

In Case You Missed It: Updates from Recent Publications and Meetings

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Financial Relationships With Ineligible Companies (Formerly Described as Commercial Interests by the ACCME) Within the Last 2 Years:

Dr Bedimo has received research funding from ViiV Healthcare and serves on the Scientific Advisory Board for Merck & Co., Inc., ViiV Healthcare, and Gilead Sciences, Inc., and Theratechnologies. (Updated 11/2/21)

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Outline

- Strategies for HIV prevention
 - HPTN 083/ HPTN 084
 - Newer Long-Acting Options
- Strategies for antiretroviral-naïve people living with HIV
 - TAF/FTC, DTG during pregnancy (IMPAACT 2010/VESTED)
- Strategies for treatment-experienced people living with HIV
 - DTG vs. DRV/r (NADIA study)
- Metabolic complications in people living with HIV
 - Weight Change with ARV Switch
- Cancer Prevention in people living with HIV
 - ANCHOR trial
- Challenges in prevention of COVID-19 in immunosuppressed
 - Do people with HIV respond well to COVID-19 vaccines?

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Unmet Needs for HIV Prevention?

IPHx (TDF/FTC) CI: 33-53
 FEM-PrEP (TDF/FTC) CI: 3-31
 TDF (TDF/FTC) CI: 22-61
 Partners PrEP (TDF/FTC) CI: 37-47, CI: 30-43, CI: 35-44, CI: 34-44
 Dapivirine ring efficacy: 27% (ASPRE); 31% (Ring)
 VOICE (TDF/FTC) CI: +3 to -18, CI: +27 to -49
 PROUD (TDF/FTC) CI: 0-54
 SPERGAT (TDF/FTC) CI: 0-54
 DISCOVER (TDF/FTC) CI: 0-54

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HPTN 083: PrEP with IM CAB vs. TDF/FTC

Phase 2b/3 randomized, double-blinded HIV PrEP international study
 Study pop: High-risk adult MSM/TGW (N=4570)
 Study reg: CAB oral (5 wks) → IM q2 mos vs. TDF/FTC po daily
 Results:
 New HIV infections:
 13 (CAB) vs. 39 (TDF/FTC)
 HIV incidence rates (/100 pt yrs):
 0.41 (CAB) vs. 1.22 (TDF/FTC)
 Safety:
 ISR 81% (CAB) vs. 31% (placebo)
 2% of CAB participants d/c
 Conclusion: CAB non-inferior and superior!

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HPTN 084: PrEP with IM CAB vs. TDF/FTC

Phase 2b/3 randomized, double-blinded HIV PrEP international study
 Study pop: High-risk cis-gender women (N=3224)
 Study reg: CAB oral (5 wks) → IM q2 mos vs. TDF/FTC po daily
 Results:
 New HIV infections:
 4 (CAB) vs. 36 (TDF/FTC)
 HIV incidence rates (/100 pt yrs):
 0.20 (CAB) vs. 1.86 (TDF/FTC)
 Safety:
 Conclusion: CAB non-inferior and superior!

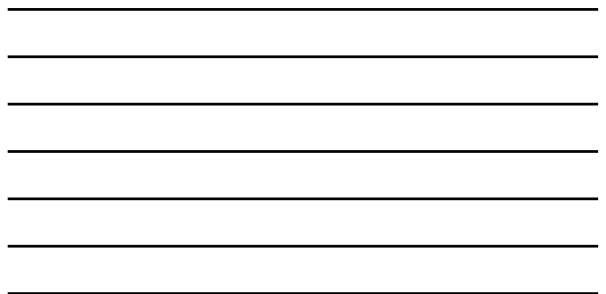
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Unmet Needs for Treatment Experienced with Current Antiretroviral Options?

