UPDATE FROM 22nd CROI

Seattle, February 23-26, 2015

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Disclosures

- **None**

Summary

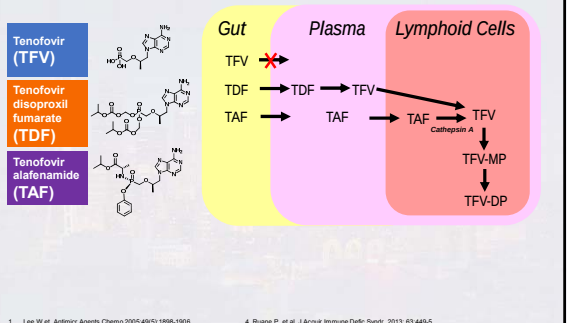
- **Lots on PrEP**
- **Some new drugs**
- **Just a little bit of rain**

- **Ones to watch**
  - Raphael Landovitz – PrEP Plenary
    - Tuesday, 8:30-9:00am, Abstract 20
  - Steven Grinspoon – Cardiovascular Disease Plenary
    - Thursday, 8:30-9:00am, Abstract 134

- **These slides adapted from Postgraduate Institute for Medicine and ViralEd, Inc CME activities**

NEW DRUGS

Tenofovir alafenamide (TAF)



1. Lee W et. Antimicr Agents Chemo 2005;49(5):1898-1906.
2. Birkus G et al. Antimicr Agents Chemo 2007;51(2):543-550.
3. Babusis D. et al. Mol Pharm 2013;10(2):459-66.
4. Ruane P, et al. J Acquir Immune Defic Syndr 2013; 63:449-5.
5. Sax P, et al. JAIDS 2014; 2014 Sep 1;67(1):52-8.
6. Sax P, et al. CROI 2015. Seattle, WA. #143LB

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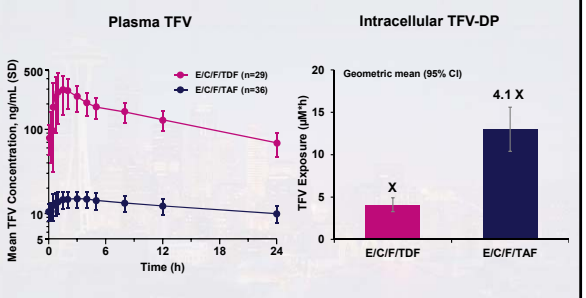
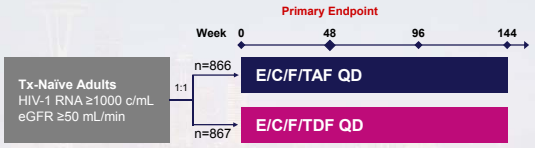
Tenofovir Alafenamide (TAF): Plasma & Cell pK



Sax P, et al. 22nd CROI; Seattle, WA; February 23-26, 2015. Abst. 143LB.

TAF vs TDF: Study Design



Wohl D, et al. 22nd CROI; Seattle, WA; February 23-26, 2015. Abst. 113LB.

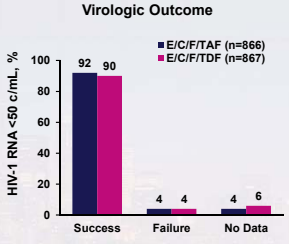
TAF vs. TDF: Baseline Characteristics

	E/C/F/TAF n=866	E/C/F/TDF n=867
Median age, years	33	35
Sex, %		
Male	85	85
Female	15	15
Race/ethnicity, %		
Black or African descent	26	25
Hispanic/Latino ethnicity	19	19
Median HIV-1 RNA, $\log_{10}$ c/mL	4.58	4.58
% with HIV-1 RNA >100,000 c/mL	23	23
Median CD4 count, cells/μL	404	406
% with CD4 count <200	13	14
Median estimated GFR*, mL/min	117	114

*Cockcroft-Gault.

Wohl D, et al. 22nd CROI; Seattle, WA; February 23-26, 2015. Abst. 113LB.

TAF vs. TDF: Virologic Results



- **E/C/F/TAF was non-inferior to E/C/F/TDF at Week 48 in each study**
  - 93% E/C/F/TAF vs 92% E/C/F/TDF (Study 104)
  - 92% E/C/F/TAF vs 89% E/C/F/TDF (Study 111)

Similar response rates, regardless of age, sex, race, HIV-1 RNA, or CD4 cell count

Wohl D, et al. 22nd CROI; Seattle, WA; February 23-26, 2015. Abst. 113LB.

TAF vs. TDF: Resistance

		E/C/F/TAF n=866	E/C/F/TDF n=867
Patients analyzed for resistance, n (%)		16 (1.8)	19 (2.2)
Primary Genotypic Resistance	Any, n (%)	7 (0.8)	5 (0.6)
	Study 104, n	3	3
	Study 111, n	4	2
NRTI Resistance, n	Any	7	5
	M184V/I	6	3
	M184V/I + K65R	1	2
INSTI Resistance, n	Any	5	3
	T66A	1	0
	E92Q	2	1
	Q148R	0	1
	Q148R + T66I/A	1	0
	Q148R + E92Q	0	1
	N155H	1	0

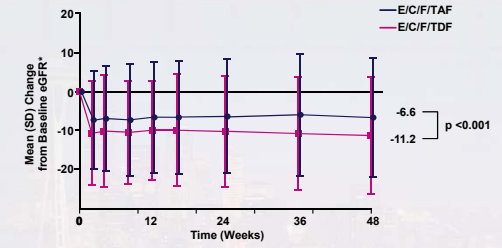
Wohl D, et al. 22nd CROI; Seattle, WA; February 23-26, 2015. Abst. 113LB.

