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

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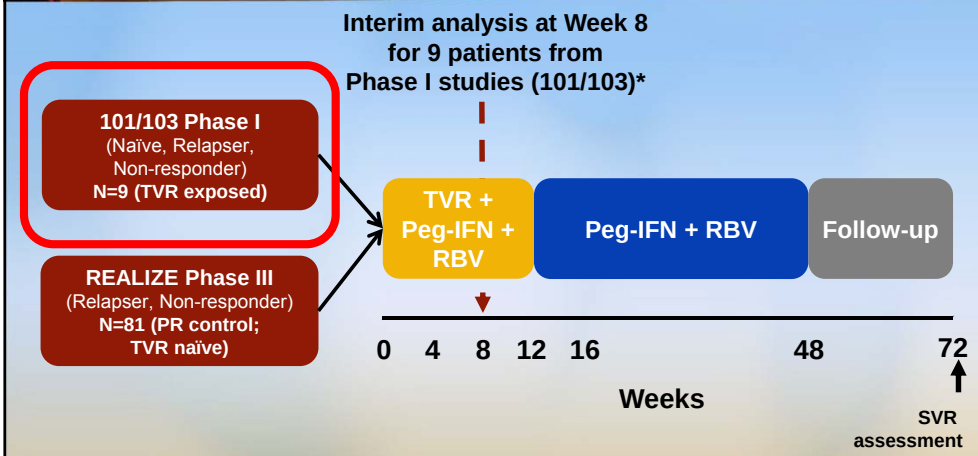
Retreatment with telaprevir/Peg-IFN/RBV after a short exposure to telaprevir in Phase I studies: interim results from a Phase IIIb rollover trial (C219)

C. Sarrazin; H.W. Reesink; S. Zeuzem; C.J. Weegink; D. Luo; J. Witek; T.L. Kieffer; D.J. Bartels; I. Dierynck; S. De Meyer; G. Picchio

Abstract 35

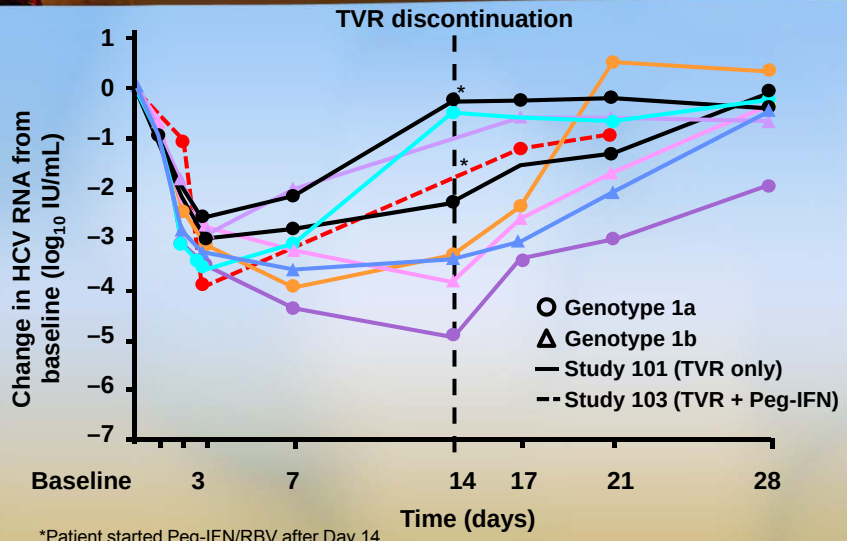
C219: Phase IIIb, Open-label, Roll-over Study



*All 9 patients had completed Week 8 of treatment at the time of the analysis; Peg-IFN: P: Peg-IFN alfa-2a = 180µg/week;
RBV: R = 1000–1200mg/day; TVR = telaprevir 750mg every 8 hours; HCV RNA determined using Roche COBAS TaqMan® assay version 2.0 (lower limit of quantification 25 IU/mL, lower limit of detection approximately 10 IU/mL)

Serrazin C, et al. 62nd AASLD; San Francisco, CA; November 04-08, 2011. Abst. 35.

