NORTHWEST AIDS EDUCATION AND TRAINING CENTER

2012 CROI Update: Selected Studies

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2012 CROI Update: Selected Studies

- Telaprevir in HCV Treatment Naïve
- Drug Interactions with Boceprevir and PIs
- Boceprevir in HCV Treatment Naïve
- Quad Pill versus Atripla in Treatment Naïve
- Dolutegravir in Treatment Naïve

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Telaprevir in HCV Treatment Naive
Study 110

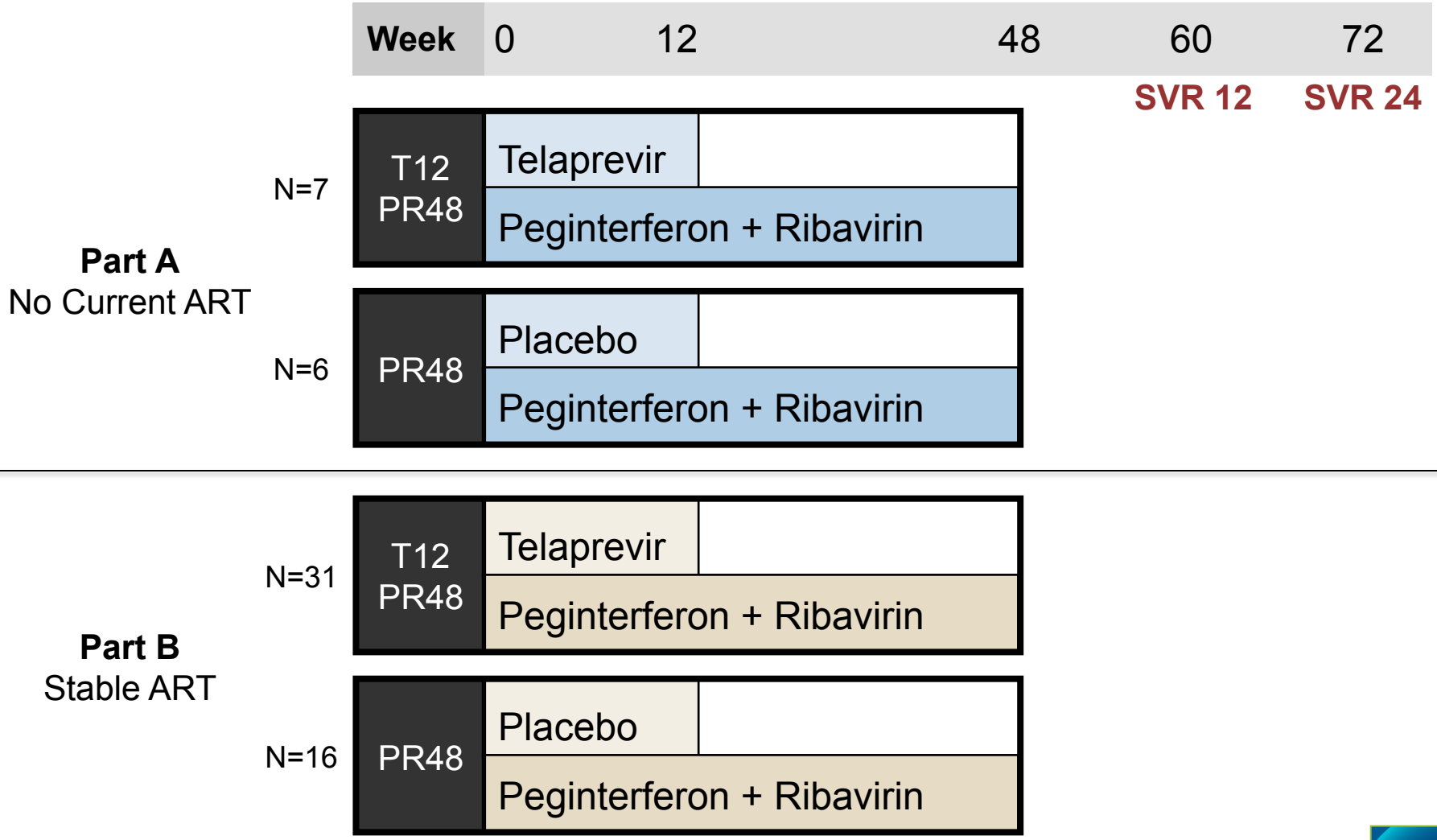
Telaprevir plus Peginterferon/Ribavirin in HIV/HCV Coinfection
Study 110: Design

