HEPATITIS C VIRUS REINFECTION AND INJECTING RISK BEHAVIOR FOLLOWING ELBASVIR/GRAZOPREVIR TREATMENT IN PARTICIPANTS ON OPIATE AGONIST THERAPY: C-EDGE CO-STAR PART B

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DISCLOSURES

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BACKGROUND

EBR/GZR is a fixed-dose combination tablet administered once daily without regard to food intake, and is approved for the treatment of HCV GT1 and 4 infections in a number of countries, including the US, Canada, and EU

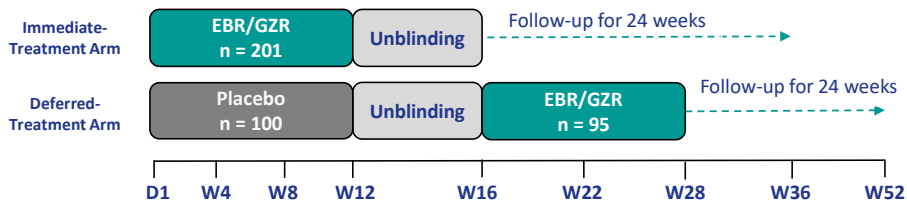
- Retains in vitro activity against many clinically relevant RASs[1-3]
- Efficacious in treatment-naive and -experienced compensated cirrhotic and noncirrhotic people with HCV, and in HIV/HCV co-infected people[4-8]
- Safety and efficacy demonstrated in special populations, including those with stage 4/5 chronic kidney disease or inherited blood disorders[5,8]

EBR, elbasvir; GT, genotype; GZR, grazoprevir; HCV, hepatitis C virus; RAS, resistance-associated substitution.

1. Summa V et al. *Antimicrobial Agent Chemother*. 2012;56:4161-4167. 2. Coburn CA et al. *ChemMedChem.* 2013;8:1930-1940. 3. Harper S et al. *ACS Med Chem Lett.* 2012;3:332-336. 4. Kwo P et al. *Gastroenterology*. 2017;152:164-175.e4. 5. Roth D et al. *Lancet*. 2015;386:1537-1545. 6. Rockstroh JK et al. *Lancet HIV*. 2015;2:e319-e327. 7. Zeuzem S et al. *Ann Intern Med*. 2015;163:1-13. 8. Hézode C et al. *Hepatology*. 2017;66:736-745.

PART A: TRIAL DESIGN

- Phase 3, randomized trial of EBR/GZR for 12 weeks
- Participants with GT1, 4, or 6 infection on OST for ≥3 months
  - Consistently kept ≥80% of scheduled appointments while on OST
- Urine drug screen performed at each visit
  - Participants with positive results not excluded

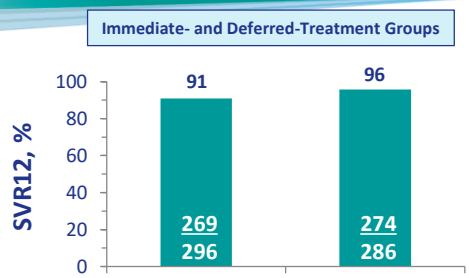


D, day; OST, opioid substitiution therapy; W, week.

PART A: EFFICACY RESULTS

SVR12

- Full analysis set (FAS): 90.9%
  - Includes nonvirologic failures
  - Categorizes reinfection as failures
- Modified FAS (mFAS)[a]: 95.8%
  - Excludes nonvirologic failures
  - Categorizes reinfections as success
- High adherence
  - Ninety-seven percent of participants demonstrated >95% adherence

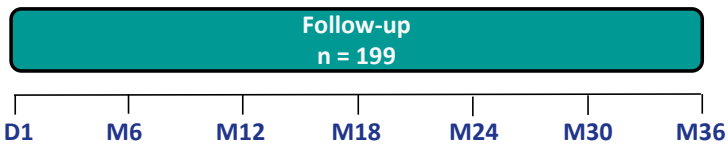


	Non-SVR	**Non-SVR**
Virologic failure	10	10
Administrative failure	1	1
D/c due to AE	1	1
	Non-SVR	**Excluded**
D/c or LTFU	**10**	**10**
	Non-SVR	**SVR**
Reinfection[b]	5	5

