Treatment of acute HCV infection in HIV co-infection: Influence of HCV genotype and ribavirin upon treatment outcome

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Background II

- Current treatment recommendations are:
  - Consensus recommendation on treatment of acute hepatits C infection
    1) Pegylated IFN and weight-based ribavirin is recommended for the treatment of acute hepatitis C in HIV infected patients (grade A, level II)
       - Acute hepatitis C in HIV-infected individuals: recommendations from the European AIDS Treatment Network (NEAT) consensus conference
       - The European AIDS Treatment Network (NEAT) Acute Hepatitis C Infection Consensus Panel
- Whether HCV genotype and addition of RBV leads to differences in treatment outcome in acute HCV with different genotypes in HIV co-infection remains unknown so far

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Acute HCV Case Definition

- Acute HCV was defined as
  (3 out of 4 within the preceding 4 months):
  - Known or suspected exposure to HCV
  - Detectable HCV-RNA (PCR)
  - Documented seroconversion to positivity for anti-HCV IgG
  - Serum alanine transferase of more than 350 U/l with a documented normal value within the preceding 12 months

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Treatment

	All n=303	GT 1/4 n=258	GT 2/3 n=45	p-value
Duration of therapy* [%]				0,096
24 weeks	61,2	59,3	73,3	
48 weeks	38,5	40,7	26,7	
Median time to treatment initiation [weeks] (IQR)	10 (4,9-16,7)	10 (4,9-17)	9,4 (4,9-14,5)	0,567
Median time to first negative HCV RNA [weeks] (IQR)	8 (4-12)	8 (4-12)	5 (4-11)	0,182

*Based upon discretion of investigator

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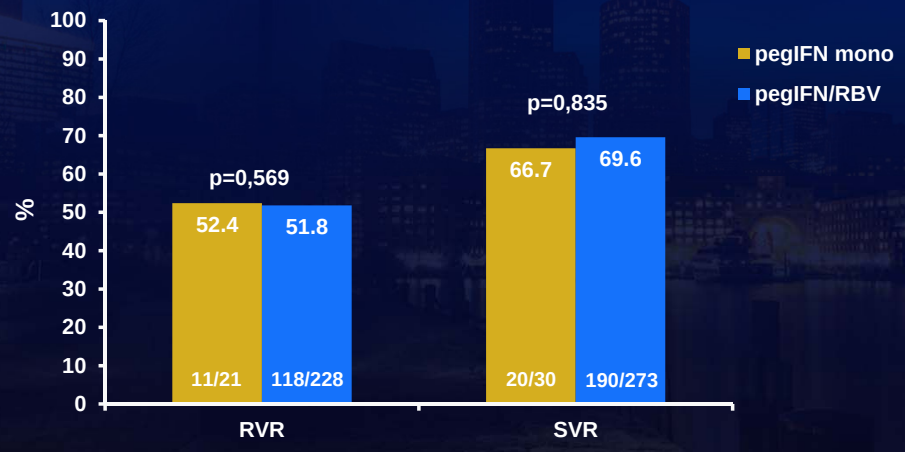
RVR & SVR all GT



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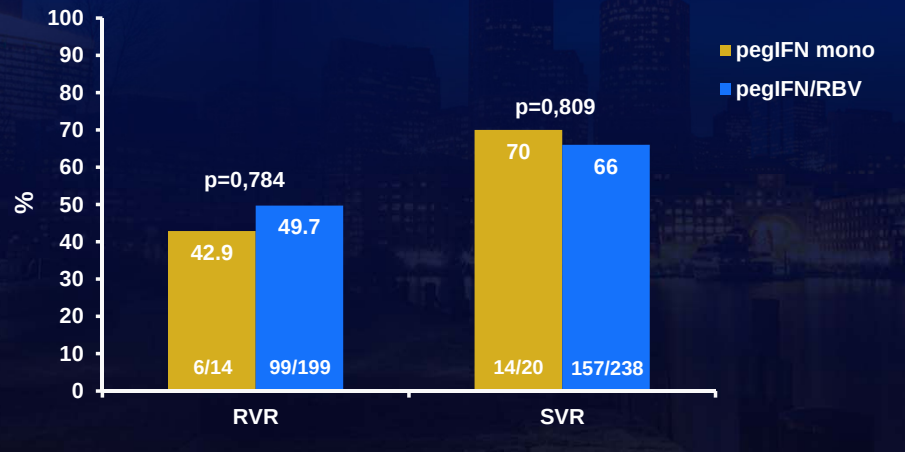
RVR & SVR GT 1/4



