New Data with Grazoprevir + Ruzasvir + Uprifosbuvir

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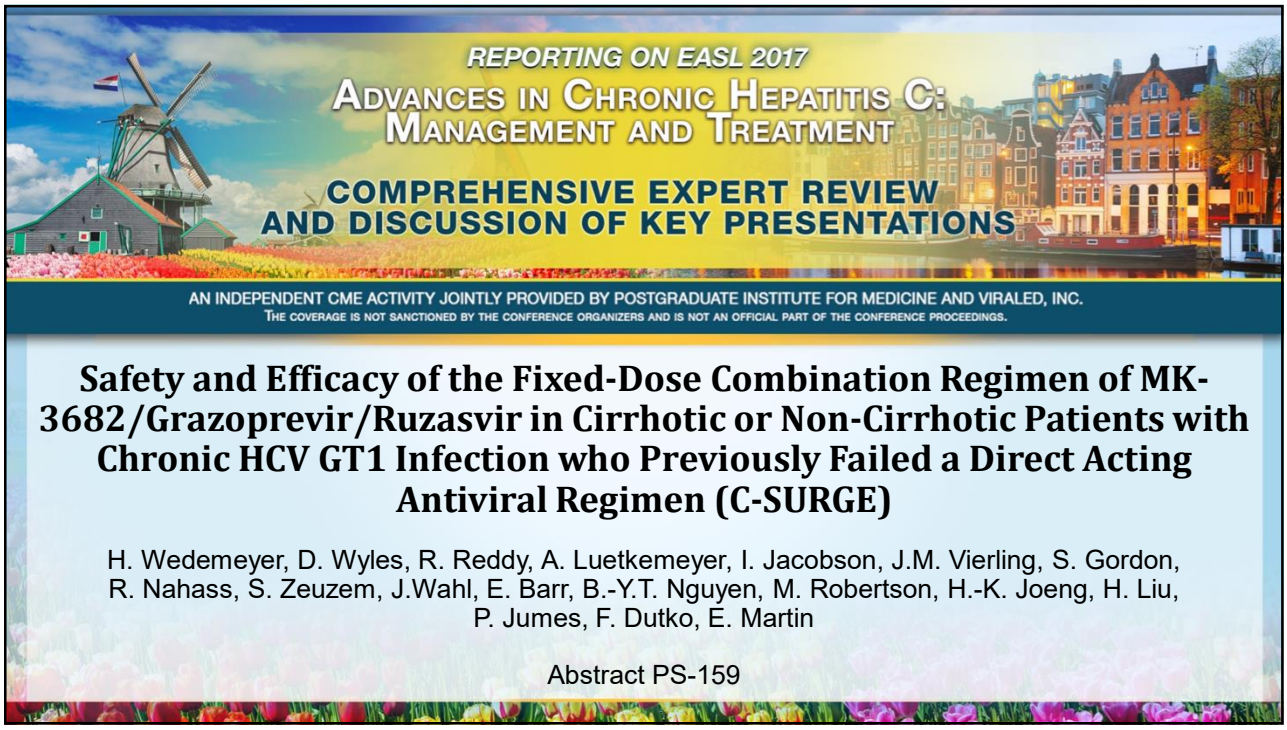


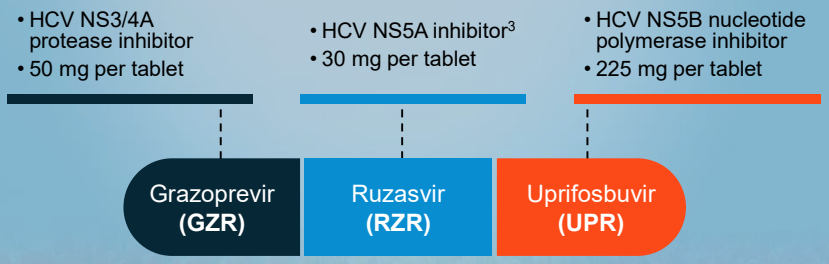
Safety and Efficacy of the Fixed-Dose Combination Regimen of MK-3682/Grazoprevir/Ruzasvir in Cirrhotic or Non-Cirrhotic Patients with Chronic HCV GT1 Infection who Previously Failed a Direct Acting Antiviral Regimen (C-SURGE)