AE, adverse event; D/c, discontinuation; LTFU, lost to follow-up; SVR12, sustained virologic response at 12 weeks.
[a]The primary efficacy analysis is the mFAS, which excluded nonvirologic failures.
[b]Reinfection was defined as a new HCV infection confirmed by sequencing analysis in participants who initially cleared the original or primary HCV infection.

PART B: 3-YEAR OBSERVATIONAL FOLLOW-UP TRIAL

- Open to all participants who received ≥1 dose of EBR/GZR in Part A
- Assessments every 6 months
  - HCV RNA[a]
    - Comparison of viral sequences at baseline and virologic recurrence to determine reinfection[b]
  - Urine drug screen
  - Participant-reported behaviors
    - Behavioral questionnaire: self-reported drug use



M, month.
[a]HCV RNA determined with Cobas® AmpliPrep/Cobas® Taqman™ HCV Test, version 2.0.
[b]Genotype determined by Abbott RealTime HCV Genotype II . Next-generation sequencing performed on sequences at the NS3 and NS5A regions with ≈1% sensitivity threshold.

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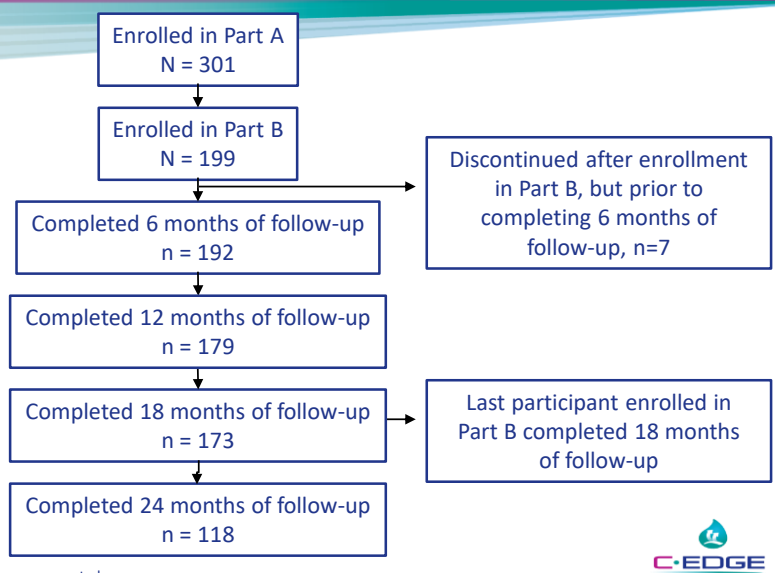
TRIAL DISPOSITION[a]



[a]Results from enrollment and through all available visits are presented.

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BASELINE CHARACTERISTICS

	Participants enrolled in Part B (n = 199)	Participants not enrolled in Part B (n = 97)
Male, n (%)	151 (76)	76 (78)
Age, years, median (range)	**48.6 (24-66)**	**44.1 (23-64)**
Race, n (%)		
White	158 (79)	80 (82)
African American	31 (16)	6 (6)
Asian/other	10 (5)	11 (11)
HCV/HIV co-infected, n (%)	16 (8)	5 (5)
OAT at day 1 active treatment, n (%)		
Methadone	159 (80)	75 (77)
Buprenorphine	39 (20)	21 (22)
Genotype, n (%)		
1a	144 (72)	81 (84)
1b	39 (20)	5 (5)
4	7 (4)	2 (2)
6	2 (1)	5 (5)
Mixed	7 (4)	4 (4)