TAF vs. TDF: Adverse Events

	E/C/F/TAF n=866	E/C/F/TDF n=867
% (n) d/c	0.9% (8)	1.5% (13)
AEs in ≥5% of patients, %		
Diarrhea	17	19
Nausea	15	17
Headache	14	13
Upper respiratory tract infection	11	13
Nasopharyngitis	9	9
Fatigue	8	8
Cough	8	7
Vomiting	7	6
Arthralgia	7	5
Back pain	7	7

Wohl D, et al. 22nd CROI; Seattle, WA; February 23-26, 2015. Abst. 113LB.

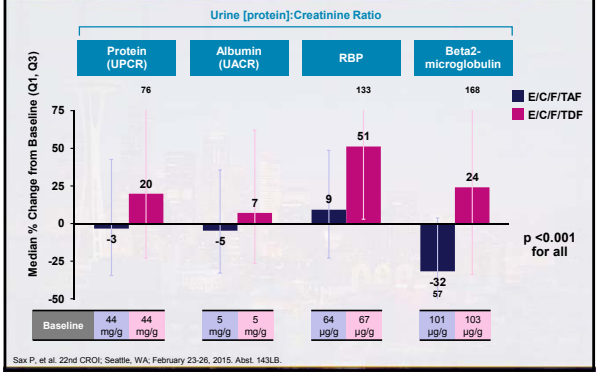
TAF vs. TDF: Renal Safety



n (%)		E/C/F/TAF n=866	E/C/F/TDF n=867
Events	Renal adverse events leading to discontinuation	0	4 (0.5)
	Tubulopathy/Fanconi syndrome	0	0

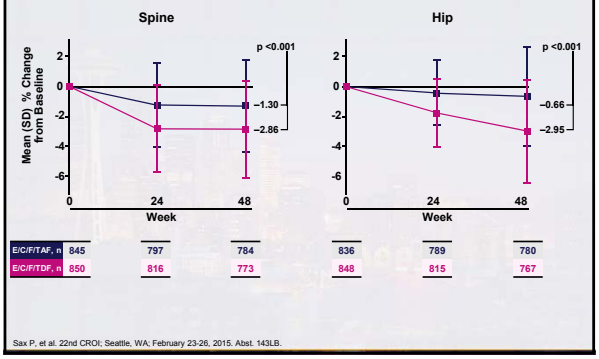
Sax P, et al. 22nd CROI; Seattle, WA; February 23-26, 2015. Abst. 143LB.

TAF vs. TDF: Quantitative Proteinuria



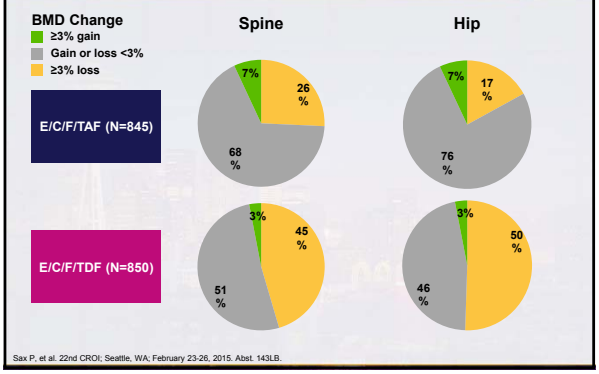
Sax P, et al. 22nd CROI; Seattle, WA; February 23-26, 2015. Abst. 143LB.

TAF vs. TDF: Spine and Hip BMD



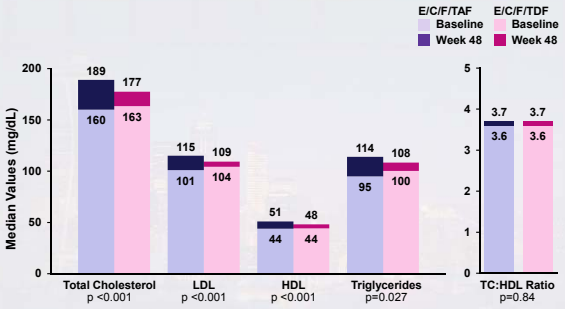
Sax P, et al. 22nd CROI; Seattle, WA; February 23-26, 2015. Abst. 143LB.

TAF vs. TDF: Bone Mineral Density (BMD)



Sax P, et al. 22nd CROI; Seattle, WA; February 23-26, 2015. Abst. 143LB.