H. Wedemeyer, D. Wyles, R. Reddy, A. Luetkemeyer, I. Jacobson, J.M. Vierling, S. Gordon, R. Nahass, S. Zeuzem, J.Wahl, E. Barr, B.-Y.T. Nguyen, M. Robertson, H.-K. Joeng, H. Liu, P. Jumes, F. Dutko, E. Martin

Abstract PS-159

C-SURGE Study: Grazoprevir + Ruzasvir + Uprifosbuvir

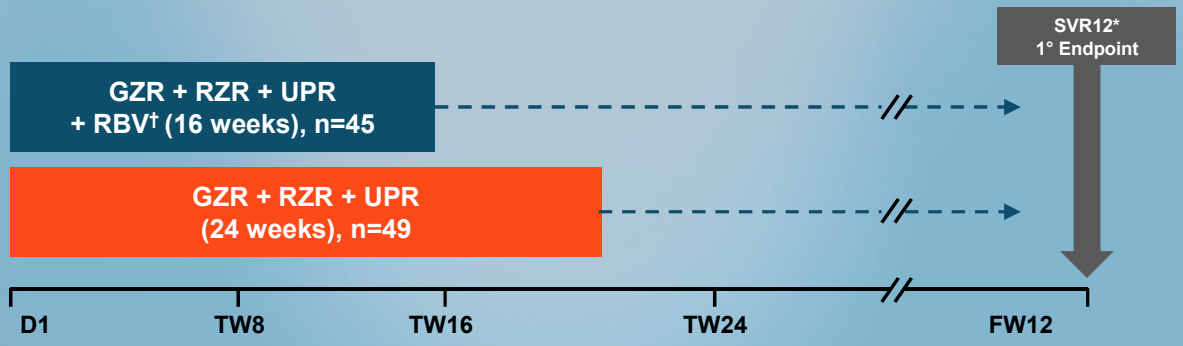
- Co-formulated as a fixed-dose combination tablet; administered as 2 tablets once-daily for a total daily dose of 100 mg grazoprevir (GZR), 60 mg ruzasvir (RZR), and 450 mg of uprifosbuvir (UPR; MK -3682)
- GZR + RZR + UPR has been shown to be effective, safe, and well tolerated for treatment-naïve and peg-interferon/ribavirin-treatment experienced HCV GT1, 2 and 3-infected persons with SVR rates >90%



Gane EJ et al., EASL, abstract SAT-139, 2016
Gane EJ et al., AASLD, abstract LB-15, 2015
Tong, et al., J Med Chem 60:290, 2017

C-SURGE Study: Study Design

- This multicenter, open-label trial randomized 94 HCV GT1-infected participants who relapsed after a regimen of LDV/SOF or EBR/GZR (randomized 1:1;stratified by GT1a/1b and cirrhosis)



GZR:100 mg once-daily; RZR: 60 mg once-daily; UPR: 450 mg once-daily; TW+ treatment week; FW=follow-up week; LDV=ledipasvirl SOF=sofosbuvir.
*SVR12 = HCV RNA <15 IU/mL at 12 weeks after end of treatment (COBAS™ AmpliPrep/COBAB™ Taqman™ HCV Test, v2.0™).
† RBV dose based on body weight (<65 kg=800 mg/d; 65-85 kg=100- mg/d; >85-105 kg=1200 mg/d; >105 kg=1400 mg/d).
Individuals could not be compensated cirrhotic (platelet cutoff+75,000/µL; excluded Child-Pugh B & C) or non-cirrhotic individuals.

Wedemeyer H, et al. 52nd EASL; Amsterdam, Netherlands; April 19-23, 2017. Abst. PS-159.

