A CONTINUING MEDICAL EDUCATION ACTIVITY

THE 46TH ANNUAL MEETING OF THE EUROPEAN ASSOCIATION FOR THE STUDY OF THE LIVER (EASL)

Online Expert Poster Review and Discussion

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REALIZE Trial Final Results: Telaprevir-based Regimen for Genotype 1 Hepatitis C Virus Infection in Patients with Prior Null Response, Partial Response or Relapse to Peginterferon/Ribavirin

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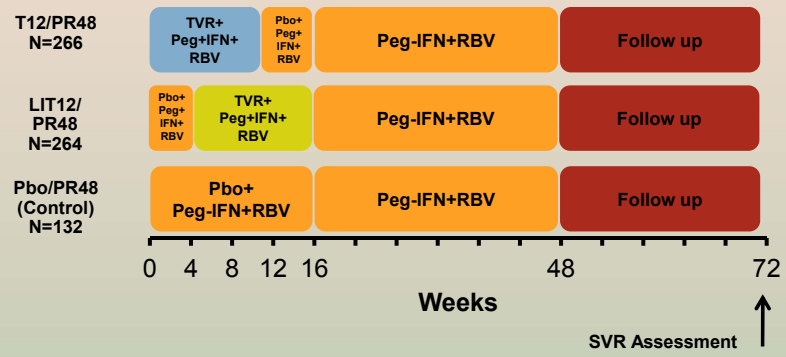
Abstract 5

REALIZE: Study Design (N=662)



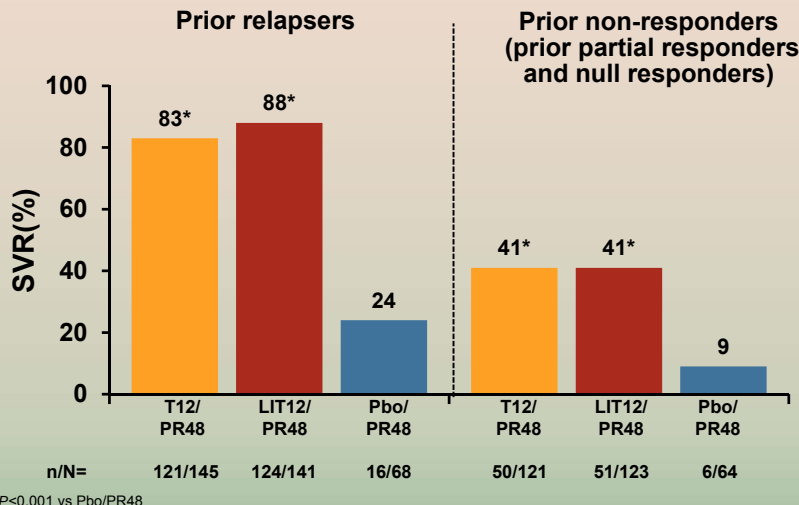
Randomization was stratified by viral load and prior response. Stopping rules applied for TVR (Weeks 4, 6, and 8 for T12/PR48; Weeks 8,10 and 12 for LI T12/PR48) and Peg-IFN/RBV (Weeks 12, 24, and 36 for T12/PR48; Weeks 16, 24, and 36 for LI T12/PR48)
Peg-IFN: Peg-IFN alfa-2a= 180µg/week;RBV=1000-1200mg/day;TVR=750mg every 8 hours
ClinicalTrials.gov identifier: NCT00703118
LI = lead-in; Pbo = placebo; TVR = telaprevir

REALIZE: Baseline Characteristics

Characteristic	T12/PR48 (N=266)	LI T12/PR48 (N=264)	Pbo/PR48 (N=132)
Male, n(%)	183 (69)	189 (72)	88 (67)
Caucasian race, n (%)	246 (92)	252 (95)	117 (89)
Black race, n (%)	11 (4)	8 (3)	11 (8)
Years of age, median (range)	51 (23-69)	51 (24-70)	50 (21-69)
HCV RNA ≥ 800,000 IU/mL, n (%)*	238 (89)	234 (89)	114 (86)
Body mass index, mean (SD)	28 (5.0)	27 (4.8)	27 (4.6)
HCV genotype, n (%)‡			
1a	136/262 (52)	149/262 (57)	67/128 (52)
1b	126/262 (48)	113/262 (43)	61 /128(48)
Prior response, n (%)			
Null responder	72 (27)	75 (28)	37 (28)
Partial responder	49 (18)	48 (18)	27 (20)
Relapser	145 (55)	141 (54)	68 (52)
Bridging fibrosis, n (%)§	60 (23)	58 (22)	29 (22)
Cirrhosis, n (%)§	72 (27)	67 (25)	30 (23)

