AETC AIDS Education & Training Center Program Mountain West

Virtual CROI 2021: Key Treatment Studies

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Disclosures

No conflicts of interest or relationships to disclose.

Outline

1. Update from IMPAACT 2010
2. Update from ATLAS-2M
3. Lenacapavir: Capella Study

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Update from IMPAACT 2010

Background: IMPAACT 2010

- ART options in pregnancy remain limited
- IMPAACT 2010 is a global, multicenter, randomized trial of ART-naïve pregnant women with HIV started on:
  - TAF/FTC + DTG vs
  - TDF/FTC + DTG vs
  - TDF/FTC/EFV
- Interim results through delivery outcome (CROI 2020)
  - DTG-containing arms had superior virologic efficacy
  - TAF/FTC + DTG had lowest rate of adverse pregnancy outcomes

Chinula L et al, Virtual CROI 2021, Abstract #177

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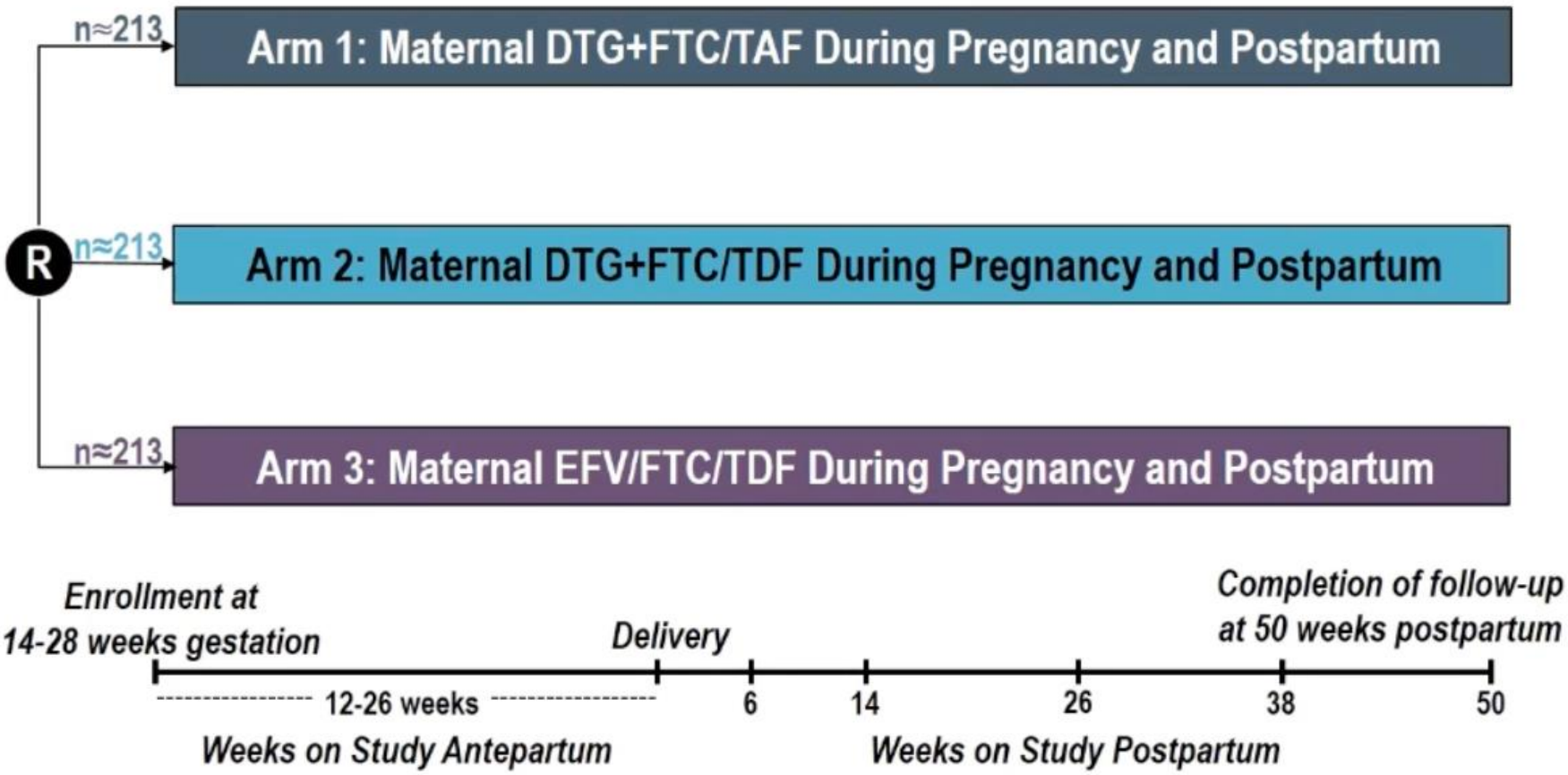
Study Design: IMPAACT 2010



