A year review: Top ten papers in infectious diseases

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Top 5 papers in HIV/AIDS

Landmarks papers relevant to:

- Advances in antiretroviral therapy
- Antiretroviral therapy in pregnant women
- Adverse effects of antiretroviral therapy
- HIV and opportunistic infections
- HIV prevention

Paper

Long acting antiretroviral therapy

Could we do more for ART?

- Prolonged daily regimens can engender dissatisfaction, contribute to stigma, and increase the risk of nonadherence and treatment failure.
- Alternatives:
  - Two-drug regimens
  - Long-acting injectables
- Benefits as an initial regimen and/or a switching therapy?

Orkin C, et al . N Engl J Med. 2020;382:1124-35.

Paper 1.1

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

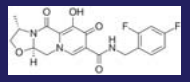
Long-Acting Cabotegravir and Rilpivirine after Oral Induction for HIV-1 Infection

N ENGL J MED 382;12 NEJM.ORG MARCH 19, 2020

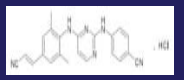
Orkin C, et al . N Engl J Med. 2020;382:1124-35.

The long-acting injectable formulations

Cabotegravir (INSTI)



Rilpivirine (NNRTI)

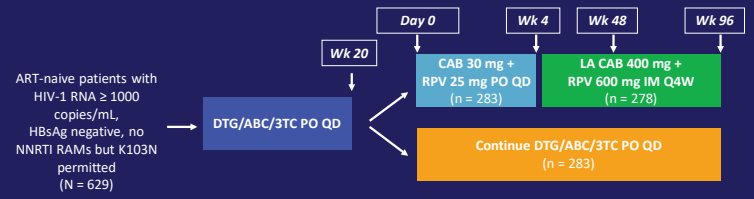


Cabotegravir (CAB) + Rilpivirine (RPV) LA with lead-in oral CAB

Margolis DA, et al . Lancet 2017; 390: 1499-510 (LATTE-2 Study).

FLAIR: The First Long-Acting Injectable Regimen

- Phase 3, randomized, multicenter, open-label, noninferiority trial



- The primary end point was the percentage of participants who had a plasma HIV-1 RNA level of 50 copies per milliliter or higher at week 48 of the maintenance phase (FDA snapshot)

Orkin C, et al . N Engl J Med. 2020;382:1124-35.

Slide credit: clinicaloptions.com

FLAIR: Results

- Balanced randomization

Outcome	Long-Acting Therapy (N = 283)	Oral Therapy (N = 283)	Difference (95% CI)	Adjusted Difference (95% CI)*
			percentage points	
Intention-to-treat exposed population				
HIV-1 RNA level — no. (%)				
<50 copies/ml	265 (93.6)	264 (93.3)	0.4 (−3.7 to 4.4)	0.4 (−3.7 to 4.5)
≥50 copies/ml†	6 (2.1)	7 (2.5)	−0.4 (−2.8 to 2.1)	−0.4 (−2.8 to 2.1)
Subgroup analysis of HIV-1 RNA level ≥50 copies/ml — no./total no. (%)‡				
Sex at birth				
Female	3/63 (4.8)	1/64 (1.6)	3.2 (−4.3 to 12.0)	—
Male	3/220 (1.4)	6/219 (2.7)	−1.4 (−4.7 to 1.6)	—
Baseline HIV-1 RNA level				
<100,000 copies/ml	4/227 (1.8)	5/227 (2.2)	−0.4 (−3.6 to 2.5)	—
≥100,000 copies/ml	2/56 (3.6)	2/56 (3.6)	0.0 (−9.2 to 9.2)	—

Orkin C, et al . N Engl J Med. 2020;382:1124-35.

FLAIR: Results

- Adverse events

Event Category	Long-Acting Therapy (N = 283)	Oral Therapy (N = 283)
	number of participants (percent)	
Any adverse event	267 (94)	225 (80)
Any adverse event, excluding injection-site reactions	246 (87)	225 (80)
Grade ≥3 adverse events	31 (11)	11 (4)
Grade ≥3 adverse events, excluding injection-site reactions	22 (8)	11 (4)
Adverse events that led to withdrawal from the trial†	9 (3)	4 (1)
Serious adverse events‡	18 (6)	12 (4)
Adverse events that led to death	0	0

- The most common AE of LA group was pain at injection site (82%) – (mild 87% and moderate 13%).
- The AEs that were reported higher in LA group were headache and pyrexia.