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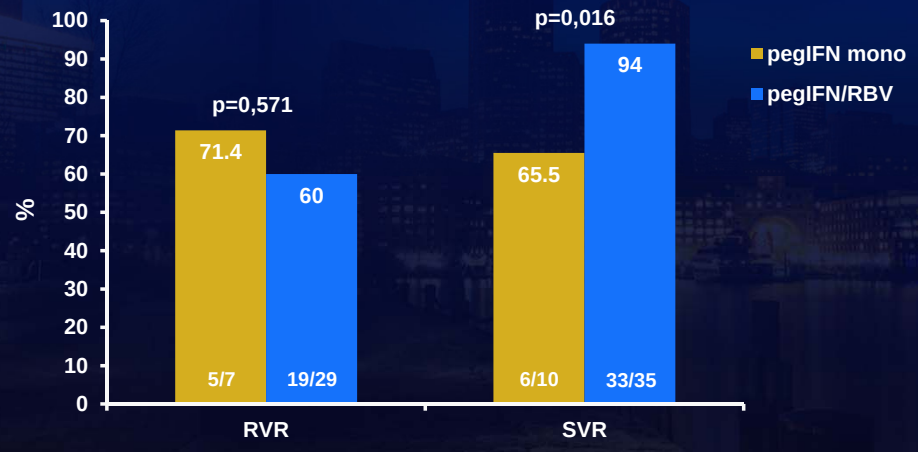
RVR & SVR GT 2/3



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Safety

- No significant differences in total numbers or severity of adverse events
- Ribavirin dose reduction occurred in 10.2% of cases
- Interferon dose reduction occurred in 5.6% of cases
- Treatment was stopped in 17 patients (6%) due to toxicities

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Telaprevir in Combination with Peginterferon Alfa-2a/Ribavirin in HCV/HIV Co-infected Patients: SVR24 Final Study Results

Mark S. Sulkowski, Kenneth E. Sherman, Vincent Soriano, Jürgen K. Rockstroh, Douglas T. Dieterich, Pierre-Marie Girard, Mohammad Bsharat, Joshua Henshaw, Raymond A. Rubin, Varun Garg, Nathalie Adda

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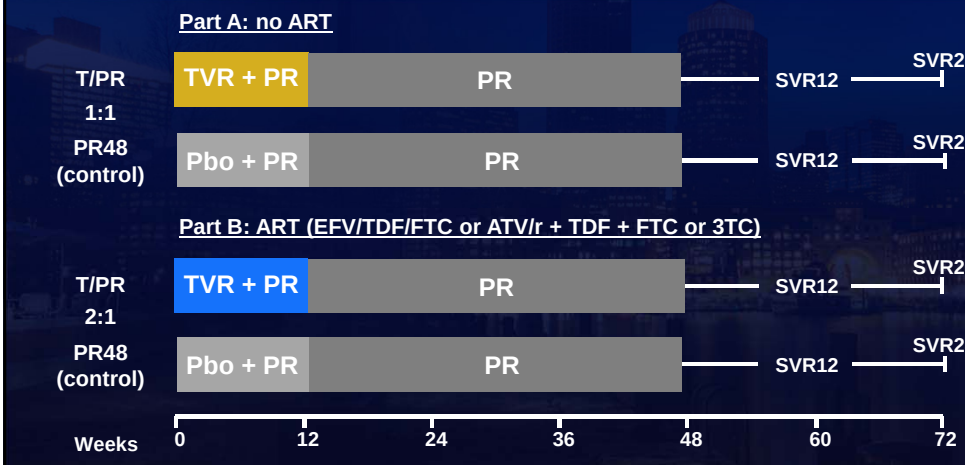
Study Design: Randomized, Double-blind, Placebo-controlled Trial