TAF vs. TDF: Fasting Lipids

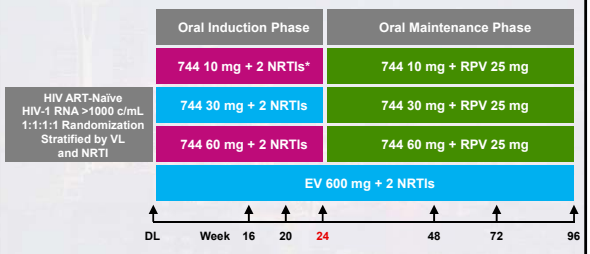


Patients initiating lipid-modifying medications: 3.6% E/C/F/TAF vs 2.9% E/C/F/TDF (p=0.42)

Sax P, et al. 22nd CROI; Seattle, WA; February 23-26, 2015. Abst. 143LB.

LATTE: Study Design

- **Phase IIb, randomized, multicenter, partially blind, dose-ranging study**
- **Patients on GSK-744 + NRTIs: If week 20 VL <50 c/mL – simplify to 744/RPV at week 24**



Margolis D, et al. 22nd CROI; Seattle, WA; February 23-26, 2015. Abst. 554LB.

LATTE: Baseline Characteristics

		744 10 mg n=60	744 30 mg n=60	744 60 mg n=61	EFV 600 mg n=62
Age	Median (y)	32.0	32.5	36.0	32.5
Gender	Male	95%	97%	93%	98%
Race	White	62%	65%	59%	63%
	African American/African	35%	28%	30%	32%
Ethnicity	Hispanic/Latino	15%	27%	23%	19%
Baseline HIV-1 RNA	Median (log_{10} c/mL)	4.281	4.178	4.349	4.343
	>100,000 c/mL	13%	12%	20%	13%
Baseline CD4+	Median (cells/mm^3)	415.0	404.0	420.0	416.5
	<200 cells/mm^3	3%	7%	3%	2%
Hepatitis coinfection	HCV	0	5 (8%)	4 (7%)	1 (2%)
Investigator-selected dual NRTIs at Day 1	TDF/FTC	37 (62%)	37 (62%)	37 (61%)	38 (61%)
	ABC/3TC	23 (38%)	23 (38%)	24 (39%)	24 (39%)

Margolis D, et al. 22nd CROI; Seattle, WA; February 23-26, 2015. Abst. 554LB.

LATTE: HIV-1 RNA <50 c/mL

Week 96 Treatment Outcomes

Outcome at Week 96	CAB 10 mg	CAB 30 mg	CAB 60 mg	CAB Total	EFV 600 mg
% <50 c/mL at W96 Snapshot (ITT-E)	41/60 (68%)	45/60 (75%)	51/61 (84%)	137/181 (76%)	39/62 (63%)
Protocol-defined Virologic Failure	3 (5%)	2 (3%)	1 (2%)	6 (3%)	6 (10%)
Failure – Adverse Event	1 (2%)	1 (2%)	4 (7%)	6 (3%)	9 (15%)
Failure – HIV-1 RNA ≥50 c/mL	5 (8%)	1 (2%)	2 (3%)	8 (4%)	2 (3%)
Failure - Other[a] Reasons while ≥50 c/mL	2 (3%)	2 (3%)	1 (2%)	5 (3%)	3 (5%)
Failure - Other[a] Reasons while <50 c/mL	8 (13%)	9 (15%)	2 (3%)	19 (10%)	3 (5%)
% <50 c/mL at W96 Snapshot (ITT-ME)	41/52 (79%)	45/53 (85%)	51/55 (93%)	137/160 (86%)	39/47* (83%)
Protocol-defined virologic failure	2 (4%)	1 (2%)	0	3 (2%)	2 (4%)
Failure – Adverse Event	1 (2%)	0	1 (2%)	2 (1%)	2 (4%)
Failure – HIV-1 RNA ≥50 c/mL	4 (8%)	1 (2%)	1 (2%)	6 (4%)	2 (4%)
Failure - Other[a] Reasons while ≥50 c/mL	1 (2%)	1 (2%)	1 (2%)	3 (2%)	0
Failure - Other[a] Reasons while <50 c/mL	3 (6%)	5 (9%)	1 (2%)	9 (6%)	2 (4%)

Margolis D, et al. 22nd CROI; Seattle, WA; February 23-26, 2015. Abst. 554LB.