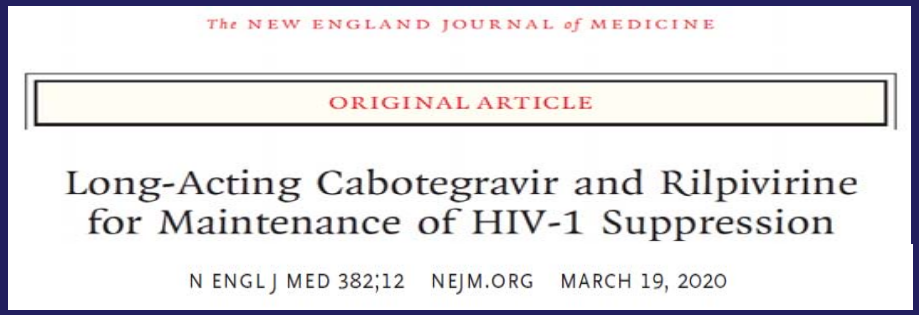
Orkin C, et al . N Engl J Med. 2020;382:1124-35.

FLAIR: Results

- At week 48, the HIVTSQc total score for satisfaction with current treatment as compared with induction treatment was higher in the LA group than in the oral group (adjusted mean difference, 4.1 points; 95% CI, 2.8 to 5.5).
- 99% of the participants who received long-acting therapy preferred the long-acting regimen over the previous oral therapy.
- Adherence to therapy was not significantly different between LA and oral groups (98% vs. >90%).

Orkin C, et al . N Engl J Med. 2020;382:1124-35.

Paper 1.2


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

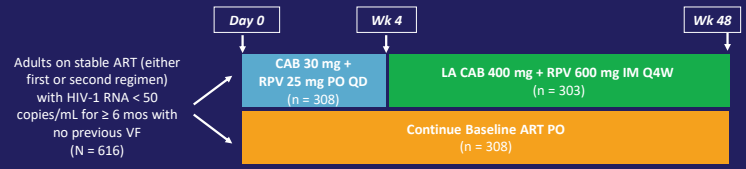
Long-Acting Cabotegravir and Rilpivirine for Maintenance of HIV-1 Suppression

N ENGL J MED 382;12 NEJM.ORG MARCH 19, 2020

Swindells S, et al . N Engl J Med 2020;382:1112-23.

ATLAS: Antiretroviral Therapy as Long Acting Suppression

- Phase 3, randomized, multicenter, parallel-group, open-label trial



- The primary end point was the percentage of participants with plasma HIV-1 RNA levels of 50 copies per milliliter or higher at week 48 (FDA snapshot).

Swindells S, et al . N Engl J Med 2020;382:1112-23.

Slide credit: clinicaloptions.com

ATLAS: Results

- Balanced randomization

Outcome	Long-Acting Therapy (N=308)	Oral Therapy (N=308)	Difference (95% CI)	Adjusted Difference (95% CI)†
			percentage points	
Intention-to-treat exposed population				
HIV-1 RNA level — no. (%)				
<50 copies/ml	285 (92.5)	294 (95.5)	−2.9 (−6.7 to 0.8)	−3.0 (−6.7 to 0.7)
≥50 copies/ml‡	5 (1.6)	3 (1.0)	0.6 (−1.1 to 2.4)	0.6 (−1.2 to 2.5)
Subgroup analysis of HIV-1 RNA level ≥50 copies/ml — no./total no. (%)				
Sex at birth				
Female	2/99 (2.0)	0/104	2.0 (−1.7 to 7.1)	—
Male	3/209 (1.4)	3/204 (1.5)	0.0 (−3.0 to 2.9)	—
Baseline third-agent class				—
PI	1/51 (2.0)	0/54	2.0 (−5.0 to 10.6)	—
INSTI	0/102	2/99 (2.0)	−2.0 (−7.1 to 1.8)	—
NNRTI	4/155 (2.6)	1/155 (0.6)	1.9 (−1.3 to 5.9)	—

Swindells S, et al . N Engl J Med 2020;382:1112-23.

ATLAS: Results

- Adverse events

Event Category	All Adverse Events	
	Long-Acting Therapy (N=308)	Oral Therapy (N=308)
Any event	294 (95)	220 (71)
Any event, excluding injection-site reactions	264 (86)	220 (71)
Grade 3 or 4 events	35 (11)	23 (7)
Grade 3 or 4 events, excluding injection-site reactions	25 (8)	23 (7)
Events leading to withdrawal†	14 (5)‡	5 (2)
Any serious adverse events	13 (4)	14 (5)

- The most common AE of LA group was pain at injection site (75%) – (grade 3 - 3%).
- Other AEs, such as headache, pyrexia, fatigue, diarrhea and flu-like symptoms were comparable between the two groups.

Swindells S, et al . N Engl J Med 2020;382:1112-23.

ATLAS: Results

- Resistant mutations in the LA group (3 participants with VF)
  - E138A/K, V108I, N155H
- After 44 weeks, participants in the LA group reported greater improvement from baseline in treatment satisfaction
- At week 48 in the LA group, 86% of participants in selected the injectable regimen over daily oral therapy.
- Adherence rate of the LA group was 98%.