Changes in HCV RNA Over Time During Previous Phase I Studies (101/103)



*Patient started Peg-IFN/RBV after Day 14

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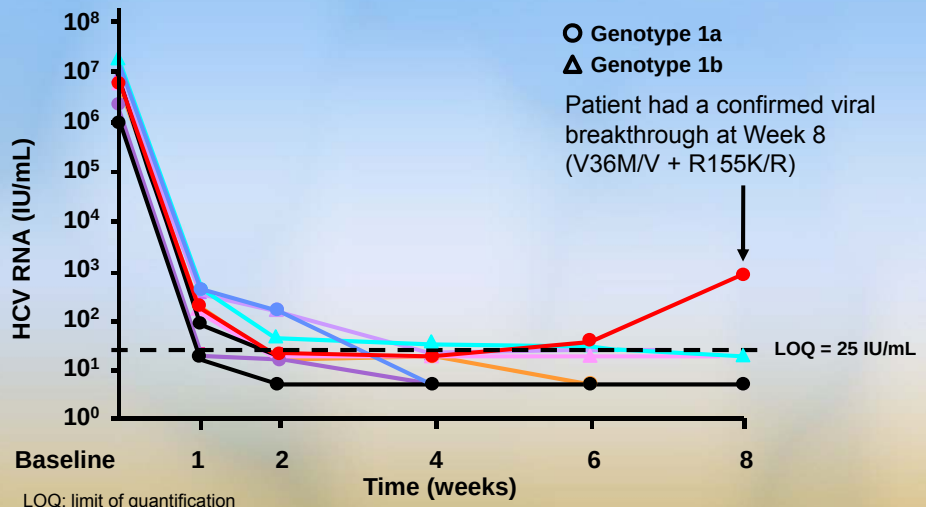
C219: HCV RNA Values Over Time (Week 8 Interim Analysis, TVR-exposed)

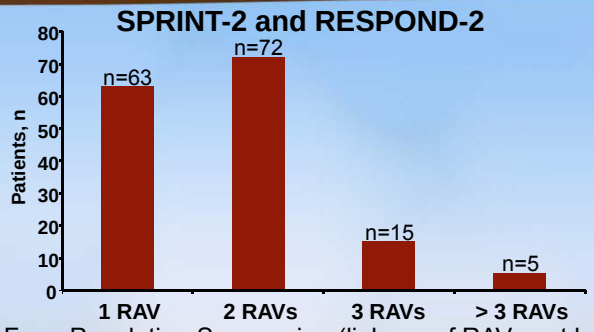


LOQ: limit of quantification

HCV RNA values below LOQ are imputed with an arbitrary value: 17.5 for <25 IU/mL detectable and 5 for <25 IU/mL undetectable

Serrazin C, et al. 62nd AASLD; San Francisco, CA; November 04-08, 2011. Abst. 35.

Analysis of Resistance-Associated Amino Acid Variants (RAVs) in Non-SVR Patients Enrolled in a Retrospective Long-term Follow-up Analysis of Boceprevir Phase 3 Clinical Studies

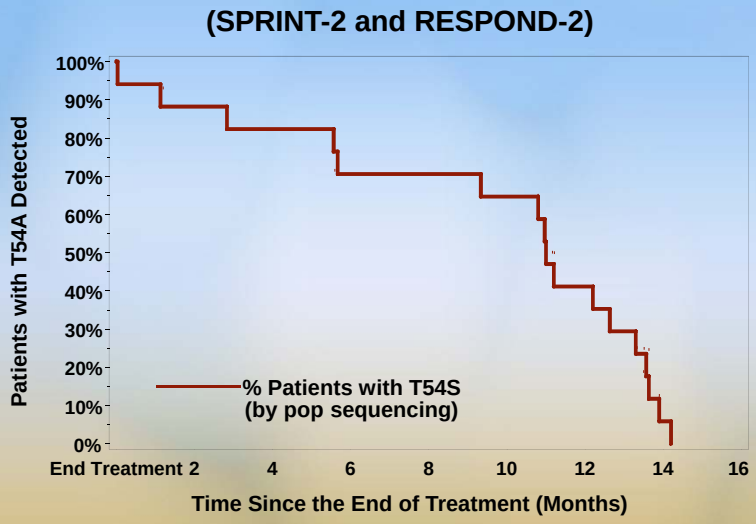


Data From Population Sequencing (linkage of RAVs not known)

1 RAV Detected		2 RAVs Detected		3 RAVs Detected		> 3 RAVs Detected	
RAV	Patients, n	RAV	Patients, n	RAV	Patients, n	RAV	Patients, n
V36M	18	V36M, R155K	37	V36M, T54S, R155K	4	V36M, T54S, R155K, R155T	1
R155K	11	T54S, R155K	8	T54A, T54S, A156S	2	V36M, T54S, R155K, A156S	1
T54A	10	R155K, V158I	4	V36L, R155K, V158I	2	V36L, R155K, V158I, I170F	1
R155T	5	T54S, A156S	4	T54A, V170A, M175L	1	T54A, T54C, T54S, V55A, A156S	1