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Study Design: Maternal Baseline Characteristics

	DTG+FTC/TAF (n=217)	DTG+FTC/TDF (n=215)	EFV/FTC/TDF (n=211)	Total (n=643)
Age (median years)	26.8	26.0	26.6	26.6
Enrolled in Africa	187 (86%)	189 (88%)	188 (89%)	564 (88%)
Gestational age (median weeks)	22.1	21.3	22.1	21.9
CD4 count (median cells/mm^3)	407	481	439	466
HIV-1 RNA (median copies/mL)	781	715	1357	903
HIV-1 RNA <50	36 (16%)	37 (17%)	27 (13%)	100 (16%)
ART in pregnancy prior to entry	176 (81%)	180 (84%)	176 (83%)	532 (83%)
Median days on ART	6	6	6	6
BMI* (kg/m2), median (Q1,Q3)	25.1 (22.5, 29.4)	24.5 (22.0, 28.1)	24.2 (21.5, 28.0)	24.7 (22.0, 28.4)

Median duration of antepartum follow-up: 17.4 weeks, *Pre-pregnancy BMI was not available

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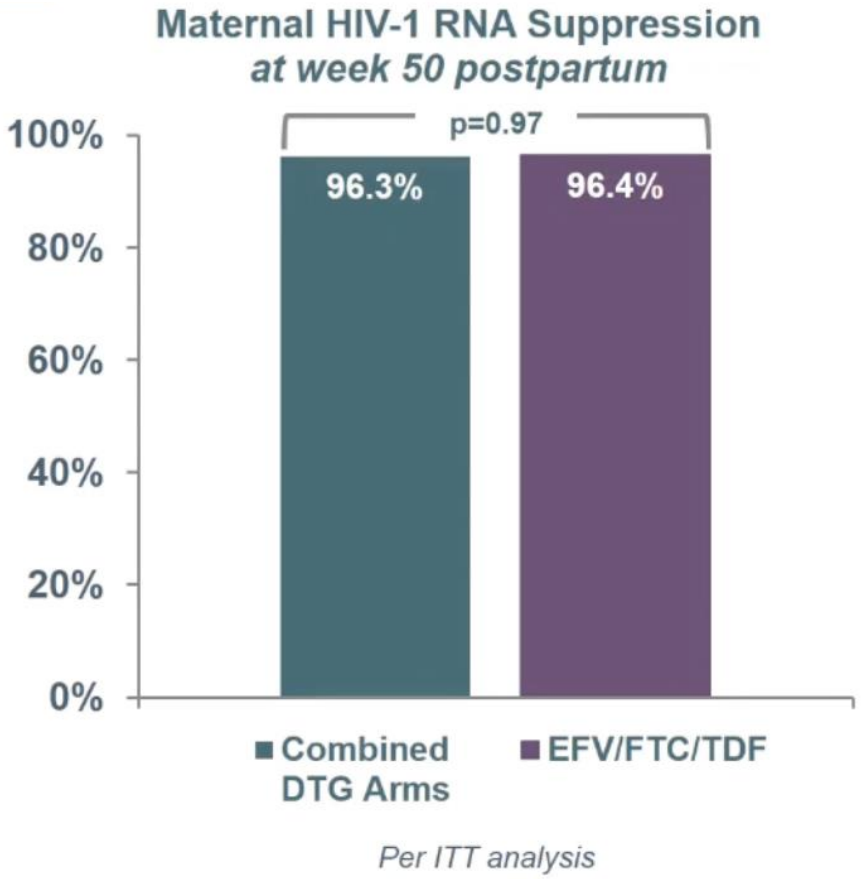
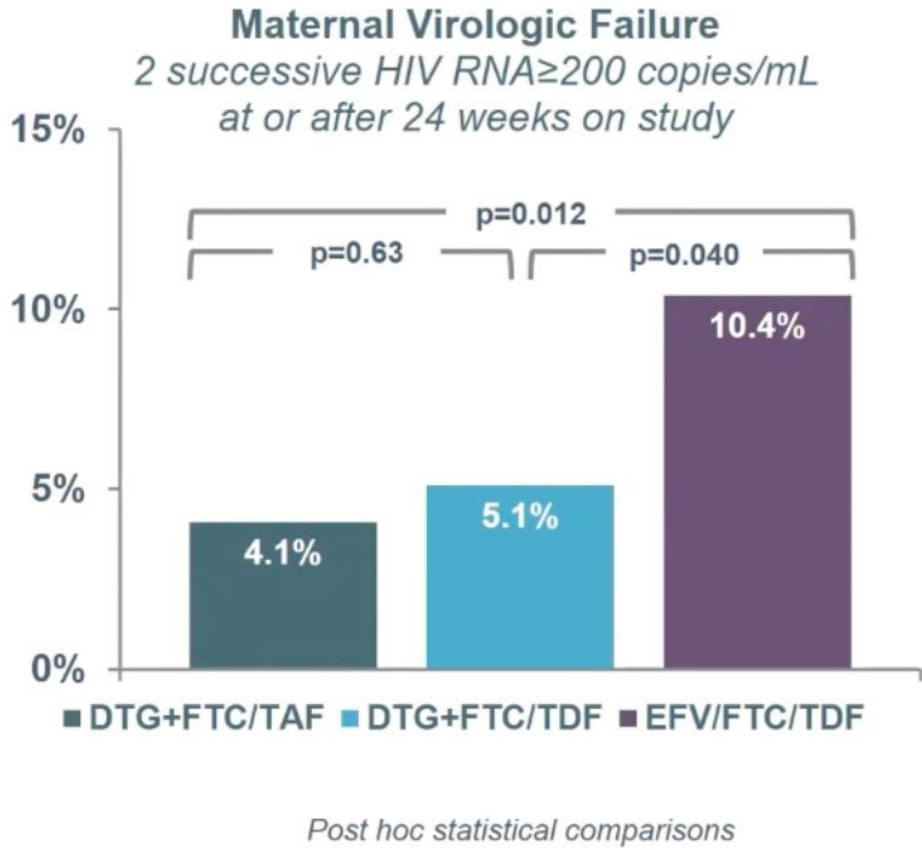
Study Design: Outcomes Evaluated

