ARV Therapies and Therapeutic Strategies

REPORTING ON IAS 2015

Comprehensive Expert Review and Discussion of Key Presentations

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Efficacy and Safety of Doravirine 100mg QD vs Efavirenz 600mg QD with TDF/FTC in ART-Naive HIV-Infected Patients: Week 24 Results

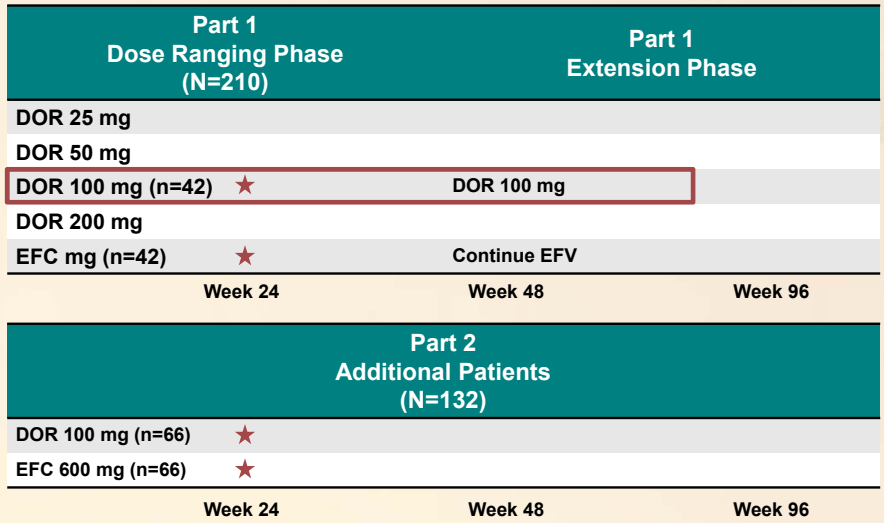
Jose M. Gatell, Francois Raffi, Andreas Plettenberg, Don Smith, Joaquin Portilla, Christian Hoffmann, Keikawus Arasteh, Melanie Thompson, Debbie P. Hagins, Javier O. Morales-Ramirez, Xia Xu, Hedy Teppler

Abstract TUAB04

TDF/FTC + Doravirine vs EFV: Study Design

Patients:

- HIV-1+ ART-naïve
- HIV RNA ≥1,000 c/ml
- CD4 count ≥100 cells/μL



Note: blinding maintained through Week 96 study visit

Gatell J, et al; 8th IAS, Vancouver, Canada, July 19-22, 2015; Abst. TUAB04.

TDF/FTC + Doravirine vs EFV: Baseline Characteristics

	Doravirine 100 mg (N=108)	Efavirenz 600 mg (N=108)
% Male	91.7	93.5
Age (years), median (range)	35 (19 – 67)	34 (20 – 57)
% White	79.6	79.6
% with AIDS	3.7	6.5
HIV RNA (log_{10} c/mL), median (range)	4.6 (2.6 – 6.5)	4.6 (3.0 – 6.7)
% with HIV RNA >100,000 c/mL, at screening	35.2	37.0
CD4 Count (cells/µL), median (range)	402 (92 – 1110)	430 (118 – 1121)
% with CD4 count ≤ 200 cells/µL	6.5	9.3
% with Clade B viral subtype	69.4	79.6