C-SURGE Study: Demographics

Demographics	16 Weeks + RBV, n=44*	24 Weeks without RBV, n=49	Overall GT1 N=93*
Male, n (%)	37 (84)	43 (88)	80 (86)
Age, median years, (range)	61.0 (33 to 70)	60.0 (25 to 71)	60.0 (25 to 71)
Race, White, n (%)	31 (71)	37 (76)	68 (73)
HCV Genotype 1a, n (%)	40 (91)	40 (82)	80 (86)
Non-cirrhotic, n (%) Cirrhotic, n (%)	25 (57) 19 (43)	27 (55) 21 (43)†	52(56) 40 (43)
NS5A RASs at baseline, n (%)‡ NS3 RASs at baseline, n (%)‡	32 (79) 25 (57)	46 (94) 35 (71)	78 (84) 60 (65)
Baseline HCV RNA >2,000,000 IU/mL, n (%)	29 (66)	33 (67)	62 (67)
Median baseline HCV RNA (log_{10}IU/mL)	6.5	6.4	6.5
Previously failed: 12-24 weeks of LDV/SOF 8 weeks of LDV/SOF 12 weeks of EBR/GZR	 26 (59) 9 (20) 9 (20)	 31 (63) 5 (10) 13 (27)	 57 (61) 14 (15) 22 (24)

* Does not include 1 participant in the 16 week + RBV arm who withdrew prior to beginning treatment.
Cirrhosis = Liver biopsy at any time showing cirrhosis, Fibroscan result of >12.5kPa within 12 month of enrollment, or Fibrotest >0.75 and APRI >2 at time of enrollment.
† One participant in 24 week arm had unknown cirrhosis status
‡ NS5A RASs = any change from wild-type at 4 positions (28, 30, 31, or 93). NS3 RASs = any change from wild-type at 14 positions (36, 54, 55, 56, 80, 107, 122, 132, 155, 156, 168, 170, or 175). RASs detected by next generation sequencing performed with a 15% sensitivity threshold.

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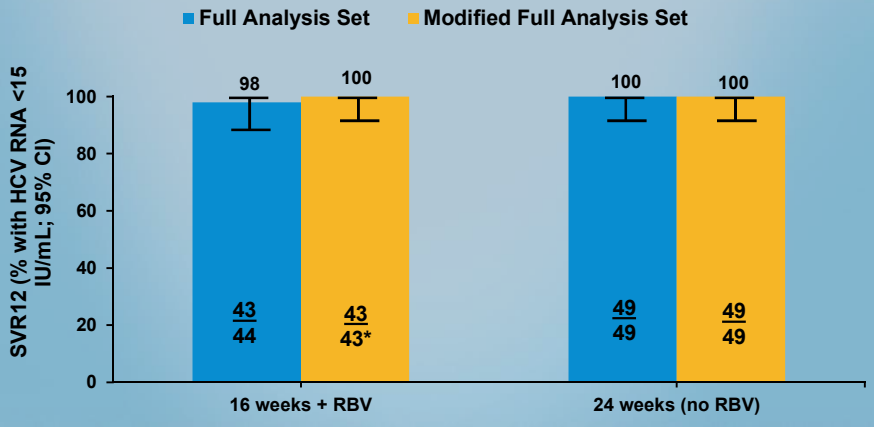
C-SURGE Study: Efficacy Results



SVR12 = % of participants with HCV RNA <15 IU/mL at 12 weeks after end of treatment.
Full analysis set = all patients who received at least one dose of study medication;
*Modified full analysis at excluded one participant from the 16-week + RBV arm who withdrew from the study after taking 3 doses of study medication.

