Supplemental Table 1. Participating sites and principal investigators

SITES	Principal Investigator	State
Liver Wellness of Arkansas	Alonzo Williams, MD/Lynn Frazier, NP	AR
University of California, San Francisco	Norah A. Terrault, MD, MPH	CA
University of California, San Diego	Irine Vodkin, MD	CA
San Francisco General Hospital	Mandana Khalili, MD	CA
Stanford	Glen Lutchman, MD	CA
Yale University	Joseph K. Lim, MD	CT
Georgetown University	Coleman Smith, MD/Dawn Fishbein, MD	DC
Howard University	Charles D. Howell, MD	DC
University of Florida	Miguel Malespin, MD - JAX Giuseppe Morelli, MD - GNV	FL
Orlando Immunology Center	Federico Hinestrosa, MD	FL
University of Miami	Eugene R. Schiff, MD/Ram Bhamidimarri, MD	FL
Center for Hepatitis at Atlanta Medical Center	Brian L. Pearlman, MD, FACP	GA
Northwestern University	Josh Levitsky, MD	IL
Indiana University	Marco Lacerda, MD	IN
Massachusetts General Hospital	Raymond T. Chung, MD	MA
Johns Hopkins University	Mark S. Sulkowski, MD	MD
University of Michigan	Anna Lok, MD, FRCP	MI
University of Minnesota	Mohamed Hassan, MD	MN
St. Louis University	Adrian M. Di Bisceglie, MD, FACP	MO
The University of North Carolina at Chapel Hill	Michael W. Fried, MD	NC
Duke University Medical Center	Andrew J. Muir, MD, MHS	NC

SITES	Principal Investigator	State
UNMC/Nebraska	Mark Mailliard, MD	NE
Southwest CARE Center	Vanessa Acosta, MD	NM
Mountain View Medical Practice	Ananthakrishnan Ramani, MD	NY
Columbia University Medical Center	Elizabeth Verna, MD	NY
Weill Cornell Medical College	Robert Brown, MD, MPH	NY
New York University	James Park, MD	NY
University of Cincinnati	Kenneth Sherman, MD	OH
University of Pennsylvania	K. Rajender Reddy, MD	PA
Research Specialists of Texas	Joseph Galati, MD	TX
Bon Secours Liver Institute of Virginia/St. Mary's Hospital (Richmond & New Port News)	Mitchell Shiffman, MD/Nadege Gunn, MD	VA
Virginia Commonwealth (VCU)	Richard Sterling, MD	VA
University of Washington	Charles, Landis, MD	WA
Virginia Mason Medical Center	Alexander Kuo, MD	WA

Supplemental Table 2. Patient who did not achieve SVR due to on-treatment viral non-response or post-treatment viral relapse.