Protocol Features for Study 110

- Phase 2a trial; randomized, placebo-controlled
- Chronic HCV; Genotype 1; HCV- treatment naïve
- Randomized to Telaprevir + PegIFN+ RBV versus PegIFN + RBV
  - Part A: No Antiretroviral Rx
  - Part B: Antiretroviral Rx
- Antiretroviral Regimens in Part B:
  (1) Tenofovir-Emtricitabine-Efavirenz
  (2) Tenofovir + (Emtricitabine or Lamivudine) + Ritonavir + Atazanavir
- Drug Dosing: Telaprevir = 750 mg tid (1125 mg tid with Efavirenz)

Source: Dieterich D, et al. 19th CROI. 2012; Abstract 46.

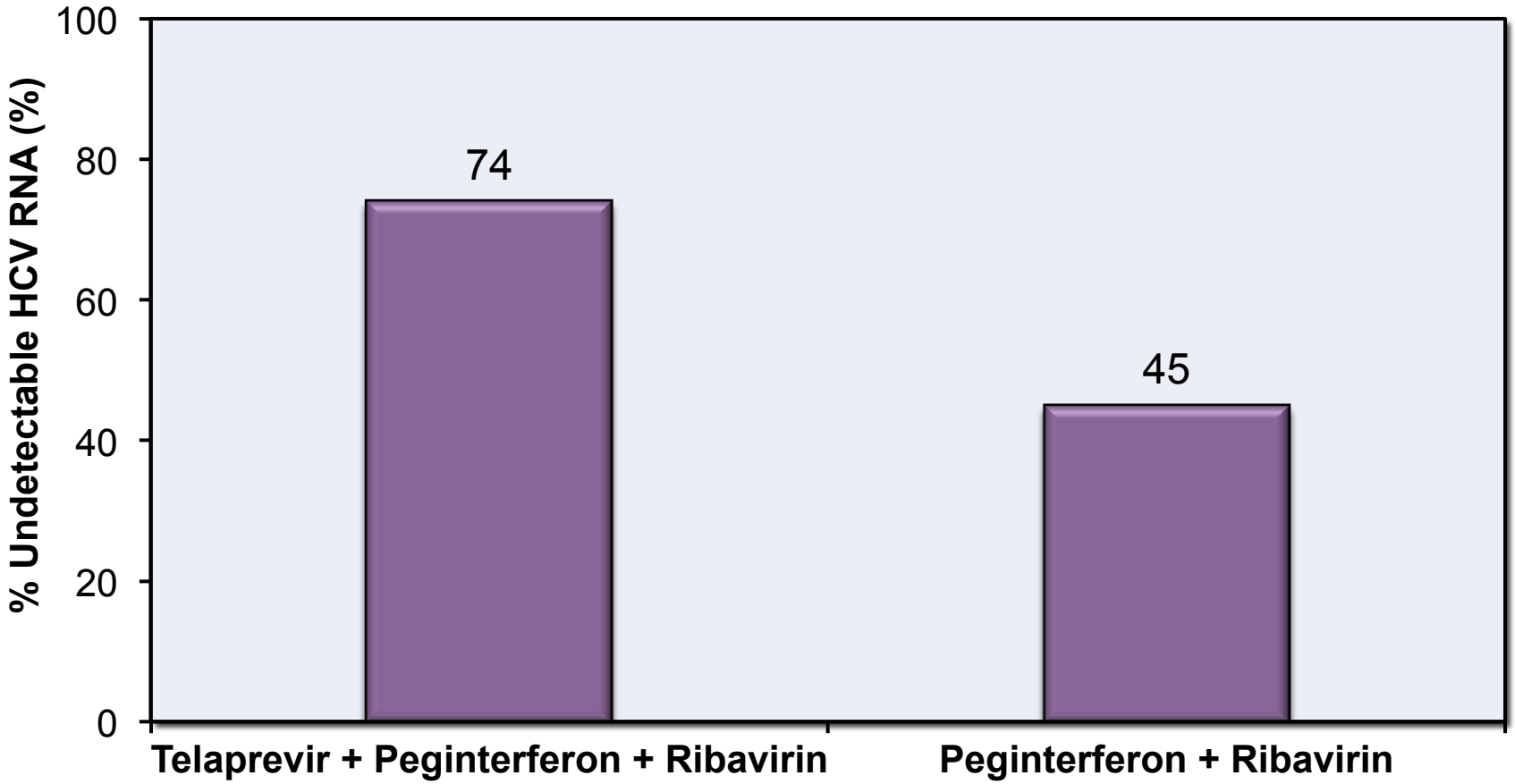
Telaprevir plus Peginterferon/Ribavirin in HIV/HCV Coinfection
Study 110: Design



Source: Dieterich D, et al. 19th CROI. 2012; Abstract 46.