Swindells S, et al . N Engl J Med 2020;382:1112-23.

My appraisal: FLAIR and ATLAS studies

PROS

- Multicenter RCTs with adequate sample size
- CAB + RPV LA after oral induction was not inferior to standard oral therapy for initial and maintenance therapy
- CAB + RPV LA was generally safe and tolerable
- CAB + RPV LA was reported to be a satisfying and preferred regimen with great adherence

CONS

- Injection-related AEs were common but only infrequently led to medication withdrawal
- Need oral induction
- Cost-effectiveness?
- Not for patients with HBV co-infection or previous VF
- Unclear relationship between drug concentrations and VF, especially, after drug discontinuation

Paper

Late initiation of ART in pregnant women

Tsepamo Update: Prevalence of neural tube defect (NTD) by ARV Exposure

Parameter	Conception			Pregnancy	HIV Negative (n = 119,630)
	DTG (n = 3591)	Non-DTG (n = 19,361)	EFV (n = 10,958)	DTG (n = 4581)	
Total NTDs per exposures, n/N	7/3591	21/19,361	8/10,958	2/4581	87/119,630
NTD prevalence, % (95% CI)					
▪ April 2019	0.30 (0.13-0.69)	0.10 (0.06-0.17)	0.04 (0.01-0.11)	0.03 (0.00-0.15)	0.08 (0.06-0.10)
▪ April 2020	0.19 (0.09-0.40)	0.11 (0.07-0.17)	0.07 (0.03-0.17)	0.04 (0.01-0.16)	0.07 (0.06-0.09)
Prevalence diff. with DTG conception, Apr 2020, % (95% CI)	Ref	0.09 (-0.03 to 0.30)	0.12 (0 to 0.32)	0.15 (0 to 0.36)	0.12 (0.01 to 32.0)
NTDs per exposures between April 2019 and April 2020, n/N	2/1908	6/4569	5/2999	1/741	17/30,258

DTG in late pregnancy in clinical trial settings?

Zash. AIDS 2020. Abstr OAXLB01. Zash. NEJM. 2019;381:827. Zash. IAS 2019. Abstr MOAX0105LB.

Slide credit: clinicaloptions.com

Articles

Dolutegravir versus efavirenz in women starting HIV therapy in late pregnancy (DolPHIN-2): an open-label, randomised controlled trial

Lancet HIV 2020; 7: 332–39

Kintu K, et al. Lancet HIV 2020;7:332-9.

DOLPHIN-2

- A phase III randomized, multicenter, open-label trial in South Africa and Uganda

Adult women with HIV infection at ≥ 28 wks of gestation; no ART within 12 mos, prior INSTIs, NNRTI failure, or EFV intolerance (N = 268)

→ Dolutegravir + 2 NRTIs (n = 137)

→ Efavirenz + 2 NRTIs (n = 131)

→ *Treatment and follow-up continued to postpartum Wk 72*

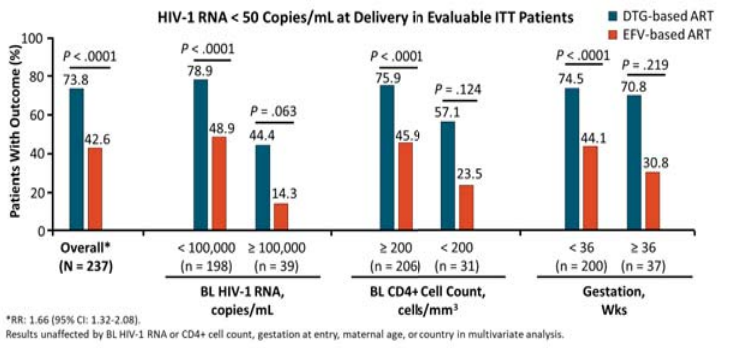
- Primary endpoint: HIV-1 RNA < 50 copies/mL at delivery
- Secondary endpoints: HIV-1 RNA < 1000 copies/mL at delivery, MTCT, maternal and infant safety

Kintu K, et al. Lancet HIV 2020;7:332-9.

Slide credit: clinicaloptions.com

DOLPHIN-2

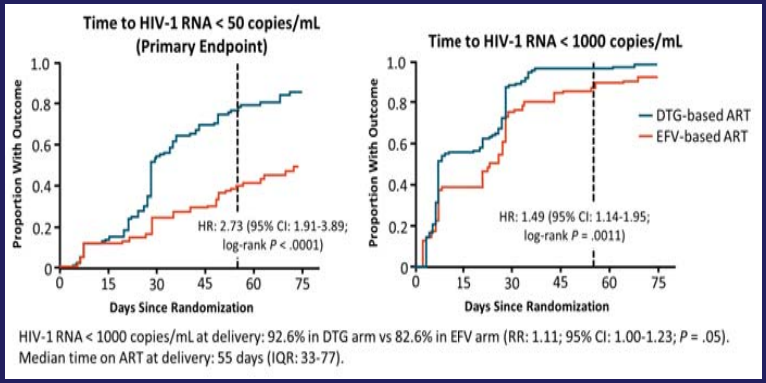
- Balanced randomization



Kintu K, et al. Lancet HIV 2020;7:332-9.

