ONLINE EXPERT POSTER REVIEW AND DISCUSSION

Advances in Chronic Hepatitis C Management and Treatment

Reporting From

THE 62ND AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES ANNUAL MEETING

(This coverage is not sanctioned by the conference organizers and is not an official part of the conference proceedings.)

Jointly Sponsored by the Postgraduate Institute for Medicine and ViralEd, LLC.

BMS-790052, A NS5A Replication Complex Inhibitor, Combined with Peginterferon-Alfa-2a and Ribavirin in Treatment-Naive HCV-Genotype 1 or 4 Subjects: Phase 2b AI444010 Study Interim Week 12 Results

C Hézode, GM Hirschfield, W Ghesquiere, W Sievert, M Rodriguez-Torres, S Shafran, PJ Thuluvath, HA Tatum, I Waked, G Esmat, EJ Lawitz, VK Rustgi, S Pol, N Weis, P Pockros, M Bourlière, L Serfaty, JM Vierling, MW Fried, O Weiland, MR Brunetto, GT Everson, S Zeuzem, PY Kwo, M Sulkowski, PD Yin, U Diva, EA Hughes, M Wind-Rotolo, S Schnittman

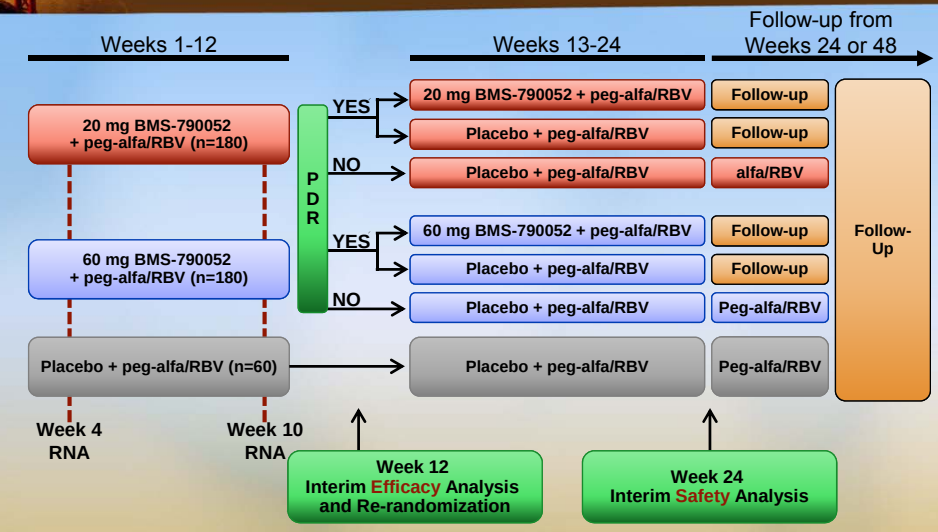
Abstract 227

Methods

- Randomized, blinded, controlled, Phase 2b clinical trial
- Patients
  - HCV genotype 1 (n=365) or 4 (n=30) infection, treatment naïve, aged 18–70 years, METAVIR stage F0–F4
- Treatment
  - 20 mg or 60 mg BMS-790052 or placebo once daily in combination with weekly peg-alfa/RBV
- Molecular diagnostics
  - HCV RNA assessed by Roche Cobas TaqMan®: limit of detection 10 IU/mL; lower limit of quantification 25 IU/mL
  - HCV genotype determined by TRUGENE 5'NC
- Efficacy data through week 12 and safety data through week 24 are presented

PDR: HCV RNA <LLQ (25 IU/mL) at week 4 and undetectable (<LLD: ≤ 10 IU/mL) at week 10.

Study Design



PDR (protocol-defined response): HCV RNA <LLQ (25 IU/mL) at week 4 and undetectable (<10 IU/mL) at week 10.