EFV = efavirenz; TDF = tenofovir; FTC = emtricitabine; ATV/r = ritonavir-boosted atazanavir; 3TC = lamivudine;
T/TVR = telaprevir 750 mg q8h or 1125 mg q8h (with EFV); Pbo=Placebo; P/Peg-IFN = pegylated interferon alfa-2a (40 kD) 180 µg/wk);
SVR = sustained virologic response

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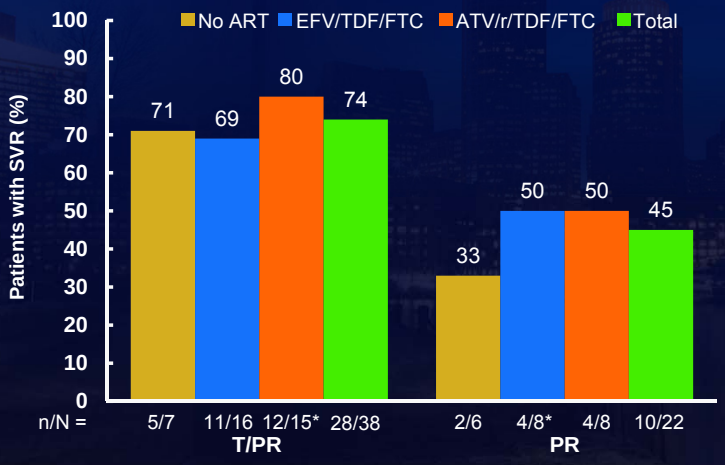
SVR at post-treatment week 24 (SVR_{24})



*Prior to Week 24 visit, 1 patient in this cohort was lost to follow up. SVR24 was imputed based on SVR12 for this patient.

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Events of Special Interest: Overall Treatment Phase

n (%)	T/PR N=38	PR N=22
Severe rash	0 (0)	0 (0)
Mild and moderate rash	13 (34)	5 (23)
Any anemia (hemoglobin <10g/dL)	7 (18)	4 (18)
Severe anemia (hemoglobin 7.0-8.9 g/dL or decrease from baseline ≥4.5 g/dL)	11 (29)	5 (23)
Use of erythropoietin stimulating agent	3 (8)	1 (5)
Blood transfusions	4 (11)	1 (5)
Discontinuation due to AE	3 (8)	0 (0)

- No HIV breakthrough; CD4 counts declined in T/PR and PR groups; CD4% unchanged
- 3 T/PR patients discontinued due to adverse event (3 T/PR)

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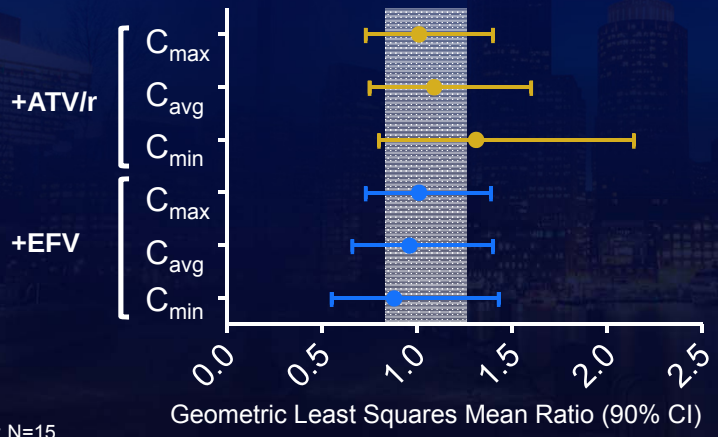
Pharmacokinetics of Telaprevir Similar Among ART Groups