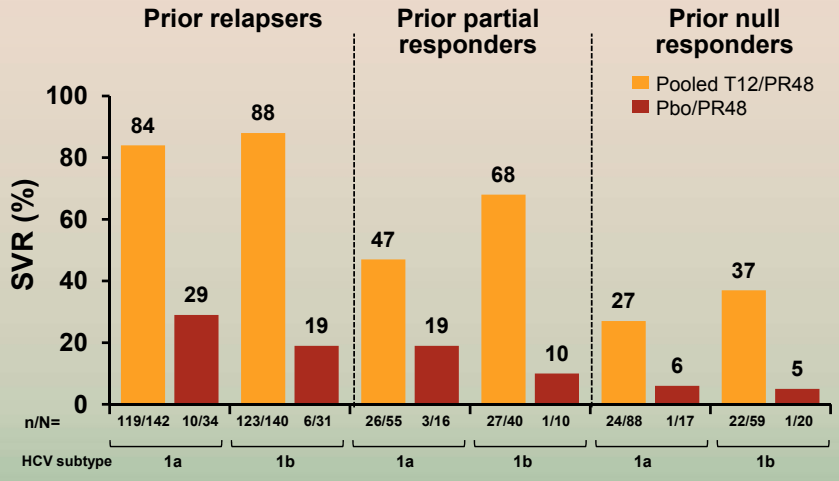
*Determined using the HCV COBAS TaqMan® assay version 2.0; ‡ Determined by NS3 sequencing; § Defined by local pathologists

REALIZE Primary Endpoint: Proportion of Patients with SVR

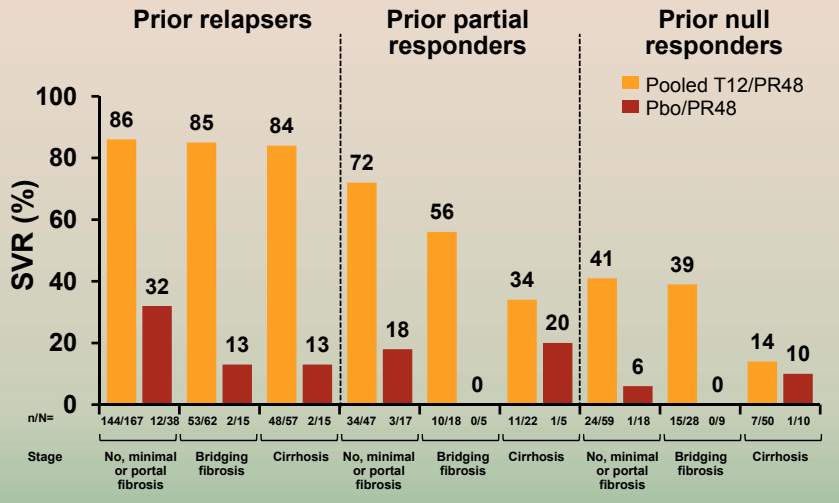


*P<0.001 vs Pbo/PR48

REALIZE: SVR by HCV Subtype and Prior Response



REALIZE: SVR by Baseline Fibrosis Stage and Prior Response



REALIZE: Patients Who Did Not Achieve an SVR

Category, n(%)	T12/PR48 (N=266)	LI T12/PR48 (N=264)	Pbo/PR48 (N=132)
Patients without SVR	95 (36)	89 (34)	110 (83)
On-treatment virologic failure*	52 (20)	45 (17)	68 (52)
Prior relapsers	2 (1)	1 (<1)	18 (14)
Prior partial and null responders	50 (19)	44 (17)	50 (38)
Detectable HCV RNA at EOT, no viral breakthrough	11 (4)	9 (3)	12 (9)
Relapse‡	26 (10)	27 (10)	30 (23)
Completed treatment	14 (5)	18 (7)	28 (21)
Prematurely discontinued treatment	12 (5)	9 (3)	2 (2)
Undetectable HCV RNA at EOT, discontinued study before SVR	6 (2)	8 (3)	0

*Includes patients with viral breakthrough and/or patients who discontinued due to a virologic stopping rule
‡ Relapse rate calculated relative to total number of patient in full analysis set; EOT = end of treatment