Telaprevir plus Peginterferon/Ribavirin in HIV/HCV Coinfection
Study 110: Design

Week 12 Post Treatment (SVR-12)



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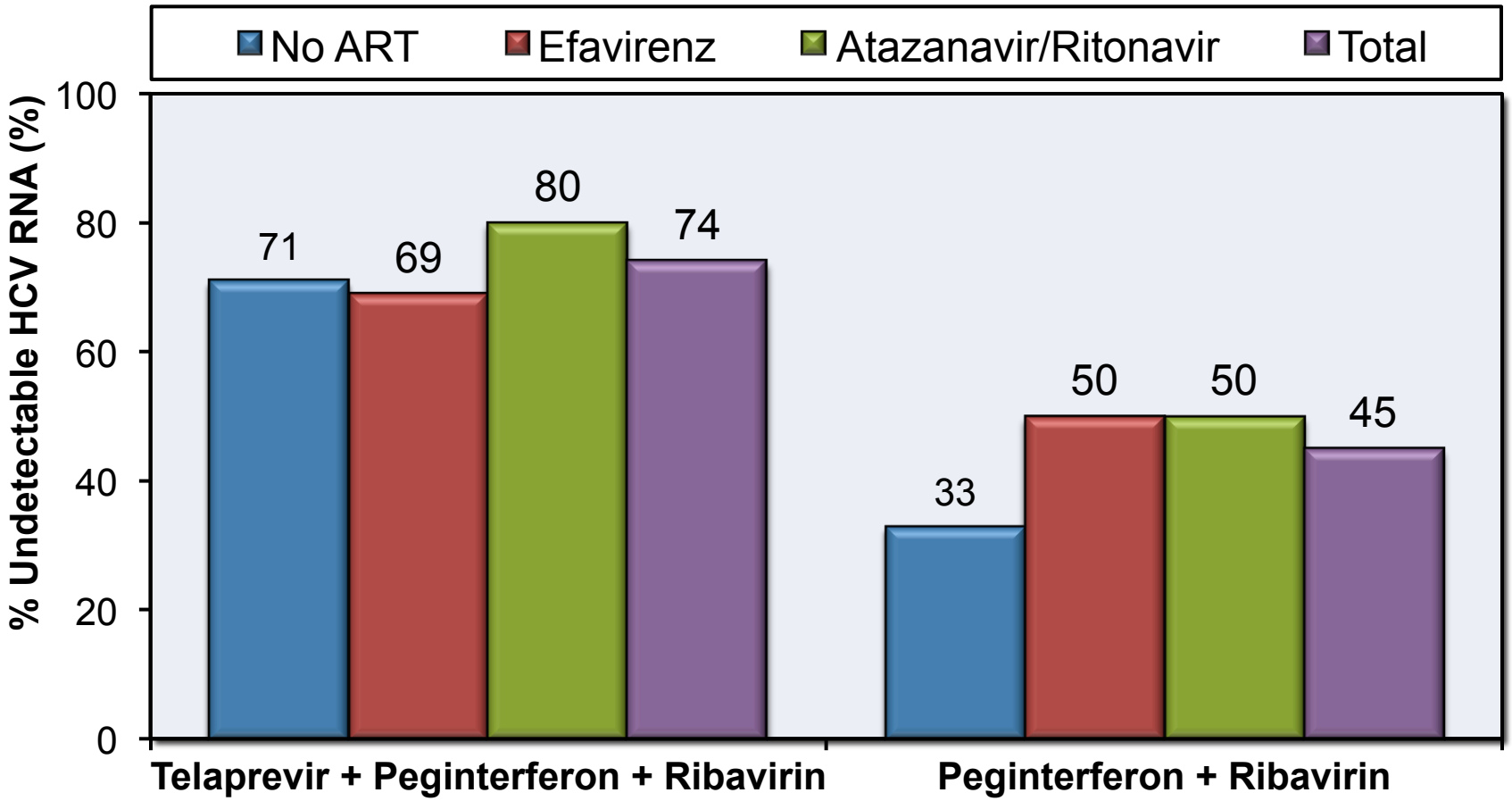
Telaprevir plus Peginterferon/Ribavirin in HIV/HCV Coinfection
Study 110: Design

Week 12 Post Treatment (SVR-12)



Source: Dieterich D, et al. 19th CROI. 2012; Abstract 46.