LATTE: Adverse Events

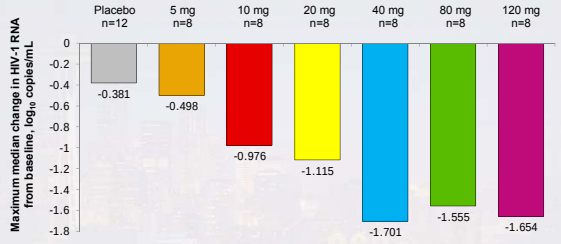
	CAB 10 mg n=60	CAB 30 mg n=60	CAB 60 mg n=61	EFV 600 mg n=62
Grade 2-4 Drug-related Events (>3% Any Arm)	5 (8%)	8 (13%)	13 (21%)	12 (19%)
Insomnia	1 (2%)	2 (3%)	0	4 (6%)
Depression	0	0	2 (3%)	0
Nausea	0	2 (3%)	3 (5%)	1 (2%)
Fatigue	0	2 (3%)	1 (2%)	1 (2%)
Headache	1 (2%)	1 (2%)	3 (5%)	0
Rash Macular	0	0	0	3 (5%)
% <50 c/mL at W96 Snapshot (ITT-ME)	1 (2%)	2 (3%)	3 (5%)	2 (3%)
Serious AEs	7 (12%)	5 (8%)	7 (11%)	4 (6%)*
Serious AEs (W24+)	5 (8%)	5 (8%)	5 (8%)	2 (3%)
AEs Leading to Withdrawal (>1 Subject)	1 (2%)	2 (3%)	4 (7%)	9 (18%)
Dizziness	0	0	0	2 (4%)
ALT Increased	0	0	2 (3%)**	0
Grade 1-4 ALT Abnormalities	8 (13%)	12 (20%)	17 (28%)	13 (21%)
Select Grade 3-4 Laboratory Abnormalities				
Creatine Phosphokinase (CPK)	7 (12%)	7 (12%)	5 (8%)	9 (15%)
Alanine Aminotransferase (ALT)	0	1 (2%)	2 (3%)**	1 (2%)
Lipase	3 (5%)	2 (3%)	6 (10%)	1 (2%)
Total Bilirubin	0	0	0	0
Total Neutrophils	1 (2%)	1 (2%)	2 (3%)	2 (3%)
Creatinine	0	0	0	0

Margolis D, et al. 22nd CROI; Seattle, WA; February 23-26, 2015. Abst. 554LB.

Maturation Inhibitors (MIs)

- **Interferes with viral maturation**
  - Disrupts final step in the processing of HIV-1 gag protein
- **Unlike PIs, MIs bind gag protein, not protease**
- **BMS-955176: >1 $\log_{10}$ c/mL in HIV-1 RNA at 20–120 mg QD**
  - Unlike 1st-generation MIs (e.g. beviramat), similar antiviral activity in subjects with wild-type HIV-1 or HIV-1 with Gag polymorphisms

BMS-955176: Phase II Trial

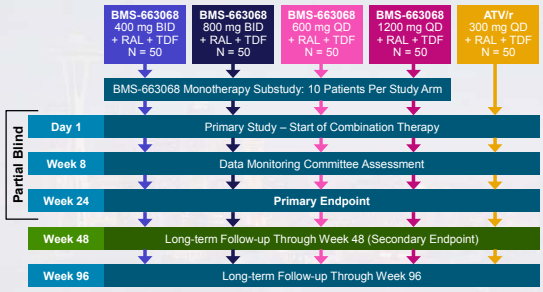


BMS-955176, a 2nd generation maturation inhibitor, demonstrated similar antiviral activity against both wild-type HIV-1 and HIV-1 with Gag polymorphisms not responsive to a 1st-generation MI

Hwang C, et al. 22nd CROI; Seattle, WA; February 23-26, 2015. Abst. 114KLB.

Attachment Inhibitor BMS-663068: Design

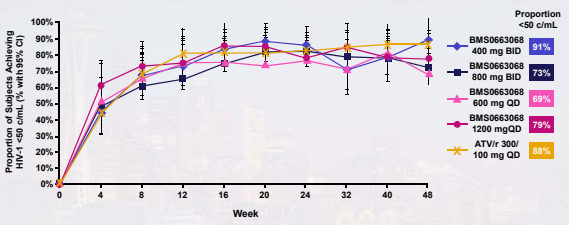
Treatment experienced patients, sensitive to all study drugs



Thompson M, et al. 22nd CROI; Seattle, WA; February 23-26, 2015. Abst. 545.

BMS-663068: Results

Treatment experienced patients, sensitive to all study drugs

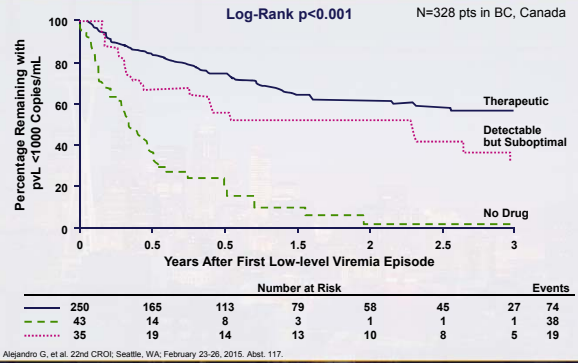


On Treatment Analysis

Thompson M, et al. 22nd CROI; Seattle, WA; February 23-26, 2015. Abst. 545.

ARV Strategies

Untimed Drug Levels and Resistance in Patients with Low Level Viremia



Alejandro G, et al. 22nd CROI; Seattle, WA; February 23-26, 2015. Abst. 117.

Untimed Drug Levels Predicted Time to VL >1000

Predictors of Virological Failure (N=328)

Variable		Unadjusted OR (95% CI)	P-value	Adjusted OR (95% CI)	P-value
Untimed Drug Level:	**Therapeutic**	1.00	<0.001	1.00	**<0.001**
	Suboptimal	3.37 (2.38-4.77)		2.53 (1.72-3.72)	
GSS: ≥3		1.00	0.003	1.00	0.04
<3		1.86 (1.24-2.78)		1.55 (1.02-2.34)	
Age (years)		0.97 (0.95-0.99)	0.012	0.98 (0.96-1)	0.087
pVL at Low-level Viremia:	0-249	1.0	<0.001	1.0	<0.001
(copies/mL)	250-499	2.55 (1.02-6.38)		2.48 (0.99-6.22)	
	500-749	2.79 (1.09-7.18)		2.36 (0.91-6.11)	
	750-999	5.42 (2.15-13.66)		3.65 (1.42-9.39)	

All p-value are derived from Cox Proportional Hazard Models
Alejandro G, et al. 22nd CROI; Seattle, WA; February 23-26, 2015. Abst. 117.