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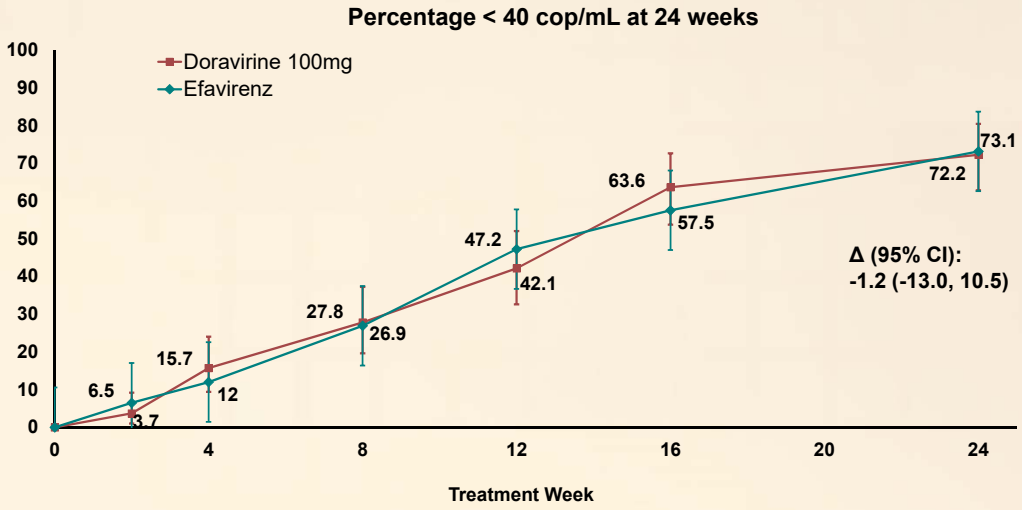
TDF/FTC + Doravirine vs EFV: Primary Endpoint



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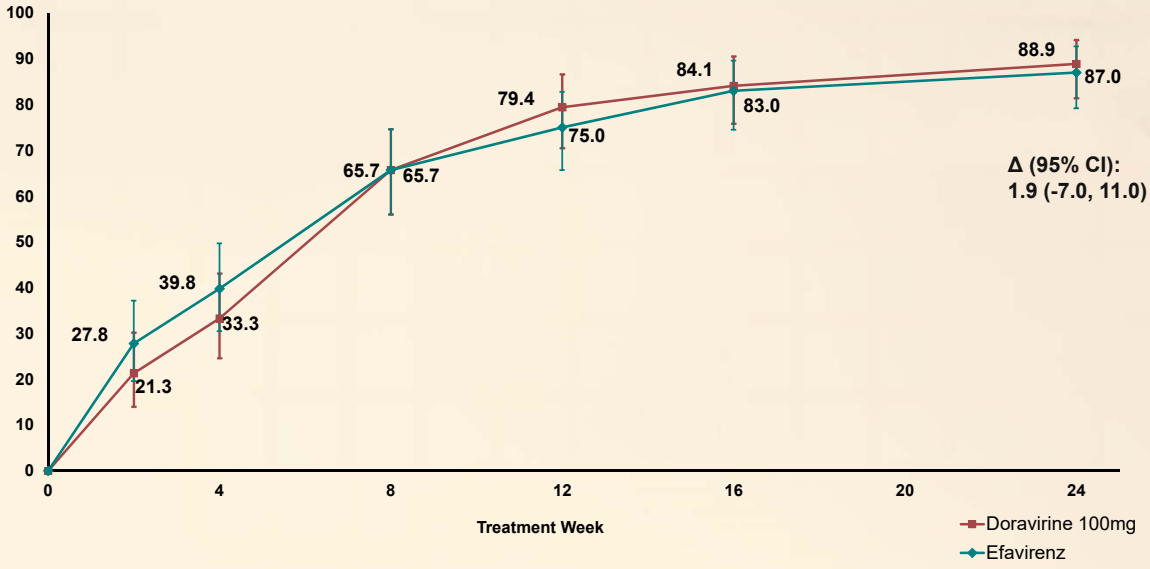
Patients with HIV RNA <200 c/mL, % (95% CI)
Non-completer = Failure Approach



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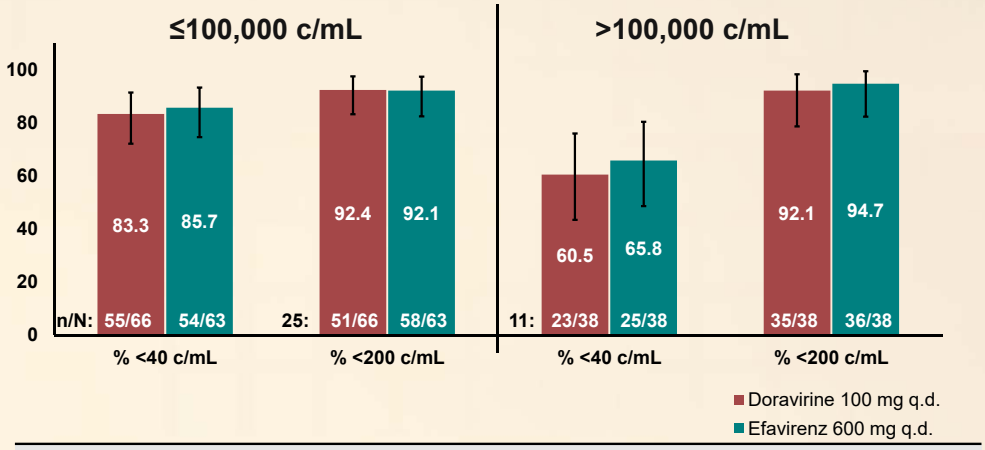
TDF/FTC + Doravirine vs EFV:
Results by Baseline HIV RNA