Boceprevir Interactions with Ritonavir-Boosted PIs

Interaction Between Boceprevir and Ritonavir-Boosted Protease Inhibitors in Healthy Volunteers

Impact of Boceprevir on Levels of Ritonavir-Boosted Protease Inhibitors			
Protease Inhibitor	**Cmin (trough)**	**Mean AUC**	**Cmax (peak)**
Atazanavir	↓ 49%	↓ 35%	↓ 25%
Darunavir	↓ 59%	↓ 44%	↓ 36%
Lopinavir	↓ 43%	↓ 34%	↓ 30%

Source: Hulskotte EGJ, et al. 19th CROI. 2012; Abstract 771LB.

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Victrelis (boceprevir) and Ritonavir-Boosted HIV Protease Inhibitor Drugs - Drug Interactions

The U.S. Food and Drug Administration (FDA) is notifying healthcare professionals and patients that drug interactions between the hepatitis C virus (HCV) protease inhibitor Victrelis (boceprevir) and certain ritonavir-boosted human immunodeficiency virus (HIV) protease inhibitors (atazanavir, lopinavir, darunavir) can potentially reduce the effectiveness of these medicines when they are used together.

Patients should not stop taking any of their medicines without talking to their healthcare professional. Patients should contact their healthcare professional if they have any questions or concerns.

Healthcare professionals who have started patients infected with both chronic HCV and HIV on Victrelis and antiretroviral therapy containing a ritonavir-boosted protease inhibitor should closely monitor patients for HCV treatment response and for potential HCV and HIV virologic rebound.

A drug interaction study showed that taking boceprevir (Victrelis) with ritonavir (Norvir) in combination with atazanavir (Reyataz) or darunavir (Prezista), or with Kaletra (lopinavir/ritonavir) reduced the blood levels of the HIV medicines and boceprevir in the body (see Data Summary below). FDA will be updating the Victrelis drug label to include information about these drug interactions.

Merck and Company has issued a Dear Healthcare Professional letter (PDF - 67KB) with information about this drug interaction study.

Facts about Victrelis (boceprevir) and HIV protease inhibitors

- Victrelis is a hepatitis C virus (HCV) protease inhibitor used with the medicines peginterferon alfa and ribavirin to treat chronic (long-lasting) hepatitis C infection in adults who have not been treated before or who have failed previous treatment.
- HIV protease inhibitors are a class of anti-viral drugs used to treat HIV infection.
- Ritonavir is an HIV protease inhibitor used to "boost" other HIV protease inhibitors, increasing their levels in the blood and making them more effective.

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Boceprevir in HCV Treatment Naïve

Boceprevir with Antiretroviral Therapy Study : Design

Protocol Features

- N = 100 HIV/HCV coinfected, Age 18-65
- Phase 2a trial; randomized, placebo-controlled
- Chronic HCV; Genotype 1; HCV- treatment naïve
- CD4 $\geq$ 200 cells/mm^3; HIV RNA < 50 copies/ml on ARV therapy
- Some ARVs Not Allowed: NNRTI, unboosted PI, ZDV, d4T
- Randomized: (1:2) and all had 4-week lead in with PegIFN+ Ribavirin
  (1x) Peginterferon + Ribavirin (n = 34)
  (2x) Boceprevir + Peginterferon + Ribavirin (n = 64)

Source: Sulkowski M, et al. 19th CROI. 2012; Abstract 47.