Withdrawing Inactive NRTIs in Subjects with Suppressed Viremia

Multi-Centered Trial Design in Spain

NRTIs Removed in the Experimental Arm (n=45)

Removed 1 NRTI (32/45, 71,1%)		Removed 2 NRTIs (13/45, 28,9%)	
Tenofovir	12	Tenofovir + Emtricitabine	9
Emtricitabine	9	Abacavir + Lamivudine	3
Lamivudine	8	Abacavir + Tenofovir	1
Abacavir	2		
Didanosine	1		

Llibre J, et al. 22nd CROI; Seattle, WA; February 23-26, 2015. Abst. 553.

Withdrawing Inactive NRTIs: Results

Virological Outcome at 48 Weeks

	Experimental (n=45)	Control (n=45)
Virologic Success at Week 48		
HIV-1 RNA <50 copies	41 (91.1%)	44 (97.8%)
Virologic Failure (VF) at Week 48		
HIV-1 RNA ≥50 copies/mL	1 (2.2%)	0
Discontinued due to lack of efficacy	2 (4.4%)	0
No Virologic Data in Week 48 Window		
Discontinued study drug due to AE	1 (2.2%)	0
Discontinued study drug due to other reasons and last available HIV-1 RNA <50 copies/mL	0	1 (2.2%)

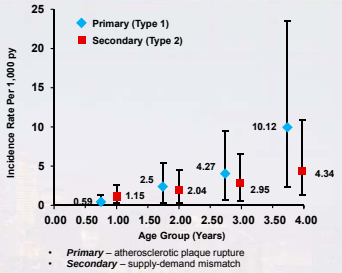
Llibre J, et al. 22nd CROI; Seattle, WA; February 23-26, 2015. Abst. 553.

Adverse Events and Co-Morbidities

NA-ACCORD: MI-Associated Factors

Key Risk Factors

- Age
- Ever Smoke RR1.75
- Hypertension RR 1.83
- Diabetes RR 1.56
- Low HDL RR 1.47
- eGFR <30 RR 5.49
- No statin RR 2.01
- Lower CD4
- Detectable HIV RNA
- History of AIDS



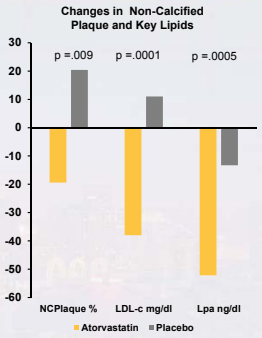
- ***Primary*** – atherosclerotic plaque rupture
- ***Secondary*** – supply-demand mismatch

- Role of ABC
- ABC use higher in older, smokers, hypertensive, low HDL, high TC, black, Hx of IDU, HCV, CD4<200, detectable VL, Hx of AIDS
- Unadjusted RR for ABC 1.88 (1.35-2.60), Adjusted RR for ABC 1.34 (0.96-1.88)

Drozd D, et al. 22nd CROI; Seattle, WA; February 23-26, 2015. Abst. 749LB.

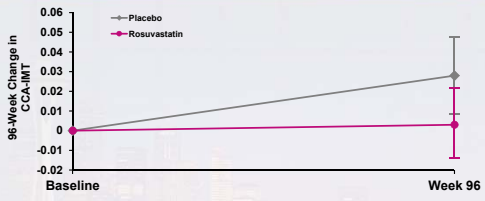
Atorvastatin for Non-Ca++ Coronary Plaques

- 40 HIV-infected pts with subclinical coronary atherosclerosis and low density lipoprotein (LDL) cholesterol <130mg/dL
- Coronary atherosclerotic plaque as assessed by coronary computed tomography angiography
- Statin therapy was well-tolerated, with low incidence of clinical adverse events or laboratory abnormalities



Lo J, et al. 22nd CROI; Seattle, WA; February 23-26, 2015. Abst. 136.

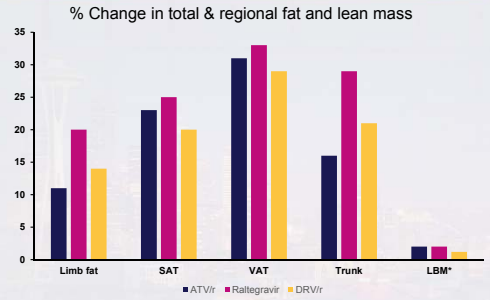
SATURN: Rosuvastatin & Carotid Intimal Media Thickening (CIMT) in Treated HIV



	Mean 96 Week Change	95% Confidence Interval	Within Group P-value	Between Group P-value
Placebo	+0.028mm	0.008-0.047	0.006	0.074
Rosuvastatin	+0.003mm	-0.014-0.021	0.714	

Longenecker C, et al. 22nd CROI; Seattle, WA; February 23-26, 2015. Abst. 137.