Virologic failures: DRV 17, EFV 11 -- mostly due to low-level viremia at week 24 (no resistance detected)
1 or more CNS adverse events: DRV 27%, EFV 46% -- difference -19.4% (95% CI -31.7, -6.6)

Gatell J, et al; 8th IAS, Vancouver, Canada, July 19-22, 2015; Abst. TUAB04.

Protocol-defined Virologic Failures by Week 24

	Doravirine 100 mg (N=108)	Efavirenz 600 mg (N=108)
Virologic failure ≥40 c/mL, n (%)		
Non-response†	17 (15.7)	10 (9.3)
Rebound‡	0	1 (0.9)
Virologic failure ≥200 c/mL, n (%)		
Non-response†	4 (3.7)	0
Rebound‡	0	1 (0.9)
Resistance testing performed*	1	1
NNRTI mutations detected	0	0
NRTI mutations detected	0	0

† Non-response: patient did not achieve vRNA <40 (or <200) c/mL by Week 24.
‡ Rebound: after initial response of vRNA <40 (or <200) c/mL, patient had 2 consecutive measurements ≥40 (or ≥200) c/mL at least 1 week apart, at or after Week 24. (Rebound after Week 24 not included here.)
* vRNA > 500 copies/mL required for resistance testing.

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Number of Protocol-defined Virologic Failures by Week 24 (≥40 c/mL, confirmed)

	vRNA (copies/mL) at time of Virologic Failure				
Type of VF	**40 - 50**	**>50 - 100**	**>100 - 200**	**>200**	**Total**
Rebound†					
Doravirine	0	0	0	0	0
Efavirenz	0	0	0	1	1
Non-Response‡					
Doravirine	4	7	2	4	17
Efavirenz	4	6	0	0	10

† Rebound: after initial response of vRNA <40 (or <200) c/mL, patient had 2 consecutive measurements ≥40 (or ≥200) c/mL at least 1 week apart, at or after Week 24. (Rebound after Week 24 not included here.)
‡ Non-response: patient did not achieve vRNA <40 (or <200) c/mL by Week 24.

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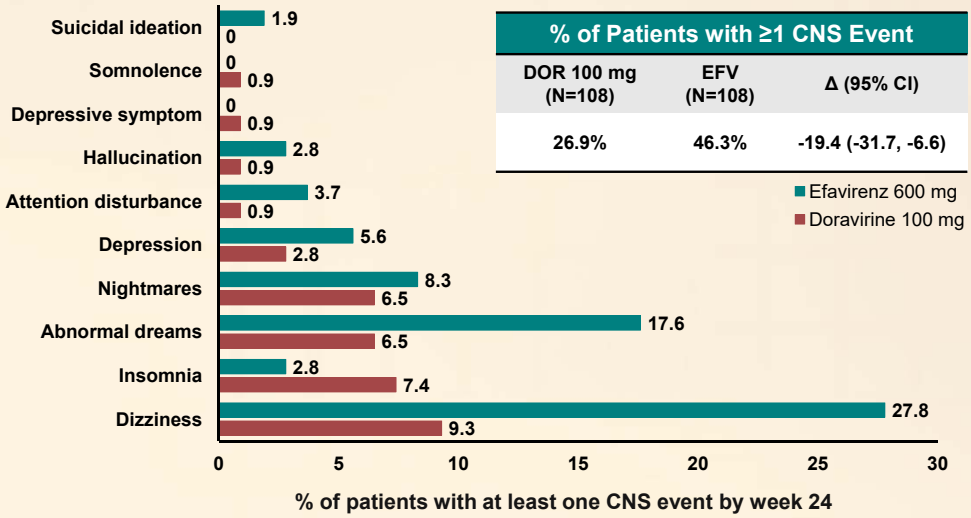
Primary Safety Comparison: CNS Events, All Causality