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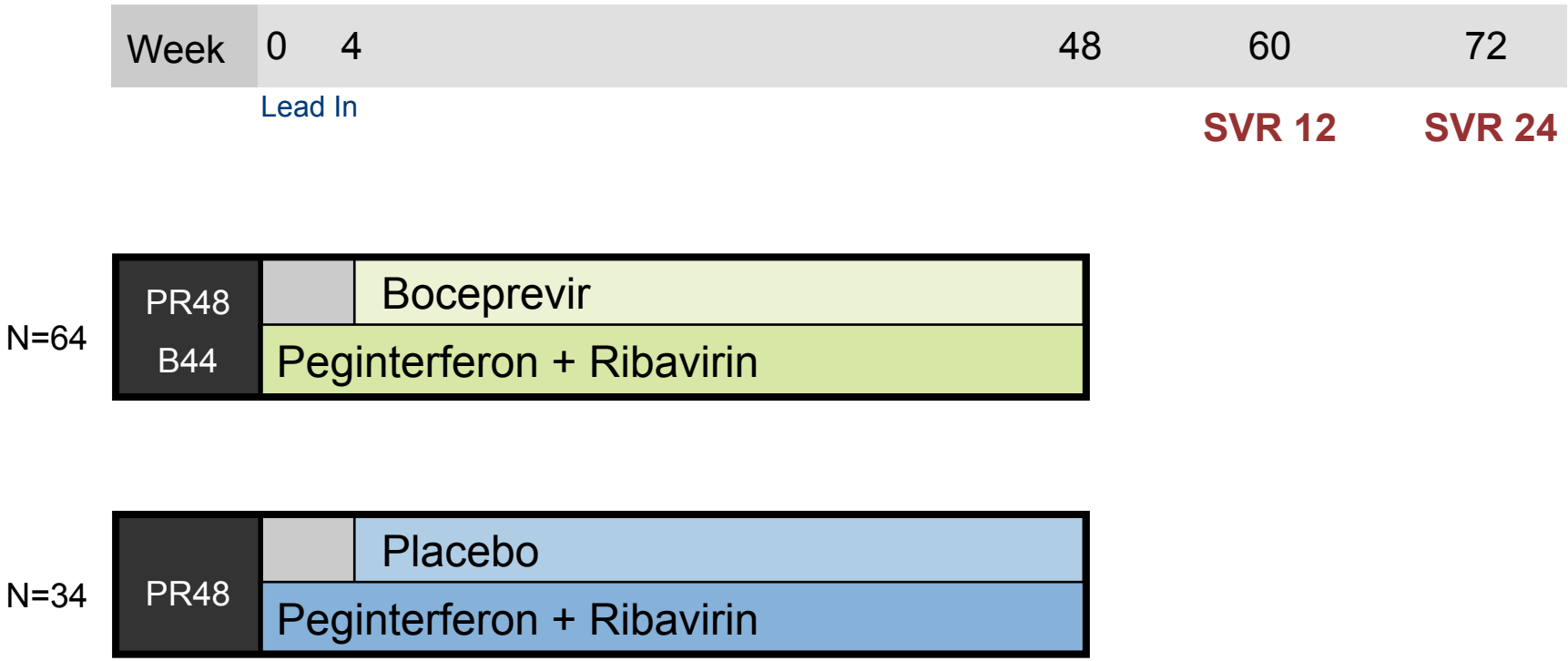
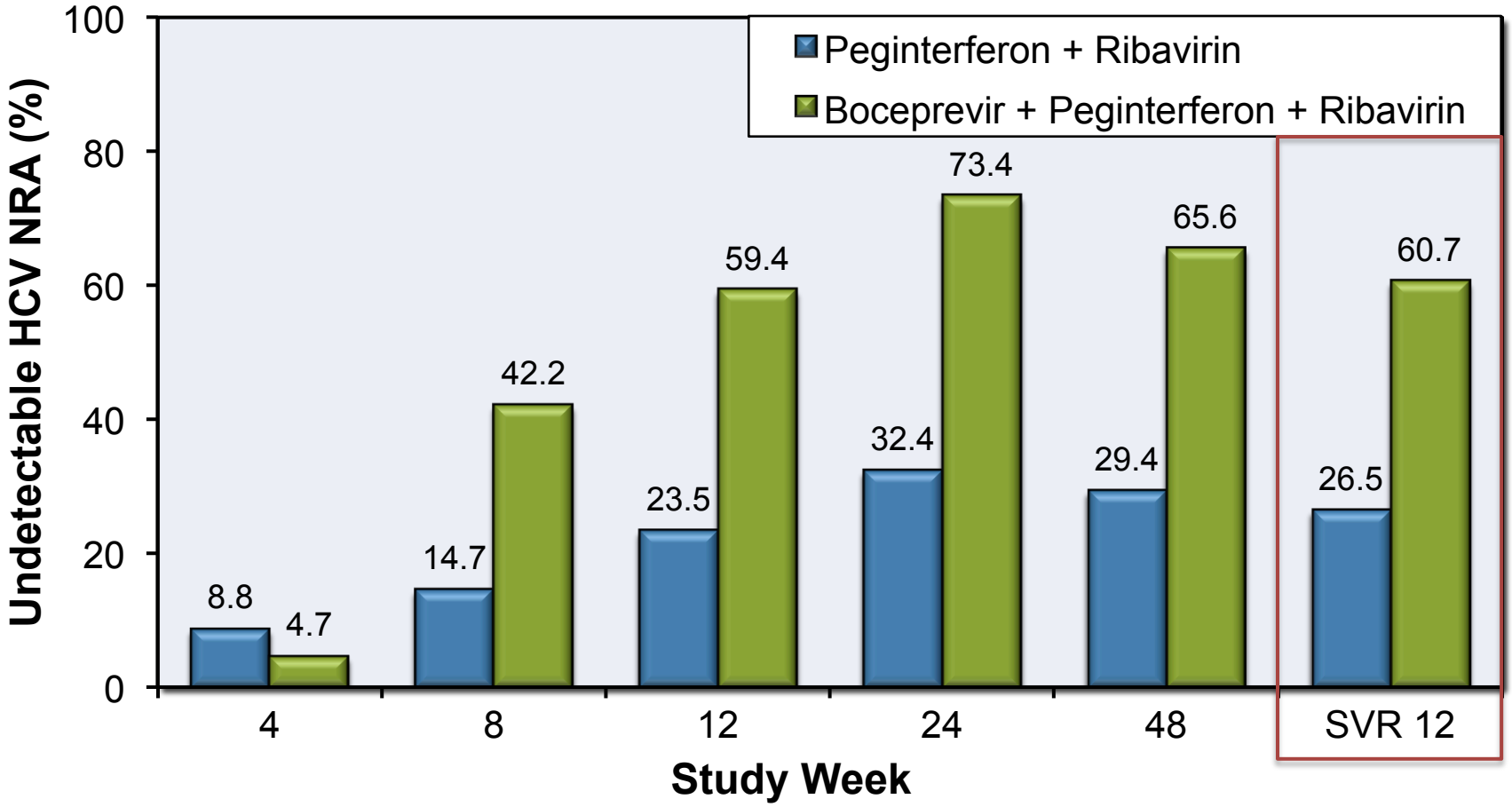
Boceprevir plus Peginterferon/Ribavirin in HIV/HCV Coinfection
Study: Design