ACTG 5260s: Body Composition over 96 weeks

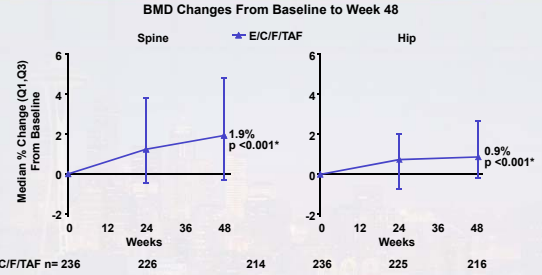


*p=0.05 ATV/r vs DRV/r

n=328

McComsey G, et al. 22nd CROI; Seattle, WA; February 23-26, 2015. Abst. 140.

Switch to E/C/F/TAF in Mild-Moderate Renal Disease: Spine and Hip Bone Mineral Density



*Two-sided Wilcoxon signed-rank test.

Pozniak A, et al. 22nd CROI; Seattle, WA; February 23-26, 2015. Abst. 795.

Risk of Cancer Among HIV+ and HIV-, Age >65yrs

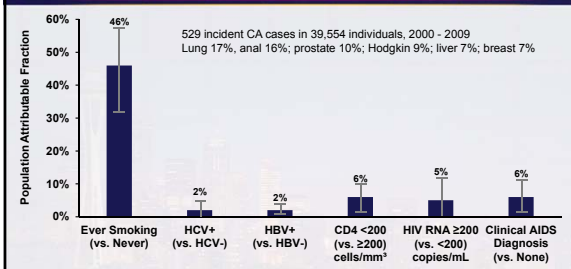
National Cancer Institute: 835,450 in US CA registry; HIV+ from 5% Medicare, 469,954 pts

	Incidence Rate* (N)		Hazard Ratio (95% CI)	
Cancer Type	HIV+	HIV-	Unadjusted	Adjusted†
Kaposi Sarcoma	63.5 (12)	0.9 (398)	68.81 (38.14-124.15)	**104.49 (56.66-192.69)**
Non-Hodgkin Lymphoma	304.0 (57)	113.2 (49,918)	2.63 (1.97-3.51)	**3.48 (2.59-4.67)**
Diffuse Large B-cell Lymphoma	139.0 (26)	30.1 (13,235)	4.53 (3.02-6.80)	**6.24 (4.14-9.41)**
Burkitt Lymphoma	16.1 (3)	0.7 (304)	22.73 (7.24-71.37)	**25.15 (7.99-79.14)**
Other Specified	75.0 (14)	68.3 (30,071)	1.07 (0.62-1.83)	1.36 (0.79-2.34)
Unspecified	75.0 (14)	14.4 (6,308)	5.10 (2.97-8.76)	**7.61 (4.41-13.12)**
Hodgkin Lymphoma	42.3 (8)	4.0 (1,752)	10.50 (5.18-21.29)	**11.50 (5.65-23.42)**
Anus	141.9 (27)	5.0 (2,212)	27.68 (18.56-41.27)	**29.96 (19.98-44.92)**
Liver	116.5 (22)	22.2 (9,806)	5.15 (3.33-7.98)	**4.86 (3.12-7.56)**
Lung	582.0 (111)	336.6 (148,217)	1.69 (1.35-2.12)	**1.78 (1.42-2.23)**
Colorectum	212.6 (40)	230.0 (101,085)	0.91 (0.65-1.27)	1.08 (0.77-1.51)
Breast‡	325.5 (16)	362.1 (94,257)	0.88 (0.51-1.52)	0.96 (0.56-1.65)
Prostate‡	805.1 (111)	854.2 (148,504)	0.92 (0.73-1.17)	**0.78 (0.61-0.99)**

*Incidence is per 100,000 person-years.
†Hazard ratios are adjusted for sex, race, age at start of follow-up, and calendar year at start of follow-up.
‡Breast cancer incidence was only assessed among women. Prostate cancer incidence was only assessed among men.

Yanik E, et al. 22nd CROI; Seattle, WA; February 23-26, 2015. Abst. 725.

NA-ACCORD: Smoking and HIV-related Risk Factors for Non-AIDS-defining Cancers



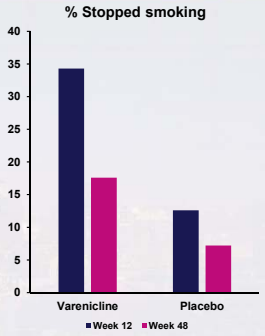
Prevalence	68%	12%	3%	26%	68%	21%
aHR* (95% CI)	2.2 (1.7, 2.9)	1.2 (0.9, 1.3)	1.8 (1.3, 2.6)	1.4 (1.1, 1.7)	1.1 (0.9, 1.3)	1.2 (1.0, 1.5)

*aHRs were adjusted for age, sex, race, cohort, and all the risk factors shown in the figure

Althoff K, et al. 22nd CROI; Seattle, WA; February 23-26, 2015. Abst. 726.