REALIZE: AEs Occurring in ≤25% of Patients During any Treatment Phase

Patients, n(%)	T12/PR48 (N=266)	LI T12/PR48 (N=264)	Pbo/PR48 (N=132)
Fatigue	145 (55)	131 (50)	53 (40)
Pruritus	138 (52)	132 (50)	36 (27)
Headache	112 (42)	109 (41)	49 (37)
Rash	99 (37)	95 (36)	25 (19)
Nausea	94 (35)	87 (33)	31 (23)
Influenza-like illness	85 (32)	94 (36)	33 (25)
Anemia	79 (30)	94 (36)	20 (15)
Anorectal symptoms	75 (28)	59 (22)	10 (8)
Insomnia	68 (26)	84 (32)	34 (26)
Diarrhea	66 (25)	69 (26)	18 (14)
Pyrexia	60 (23)	71 (27)	36 (27)
Cough	62 (23)	66 (25)	26 (20)
Asthenia	51 (19)	60 (23)	38 (29)

Shading indicates AEs with an incidence >10% greater in the T12/PR48arm compared with Pbo/PR48

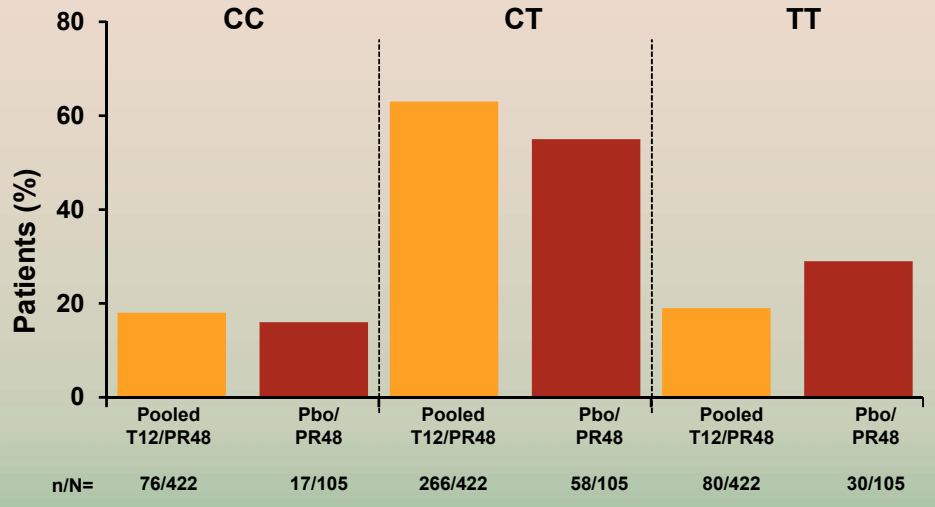
REALIZE: AEs Leading to Study Drug Discontinuation

	T12/PR48 (N=266)	LI T12/PR48 (N=264)	Pbo/PR48 (N=132)
Discontinuation of all study drugs during TVR treatment phase, n (%)			
Any AE	**17(6)**	**11(4)**	**4(3)**
Rash events	2(1)	2(1)	0
Anemia events	2(1)	2(1)	0
Pruritus	0	1(<1)	0
Anorectal signs and symptoms	2(1)	0	0
Discontinuation of all study drugs during TVR treatment phase, n (%)			
Any AE	**39(15)**	**29(11)**	**4(3)**
Rash events	12(5)	10(4)	0
Anemia events	6(2)	9(3)	0
Pruritus	1(<1)	3(1)	0
Anorectal signs and symptoms	2(1)	1(<1)	0

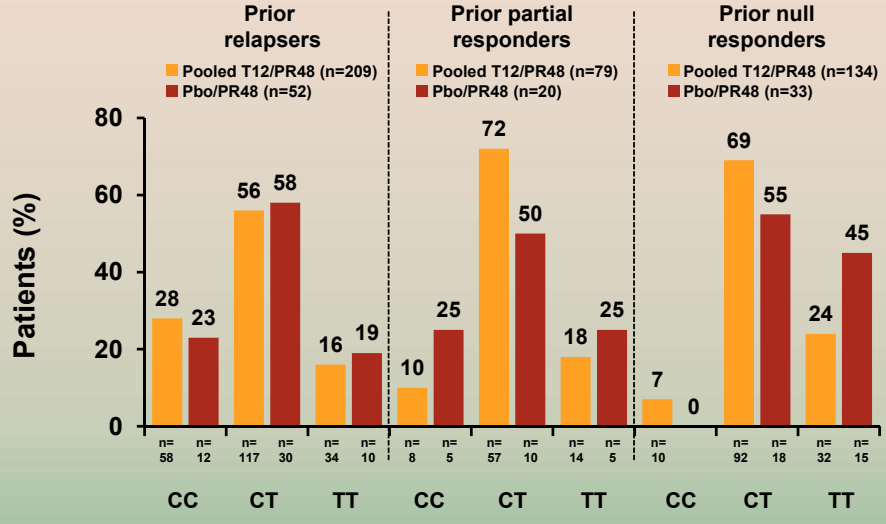
REALIZE: Conclusions

- TVC/Peg-IFN/RBV was superior to Peg-IFN/RBV alone in treatment –experienced populations including prior relapers, partial responders and null responders
- In TVR-treated patients, the use of a 4-week lead-in phase with Peg-IFN/RBV showed
  - No reduction in virologic failure and relapse rates
  - No improvement in SVR rates
- Safety data were comparable with previous TVR studies
- AEs leading to permanent discontinuation of study drugs (mainly anemia and rash events) were more frequent in the TVR group than in the control group