Source: Sulkowski M, et al. 19th CROI. 2012; Abstract 47.

Boceprevir plus Peginterferon/Ribavirin in HIV/HCV Coinfection Study: Results

Treatment Response



Source: Sulkowski M, et al. 19th CROI. 2012; Abstract 47.

HIV Breakthrough Viremia

- HIV Breakthrough Viremia (HIV RNA > 50 copies/ml on 2 consecutive visits)
  - Overall: 7 (7%) of 98 patients
  - Control Group (PR): 4 (12%) of 34
  - Boceprevir Group (B + PR): 3 (5%) of 64

Source: Sulkowski M, et al. 19th CROI. 2012; Abstract 47.

Investigational

Elvitegravir in "Quad Pill" versus *Atripla* Study 102

Elvitegravir-Cobicistat-TDF-FTC versus Efavirenz-TDF-FTC
Study 102: Design

Study Design

Protocol

- N = 700 HIV-infected Adults
- Randomized, Double-blind, Phase 3 trial
- Antiretroviral naive
- No baseline NRTI, NNRTI mutations
- HIV RNA ≥ 5,000 copies/ml
- Creatinine Clearance ≥ 70 ml/min

***Elvitegravir-Cobicistat-Tenofovir-Emtricitabine**
(n = 348)

^Efavirenz-Tenofovir-Emtricitabine
(n = 352)

*Dosing: Elvitegravir (150 mg); Cobicistat (150 mg); Tenofovir (300 mg); Emtricitabine (200mg)