REGIMEN	RBV	Viral OUTCOME	Sex	Race	Age	HCV GT	Treatment Experience	Cirrhosis	RAS 28	RAS 30	RAS 31	RAS 93	Completion / reason for non-completion	Days on Tx
EBR/GZR	Yes	VBT	Male	White	59	1a	Naive	NO	No	No	Yes	No	Complete	111
EBR/GZR	No	NR	Female	White	58	1a	Naive	YES	No	No	No	No	Complete	84
EBR/GZR	No	RELAPSE	Female	White	64	1a	Experienced	NO	No	No	No	No	Complete	85
EBR/GZR	No	RELAPSE	Male	Black	45	1a	Naive	NO	No	No	No	No	Complete	85
EBR/GZR	No	NR	Male	White	60	1a	Experienced	NO	No	No	No	No	Complete	84
EBR/GZR	No	RELAPSE	Female	White	32	1a	Naive	NO	No	No	No	No	Complete	87
EBR/GZR	No	NR	Female	Other	51	1a	Experienced	NO	No	No	No	No	Complete	85
EBR/GZR	Yes	RELAPSE	Male	Black	59	1a	Naive	NO	No	No	Yes	No	Complete	113
EBR/GZR	Yes	RELAPSE	Male	White	70	1a	Naive	NO	No	No	No	No	Complete	83
EBR/GZR	No	RELAPSE	Female	Black	56	1a	Naive	NO	No	No	No	No	Complete	93
EBR/GZR	No	RELAPSE	Male	Black	53	1a	Naive	NO	No	No	No	No	Complete	83
EBR/GZR	No	NR	Male	White	62	1a	Naive	NO	No	No	No	No	Adverse Event	13
EBR/GZR	No	RELAPSE	Female	Black	46	1b	Naive	NO	No	No	No	Yes	Complete	85
EBR/GZR	No	RELAPSE	Male	Black	47	1a	Naive	NO	No	No	No	No	Complete	108
EBR/GZR	No	NR	Male	Black	63	1b	Naive	NO	No	No	No	Yes	Complete	94
EBR/GZR	No	NR	Female	Black	65	1a	Naive	NO	No	No	No	No	Adverse Event	7
EBR/GZR	No	RELAPSE	Female	White	60	1a	Naive	NO	No	No	No	No	Complete	85
EBR/GZR	No	RELAPSE	Male	Black	64	1a	Naive	NO	No	No	No	No	Complete	91
EBR/GZR	No	NR	Female	White	41	1a	Naive	NO	No	No	No	No	Non-compliance	31
EBR/GZR	No	RELAPSE	Female	White	66	1b	Naive	YES	No	No	No	No	Complete	85
EBR/GZR	No	RELAPSE	Female	Black	37	1a	Naive	NO	No	No	No	No	Complete	86
EBR/GZR	No	RELAPSE	Male	White	45	1a	Naive	NO	No	No	No	No	Complete	87
EBR/GZR	No	RELAPSE	Male	Black	60	1b	Naive	NO	No	No	No	Yes	Complete	85
EBR/GZR	Yes	RELAPSE	Male	White	60	1a	Naive	YES	No	No	No	No	Complete	112
EBR/GZR	No	RELAPSE	Male	White	47	1a	Naive	NO	No	No	No	No	Complete	85
EBR/GZR	No	NR	Female	White	64	1a	Experienced	YES	No	No	No	No	Complete	97
EBR/GZR	Yes	NR	Male	Black	66	1a	Naive	NO	No	No	No	Yes	Complete	85
EBR/GZR	No	NR	Male	Black	56	1a	Naive	NO	No	No	No	No	Complete	84
EBR/GZR	No	NR	Male	White	59	1a	Naive	NO	No	No	No	No	Complete	103
EBR/GZR	Yes	RELAPSE	Female	White	63	1a	Experienced	NO	No	Yes	No	Yes	Complete	112
LDV/SOF	No	NR	Male	White	29	1a	Naive	NO	No	No	No	No	Complete	57
LDV/SOF	No	RELAPSE	Male	White	51	1a	Naive	NO	No	No	No	No	Complete	66
LDV/SOF	No	RELAPSE	Male	Black	61	1b	Naive	NO	No	No	Yes	No	Complete	49
LDV/SOF	No	RELAPSE	Male	Black	59	1b	Naive	YES	No	No	No	No	Complete	85
LDV/SOF	No	RELAPSE	Male	White	59	1b	Experienced	NO	No	No	Yes	Yes	Complete	103
LDV/SOF	No	RELAPSE	Male	Black	67	1b	Naive	YES	No	No	No	Yes	Complete	85
LDV/SOF	Yes	RELAPSE	Male	White	58	1a	Naive	YES	No	Yes	No	Yes	Complete	83
LDV/SOF	No	NR	Male	Black	62	1a	Naive	YES	No	No	No	No	Lack of efficacy	43
LDV/SOF	No	NR	Male	Black	64	1a	Naive	NO	No	No	No	No	Non-compliance	37
LDV/SOF	No	RELAPSE	Male	Black	61	1a	Naive	YES	No	No	Yes	No	Complete	85

VBT- viral breakthrough, NR- non-response, Tx- treatment, RAS- resistance associated substitution

Supplemental Table 3a. Sustained Virological Response 12 (SVR12) by RAS Location for patients with HCV genotype 1a infection by randomized treatment arm.