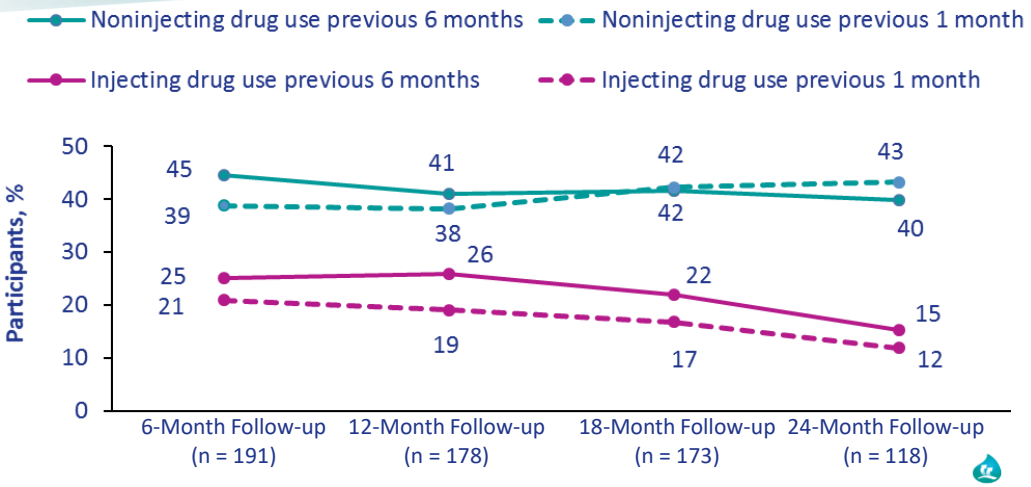
	Participants enrolled in Part B (n = 199)	Participants not enrolled in Part B (n = 97)
Presence of cirrhosis (F4), n (%)	44 (22)	18 (19)
Positive urine drug screen at enrollment of Part A, n (%)	117 (59)	66 (68)
Amphetamines	13 (7)	4 (4)
Benzodiazepines	47 (24)	36 (37)
Cannabinoids	46 (23)	42 (43)
Cocaine	19 (10)	12 (12)
Opiates	44 (22)	23 (24)

ONGOING RISK BEHAVIOR—URINE DRUG SCREEN

	Participants With Urine Drug Screen Results					
	Part A Day 1 (n = 199)	Part B Enrollment (n = 192)	6-Month Follow-up (n = 190)	12-Month Follow-up (n = 177)	18-Month Follow-up (n = 172)	24-Month Follow-up (n = 111)
Any positive urine drug screen[a]	59%	60%	59%	62%	59%	60%
Amphetamines	**7%**	**8%**	**8%**	**5%**	**6%**	**2%**
Benzodiazepines	24%	24%	23%	21%	23%	21%
Cannabinoids	23%	28%	28%	29%	28%	32%
Cocaine	**10%**	**12%**	**11%**	**14%**	**13%**	**20%**
Opioids	**22%**	**27%**	**21%**	**24%**	**27%**	**22%**

[a]Excludes methadone and buprenorphine.

ONGOING RISK BEHAVIOR—REPORTED DRUG USE[a]



[a]Participants may have reported both injection and noninjection drug use.

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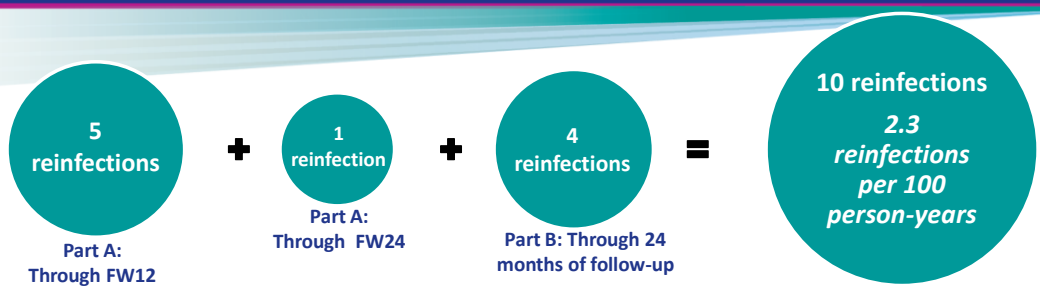
INCIDENCE OF REINFECTION