Slide credit: clinicaloptions.com

DOLPHIN-2



HIV-1 RNA < 1000 copies/mL at delivery: 92.6% in DTG arm vs 82.6% in EFV arm (RR: 1.11; 95% CI: 1.00-1.23; $P = .05$).
Median time on ART at delivery: 55 days (IQR: 33-77).

Kintu K, et al. Lancet HIV 2020;7:332-9.

Slide credit: clinicaloptions.com

DOLPHIN-2

- Infant transmissions: 3 in DTG arm vs. 0 in EFV arm

Characteristic of Transmission Event in DTG Arm	MTCT #1	MTCT #2	MTCT #3
Gestation at enrollment, wks	32	32	30
ART exposure before delivery, days	35	32	24
Time from delivery to first PCR positivity for infant, days	5	3	11
Maternal HIV-1 RNA, copies/mL			
▪ Baseline	48,969	32,844	31,354
▪ Day 7	5211	210	258
▪ Day 28	53	100	--
▪ Delivery	29	20	200

The transmissions might have been intra-utero

Kintu K, et al. Lancet HIV 2020;7:332-9.

Slide credit: clinicaloptions.com

DOLPHIN-2

- No differences in safety outcomes (DTG vs. EFV)
  - Serious adverse events related to ART (1.5% vs. 3.8%)
  - ART-unrelated stillbirths (2.9% vs. 0%)
  - Preterm < 34 weeks (4.9% vs. 5.0%)
  - ART-unrelated infant death (4.1% vs. 2.5%)

Outcome in Evaluable Live Births, n (%)	DTG-Based ART (n = 123)	EFV-Based ART (n = 119)
Any congenital, familial, genetic defect	47 (38.2)	45 (37.8)
Congenital umbilical hernia	37 (30.1)	35 (29.4)
Birth mark	18 (14.6)	18 (15.1)

Outcome in Evaluable Live Births, n (%)	DTG-Based ART (n = 123)	EFV-Based ART (n = 119)
Craniosynostosis	1 (0.8)	1 (0.8)
Cleft palate	0	1 (0.8)
Sickle cell anemia	1 (0.8)	0
Neural tube defects	0	0

Kintu K, et al. Lancet HIV 2020;7:332-9.

My appraisal: DOLPHIN-2 study

PROS

- Multicenter RCTs with adequate sample size
- DTG-based therapy conferred more rapid virologic suppression vs. EFV-based therapy
- DTG-based therapy was considered safe for mothers and infants
- Supporting the Thai national and WHO guidelines for use of DTG-based therapy in pregnant women, especially in late pregnancy

CONS

- The sample size was not sufficient to assess differences in infant transmissions
- Safety follow-up of mothers and babies was limited by the short time between third trimester initiation and the primary endpoint at giving birth

Paper

Weight gain after ART initiation

Clinical Infectious Diseases

MAJOR ARTICLE

IDSA Infectious Diseases Society of America | hivma hiv medicine association | OXFORD

Weight Gain Following Initiation of Antiretroviral Therapy: Risk Factors in Randomized Comparative Clinical Trials

Clinical Infectious Diseases® 2019;XX(XX):1–11

- An increasing prevalence of overweight and obesity has been reported in PLWH initiating ART.
- Good (return to normal health) vs. Bad (risk for CV and metabolic diseases)
- Unclear mechanism but possible risk factors (demographics, ART)

Sax P, et al. Clin Infect Dis 2019 Oct 14;ciz999. doi: 10.1093/cid/ciz999.

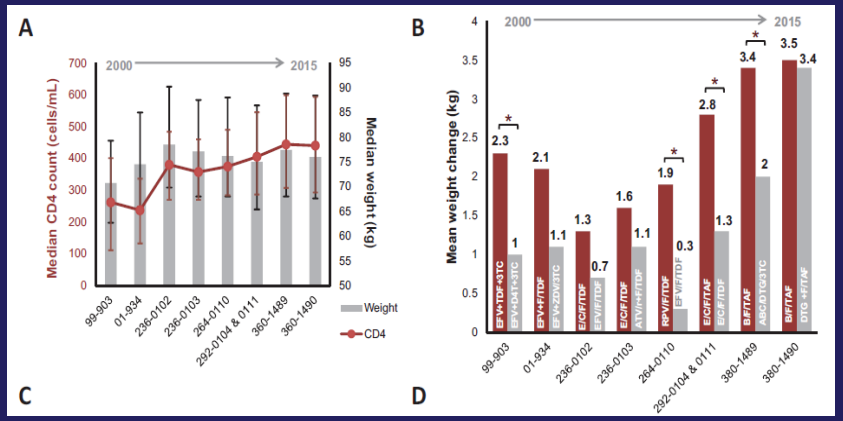
Weight Gain Following Initiation of Antiretroviral Therapy: Risk Factors in Randomized Comparative Clinical Trials