	Treatment Regimen														
	EBR/GZR (400)			EBR/GZR/RBV, 16wks (37)			EBR/GZR/RBV, Other Duration (8)			SOF/LDV (248)			SOF/LDV/RBV (12)		
RAS Position Criteria[a]	N[b]	n (%)[c]	95% Conf. Int.[d]	N[b]	n (%)[c]	95% Conf. Int.[d]	N[b]	n (%)[c]	95% Conf. Int.[d]	N[b]	n (%)[c]	95% Conf. Int.[d]	N[b]	n (%)[c]	95% Conf. Int.[d]
With Baseline RAS at Any Location (28, 30, 31, or 93)	4	4 (100.0%)	(39.8, 100.0)	34	31 (91.2%)	(76.3, 98.1)	4	3 (75.0%)	(19.4, 99.4)	24	23 (95.8%)	(78.9, 99.9)	4	3 (75.0%)	(19.4, 99.4)
With Baseline RAS at Location 28	4	4 (100.0%)	(39.8, 100.0)	20	20 (100.0%)	(83.2, 100.0)	3	3 (100.0%)	(29.2, 100.0)	10	10 (100.0%)	(69.2, 100.0)	1	1 (100.0%)	(2.5, 100.0)
-but not at Locations 30, 31, or 93	4	4 (100.0%)	(39.8, 100.0)	16	16 (100.0%)	(79.4, 100.0)	2	2 (100.0%)	(15.8, 100.0)	8	8 (100.0%)	(63.1, 100.0)	0	0 (0.0%)	--
With Baseline RAS at Location 30	0	0 (0.0%)	--	8	7 (87.5%)	(47.3, 99.7)	0	0 (0.0%)	--	5	5 (100.0%)	(47.8, 100.0)	2	1 (50.0%)	(1.3, 98.7)
-but not at Locations 28, 31, or 93	0	0 (0.0%)	--	2	2 (100.0%)	(15.8, 100.0)	0	0 (0.0%)	--	2	2 (100.0%)	(15.8, 100.0)	0	0 (0.0%)	--
With Baseline RAS at Location 31	0	0 (0.0%)	--	3	1 (33.3%)	(0.8, 90.6)	0	0 (0.0%)	--	7	6 (85.7%)	(42.1, 99.6)	1	1 (100.0%)	(2.5, 100.0)
-but not at Locations 28, 30, or 93	0	0 (0.0%)	--	3	1 (33.3%)	(0.8, 90.6)	0	0 (0.0%)	--	7	6 (85.7%)	(42.1, 99.6)	1	1 (100.0%)	(2.5, 100.0)
With Baseline RAS at Location 93	0	0 (0.0%)	--	10	9 (90.0%)	(55.5, 99.7)	2	1 (50.0%)	(1.3, 98.7)	5	5 (100.0%)	(47.8, 100.0)	2	1 (50.0%)	(1.3, 98.7)
-but not at Locations 28, 30, or 31	0	0 (0.0%)	--	6	6 (100.0%)	(54.1, 100.0)	0	0 (0.0%)	--	4	4 (100.0%)	(39.8, 100.0)	1	1 (100.0%)	(2.5, 100.0)
Without Baseline RAS at Any Location	393	373 (94.9%)	(92.2, 96.9)	2	1 (50.0%)	(1.3, 98.7)	3	3 (100.0%)	(29.2, 100.0)	223	219 (98.2%)	(95.5, 99.5)	8	8 (100.0%)	(63.1, 100.0)
Inconclusive RAS Test Result	3	3 (100.0%)	(29.2, 100.0)	1	1 (100.0%)	(2.5, 100.0)	0	0 (0.0%)	--	1	1 (100.0%)	(2.5, 100.0)	0	0 (0.0%)	--

[a] Subject could have baseline NS5A RASs in more than one position and would be counted in each one
[b] Number of subjects with virologic outcome
[c] Number of subjects achieving SVR12
[d] Based on the Clopper-Pearson (Exact) method

Supplemental Table 3b. Sustained Virological Response 12 by specific RAS location in patients with HCV genotype 1b infection and viral outcome by randomized treatment arm

