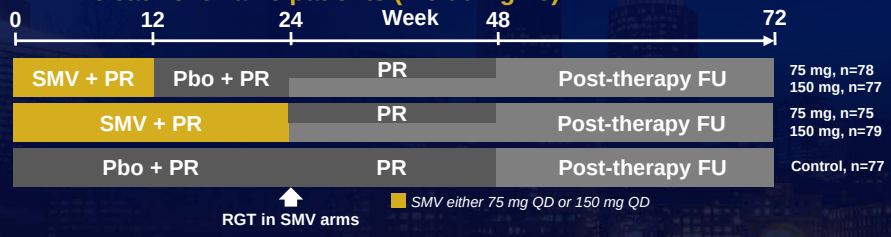
Efficacy and tolerability of simeprevir (TMC435) 150 mg once daily with peginterferon and ribavirin for treatment of HCV genotype 1 infection in patients with Metavir score F3 and F4 (PILLAR and ASPIRE trials)

Fred Poordad, Michael W. Fried, Stefan Zeuzem, Peter Ferenci, Oliver Lenz, Rekha Sinha, Katleen Callewaert, Monika Peeters, Maria Beumont-Mauviel

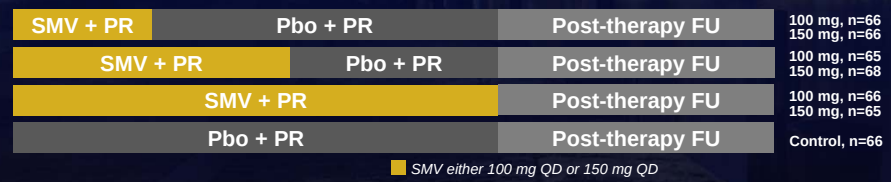
Abstract 83

International, Phase IIb studies in HCV genotype 1 treatment-naïve and -experienced patients

PILLAR: treatment-naïve patients (including F3)



ASPIRE: treatment-experienced patients (prior relapsers, partial and null responders; including F3 and F4)



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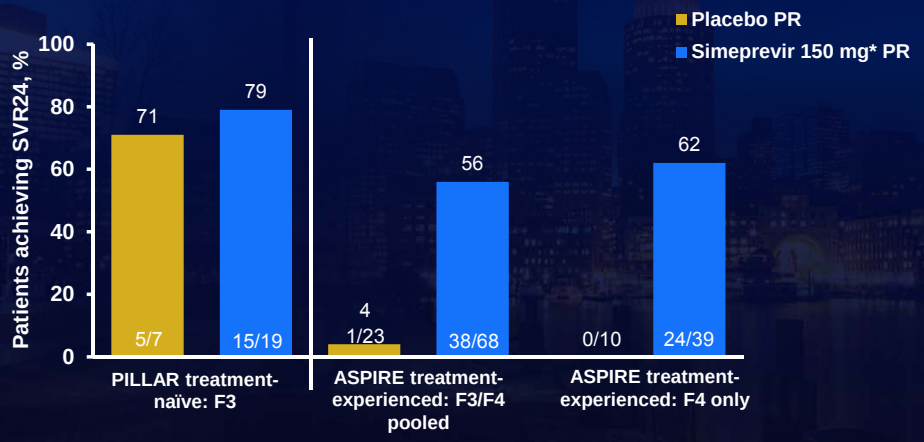
Treatment-naïve and -experienced: proportion of F3 and F4 patients achieving SVR24



*Treatment arms within PILLAR and ASPIRE with different durations pooled
PR, pegylated interferon α-2a + ribavirin; SVR24, HCV RNA <25 IU/mL undetectable 24 weeks after planned end of treatment

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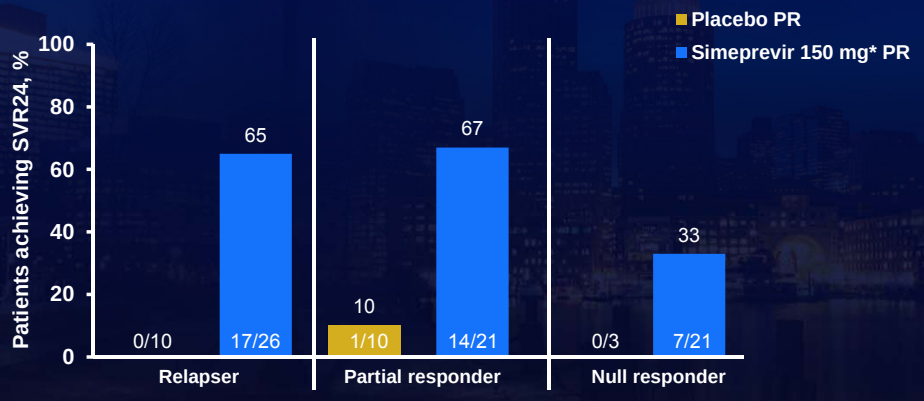
Treatment-experienced: SVR24 by prior response to PegIFN/RBV in F3/F4 patients