- Pooled analyses included 8 randomized comparative trials of participants initiating ART (2003–2015)
  - Phase 3 stage
  - Active-controlled design
  - Enrollment of treatment-naive participants
  - Follow-up duration of at least 96 weeks (baseline and every 12 weeks visit)
- 5,680 treatment-naïve patients

No. of participants	5680
Age, y	
Mean (SD)	37 (10.7)
Median (Q1, Q3)	35 (28, 44)
Sex at birth	
Male	5018 (88.3)
Female	662 (11.7)
Race	
Asian	290 (5.1)
Black	1471 (25.9)
White	3499 (61.6)
Other	415 (7.3)
Unknown[a]	4 (0.1)
Sex and race	
Male, black	1161 (20.4)
Male, non-black	3853 (67.8)
Female, black	310 (5.5)
Female, non-black	351 (6.2)

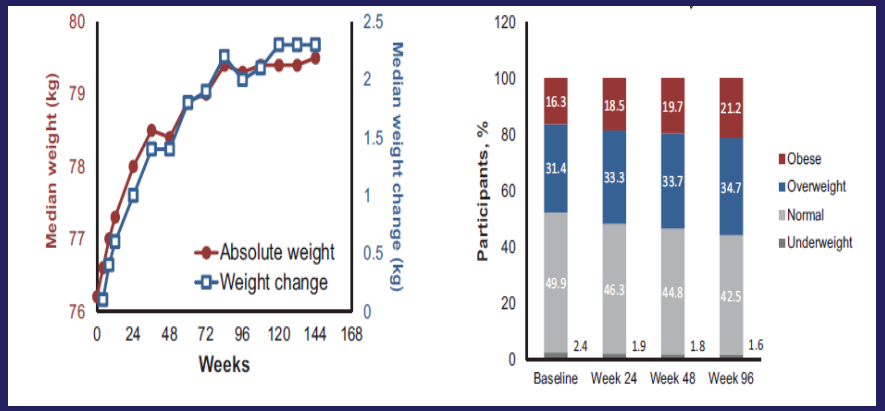
Sax P, et al. Clin Infect Dis 2019 Oct 14;ciz999. doi: 10.1093/cid/ciz999.

Trial characteristics and weight change



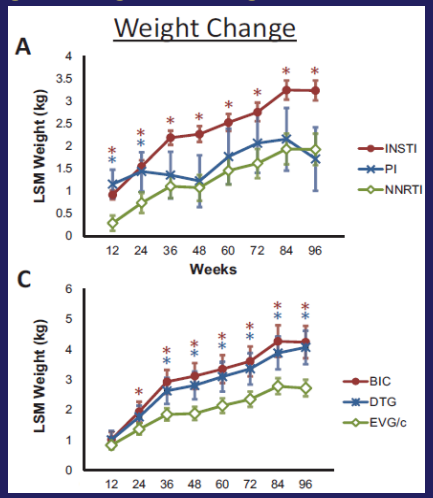
Sax P, et al. Clin Infect Dis 2019 Oct 14;ciz999. doi: 10.1093/cid/ciz999.

Weight, weight change and obesity status



Sax P, et al. Clin Infect Dis 2019 Oct 14;ciz999. doi: 10.1093/cid/ciz999.

Weight change following initiation of ART



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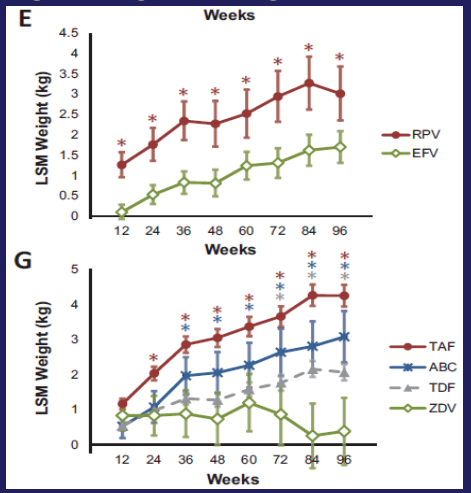


Sax P, et al. Clin Infect Dis 2019 Oct 14;ciz999. doi: 10.1093/cid/ciz999.