- Virologic efficacy to 50 weeks post-partum
- Safety outcomes to 50 weeks post-partum
  - Maternal grade 3 or higher adverse events
  - Infant grade 3 or higher adverse events
  - Infant mortality
  - Infant HIV infection

Results: IMPAACT 2010 Virologic Efficacy





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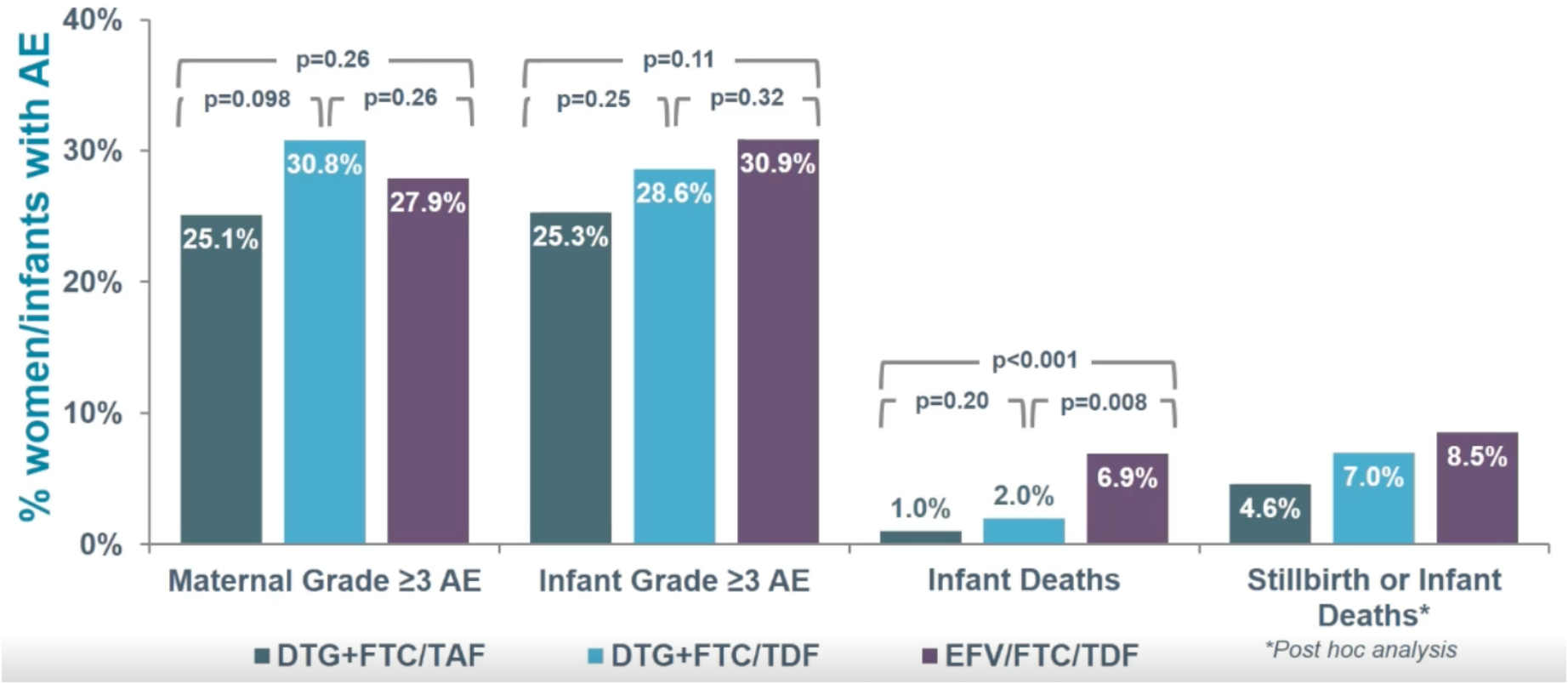
Results: IMPAACT 2010 Adverse Events