ANRS 444: Varenicline in HIV+ Smokers

- 248 smokers were randomized; 213 included in the modified intention-to-treat analysis (102 varenicline, 111 placebo)
  - Dose 0.5mg QD to 1 mg BID after 1 wk
- Median age was 45 years, 83% male, median nadir CD4+ 213/mm³, baseline CD4+ 617/mm³ and undetectable HIV RNA 73%
- Grade 3/4 drug-related effects were reported in 7 patients in each arm, including
- 9 psychiatric side effects (5 in varenicline arm vs. 4 in placebo arm)
- 3 gastrointestinal side effects (1 in varenicline arm vs. 2 in placebo arm)

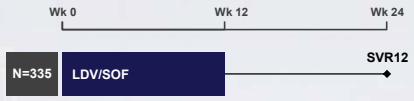


Mercie P, et al. Abstract 139

Mercie P, et al. 22nd CROI; Seattle, WA; February 23-26, 2015. Abst. 139.

Hepatitis

ION-4 Trial in HIV-HCV: Study Design



- **Phase 3, multicenter, open-label study (NCT02073656)**
- **HCV GT 1 or 4 patients in US, Canada, and New Zealand**
- **Broad inclusion criteria**
  - HCV treatment-naïve or treatment-experienced
  - 20% with compensated cirrhosis
  - Platelets ≥50,000/mm^3; hemoglobin ≥10 mg/dL, CrCl ≥60 mL/min
  - HIV-1 positive, HIV RNA <50 copies/mL; CD4 cell count >100 cells/mm^3
- **ART regimens included emtricitabine and tenofovir disoproxil fumarate plus efavirenz, raltegravir, or rilpivirine**

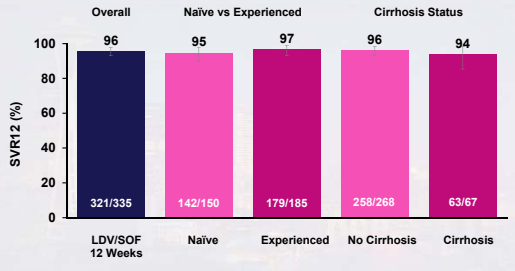
Naggie S, et al. 22nd CROI; Seattle, WA; February 23-26, 2015. Abst. 152LB.

ION-4: Baseline Characteristics

	LDV/SOF 12 weeks N=335
Mean age, y (range)	52 (26-72)
Male, n (%)	276 (82)
Black, n (%)	115 (34)
Hispanic or Latino, n (%)	56 (17)
Mean BMI, kg/m^2 (range)	27 (18-66)
IL28B CC, n (%)	81 (24)
GT 1	327 (98)
HCV treatment experienced, n (%)	185 (55)
Cirrhosis, n (%)	67 (20)
Mean HCV RNA, $\log_{10}$ IU/mL ± SD	6.7 ± 0.6
Median CD4 cell count, cells/µL (range)	628 (106-2069)
HIV ARV Regimen	
Efavirenz + FTC + TDF	160 (48)
Raltegravir + FTC + TDF	146 (44)
Rilpivirine + FTC + TDF	29 (9)

Naggie S, et al. 22nd CROI; Seattle, WA; February 23-26, 2015. Abst. 152LB.

ION-4: SVR12 by Prior Treatment and Cirrhosis

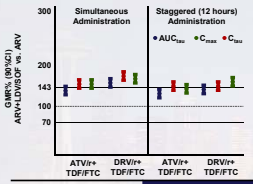


Error bars represent 95% confidence intervals.

Naggie S, et al. 22nd CROI; Seattle, WA; February 23-26, 2015. Abst. 152LB.

Drug Interactions: Ledipasvir/Sofosbuvir and ART

Effect of LDV/SOF on TDF PK



- Moderate (~ 30-60%) increases in TDF/FTC exposure with LDV/SOF added to PI/r + TDF/FTC regimen versus PI/r + TDF/FTC regimen alone
- May be attributed to persistent inhibition of efflux drug transporters

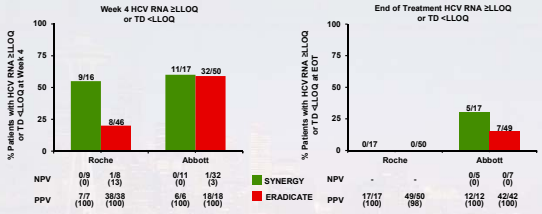
TDF PK Parameter N=24	Mean (%CV)			
	LDV/SOF + ATV/r + TDF/FTC		LDV/SOF + DRV/r + TDF/FTC	
	Simultaneous	Staggered	Simultaneous	Staggered
AUC_{tau} (ng-h/mL)	5460 (27.7)	5740 (25.0)	5490 (31.2)	4260 (24.2)
C_{max} (ng/mL)	530 (26.2)	559 (22.0)	523 (28.0)	410 (27.6)
C_{tau} (ng/mL)	120 (30.5)	116 (27.1)	117 (30.6)	87.3 (25.0)

Data presented to 3 significant figures; N=23 (LDV/SOF + DRV/r + TDF/FTC; simultaneous administration)

German P, et al. 22nd CROI; Seattle, WA; February 23-26, 2015. Abst. 82.