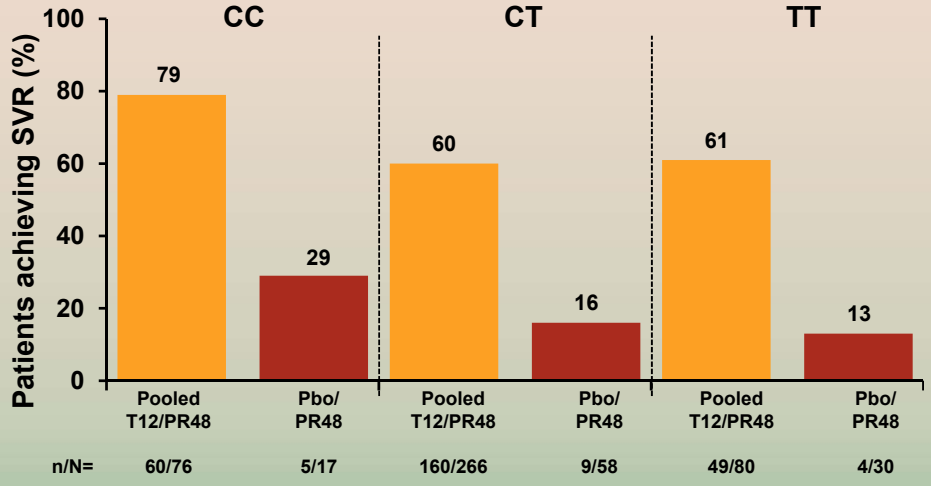
Overall Baseline IL28B Genotype Distribution



Baseline IL28B Genotype Distribution by Prior Response

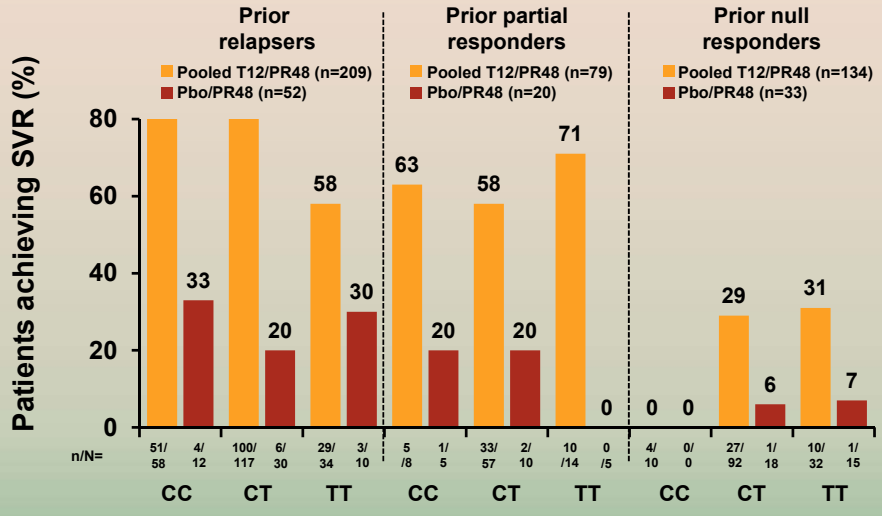


Overall SVR Rates by IL28B Genotype



In a 2-step multivariate analysis exploring factors including: treatment group, IL28B genotype, prior response category, treatment/prior response interaction and other baseline characteristics, IL28B did not have a significant impact on SVR (p=0.169 for CC, p=0.792 for TT)

SVR Rates by IL28B Genotype and Prior Response



Conclusions

- Response rates were consistently higher and relapse rates lower with TVR-based therapy versus Peg-IFN/RBV alone
- Response rates with TVR-based therapy were similar across IL28B genotypes
  - SVR rates were highest in patients with CC genotype (79%), but SVR rates for CT and TT genotypes were also high (60–61%)
  - Relapse and viral breakthrough rates similar across genotypes
  - Lower SVR rates and higher viral breakthrough rates in prior null responders, irrespective of IL28B genotype
- IL28B genotype may have limited predictive value in patients with prior Peg-IFN/RBV treatment failure receiving a TVR-based regimen