Maternal & Infant Grade 3 or Higher Adverse Events by Arm Through 50 Weeks Postpartum



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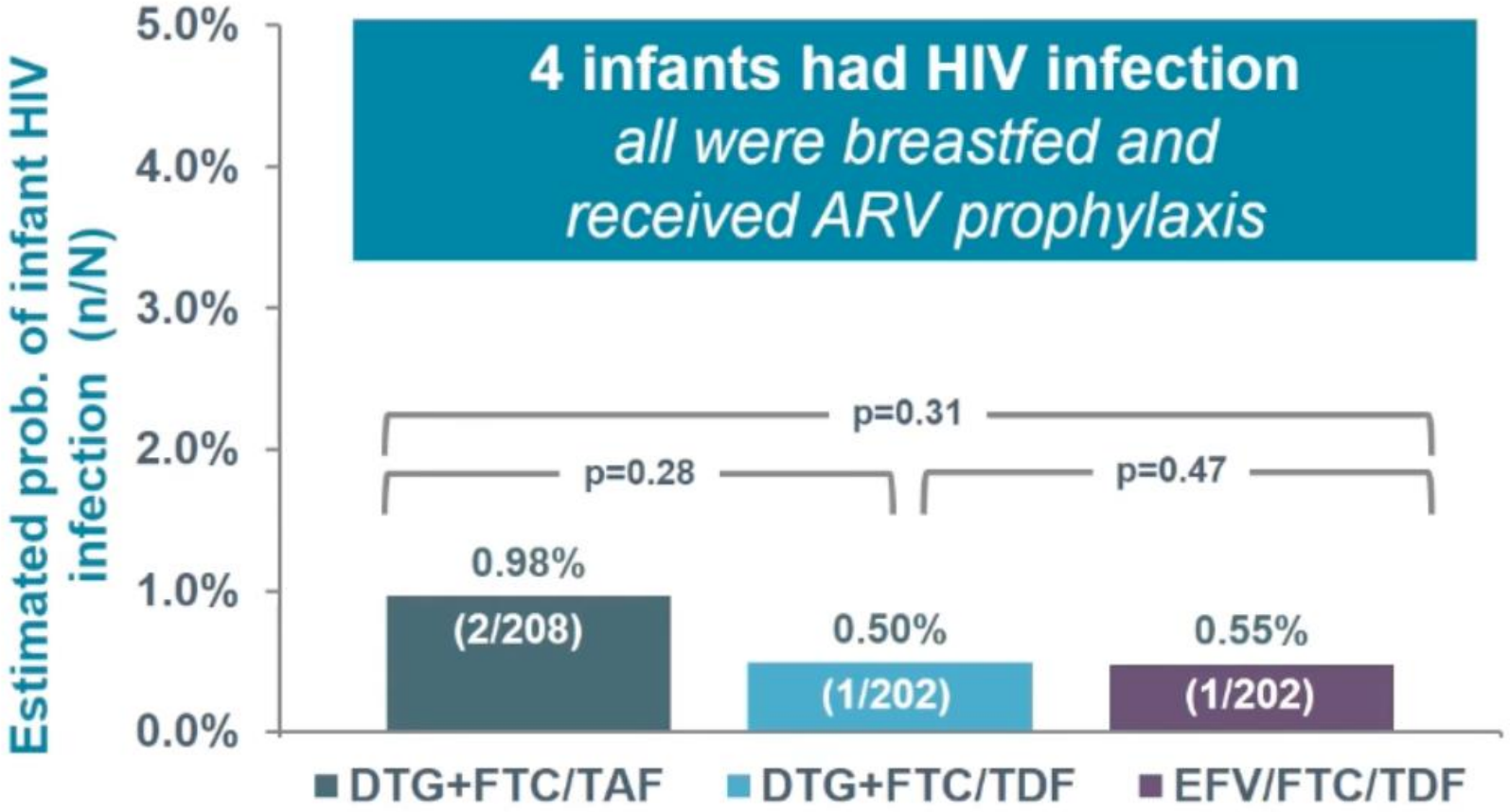
Results: IMPAACT 2010 Infant HIV Infection