	Treatment Regimen											
	EBR/GZR (140)			EBR/GZR/RBV, 16wks (1)			SOF/LDV (96)			SOF/LDV/RBV (3)		
RAS Position Criteria[a]	**N[b]**	**n (%)[c]**	**95% Conf. Int.[d]**	**N[b]**	**n (%)[c]**	**95% Conf. Int.[d]**	**N[b]**	**n (%)[c]**	**95% Conf. Int.[d]**	**N[b]**	**n (%)[c]**	**95% Conf. Int.[d]**
With Baseline RAS at Any Location (28, 30, 31, or 93)	11	8 (72.7%)	(39.0, 94.0)	1	1 (100.0%)	(2.5, 100.0)	17	14 (82.4%)	(56.6, 96.2)	2	2 (100.0%)	(15.8, 100.0)
With Baseline RAS at Location 28	1	1 (100.0%)	(2.5, 100.0)	0	0 (0.0%)	--	1	1 (100.0%)	(2.5, 100.0)	1	1 (100.0%)	(2.5, 100.0)
-but not at Locations 30, 31, or 93	1	1 (100.0%)	(2.5, 100.0)	0	0 (0.0%)	--	1	1 (100.0%)	(2.5, 100.0)	1	1 (100.0%)	(2.5, 100.0)
With Baseline RAS at Location 31	2	2 (100.0%)	(15.8, 100.0)	0	0 (0.0%)	--	8	6 (75.0%)	(34.9, 96.8)	1	1 (100.0%)	(2.5, 100.0)
-but not at Locations 28, 30, or 93	2	2 (100.0%)	(15.8, 100.0)	0	0 (0.0%)	--	5	4 (80.0%)	(28.4, 99.5)	0	0 (0.0%)	--
With Baseline RAS at Location 93	8	5 (62.5%)	(24.5, 91.5)	1	1 (100.0%)	(2.5, 100.0)	11	9 (81.8%)	(48.2, 97.7)	1	1 (100.0%)	(2.5, 100.0)
-but not at Locations 28, 30, or 31	8	5 (62.5%)	(24.5, 91.5)	1	1 (100.0%)	(2.5, 100.0)	8	7 (87.5%)	(47.3, 99.7)	0	0 (0.0%)	--
Without Baseline RAS at Any Location	125	124 (99.2%)	(95.6, 100.0)	0	0 (0.0%)	--	75	74 (98.7%)	(92.8, 100.0)	1	1 (100.0%)	(2.5, 100.0)
Inconclusive RAS Test Result	4	4 (100.0%)	(39.8, 100.0)	0	0 (0.0%)	--	4	4 (100.0%)	(39.8, 100.0)	0	0 (0.0%)	--

[a] Subject could have baseline NS5A RASs in more than one position and would be counted in each one
[b] Number of subjects with virologic outcome
[c] Number of subjects achieving SVR12
[d] Based on the Clopper-Pearson (Exact) method

Supplemental Table 4. Baseline characteristics of treated participants as randomized to EBR/GZR LDV/SOF and PrOD (Phase 1 Population)