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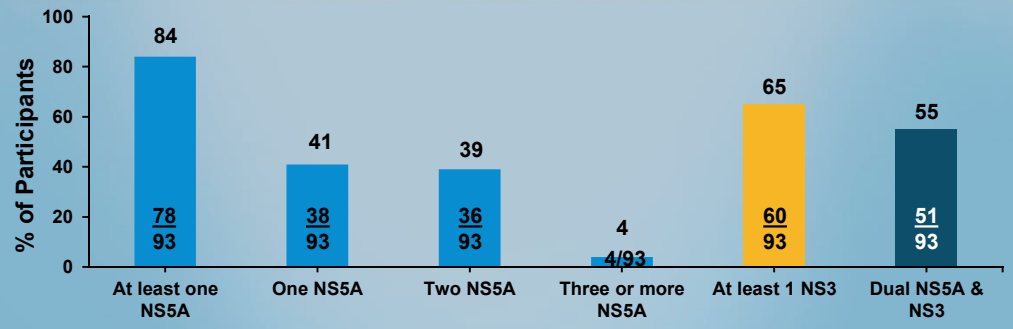
C-SURGE Study: Baseline NS5A or NS3 RASs



Number of RASs Per Participant

- RASs at NS3 position Q80K detected in 33 of 93 participants (35%)
- One participant in the 16 week + RBV treatment group had an NS3 RAS at the 168 position
  - No Participant had NS3 RASs at the 156 position

*RASs detected by next-generation sequencing with 15% sensitivity; NS5A RAS: any change from wild-type at 4 positions (28, 30, 31, or 93); NS3 RASs + any change from wild-type at 14 positions (36, 54, 55, 56, 80, 107, 122, 132, 155, 156, 158, 168, 170, or 175).

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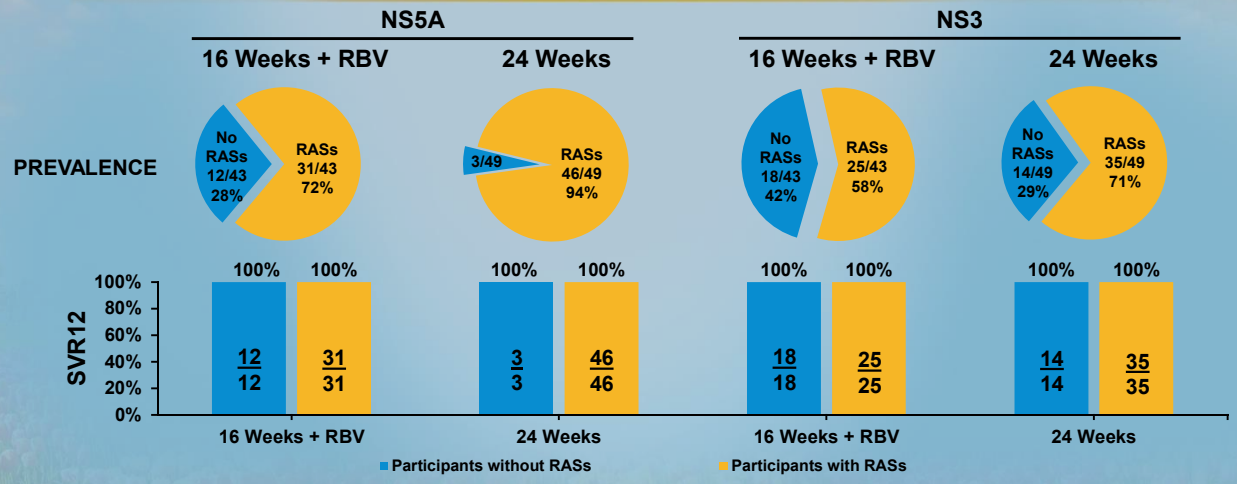
C-SURGE Study: Baseline NS5A or NS3 RASs on SVR12



SVR12= proportion of participants with HCV RNA <15 IU/mL at 12 weeks after end of treatment.
*RASs detected by next-generation sequencing with 15% sensitivity.
†Excludes 1 participant from the 16-week group who withdrew after receiving 3 doses of study medication.