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Summary: IMPAACT 2010

- TAF and DTG were safe through 50-week post-partum data
- All regimens were safe and efficacious
  - Infant mortality higher in EFV arm
  - More women had virologic failure in the EFV arm

Take-Away Point: This provides additional reassuring data about DTG and TAF use in pregnancy and post-partum

Update from ATLAS-2M

Background: ATLAS-2M

- ATLAS (CROI 2019): CAB/RPV IM q4w in treatment-experienced PWH was non-inferior to standard PO ART
  - 3 virologic failures occurred
- ATLAS-2M (CROI 2020): CAB/RPV IM q8w in treatment-experienced PWH was non-inferior to q4w at 48 weeks
  - Participants preferred q8w dosing
  - 10 virologic failures (VFs) occurred
    - 8 in q8w arm, 2 in q4w arm
  - Majority with VF failed with both NNRTI and INSTI RAMs

Overton E et al, CROI 2020, Abstract #34.

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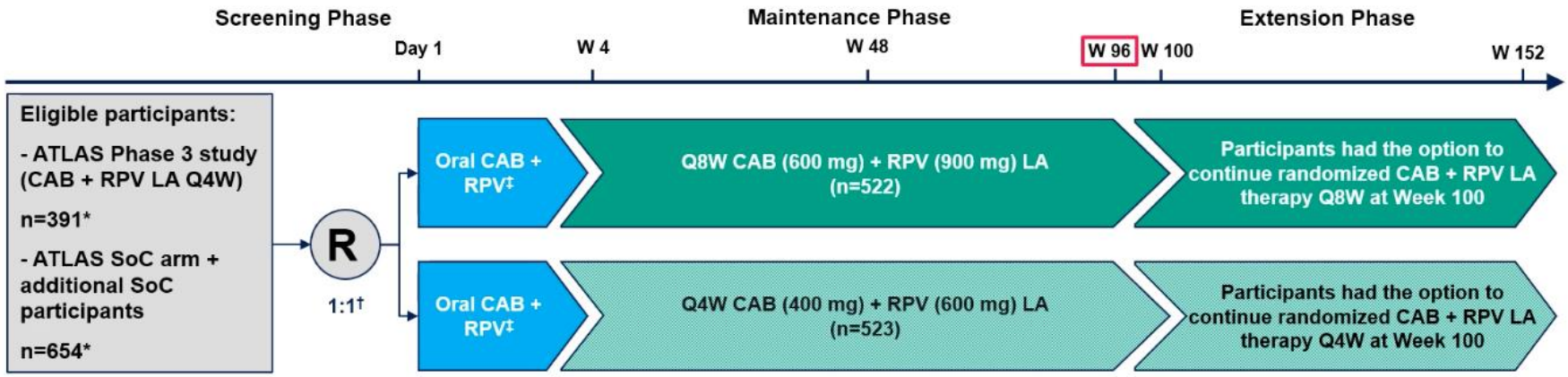
Study Design: ATLAS-2M