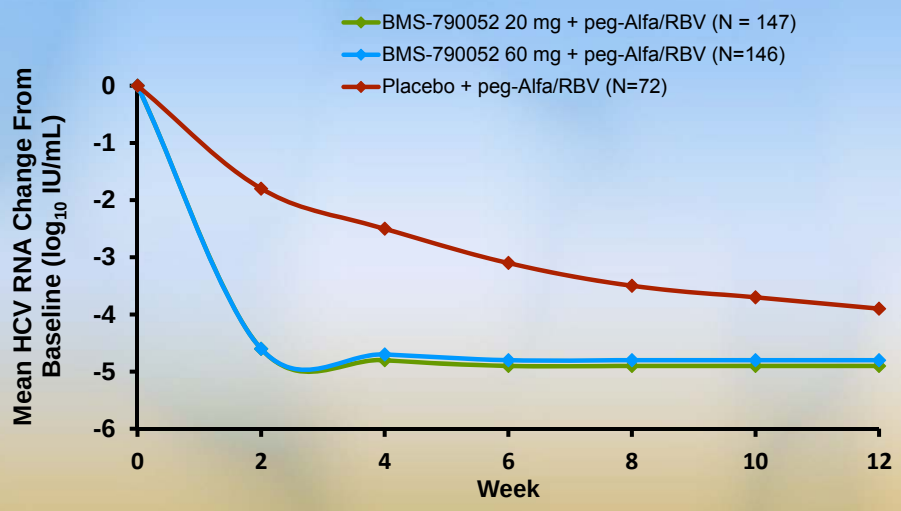
Hézode C et al. 49TH IDSA; Boston, MA; October 20-23, 2011; Abst. 227.

Baseline Demographic and Disease Characteristics

Characteristic, n (%)	BMS-790052 20 mg (n = 159)	BMS-790052 60 mg (n = 158)	Placebo (n = 78)
Median age, years (range)	51 (22-70)	50 (18-67)	50.5 (25-66)
Male sex	67	65	71
Race			
White	136 (86)	129 (82)	62 (79)
Black	15 (9)	21 (13)	9 (12)
Other	8 (5)	8 (5)	7 (9)
Mean baseline HCV RNA, (log_{10} IU/mL)	6.5	6.5	6.4
HCV genotype			
1	147 (92)	145 (92)	72 (92)
1a	106 (67)	113 (72)	56 (72)
1b	41 (26)	3 (20)	16 (21)
4	10 (6)	8 (5)	5 (6)
Not reported	2 (1)	5 (3)	1 (1)
Cirrhosis			
Absent	146 (92)	149 (94)	70 (90)
Present	13 (8)	8 (5)	8 (10)
Not reported	0	1 (1)	0
IL28B genotype (rs12979860)			
CC	53 (33)	44 (28)	23 (30)
CT	82 (52)	86 (54)	38 (49)
TT	17 (11)	18 (11)	11 (14)
Not reported	7 (4)	10 (6)	6 (8)

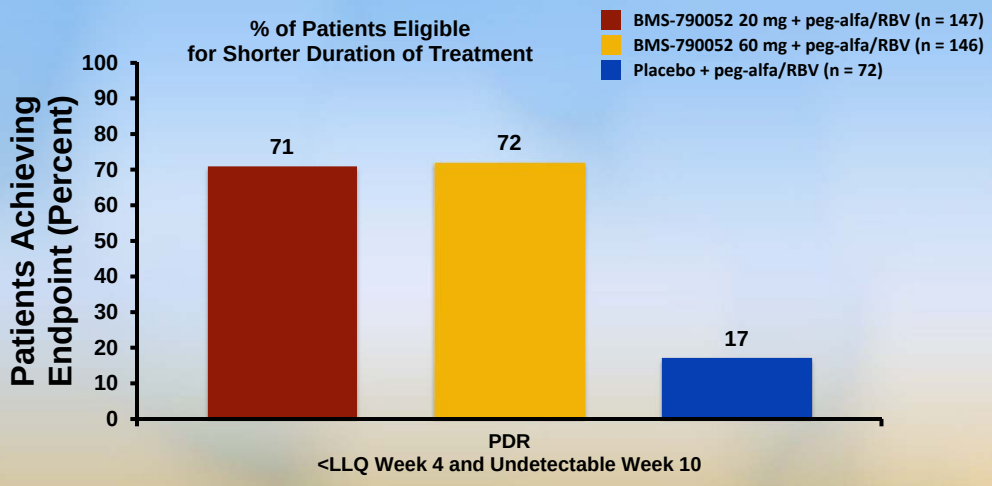
Hézode C et al. 49TH IDSA; Boston, MA; October 20-23, 2011; Abst. 227.

HCV RNA Reductions Through Week 12 in Patients With Genotype 1 Infection



Hézode C et al. 49TH IDSA; Boston, MA; October 20-23, 2011; Abst. 227.