Risk factors associated with ≥ 10% weight gain

Variable	OR	(95% CI)	*P* Value
CD4 count (<200 vs ≥200 cells/all)	4.36	(3.6–5.27)	<.001
HIV RNA (>100K vs ≤100K copies/mL)	1.98	(1.65–2.37)	<.001
BMI			
Normal vs overweight	1.54	(1.27–1.87)	<.001
Normal vs obese	1.66	(1.29–2.15)	<.001
Sex (female vs male)	1.54	(1.21–1.96)	<.001
Race (black vs non-black)	1.32	(1.10–1.59)	.003
Third ART agent			
BIC/DTG vs EFV	1.82	(1.24–2.66)	.002
EVG/c vs EFV	1.36	(1.04–1.78)	.026
RPV vs EFV	1.51	(1.03–2.20)	.035
ATV/r vs EFV	0.92	(.59–1.45)	.73
NRTI			
TAF vs ZDV	1.75	(1.04–2.95)	.034
TDF vs ZDV	1.19	(.76–1.87)	.44
ABC vs ZDV	0.93	(.47–1.8)	.82
TAF vs ABC	1.9	(1.25–2.88)	.003
TDF vs ABC	1.29	(.79–2.11)	.31
TAF vs TDF	1.47	(1.14–1.90)	.003

Sax P, et al. Clin Infect Dis 2019 Oct 14;ciz999. doi: 10.1093/cid/ciz999.

My appraisal: Weight gain after ART study

PROS

- Large sample size from pooled RCTs
- Black race and female were associated with weight gain
- Low CD4 count and high HIV VL were associated with weight gain
- INSTI (DTG and BIC > EVG), NNRTI (RPV), and NRTI (TAF) were associated with weight gain
- Reasons: Better GI tolerability, faster VL suppression or unknown

CONS

- Asian 5.1%
- Incomplete or missing data on GI tolerability, psychiatric comorbidities, concomitant medications, diet, physical activity and smoking
- Consequences of weight gain were not assessed given limited follow-up time

Paper

OI prevention among PLWH

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Isoniazid Preventive Therapy in HIV-Infected Pregnant and Postpartum Women

N ENGL J MED 381;14 NEJM.ORG OCTOBER 3, 2019

- Tuberculosis which develops during pregnancy is associated with adverse maternal, pregnancy, and infant outcomes.
- There is consensus regarding the benefits of treating active tuberculosis during pregnancy and isoniazid preventive therapy (IPT) in PLWH.
- Safety and efficacy data are lacking regarding IPT in pregnant women receiving ART.

Gupta A, et al. N Engl J Med 2019;381:1333-46.

IMPAACT P1078 TB APPRISE Study

- A prospective, double-blind, placebo-controlled, randomized, noninferiority trial at 13 sites in eight TB-endemic countries

HIV-positive, pregnant women
GA 14-34 wks, ≥18 years, ≥35 kg
within normal limit lab parameter

Immediate INH preventive therapy
Started INH after enrolment, continued for 28 wks
then placebo for 40 wks after delivery
(n = 477)

Deferred INH preventive therapy
Received placebo after enrolment, continued until week 12
after delivery, then INH for 28 weeks
(n = 479)

- The primary outcome was a composite safety outcome of maternal adverse events of grade 3 or higher related to regimen discontinuation through week 48 after delivery.

Gupta A, et al. N Engl J Med 2019;381:1333-46.

IMPAACT P1078 TB APPRISE Study

- Balanced randomization

Outcome	Immediate Group		Deferred Group		Incidence Rate Difference (95% CI)
	no./total no. (%)	*incidence rate per 100 person-yr*	*no./total no. (%)*	*incidence rate per 100 person-yr*	
Primary outcome†					
Intention-to-treat population	72/477 (15.1)	15.03	73/479 (15.2)	14.93	0.10 (−4.77 to 4.98)
Per-protocol population	64/376 (17.0)	16.00	69/388 (17.8)	16.71	−0.71 (−6.27 to 4.85)
Secondary maternal outcomes					
Any grade 3 or 4 adverse event	144/477 (30.2)	34.95	136/479 (28.4)	31.26	3.69 (−4.07 to 11.45)
Hepatotoxicity‡	29/477 (6.1)	5.80	34/479 (7.1)	6.69	−0.89 (−3.98 to 2.19)
Peripheral neuropathy	1/477 (0.2)	0.19	0/479 (0.0)	0.00	0.19 (−0.19 to 0.57)
Death	2/477 (0.4)	0.40	4/479 (0.8)	0.78	−0.39 (−1.33 to 0.56)
Tuberculosis¶	3/477 (0.6)	0.60	3/478 (0.6)	0.59	0.01 (−0.94 to 0.96)

Gupta A, et al. N Engl J Med 2019;381:1333-46.