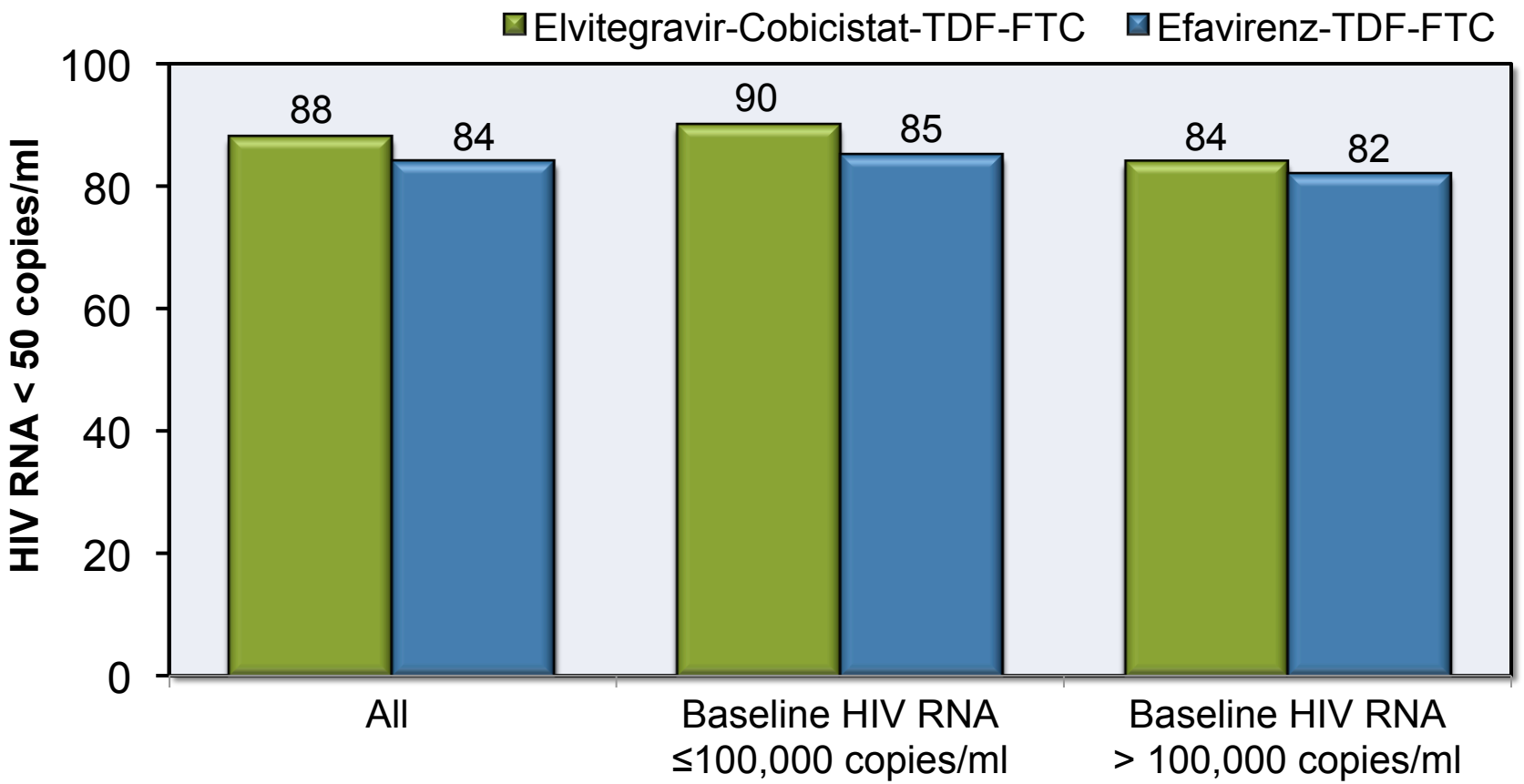
^Dosing: Efavirenz (600 mg); Tenofovir (300 mg); Emtricitabine (200mg)

Source: Sax P, et al. 19th CROI. 2012; Abstract 101.

Investigational

Elvitegravir-Cobicistat-TDF-FTC versus Efavirenz-TDF-FTC
Study 102: Results

Week 48: Virologic Response (ITT-TLOVR*)



*ITT-TLOVR = Intention to Treat-Time to Loss of Virologic Response

Source: Sax P, et al. 19th CROI. 2012; Abstract 101.

Investigational

Dolutegravir (“572”) vs. Efavirenz
SPRING-1 Study: 96 Week Data

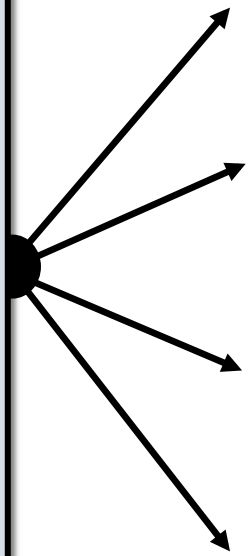
Investigational

Dolutegravir vs. Efavirenz in ARV-Naive
SPRING-1: Study Design

Study Design

Protocol

- N = 205
- Dose ranging, partially-blinded
- Multicenter, phase 2b trial
- Antiretroviral therapy-naïve
- Age ≥ 18
- HIV RNA > 1,000 copies/ml
- CD4 > 200 cells/mm^3
- No baseline NNRTI mutations
- Randomized to one of 4 arms
- All given 2 NRTIs*



Dolutegravir: 10 mg qd + 2NRTIs* (n = 53)

Dolutegravir: 25 mg qd + 2NRTIs* (n = 51)

Dolutegravir: 50 mg qd + 2NRTIs* (n = 51)

Efavirenz: 600 mg qd + 2NRTIs* (n = 50)