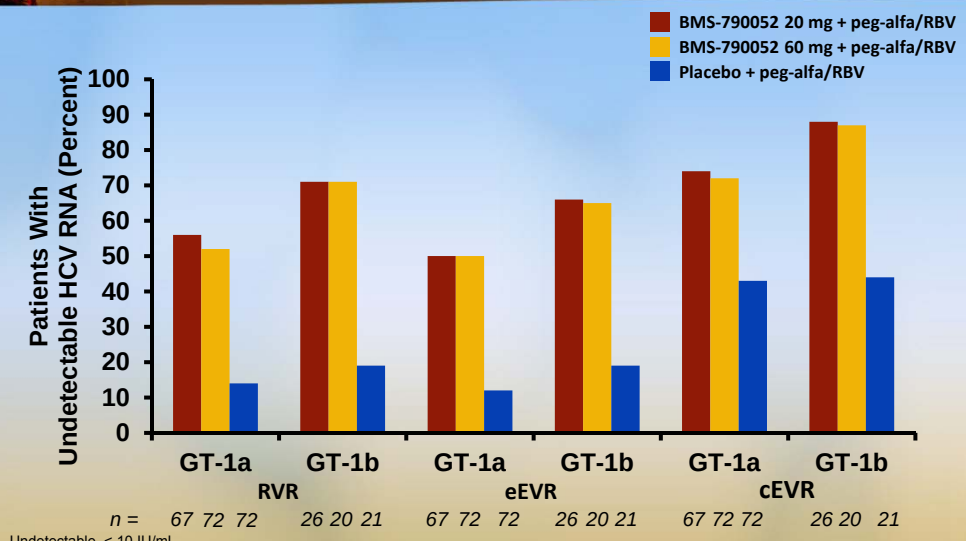
PDR Achieved by Week 12 in Patients With Genotype 1 Infection



LLQ, lower limit of quantitation = 25 IU/mL
Undetectable, < 10 IU/mL

Hézode C et al. 49TH IDSA; Boston, MA; October 20-23, 2011; Abst. 227.

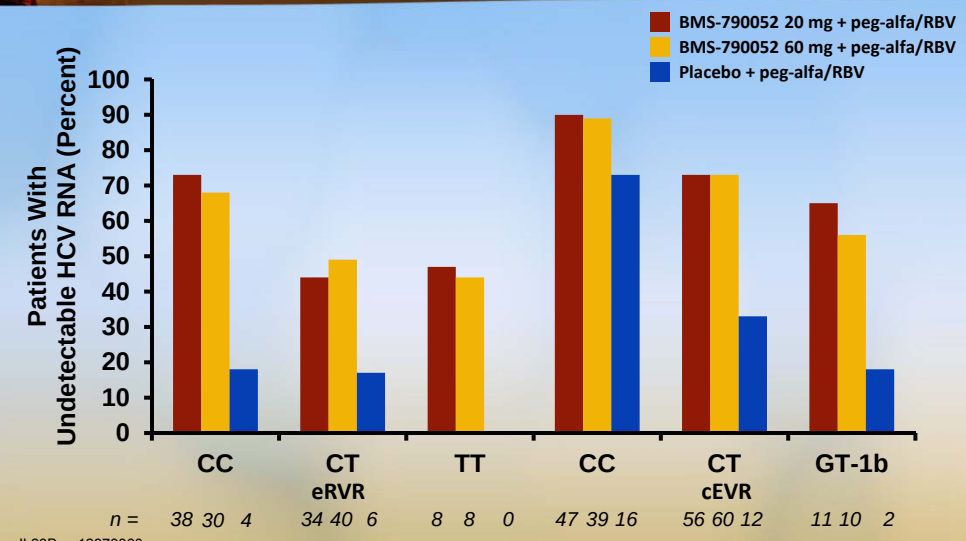
Virologic Responses Through Week 12 by HCV Genotype 1 Subtype



Undetectable, < 10 IU/mL

Hézode C et al. 49TH IDSA; Boston, MA; October 20-23, 2011; Abst. 227.