- Significantly fewer patients on DOR had ≥1 CNS event by week 24 (p<0.001)



% of Patients with ≥1 CNS Event		
DOR 100 mg (N=108)	EFV (N=108)	Δ (95% CI)
26.9%	46.3%	-19.4 (-31.7, -6.6)

Efavirenz 600 mg
Doravirine 100 mg

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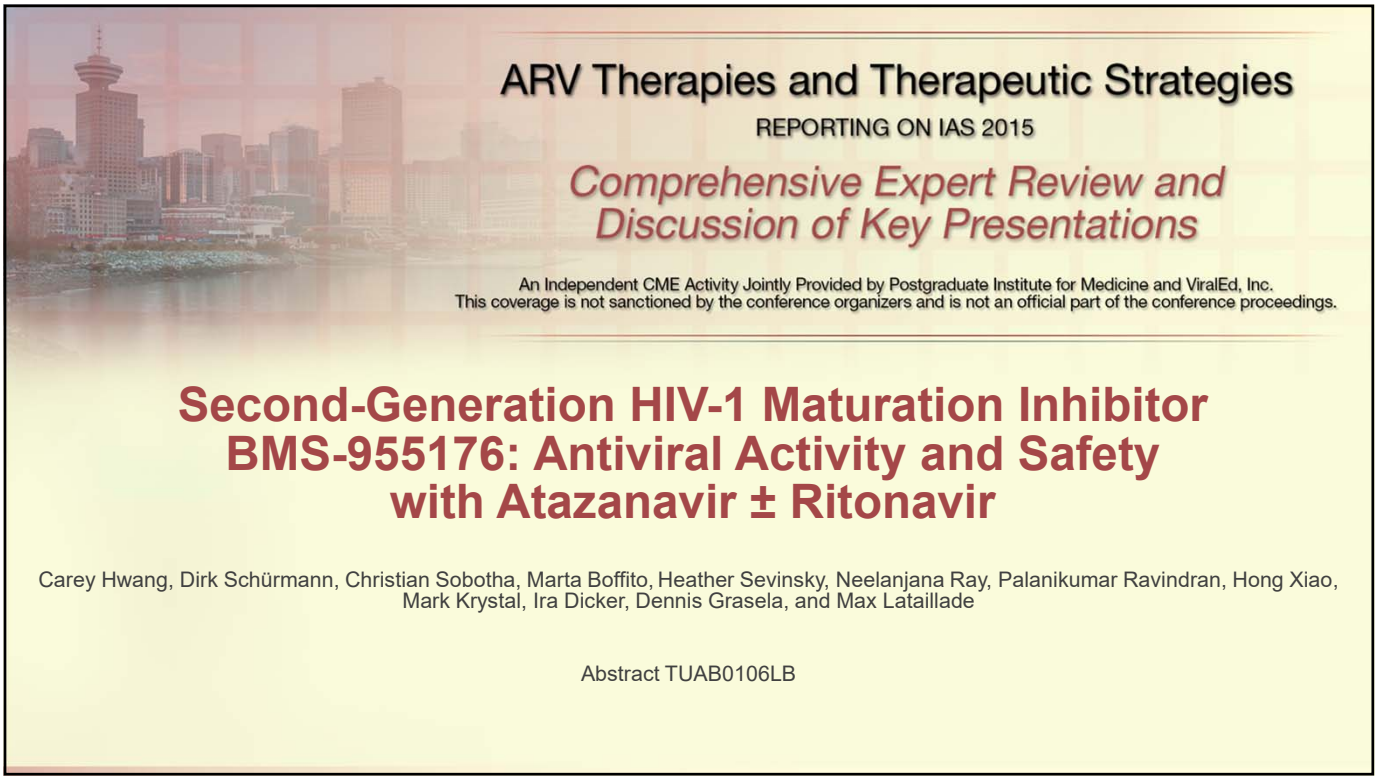