EFV: N=15
ATV/r: N=13

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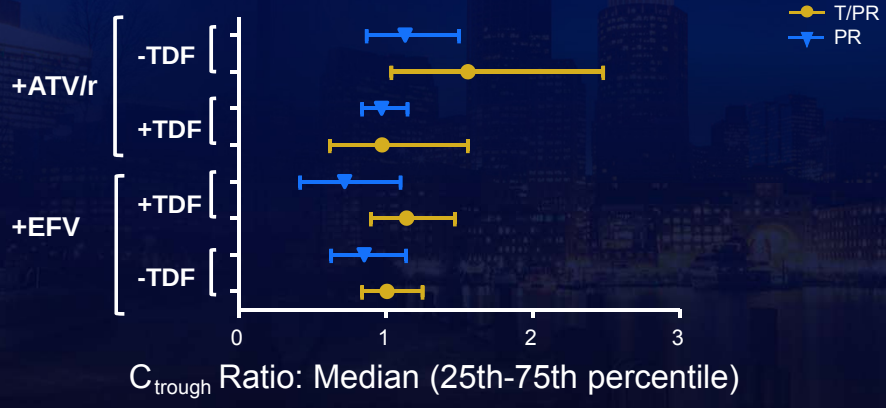
Pharmacokinetics of ART Similar Among T/PR and PR groups



ATV/r: N = 7 PR, N= 14 for T/PR
EFV: N = 8 PR, N= 15 for T/PR

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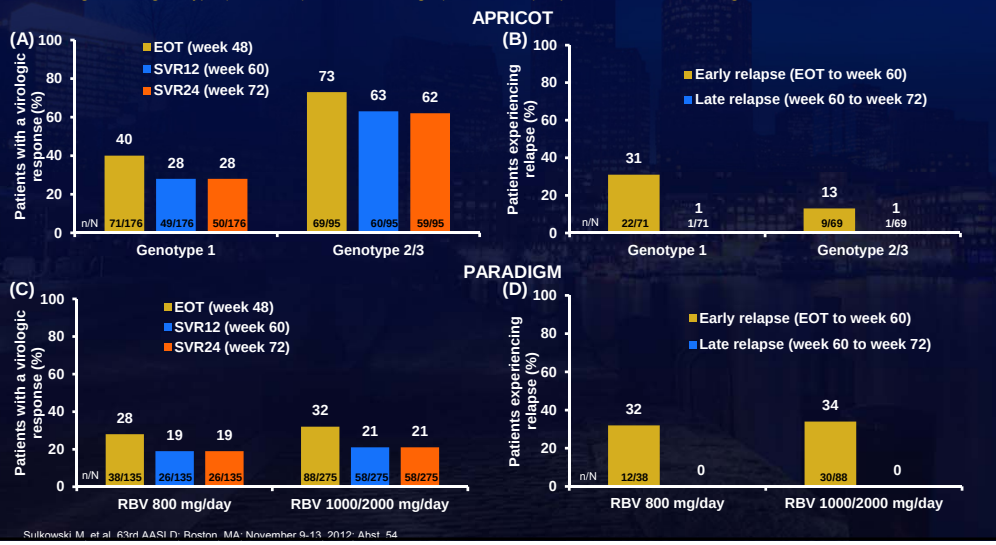
In APRICOT and PARADIGM 99% of HIV-HCV Co-Infected Patients with an SVR12 Achieved an SVR24 Validating SVR12 as an Endpoint for Trials in this Population

Overall end of treatment (EOT), SVR12, and SVR24 rates (A,C), and relapse rates by week 60 and between weeks 60 and 72 (B,D) according to HCV genotype (APRICOT) and RBV dosage (PARADIGM) in patients treated with PegIFN alfa-2a/RBV



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