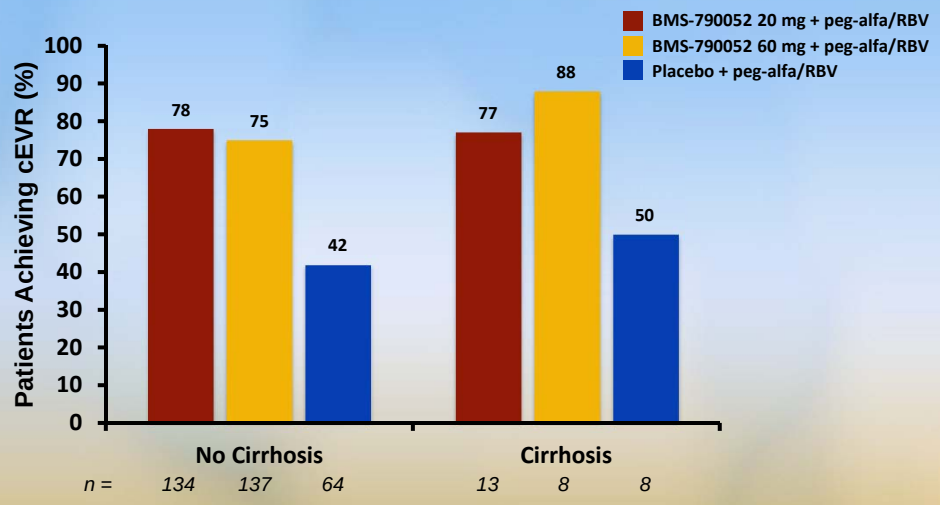
Responses By IL28B Genotype in Patients With HCV Genotype 1 Infection



IL28B: rs12979860

Hézode C et al. 49TH IDSA; Boston, MA; October 20-23, 2011; Abst. 227.

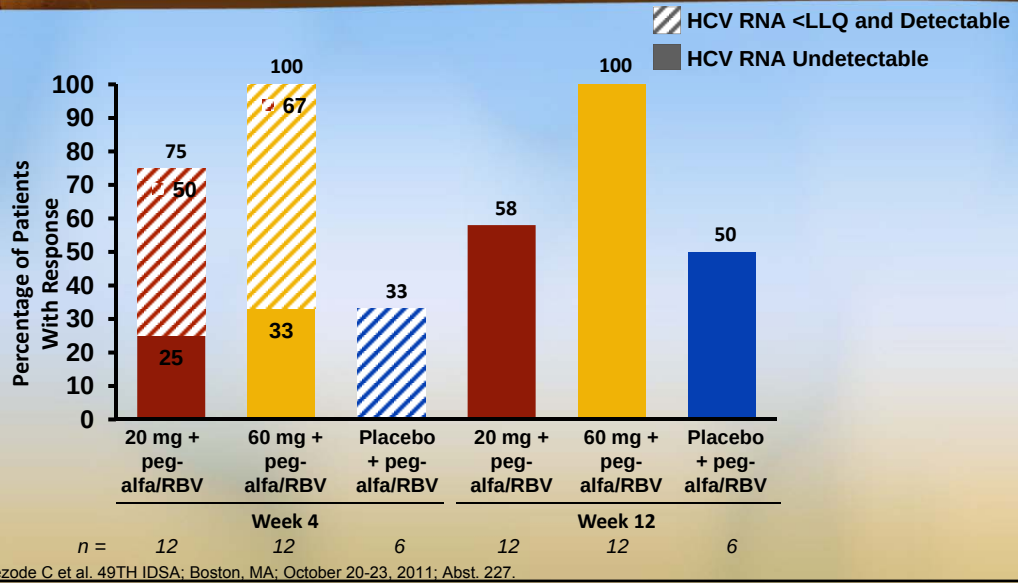
cEVR Responses by Baseline Cirrhosis StatusHCV Genotype 1 Infection



cEVR, undetectable HCV RNA at week 12

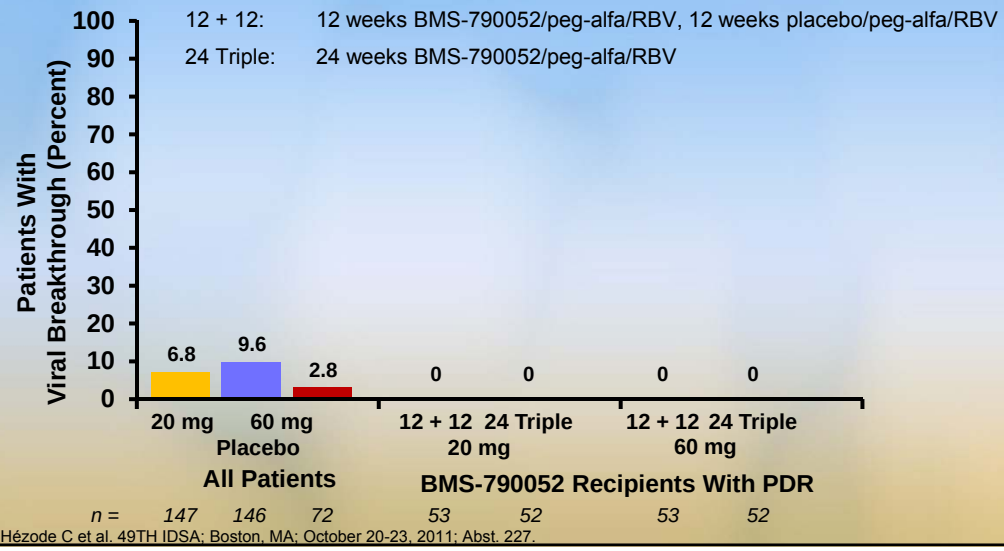
Hézode C et al. 49TH IDSA; Boston, MA; October 20-23, 2011; Abst. 227.