Hepatitis C Viral Load Monitoring with Ledipasvir/Sofosbuvir

Patients with HCV RNA ≥LLOQ or TD <LLOQ at W4 and EOT



- The majority of patients with HCV RNA ≥LLOQ or HCV RNA TD <LLOQ at week 4 achieved SVR12 (NPV <13%)
- 5 patients on SYNERGY and 7 patients on ERADICATE had HCV RNA TD <LLOQ at EOT by the Abbott assay
  - All 12 patients achieved SVR12
  - By the Roche assay, all patients had HCV RNA TND <LLOQ at EOT

Sidharthan S, et al. 22nd CROI; Seattle, WA; February 23-26, 2015. Abst. 689.

High SVR Regardless of Time to Suppression with Ombitasvir/Paritaprevir/r & Dasabuvir + RBV

Studies Included in Post-hoc Analyses

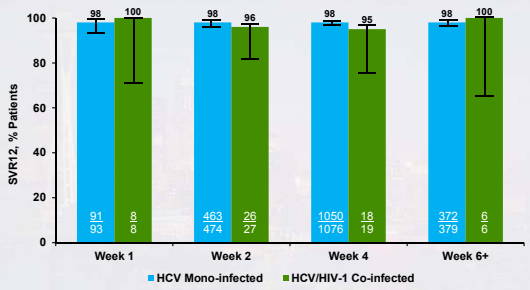
Study	N	Genotypes	pegIFN/RBV Treatment-Experienced	Cirrhosis	HIV-1 Co-Infection
SAPPHIRE-I	473	1a, 1b	No	No	No
SAPPHIRE-II	297	1a, 1b	Yes	No	No
PEARL-II	186	1b	Yes	No	No
PEARL-III	419	1b	No	No	No
PEARL-IV	305	1a	No	No	No
TURQUOISE-II	380	1a, 1b	Yes & No	Yes	No
TURQUOISE-I	63	1a, 1b	Yes & No	Yes & No	Yes

Phase 3 studies
Phase 2 study

Wyles D , et al. 22nd CROI; Seattle, WA; February 23-26, 2015. Abst. 147.

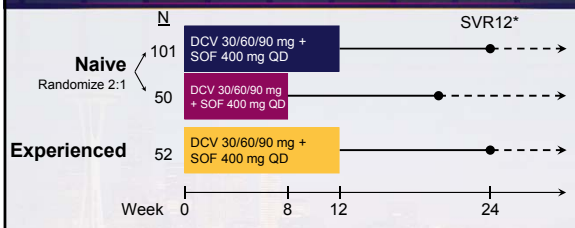
High SVR Regardless of Time to Suppression with Ombitasvir/Paritaprevir/R & Dasabuvir + RBV

SVR12 by Time to HCV RNA Suppression <15 IU/mL



Wyles D , et al. 22nd CROI; Seattle, WA; February 23-26, 2015. Abst. 147.

ALLY-2: Study Design

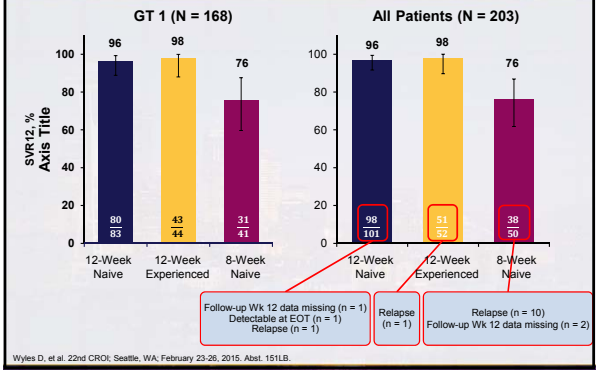


- Primary endpoint: SVR12 in treatment-naive patients with GT 1 treated for 12 weeks
- Standard DCV dose is 60 mg
- Dose-adjusted for concomitant ARV therapy: 30 mg with ritonavir-boosted PIs, 90 mg with NNRTIs except RPV

* HCV RNA <LLOQ (TD or TND) at posttreatment Week 12, assessed using the Roche HCV COBAS TaqMan Test v2.0 (LLOQ 25 IU/mL).

Wyles D, et al. 22nd CROI; Seattle, WA; February 23-26, 2015. Abst. 151LB.

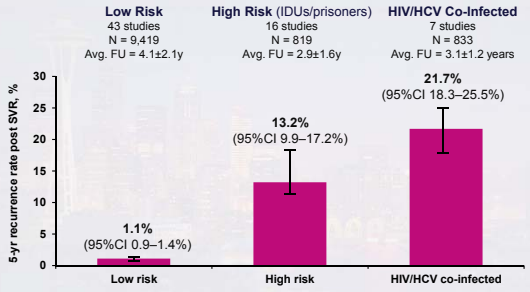
ALLY-2: SVR12



Wyles D, et al. 22nd CROI; Seattle, WA; February 23-26, 2015. Abst. 151LB.

Risk of Late Relapse or Re-Infection with HCV After SVR

Meta-Analysis of 66 Studies in 11,071 Patients
Five-Year Rate (95%CI) of Recurrence Post-SVR, by Risk Group



Hill A, et al. 22nd CROI; Seattle, WA; February 23-26, 2015. Abst. 654.