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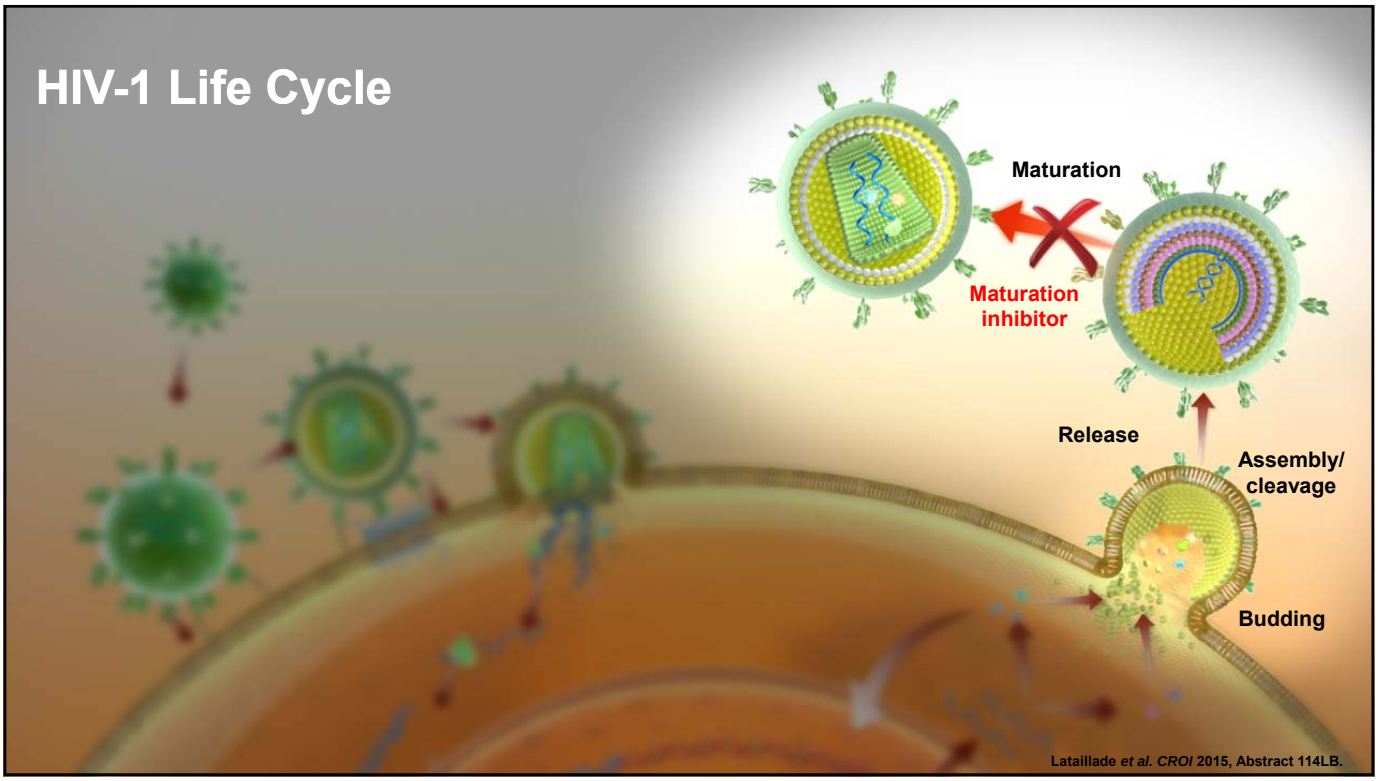
Second-Generation HIV-1 Maturation Inhibitor BMS-955176: Antiviral Activity and Safety with Atazanavir ± Ritonavir

Carey Hwang, Dirk Schürmann, Christian Sobotha, Marta Boffito, Heather Sevinsky, Neelanjana Ray, Palanikumar Ravindran, Hong Xiao, Mark Krystal, Ira Dicker, Dennis Grasela, and Max Lataillade