Virologic Responses Through Week 12: HCV Genotype 4



Hézode C et al. 49TH IDSA; Boston, MA; October 20-23, 2011; Abst. 227.

Viral Breakthrough Through Week 24



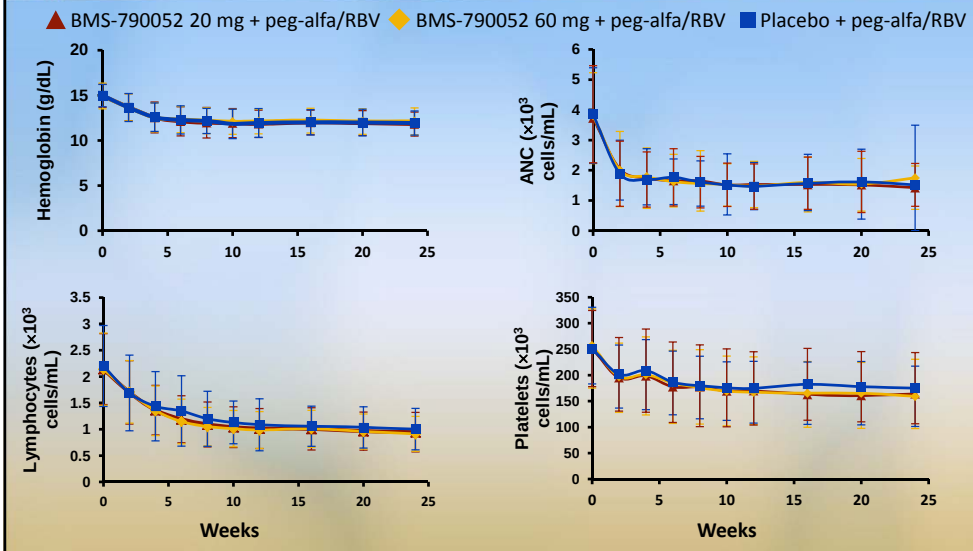
Hézode C et al. 49TH IDSA; Boston, MA; October 20-23, 2011; Abst. 227.

Key Safety Parameters at 24 Weeks

Event, n (%)	BMS-790052 20 mg + alfa/RBV (n = 159)	BMS-790052 60 mg + alfa/RBV (n = 158)	Placebo + alfa/RBV (n = 78)
Deaths	1 (0.6)	0	0
Serious adverse events	12 (7.5)	12 (7.6)	5 (6.4)
AEs leading to discontinuation	6 (3.8)	8 (5.1)	6 (7.7)
Grade 3/4 AEs	29 (18.2)	19 (12.0)	12 (15.4)
Peg-alfa dose reduction	28 (17.6)	20 (12.7)	10 (12.8)
RBV dose reduction	70 (44.0)	55 (34.8)	29 (37.2)
Concomitant filgrastim	2 (1.3)	5 (3.2)	0
Erythropoietin use	8 (5.0)	11 (7.0)	3 (3.8)

Hézode C et al. 49TH IDSA; Boston, MA; October 20-23, 2011; Abst. 227.

Hematologic Data Through Week 24



Hézode C et al. 49TH IDSA; Boston, MA; October 20-23, 2011; Abst. 227.

Conclusions

- BMS-790052 combined with peg-alfa/RBV provided higher rates of early virologic responses compared with placebo + peg-alfa/RBV
  - A high proportion of BMS-790052 recipients achieved PDR with potential to achieve SVR with shortened duration of treatment
- BMS-790052 + peg-alfa/RBV regimens were well tolerated
  - Similar adverse event profiles in BMS-790052 and placebo groups
  - Comparable safety profiles in patients treated with BMS-790052 for 12 or 24 weeks
- Data support initiation of phase 3 studies

Hézode C et al. 49TH IDSA; Boston, MA; October 20-23, 2011; Abst. 227.