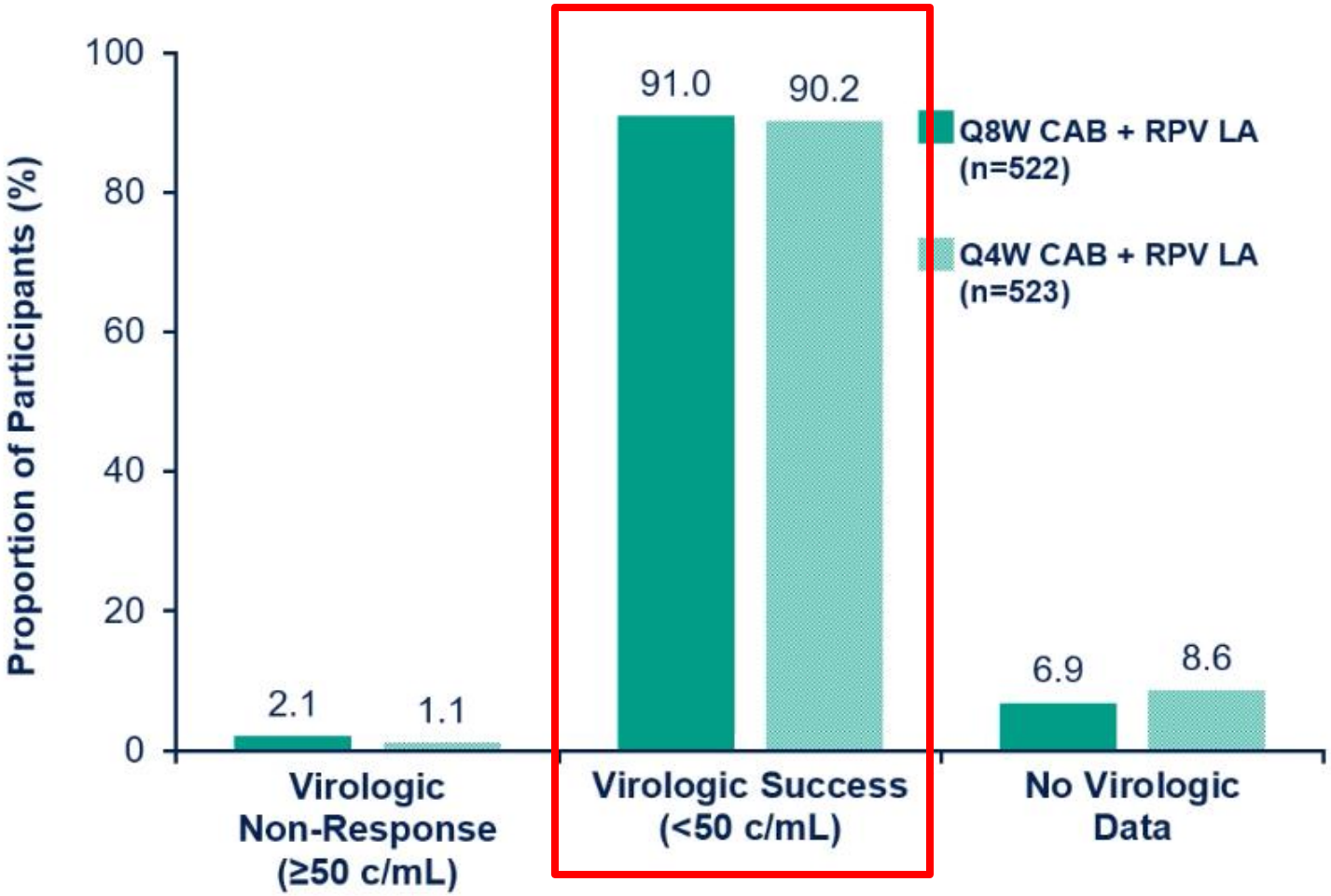


*ITT-E population. †Randomization was stratified by prior exposure to CAB + RPV (0 weeks, 1–24 weeks, >24 weeks). ‡Excluding participants with prior CAB + RPV exposure in ATLAS.
For further study design details, please see Overton et al. CROI 2020; Boston, MA. Presentation 3334.[1]
CAB, cabotegravir; CVF, confirmed virologic failure; ITT-E, intention-to-treat exposed; LA, long-acting; Q4W, every 4 weeks; Q8W, every 8 weeks; R, randomized; RPV, rilpivirine; SoC, standard of care; W, week.
Overton ET, et al. Conference on Retroviruses and Opportunistic Infections 2020; Boston, MA; March 8–11, 2020. Presentation 3334. Available from: www.croiwebcasts.org/p/2020croi/croi/34

Primary Endpoint: Proportion of participants with HIV RNA ≥ 50 copies/mL

Other Endpoints: Incidence of confirmed virologic failure (VF), incidence of viral resistance in participants with confirmed VF (CVF), safety and tolerability

Results: ATLAS-2M 96 Week Data



Jaeger H et al, Virtual CROI 2021, Abstract #401

Results: ATLAS-2M Adverse Effects

Table adapted from Jaeger H et al:

	Q8W n = 522 n (%)	Q4W n = 523 n (%)
Any adverse event (AE)	488 (93)	499 (95)
AE leading to withdrawal	18 (3)	19 (4)
# of injections	12,832	23,855
Injection site reaction (ISR) events	3400	4157
ISR pain	2662 (21)	3295 (14)
ISR nodule	188 (1)	297 (1)
ISR discomfort	134 (1)	148 (<1)
Median duration, days (IQR)	3 (2,5)	3 (2,5)
Participants withdrawing for injection-related reasons	7 (1)	11 (2)

Jaeger H et al, Virtual CROI 2021, Abstract #401

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Results: ATLAS-2M Resistance

Overall Summary of CVFs through Week 96

	n	CVFs n (%)	CVFs with RPV RAMs*	RPV RAMs observed at failure	CVFs with INSTI RAMs*	INSTI RAMs observed at failure
Q8W	522	9 (1.7)	7/9	K101E, E138E/K, E138A, Y188L, Y181C	5/9	Q148R, N155H
Q4W	523	2 (0.4)	1/2	K101E, M230L	2/2	E138E/K, Q148R, N155N/H

*For those with observed RAMs at failure: 7/7 Q8W and 1/1 Q4W CVFs had RPV resistance (fold-change >2), and 3/5 Q8W and 1/2 Q4W CVFs had CAB resistance (fold-change >2.5).