Abstract TUAB0106LB



BMS-955176 Attachment Inhibitor: Study Design

TDF/FTC 300/200 mg + ATV 300 mg + RTV 100 mg N=4	BMS-955176 40 mg + ATV 300 mg + RTV 100 mg N=8	BMS-955176 40 mg + ATV 400 mg N=8	BMS-955176 80 mg + ATV 400 mg N=8
Days 1–28	Dosing period		
Day 30	Furloughed		
Days 35	Outpatient visits		
Day 42	Discharge		

Inpatient days: Day -1 to Day 30

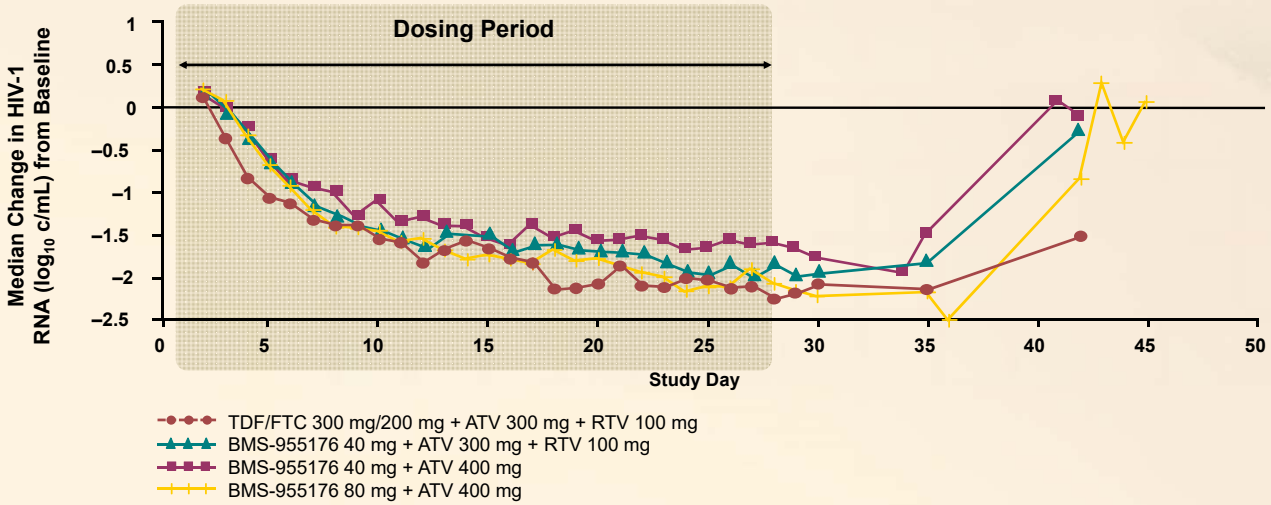
Objectives
Change in plasma HIV-1 RNA levels from baseline to Day 28
Safety and tolerability of BMS-955176 during combination therapy

Key Inclusion Criteria	
HIV-1 subtype B-infected subjects	Plasma HIV-1 RNA ≥5,000 c/mL
Treatment-naïve (<1 week of antiretroviral treatment) or -experienced (PI naïve) subjects	CD4+ T-cell count ≥200 cells/μL

Hwang C, et al; 8th IAS, Vancouver, Canada, July 19-22, 2015; Abst. TUAB0106LB

BMS-955176 Attachment Inhibitor: Median Change in HIV-1 RNA

- Median change in HIV-1 RNA at Day 29 was between -1.66 and -2.18 $\log_{10}$ c/mL for the BMS-955176 arms and was -2.22 $\log_{10}$ c/mL for the standard of care arm