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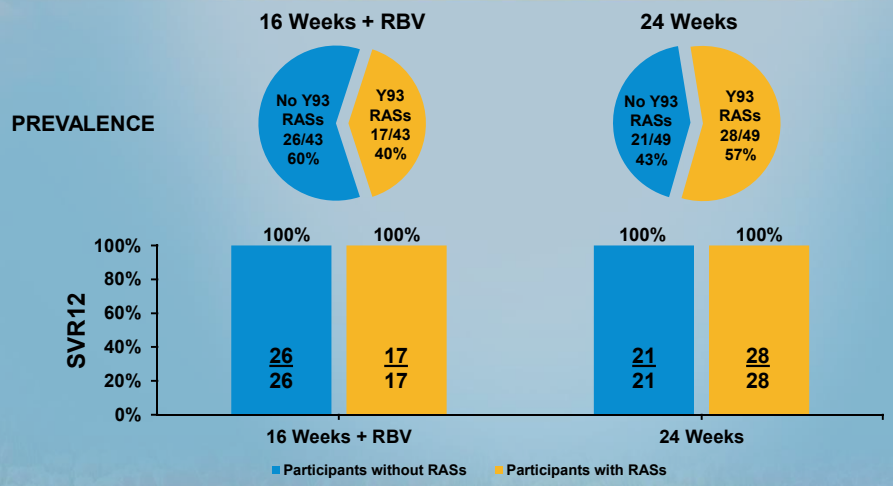
C-SURGE Study: Baseline Y93 RASs in NS5a on SVR12



SVR12= proportion of participants with HCV RNA <15 IU/mL at 12 weeks after end of treatment.
*RASs detected by next-generation sequencing with 15% sensitivity.
†Excludes 1 participant from the 16-week group who withdrew after receiving 3 doses of study medication.

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C-SURGE Study: Adverse Events

Tolerability	16 Weeks + RBV, n=44	24 Weeks Without RBV, n=49	Overall GT1 N=93
One or more AEs, n (%)	40 (91)	39 (80)	79 (85)
Drug-related AE, n (%)	32 (73)	23 (47)	55 (59)
Serious AE, n (%)	1 (2)	4 (8)	5 (5)*
Drug-related serious AE, n (%)	0 (0)	0 (0)	0 (0)
Death, n (%)	0 (0)	0 (0)	0 (0)
Discontinuation due to AE, n (%)	0 (0)	0 (0)	0 (0)
Hemoglobin <10 g/dL, n (%)	4 (9)	0 (0)	4 (4)
Direct bilirubin >5x baseline, n (%)	0 (0)	0 (0)	0 (0)
Late ALT/AST >5x ULN, n (%)	0 (0)	0 (0)	0 (0)
Creatinine grade 2 (1.4-1.8x ULN), n (%)	0 (0)	1 (2)	1 (1)
Most common AEs (>10%), n (%)			
Fatigue	21 (48)	12 (24)	33 (35)
Headache	6 (14)	6 (12)	12 (13)
Diarrhea	3 (7)	5 (10)	8 (9)
Pruritus	5 (11)	0 (0)	5 (5)
Rash	6 (14)	2 (4)	8 (9)

*SAEs all determined by the investigator to be "not drug related" : hospitalization for cervical spine disc herniation; hospitalization for chest pain; hospitalization for dizziness|; pancreatitis without hospitalization; hospitalization for shoulder cyst surgery

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C-SURGE Study: Summary

- Grazoprevir (GZR)/ruzasvir (RZR)/uprifosbuvir (UPR) ± ribavirin (RBV) was highly effective in GT1 participants who previously failed an NS5A inhibitor-containing direct-acting antiviral regimen
  - Cirrhosis had no impact on efficacy
- 16 weeks of GZR/RZR/UPR + RBV resulted in SVR12 rate of 98% (43/44)
  - One participant withdrew from the study after receiving 3 doses of study medication
- 24 weeks of GZR/RZR/UPR alone resulted in SVR12 rate of 100% (49/49)
- High efficacy was observed despite a high prevalence of baseline NS3 and NS5A RASs in this population
- Treatment was generally safe and well tolerated

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