- Total VFs from ATLAS-2M = 11 (9 in q8w arm, 2 in q4w arm)
- One additional VF occurred between weeks 48 and 96 in the q8w arm
  - K103N and Y181C detected at VF & retrospectively at baseline in PBMC
  - No INSTI RAMs present at VF or baseline, though substitution L74I was present at baseline
- 10/11 with confirmed VF resuppressed on an alternative regimen
- All with confirmed VF retained DTG susceptibility

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Summary: ATLAS-2M 96-Week Data

- Virologic efficacy, adverse events, and injection site reactions were similar in IM CAB/RPV q8w and q4w arms
- Confirmed VF occurred in 11 PWH
  - 9 in the q8w arm, 2 in the q4w arm
- Most PWH with VF acquired both NNRTI and INSTI RAMs

Take-Away Point: Q8W dosing of CAB/RPV is effective and there are few VFs, but with failure, RAMs occurred

Lenacapavir: Capella Study

Background: Lenacapavir

- Novel HIV-1 capsid inhibitor, formerly known as GS-6207, that can be given as a long-acting subcutaneous injection
- Currently in development as a component of long-acting therapy for HIV-1
- Has activity in NRTI, NNRTI, INSTI, and PI-resistant HIV-1

Segal-Maurer S et al, Virtual CROI 2021, Abstract #127

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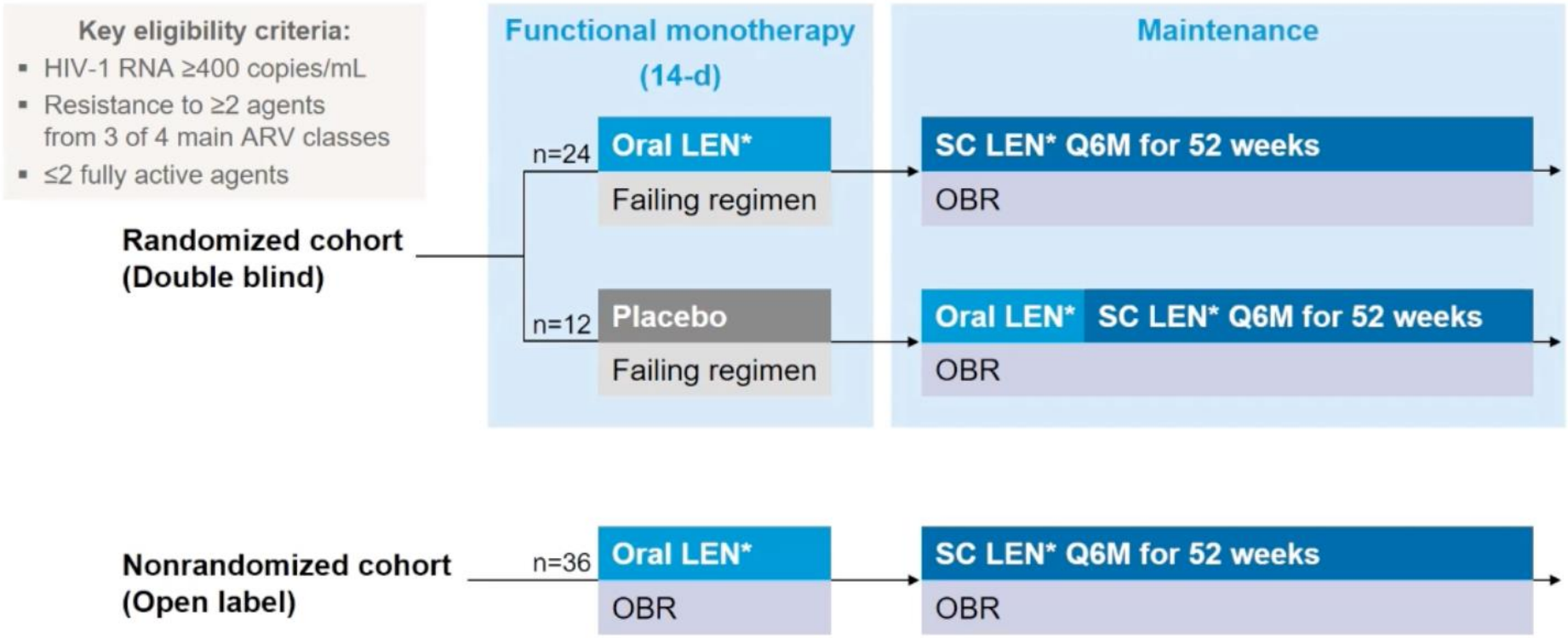
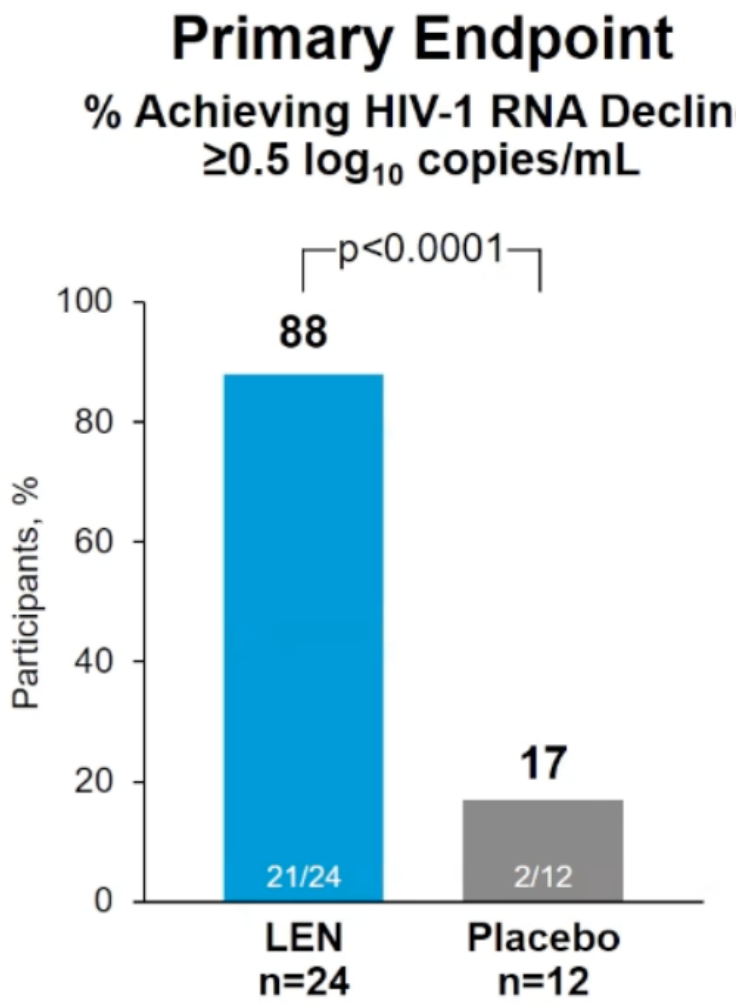
Study Design: Lenacapavir in MDR HIV-1