- 31% (4/13) null responders with cirrhosis (F4) achieved SVR24

*Treatment arms across ASPIRE with different durations combined
PR, pegylated interferon α-2a + ribavirin ; SVR24, HCV RNA <25 IU/mL undetectable 24 weeks after planned end of treatment

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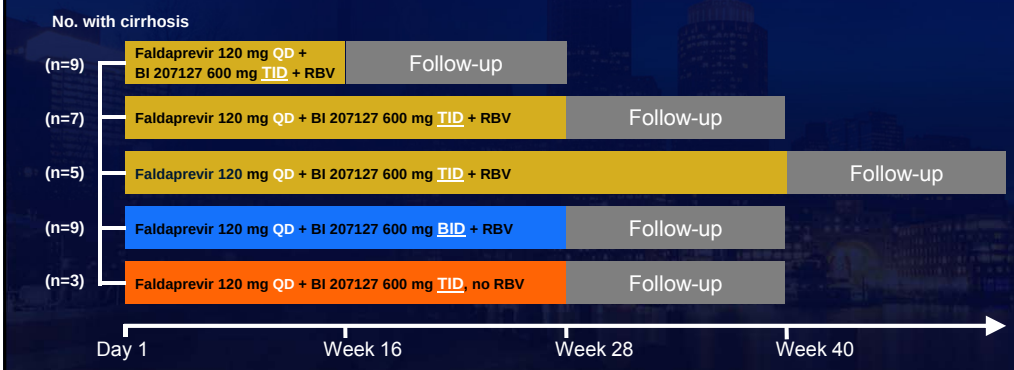
EFFICACY AND SAFETY OF THE INTERFERON-FREE COMBINATION OF FALDAPREVIR (BI 201335) + BI 207127 ± RIBAVIRIN IN TREATMENT-NAÏVE PATIENTS WITH HCV GT-1 AND COMPENSATED LIVER CIRRHOSIS: RESULTS FROM THE SOUND-C2 STUDY

Vicente Soriano, Ed Gane, Peter Angus, Felix Stickel, Jean-Pierre Bronowicki, Stuart Roberts, Michael Manns, Stefan Zeuzem, Richard Vinisko, Ivona Herichova, Wulf Böcher, Jerry Stern, and Federico Mensa

Abstract 84

Methods



- Phase IIb, multicenter, open-label, randomized (1:1:1:1:1)
  - Treatment-naïve patients with chronic HCV GT-1
- Compensated cirrhosis allowed, 18–75 years of age, HCV RNA >100 000 IU/mL
- Stopping rule: HCV RNA detectable between Weeks 6 and 8
- Primary endpoint: SVR 12 weeks after treatment completion

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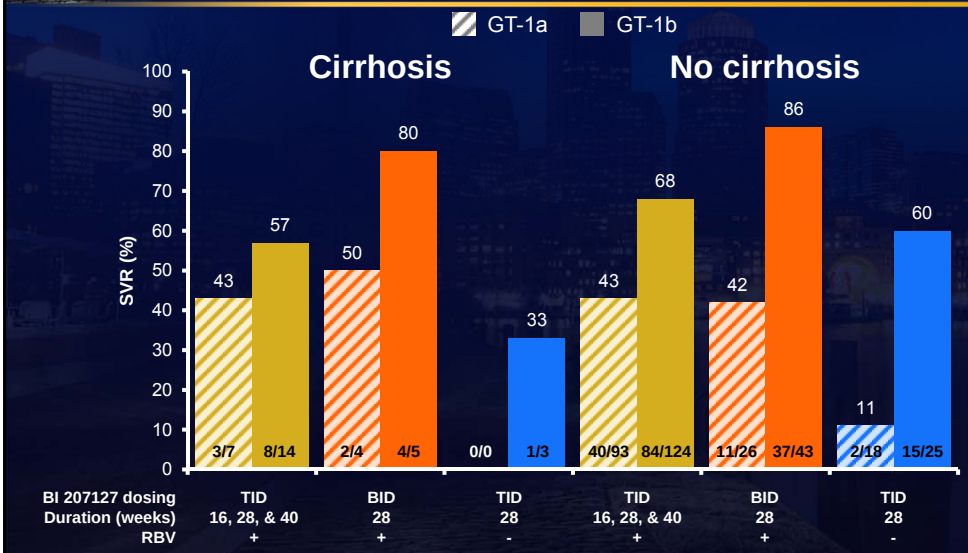
SVR_{12} rates by HCV-1 subtype