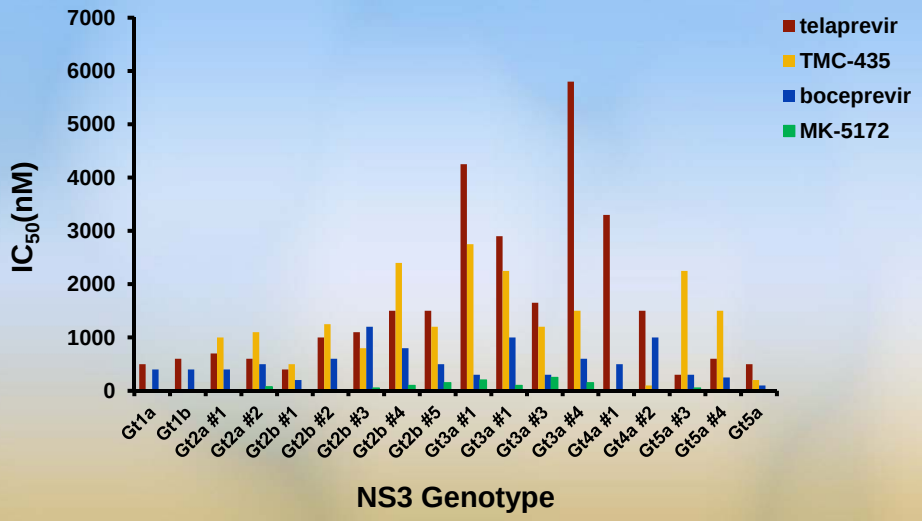
Bernard R, et al. 62nd AASLD; San Francisco, CA; November 04-08, 2011. Abst. 164.

Kaplan-Meier Plot of Patients with Viruses Harboring RAV T54A Detected During Follow-up



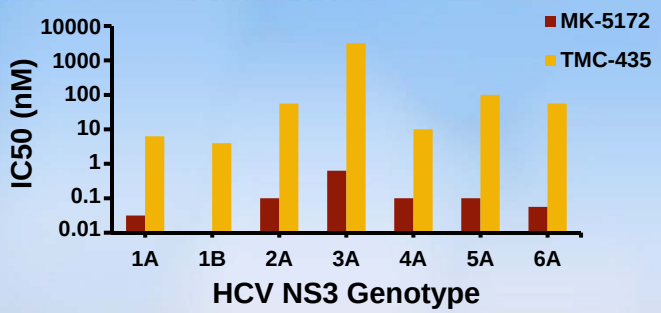
Bernard R, et al. 62nd AASLD; San Francisco, CA; November 04-08, 2011. Abst. 164.

Comparative Activity of PIs Against HCV NS3 Proteases from Genotypes 1-6 (SEAP Assay)



Graham D, et al. 62nd AASLD; San Francisco, CA; November 04-08, 2011. Abst. 370.

Activity of MK-5172 and TMC-435 Against NS3 Enzymes from Different Genotypes



- MK-5172 potently inhibited enzymes from genotypes 1-4 at IC_{50} concentrations <1 nM compared with TMC-435 (IC_{50} range 2.9-2750 nM)
- MK-5172 was >3000-fold more active against the genotype 3a enzyme than TMC-435, a finding consistent with the relative difference in clinical activity of these compounds in genotype 3 infected patients

The inhibitory activity of MK-5172 against purified NS3 proteases from different HCV genotypes was evaluated in an *in vitro* enzyme assay (data courtesy of Aileen Soriano, *In vitro* Pharmacology, Merck).

See Poster 346, Petry et al., AASLD, 2011; Moreno et al "A Phase IIa, open-label study to assess the antiviral activity of TMC-435 monotherapy in patients infected with HCV genotypes 2-6; AASLD 2010

Graham D, et al. 62nd AASLD; San Francisco, CA; November 04-08, 2011. Abst. 370.

Conclusions

- The novel macrocyclic HCV PI inhibitor, MK-5172, demonstrated potent activity against the majority of primary 1st generation PI RAVs in biochemical and a cell-based phenotype assays.
- MK-5172 inhibited patient-derived NS3 proteases across HCV genotypes 1-6 with IC50 values ranging between 0.9-259 nM
- MK-5172 fulfills the profile expected of a next-generation PI:
  - Pan-genotypic activity
  - Potent activity versus key 1st generation PI RAVs

Graham D, et al. 62nd AASLD; San Francisco, CA; November 04-08, 2011. Abst. 370.