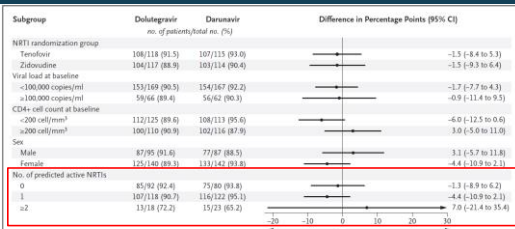
- **After Failure of NNRTI-based Therapy:**
 - INSTI-based ART in treatment-experienced. Efficacy vs. PI-based ART? Despite NRTI resistance?;
 - SECOND LINE: RAL + 2 NRTIs non-inferior to LPV/RTV + 2 NRTIs,¹
 - EARNEST: RAL + 2 NRTIs non-inferior to RAL + PI; sup to PI mono.²
 - DAWNING: DTG + 2 NRTIs superior to LPV/RTV.³
- **NADIA Trial:⁴**
 - More contemporary PI; Second-line INSTI;
 - 464 participants failing first-line NNRTI-based therapy
 - DTG vs. DRV/RTV each with TDF/FTC or ZDV/3TC
 - At baseline: 50% had K65R and 86% had M184V
 - Excellent virologic response at wk 48: DTG: 90.2%; DRV/r: 91.7% (diff. -1.5; 95% CI: -6.7 to 3.7; P=0.58)

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1. Lancet 2013; 381: 2091-99; 2. Paton. N Engl J Med 2014; 371: 234-47; 3. Aboud. Lancet Infect Dis 2019; 19: 253-64; 4. Paton. NEJM. 2021 Jul 22;385(4):330-341.



NADIA Trial: Viral Suppression at Week 48



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Paton. NEJM. 2021 Jul 22;385(4):330-341

After NNRTI therapy failure, DTG or DRV/r + TDF/FTC efficacious, regardless of amount of NRTI resistance.



Unmet Needs for ART in Pregnancy?

- **Prompt ART crucial to optimize maternal outcomes and prevent MTCT:**
 - No adequate data on safety and efficacy of Dolutegravir or Tenofovir alafenamide during pregnancy
- **IMPAACT 2010/VESTED Trial:**
 - ≥14 weeks of pregnancy; no previous ART
 - DTG + TAF/FTC vs. DTG + TDF/FTC vs. EFV/TDF/FTC
 - Viral Suppression at Delivery:

	Combined dolutegravir-containing groups (n=432)	Efavirenz, emtricitabine, and tenofovir disoproxil fumarate group (n=211)	Difference in proportions (95% CI)	p value
HIV-1 RNA <200 copies per mL				
Intention-to-treat analysis	395/405 (98%)	182/200 (91%)	6.5% (1.8-10.7)	0.0052*
Pre-protocol analysis	389/399 (98%)	171/187 (91%)	6.5% (1.6-10.3)	0.0077*
US FDA snapshot algorithm†	389/431 (90%)	171/211 (81%)	9.0% (3.0-15.0)	0.0032

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Lockman. Lancet 2021 Apr 3;397(10281):1276-1282



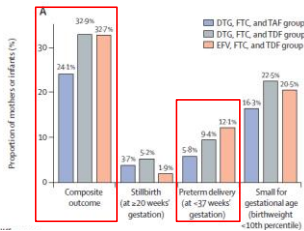
IMPACT 2010/VESTED: Adverse Outcomes

Composite adverse pregnancy outcome: spontaneous abortion (at <20 weeks), stillbirth (at ≥20 weeks), preterm delivery (at <37 weeks), or small for gestational age (birthweight <10th %ile for gestational age, adjusted for sex).

DTG+FTC/TAF vs. DTG+FTC/TDF:
-8.8% (-17.3% to -0.3%)

DTG+FTC/TAF vs. EFV/FTC/TDF:
-8.6% (-17.1% to -0.1%)

Preterm Delivery:
DTG+FTC/TAF vs. EFV/FTC/TDF:
-6.3% (-11.8% to -0.9%)



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Lockman, Lancet 2021 Apr 3:397(10281):1276-1292

Weight Gain on INSTI, TAF or Weight Loss on TDF, EFV? Likely Both...