All Reinfections: From End of Treatment Through 24 Months of Follow-up
• 10 reinfections • 426 person-years • 2.3 reinfections per 100 person-years (95% CI: 1.1, 4.3)
Persistent Reinfections: From End of Treatment Through 24 Months of Follow-up (includes only those participants with persistent HCV RNA)
• 7 reinfections • 429 person-years • 1.6 reinfections per 100 person-years (95% CI: 0.7, 3.4)
Clearance of reinfection was observed in 3/10 (30%) reinfection cases

CI, confidence interval; FW, follow-up week.

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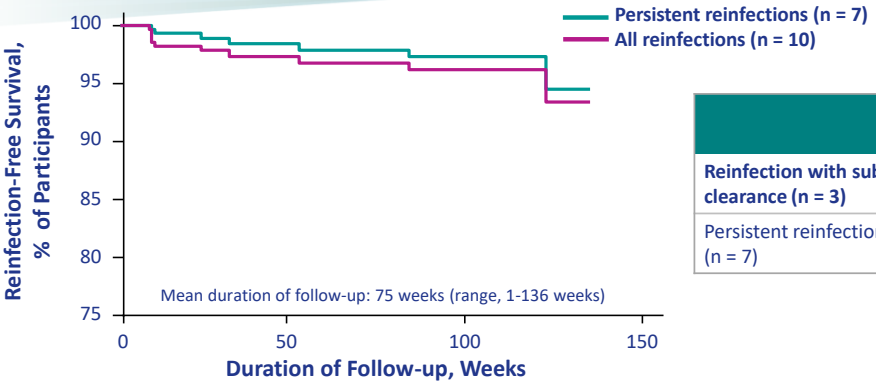
INCIDENCE OF REINFECTION (CONT'D)



	Time to Reinfection Post-EOT (weeks)
Reinfection with subsequent clearance (n = 3)	**8, 9, 9**
Persistent reinfection (n = 7)	9, 10, 24, 32, 52, 84, 125

Visit	EOT	FW12	FW24	6m FU	12m FU	18m FU	24m FU
Number at risk	296	277	265	192	179	173	118

EOT, end of treatment; FU, follow-up.

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INCREASED RISK OF REINFECTION BASED ON REPORTED INJECTION DRUG USE DURING FOLLOW-UP

199 participants enrolled in Part B

From the end of treatment through all available follow-up

74 participants (37%)

reported injection drug use

Rate of reinfection:

4.2 reinfections/100 person-years

95% CI: 1.5, 9.2

125 participants (63%)

reported NO injection drug use

Rate of reinfection:

0.4 reinfections/100 person-years

95% CI: 0.0, 2.3

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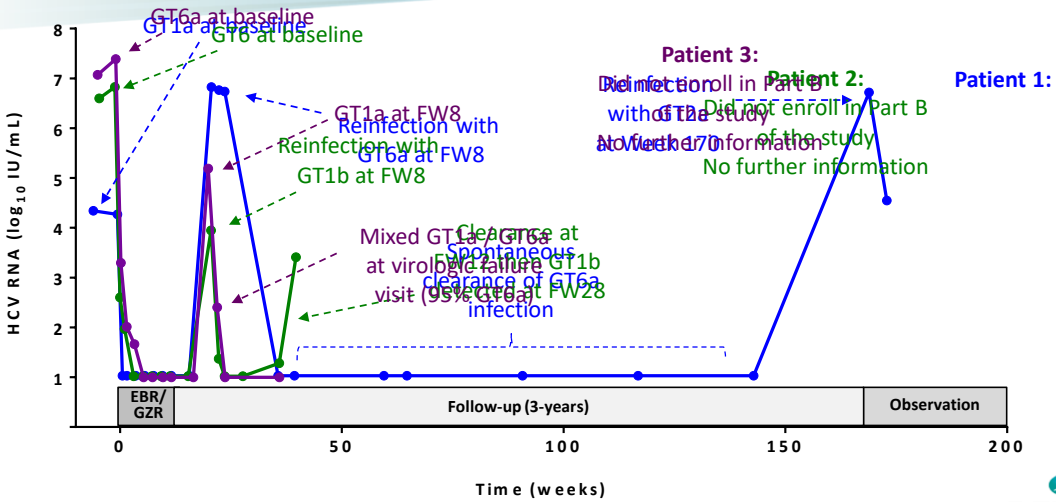
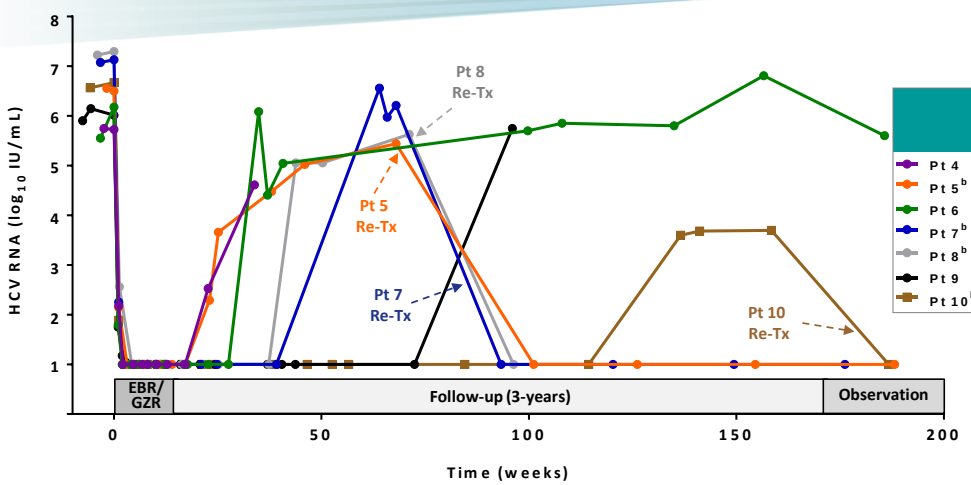
THREE PARTICIPANTS HAD RECURRENT VIREMIA AND SUBSEQUENT SPONTANEOUS CLEARANCE



[a]Serum HCV RNA was assessed using the Cobas® Taqman™ HCV Test, v2.0 with a lower limit of quantitation (LLoQ) of 15 IU/mL.

SEVEN PARTICIPANTS HAD PERSISTENT RECURRENT VIREMIA THROUGH AVAILABLE FOLLOW-UP VISITS; FOUR CLEARED WITH RETREATMENT



	Detectable HCV RNA[a] (week)	HCV RNA Cleared (week)
Pt 4	23	-
Pt 5[b]	23	102
Pt 6	35	-
Pt 7[b]	64	94
Pt 8[b]	44	97
Pt 9	96	-
Pt 10[b]	137	187

[a]Serum HCV RNA was assessed using the Cobas® Taqman™ HCV Test, version 2.0 with a LLOQ of 15 IU/mL.
[b]Four participants with reinfection subsequently achieved undetectable HCV RNA with retreatment (Pts 5 & 8, SOF/DAC; Pt 7, PrOD; Pt 10, GLE/PIB). The time that retreatment was initiated is indicated with dashed arrow.

CONCLUSIONS

- Drug use patterns relatively stable during the 24 months of follow-up
  - Rate of injection drug use in previous 6 months: 22-26% through 18 months follow-up
- Of the 10 participants with reinfection, persistence of reinfection was observed in 7 participants
- Overall, the reinfection rate was 2.3/100 person-years, with a persistent reinfection rate of 1.6/100 person-years
  - Higher rate of reinfection in early follow-up period may be due to more frequent follow-up
  - Reinfection rate of 4.2/100 person-years among participants with reported injection drug use
  - Seven of 10 reinfection cases had viral clearance (spontaneous, n=3; re-treatment, n=4)