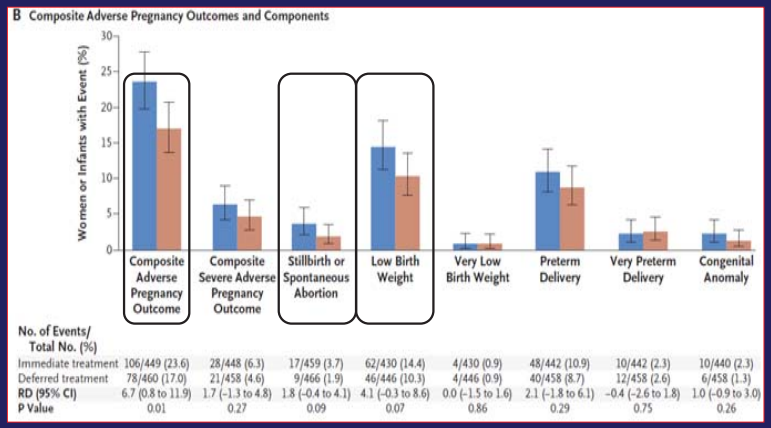
IMPAACT P1078 TB APPRISE Study

- Most common maternal AEs were elevated liver enzyme (5% vs. 7%) and weight loss (6% vs. 5%)

Outcome	Immediate Group		Deferred Group		Incidence Rate Difference (95% CI)
	no./total no. (%)	*incidence rate per 100 person-yr*	*no./total no. (%)*	*incidence rate per 100 person-yr*	
Secondary infant outcomes					
Any grade 3 or 4 adverse event	191/445 (42.9)	70.74	192/464 (41.4)	65.75	4.99 (−8.69 to 18.67)
HIV infection	3/439 (0.7)	0.79	7/458 (1.5)	1.75	−0.96 (−2.54 to 0.61)
Infant death: 0–48 wk after birth	11/445 (2.5)	2.99	17/464 (3.7)	4.42	−1.43 (−4.17 to 1.32)
Neonatal death: 0–7 days after birth	4/445 (0.9)	—	5/464 (1.1)	—	—
Tuberculosis**	0/445 (0.0)	0.54	1/464 (0.2)	0.52	0.02 (−1.02 to 1.07)

Gupta A, et al. N Engl J Med 2019;381:1333-46.

IMPAACT P1078 TB APPRISE Study



Gupta A, et al. N Engl J Med 2019;381:1333-46.

My appraisal: IMPAACT P1078 TB APPRISE

PROS

- Multicenter DB RCT trial
- No differences in maternal outcomes (INH-related AEs, death and tuberculosis) and infant outcomes (INH-related AEs, HIV infection, death and tuberculosis) between immediate vs. deferred groups
- New findings: higher composite pregnancy adverse outcome (stillbirth, abortion, low birth weight) in immediate group

CONS

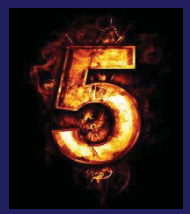
- Exclusion of first-trimester pregnancy
- Exclusion of those with recent TB contact
- Low rate of active TB development
- Only 30% of participants had a confirmed LTBI diagnosis (positive IGRA result).

Thai National guidelines for HIV/AIDS management 2020

LTBI screening and treatment among pregnant PLWH

- For close contact (high-risk exposure), initiating LTBI treatment upon entering care.
- For others, if LTBI treatment is indicated (CD4 <200 cells/μL or CD4≥ 200 cells/μL and positive TST or IGRAs), delaying LTBI treatment until 12 weeks after delivery.

Paper



Pre-exposure prophylaxis

Articles

Emtricitabine and tenofovir alafenamide *vs* emtricitabine and tenofovir disoproxil fumarate for HIV pre-exposure prophylaxis (DISCOVER): primary results from a randomised, double-blind, multicentre, active-controlled, phase 3, non-inferiority trial

Lancet 2020; 396: 239–54

- Increasing population-level uptake of PrEP is associated with declining HIV incidence (TDF/FTC daily regimen).
- TAF vs. TDF
  - Faster increase in drug concentration in PBMCs (1-2 hours vs. ≥ 3 days) and higher concentration in PBMCs (at least 4 times higher)
  - Less renal AEs
  - Less BMD AEs

Meyer KH, et al. Lancet 2020;396:239-54.

