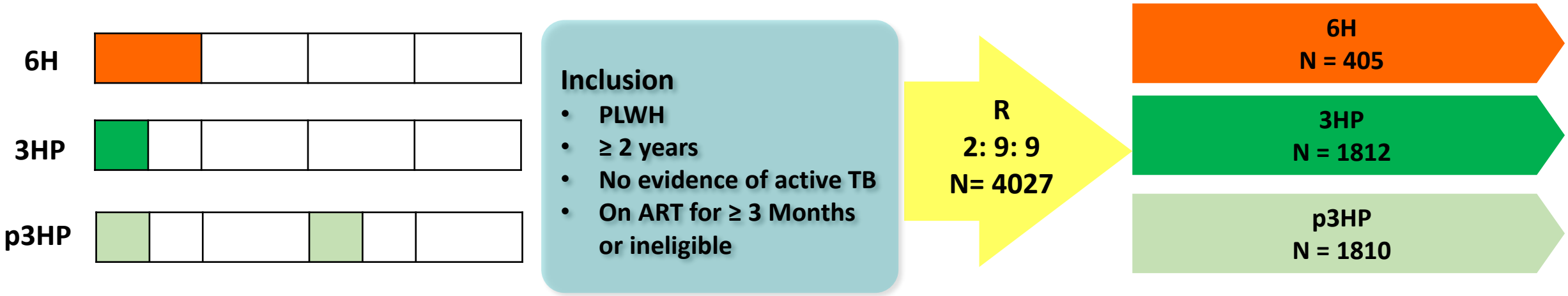
Chinula L, CROI 2020, Abs. 130LB

WHIP3TB: Effectiveness of 3HP annually vs once in PLWH

- **Primary objective :**

Part A: Treatment completion rates and effectiveness of 3HP vs. 6H

Part B: The effectiveness of 3HP given annually vs. once



p3HP = periodic (annual)3HP

Churchyard G, CROI 2020, Abs. 143LB

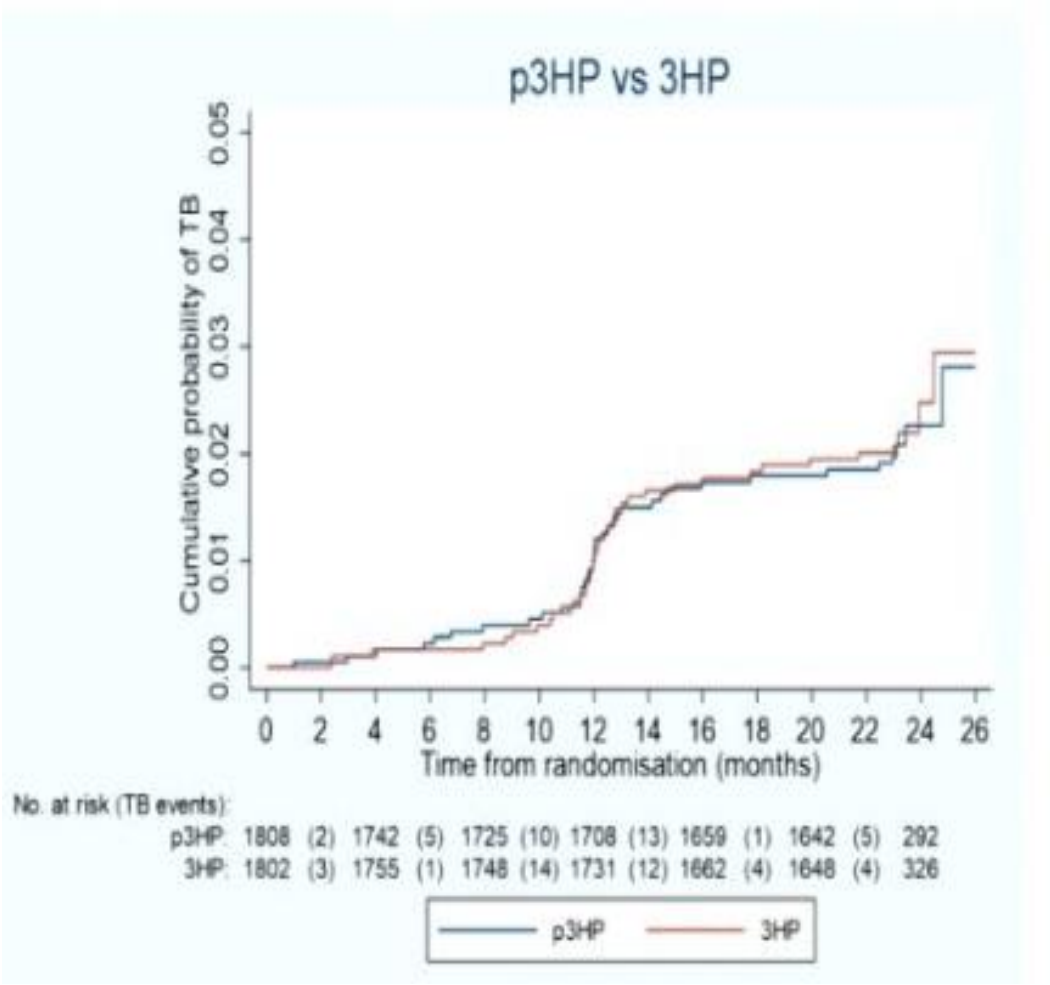
WHIP3TB: Primary outcome

Part A: Treatment completion

Arm	n/N	Treatment Completion (%)	Risk difference, % (95% CI)	Risk Ratio (95% CI)
6H	204/404	50.5	0	1
3HP	3264/3610	90.4	39.9 (35.0-44.9)	1.79 (1.62-1.97)

Part B: TB incidence over 24 months

Arm	n	TB rate/ 100 pyrs	Hazard ratio (95% CI)	P-value
3HP	1802	1.26	1	
p3HP	1808	1.21	0.96 (0.61-1.50)	0.85



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