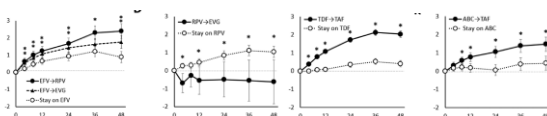
Study or Subgroup	TDF		non-TDF		Odds Ratio	M-H, Random, 95% CI
	Events	Total	Events	Total		
1.2.1 TDF or TDF/FTC vs Placebo						
SBR (TDF or Placebo)	140	1204	135	1209	24.7%	1.05 [0.81, 1.33]
TDM-F (TDF/FTC vs Placebo)	1	1205	0	1033	0.0%	2.37 [0.18, 61.24]
PRV (TDF/FTC vs Placebo)	34	1251	19	1248	12.4%	1.81 [1.45, 2.26]
Parvov (TDF/FTC vs Placebo)	13	1183	6	1584	5.0%	1.09 [0.41, 2.86]
TDF vs TDF/FTC vs Placebo	313	611	72	608	23.8%	2.07 [1.52, 2.81]
EVG (TDF or TDF/FTC vs Placebo)	49	2030	17	1009	12.0%	1.48 [1.04, 2.14]
Subtotal (95% CI)	944	6095	6095	7208	17.8%	1.48 [1.06, 2.07]
Total events	370		249			
Heterogeneity: Tau ² = 0.00; Chi ² = 12.82, df = 5, P = 0.03; I ² = 60%						
Test for overall effect: Z = 2.28 (P = 0.02)						
1.2.2 TDF/FTC vs Cabotegravir						
SPR (TDF/FTC vs CAB)	101	1830	78	1814	22.2%	1.32 [0.97, 1.79]
Subtotal (95% CI)	101	1830	78	1814	22.2%	1.32 [0.97, 1.79]
Total events	101		78			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.78 (P = 0.07)						
Total (95% CI)	1054	8925	8073	10002	19.0%	1.44 [1.12, 1.83]
Total events	471		327			
Heterogeneity: Tau ² = 0.05; Chi ² = 12.53, df = 6, P = 0.03; I ² = 52%						
Test for overall effect: Z = 2.81 (P = 0.005)						
Test for subgroup differences: Chi ² = 0.25, df = 1, P = 0.62; I ² = 0%						

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Shah et al. IDWeek 2021

Weight Gain on INSTI, TAF or Weight Loss on TDF, EFV? Likely Both...

- Pooled analysis of 12 prospective clinical trials of switch in virologically suppressed (n = 4166) vs. remaining on SBR (n = 3150)
- Greatest risk with switch from EFV to RPV or EVG/cobi and switch from TDF to TAF. Switch from ABC to TAF was associated with less weight gain than switch from TDF to TAF



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Erlandson, Clin Infect Dis. 2021 Oct 20;73(8):1440-1451.

Treating Anal Cancer Precursor Lesions Reduces Cancer Risk for People With HIV

- 4446 PLWH with high-grade squamous intraepithelial lesions (HSIL) randomized to either HSIL treatment or active monitoring.¹
- 21 clinical sites around the United States
- Treatment arm: HRA-guided ablative therapy (most patients) or topical (imiquimod thrice weekly x 16 wks, fluorouracil bid x 5d then q2 wks x 16 wks, or trichloroacetic acid q 3 weeks x 12 wks)
- Treatment arm: recurrent HSIL were re-treated; active monitoring arm: watched closely with HRA and yearly biopsy to check for progression to ASCC.
- All participants received HRA q 6 months, and rates of anal squamous cell cancer compared b/w groups.
- ***Chances of progression to anal cancer were significantly reduced***^{2,3}

1. <https://www.clinicaltrials.gov> NCT 02135419
2. <https://iansociety.org>. Accessed October 8, 2021
3. Goldstone. *Diseases of the Colon & Rectum*: November 1, 2021

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Acknowledgments

- Raj Gandhi
- Trip Gulick

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Question-and-Answer Session