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Safety and Sustained Viral Response of MK-5172 for 12 Weeks in Combination With Pegylated Interferon Alfa-2b and Ribavirin for 24 Weeks in HCV Genotype 1 Treatment-Naive Noncirrhotic Patients

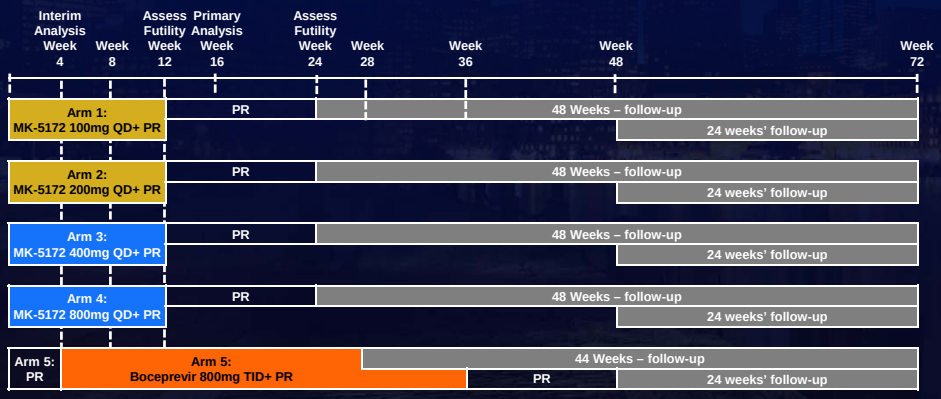
Patrick Marcellin, John M Vierling, Bruce R Bacon, Michael Manns, Christine Fandozzi, Jacqueline Gress, Luzelena Caro, Christopher Gilbert, Peggy Hwang, Janice Wahl, Michael P Cooreman, Niloufar Mobashery

Abstract 766

Study Design

MK-5172 is a once-daily, potent, next-generation NS3/4A protease inhibitor (PI)

- Potent in vitro activity against a broad enzyme panel including all major hepatitis C virus (HCV) genotypes (G)1
- In vitro activity against resistance-associated variants (RAVs) found in patients who failed therapy with first-generation PIs (boceprevir,telaprevir, and TMC-435)2
- 5 log10 drop in HCV RNA levels in patients with HCV G1 following monotherapy of ≥30 mg once daily (qd) for 7 days3



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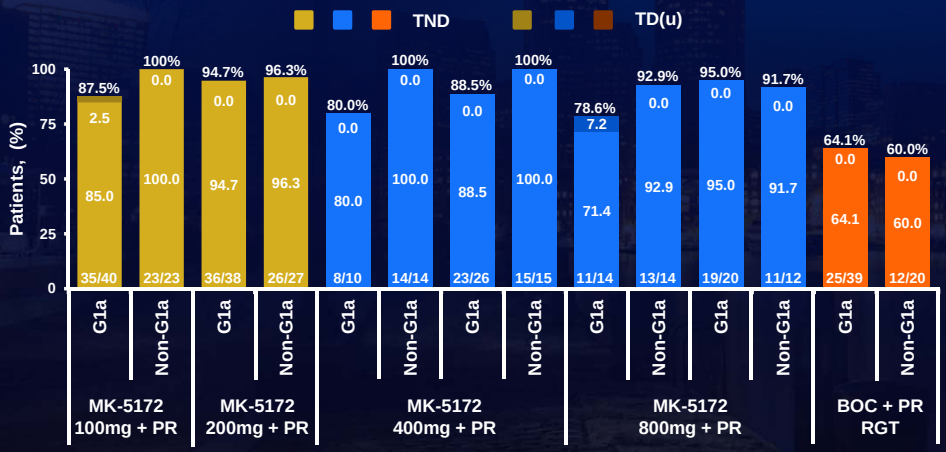
MK 5172 will be studied in combination with NS5a MK 8742 in all oral protocol

Figure 6. Sustained virologic response at week 4 follow-up (SVR4) according to genotype 1 subtype (G1a vs non-G1a) – combined cohort, FAS population.



BOC, boceprevir; PR, peginterferon alfa-2b + ribavirin; RGT, response-guided therapy; SC, second cohort; TD(u), HCV target detected unquantifiable; TND, HCV target not detected; VC, vanguard cohort

Marcellin P, et al. 63rd AASLD; Boston, MA; November 9-13, 2012; Abst. 766.