*Oral LEN administered as 600 mg on Days 1 and 2, 300 mg on Day 8; SC LEN administered as 927 mg (2 x 1.5 mL) in the abdomen on Day 15.
OBR, optimized background regimen (investigational agents, such as fostemsavir, were allowed; ATV, ATV/co, ATV/r, EFV, ETV, NVP, TPV were not allowed).

Results: Lenacapavir in MDR HIV-1



Participant Characteristics:

- Median age: 52
- Median CD4 cell count: 150 cells/mm^3
- Median number of prior ARV regimens: 11
- Median years since HIV diagnosis: 24

Segal-Maurer S et al, Virtual CROI 2021, Abstract #127

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Summary: Lenacapavir in MDR HIV-1

- In the Capella study, early data shows that use of lenacapavir demonstrated antiviral activity against MDR HIV after 14 days and led to virologic suppression when paired with an OBR

Take-Away Point: Although much more data is needed, lenacapavir has the potential to become an important tool against MDR HIV in heavily treatment experienced PWH

Segal-Maurer S et al, Virtual CROI 2021, Abstract #127

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ART Conclusions from Virtual CROI 2021

1. IMPAACT 2010: Data at 50 weeks post-partum show that TDF/FTC + DTG, TAF/FTC + DTG, and TDF/FTC/EFV are safe ART options during pregnancy and in the post-partum period
2. ATLAS-2M: Data at 96 weeks demonstrated virologic efficacy and safety of CAB/RPV IM q8w dosing, as compared to q4w dosing, with 11 total VFs (and RAMs)
3. Capella Study: Early data of lenacapavir, a novel capsid inhibitor that can be administered in a long-acting fashion, demonstrated antiviral activity against MDR HIV

Chinula L et al, Virtual CROI 2021, Abstract #177; Jaeger H et al, Virtual CROI 2021, Abstract #401; Segal-Maurer S et al, Virtual CROI 2021, Abstract #127

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