DISCOVER study

- Randomized, double-blind phase III noninferiority trial in Europe and North America

cis-MSM and TG women at high risk of HIV (≥ 2 episodes of condomless anal sex in past 12 wks or rectal gonorrhea/chlamydia or syphilis in past 24 wks), HBV negative, and eGFR ≥ 60 mL/min
(N = 5387)

→ **TAF/FTC QD** (n = 2694)

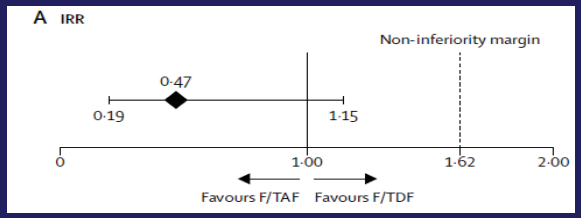
→ **TDF/FTC QD** (n = 2693)

- Primary endpoint: HIV incidence/100 PY (noninferiority upper bound of 95% CI for IRR of FTC/TAF vs FTC/TDF: < 1.62; expected incidence 1.44/100 PY based on prior studies).

Meyer KH, et al. Lancet 2020;396:239-54.

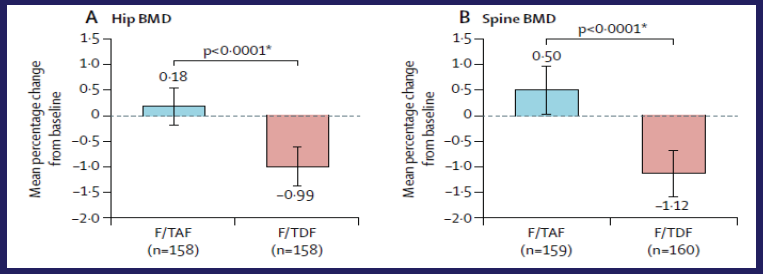
DISCOVER study

- Balanced randomization
- TAF/FTC was non-inferior to TDF/FTC for primary endpoint of HIV incidence/100 PY at week 48
  - 0.16 vs 0.34 (IRR: 0.47; 95% CI: 0.19-1.15)



Meyer KH, et al. Lancet 2020;396:239-54.

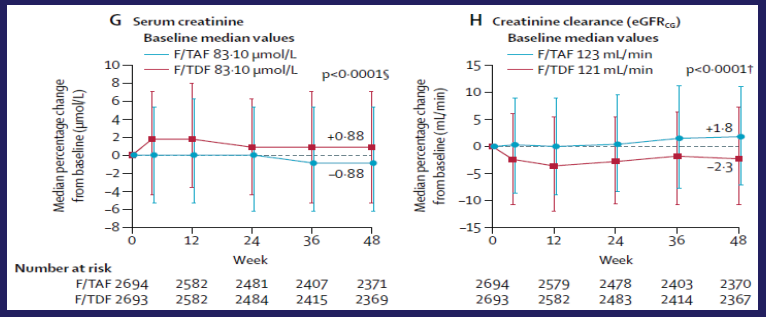
DISCOVER study



- Hip and spine BMD changes were significantly more favorable with TAF/FTC in overall groups.

Meyer KH, et al. Lancet 2020;396:239-54.

DISCOVER study



- eGFR and serum creatinine changes were significantly more favorable with TAF/FTC in overall groups.

Meyer KH, et al. Lancet 2020;396:239-54.

DISCOVER study

No differences between TAF/FTC and TDF/FTC in regards to:

- Adherence rate (98% vs. 98%)
- Drug discontinuation due to AEs (1% vs. 2%)
- Grade 3-4 laboratory abnormalities (7% vs. 8%)
- STIs

Common adverse events (≥10% in either group)		
Rectal chlamydia	770 (29%)	792 (29%)
Oropharyngeal gonorrhoea	740 (27%)	722 (27%)
Rectal gonorrhoea	693 (26%)	671 (25%)
Syphilis	342 (13%)	321 (12%)
Urethral chlamydia	280 (10%)	259 (10%)

Meyer KH, et al. Lancet 2020;396:239-54.

DISCOVER study

TAF/FTC vs. TDF/FTC had a significantly differences in mean changes of:

- Bodyweight (+1.1 kg vs. -0.1 kg; p<0.0001)
- Total cholesterol (-0.03 mmol/L vs. -0.28 mmol/L; p<0.0001)
- LDL (+0.03 mmol/L vs. -0.18 mmol/L; p<0.0001)
- HDL (-0.05 mmol/L vs. -0.13 mmol/L; p<0.0001)

Meyer KH, et al. Lancet 2020;396:239-54.

My appraisal: DISCOVER study

PROS

- Multicenter DB RCT trial
- TAF/FTC was not inferior than TDF/FTC as PrEP for cis-gender MSM and TG
- TAF/FTC had more favorable BMI and renal profiles (consistent with treatment trials)
- TAF/FTC had poorer outcomes on weight gain and lipid profiles

CONS

- Not include cis-gender women
- Lower than-expected number of HIV infections observed reduced the statistical power
- Active control (not placebo control) limited assessing the impact of low HIV prevalence and viral load suppression among partners
- Cost-effectiveness was not studied