Up to 100% SVR4 rates with ritonavir-boosted danoprevir (DNVr), mericitabine and ribavirin with or without peginterferon alfa-2a (40KD) in HCV genotype 1-infected partial and null responders: results from the MATTERHORN study

J.J. Feld, I.M. Jacobson, D.M. Jensen, G.R. Foster, S. Pol, E. Tam, H. Berak, J.M. Vierling, J.A. Tavel, M.T. Navarro, S. Shahdad, R. Kulkarni, S. Le Pogam, I. Najera, C.Y. Lim, N.S. Shulman, E.S. Yetzer

Abstract 81

MATTERHORN: phase 2 study design

Randomized (1:1:1), open-label, multicenter, parallel study of two cohorts
Stratification: G1a/G1b and *IL28B*

Cohort A: G1 prior partial responders

n=52	IFN-free: MCB + DNVr + RBV	Follow-up	→ G1a pts added P/R and are excluded from this analysis
n=49	Triple: DNVr + P/R	Follow-up	
n=50	QUAD: MCB + DNVr + P/R	Follow-up	

Cohort B: G1 prior null responders

n=77	IFN-free: MCB + DNVr + RBV	Follow-up	→ G1a pts added P/R and are excluded from this analysis
n=77	QUAD: MCB + DNVr + P/R	Follow-up	
n=74	QUAD: MCB + DNVr + P/R	P/R	Follow-up → Ongoing

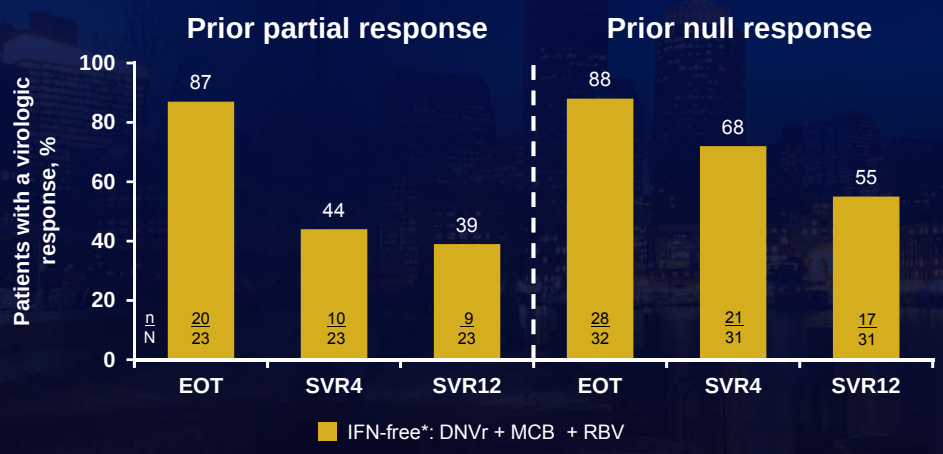
0 — 12 — 24 — 36 — 48 — 72

Weeks

DNVr = danoprevir/ritonavir 100 mg/100 mg bid; MCB = mericitabine 1000 mg bid;
P/R = peginterferon alfa-2a (40KD) 180 µg/week plus ribavirin 1000 mg or 1200 mg/day
ClinicalTrials.gov Identifier: NCT01331850
G1a patients in IFN-free arms offered 24-week P/R + assigned treatment due to unacceptable relapse rates

Meld J, et al. 63rd AASLD; Boston, MA; November 9-13, 2012; Abst. 81.

Efficacy of IFN-free treatment for G1b



Characteristics: partial vs. null responders

- Similar IL28B genotype, BMI, age
- Partials: higher baseline viral load (Median: 7.0 vs. 6.7 IU/mL; ≥7 log10 IU/mL: 52% vs. 34%)

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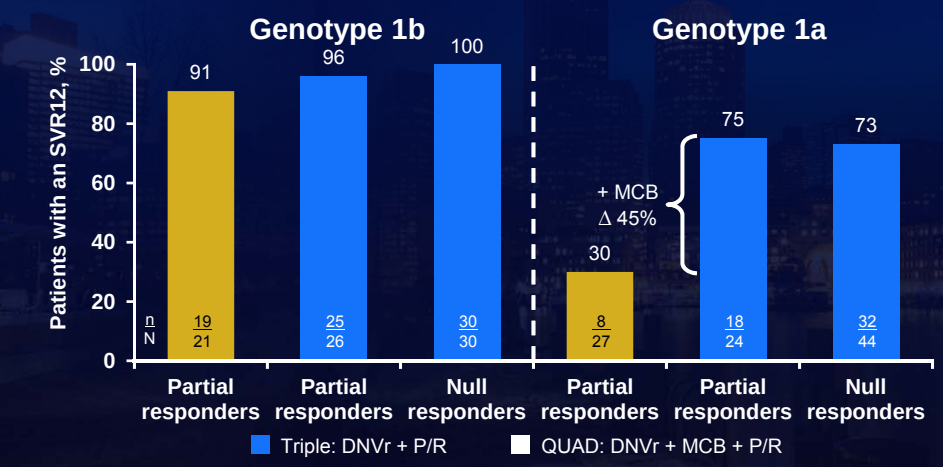
SVR12 by subtype
Addition of MCB improves SVR12 in G1a by 45% (absolute)



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