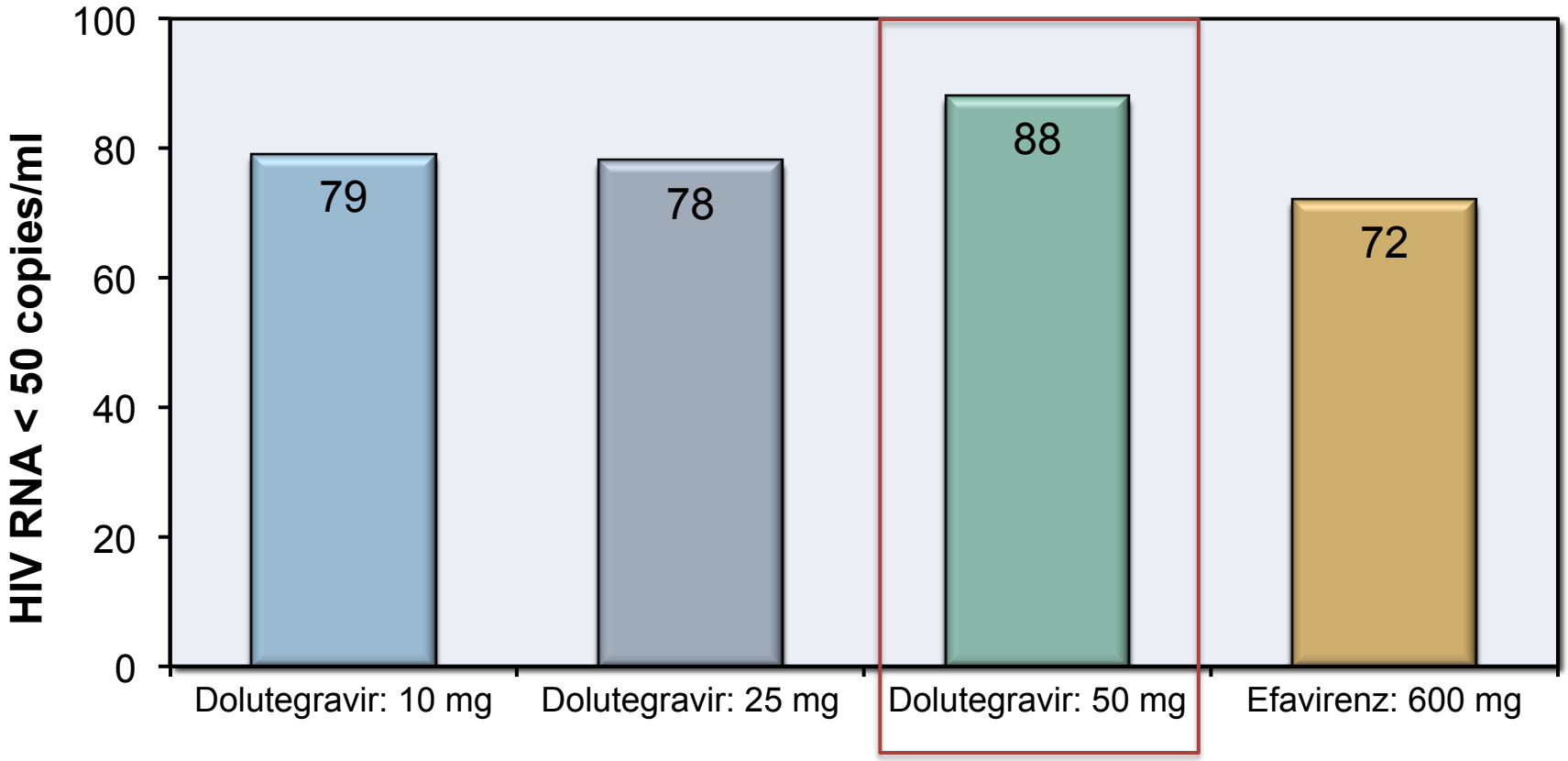
*2 NRTIs: Tenofovir-Emtricitabine + (67%); Abacavir-Lamivudine (33%)

Source: Stellbrink HJ, et al. 19th CROI; 2012;Abrastact 102LB.

Investigational

Dolutegravir vs. Efavirenz in ARV-Naive SPRING-1: Study Results

96 Week Data: Virologic Response (TLOVR)



All regimens included 2 NRTIs: Tenofovir-Emtricitabine or Abacavir-Lamivudine

Source: Stellbrink HJ, et al. 19th CROI; 2012;Abstract 102LB.

End