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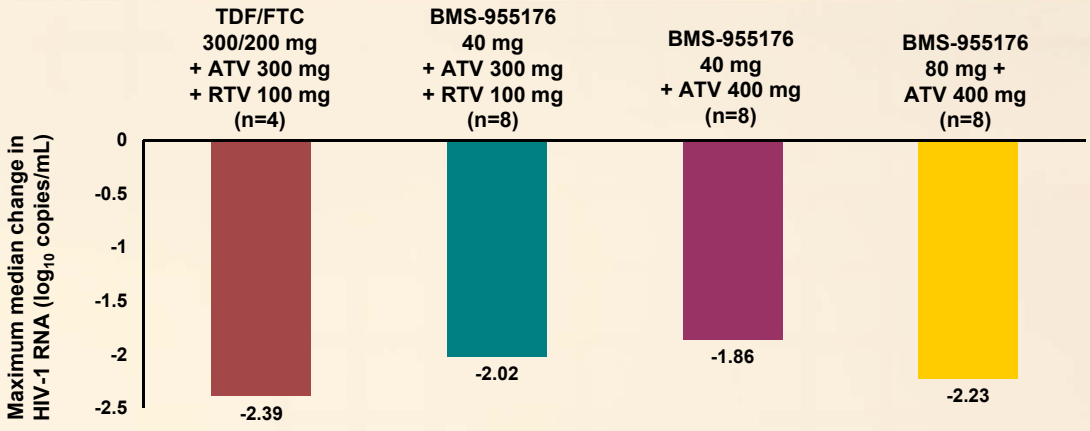
BMS-955176 Attachment Inhibitor: Maximum Median Decline in HIV-1 RNA from Baseline



- BMS-955176 80 mg + ATV and BMS-955176 40 mg + ATV + RTV had similar maximum median changes in HIV-1 RNA compared with the standard of care arm
- Greatest elevations in bilirubin seen in maturation inhibitor plus boosted ATV (arm 2)

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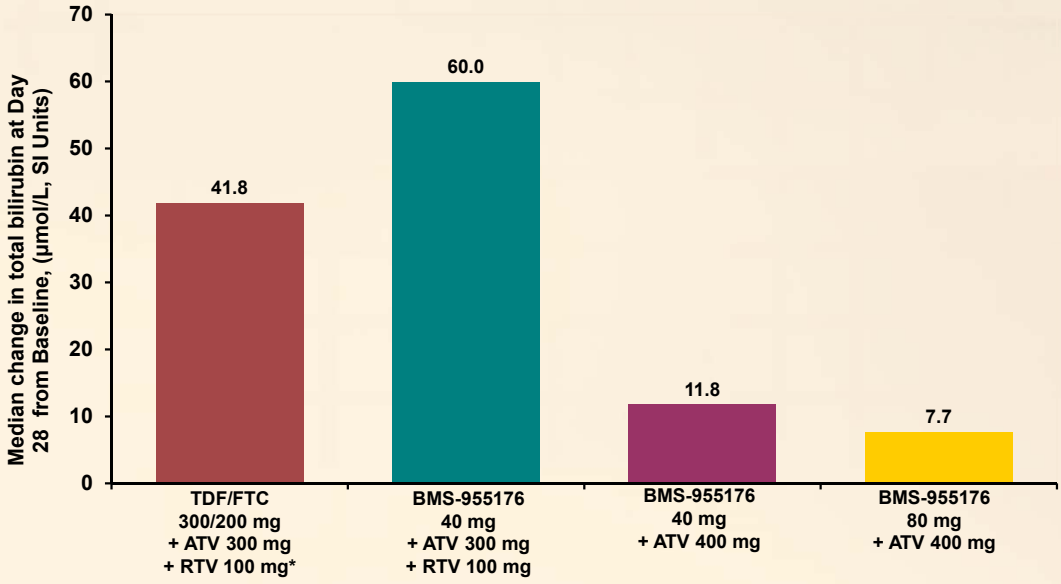
AI468002: Median Change in Bilirubin at Day 28 from Baseline



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Conclusions

- BMS-955176 is a potent, once-daily, second-generation MI
- BMS-955176 80 mg + ATV and BMS-955176 40 mg + ATV + RTV demonstrated similar antiviral activity (~2.2 $\log_{10}$ c/mL median decline) compared to the standard of care control over the 28-day treatment period
- BMS-955176 was generally well tolerated
  - There were no SAEs or AEs leading to discontinuation
  - BMS-955176 + unboosted ATV was associated with lower median changes from baseline in bilirubin levels compared to the arms with boosted ATV
- A Phase IIb study investigating BMS-955176 + ATV in a booster-sparing and nucleot(s)ide-sparing regimen in treatment-experienced patients initiated July 2015

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