	EBR/GZR	**LDV/SOF**	**PrOD**
Participants who started treatment n	147	111	147
Age, years mean (range)	54.3 (22.0-79.0)	56.2 (23.0-82.0)	56.3 (23.0-86.0)
Sex n (%)			
Female	48 (32.7)	44 (39.6)	51 (34.7)
Male	99 (67.3)	67 (60.4)	96 (65.3)
Race n (%)			
White	70 (47.6)	65 (58.6)	81 (55.1)
Black	65 (44.2)	41 (36.9)	59 (40.1)
Other	12 (8.2)	5 (4.5)	7 (4.8)
HCV GT1 Subtype n (%)			
1a	106 (72.1)	75 (67.6)	105 (71.4)
1b	41 (27.9)	36 (32.4)	42 (28.6)
Cirrhosis n (%)			
yes	23 (15.6)	22 (19.8)	24 (16.3)
no	124 (84.4)	89 (80.2)	123 (83.7)
NS5a RAS n (%)			
RAS at any 28/30/31/93	19 (12.9)	14 (12.6)	22 (15.0)
RAS at 28 only	6 (4.1)	1 (0.9)	9 (6.1)
RAS at 30 only	4 (2.7)	2 (1.8)	3 (2.0)
RAS at 31 only	3 (2.0)	7 (6.3)	6 (4.1)
RAS at 93 only	8 (5.4)	7 (6.3)	7 (4.8)
Ribavirin administration n (%)			
yes	13 (8.8)	6 (5.4)	99 (67.3)
no	134 (91.2)	105 (94.6)	48 (32.7)
HIV co-infection n (%)			
yes	22 (3.1)	13 (3.0)	5 (3.4)
no	678 (96.9)	415 (97.0)	142 (96.6)
Hepatocellular carcinoma history			
yes	6 (4.1)	3 (2.7)	5 (3.4)
no	140 (95.2)	108 (97.3)	142 (96.6)
Type of health insurance n (%)			
Medicaid	55 (37.4)	21 (18.9)	51 (34.7)
Medicare	33 (22.4)	28 (25.2)	33 (22.4)
Commercial	54 (36.7)	51 (45.9)	54 (36.7)
Other	5 (3.4)	11 (9.9)	9 (6.1)
Platelets (x1000/ml) mean (range)	216.2 (73.0-426.0)	218.5 (79.0-446.0)	215.9 (52.0-434.0)

Phase 1- all patients randomized up to the last patient randomized to PROD (1/4/17)

HCV = hepatitis C virus, RAS = NS5A resistance-associated substitutions, EBR/GZR = elbasvir/grazoprevir, LDV/SOF = ledipasvir/sofosbuvir.

Supplemental Table 5a. Exploration of subgroup differences based on unadjusted SVR12 frequencies- Phase 1 Population -- EBR/GZR vs. PrOD

		EBR/GZR[1]		PrOD[1]	EBR/GZR vs. PrOD
Sub-population	**n/N**	**Percentage (CI)**	**n/N**	**Percentage (CI)**	**Difference (CI)**
Overall	**117/123**	**95.1 [89.7, 98.2][2]**	**119/122**	**97.5 [93, 99.5] [2]**	**-2.4 [-7.9, 2.8]**
With RBV	9/10	90.0 [55.5, 99.7]	77/80	96.3 [89.4, 99.2]	-6.3 [-36.8, 4.4]
Without RBV	108/113	95.6 [90,98.5]	42/42	100 [91.6, 100]	-4.4 [-9.9, 4.4]
Black	56/57	98.2 [90.6, 100]	44/47	93.6 [82.5, 98.7]	4.6 [-4, 15.5]
Non-black	61/66	92.4 [83.2,97.5]	75/75	100 [95.2, 100]	-7.6 [-16.6, -1.1]
Prior HCV treatment	17/19	89.5 [66.9, 98.7]	16/16	100 [79.4, 100]	-10.5 [-31.4, 10.3]
No prior HCV treatment	100/104	96.2 [90.4, 98.9]	103/106	97.2 [92.0, 99.4]	-1.0 [-6.9, 4.7]
Male	78/81	96.3 [89.6, 99.2]	80/83	96.4 [89.8, 99.2]	-0.1 [-7.1, 6.8]
Female	39/42	92.9 [80.5, 98.5]	39/39	100 [91.0, 100]	-7.1 [-19, 3]
GT 1a	83/89	93.3 [85.9, 97.5]	81/84	96.4 [89.9, 99.3]	-3.2 [-10.7, 4.2]
GT 1b	34/34	100 [89.7, 100]	38/38	100 [90.7, 100]	0.0
Cirrhosis	19/19	100 [82.4, 100]	23/23	100 [85.2, 100]	0.0
No Cirrhosis	98/104	94.2 [87.9, 97.9]	96/99	97 [91.4, 99.4]	-2.7 [-9.3, 3.6]
NS5a RAS	12/13	92.3 [64.0, 99.8]	18/19	94.7 [74.0, 99.9]	-2.4 [-28.4, 18.0]
No NS5a RAS	104/109	95.4 [89.6, 98.5]	94/95	98.9 [94.3, 100]	-3.5 [-9.3, 1.8]

EBR/GZR = elbasvir/grazoprevir, PrOD= paritaprevir/ritonavir/ombitasvir + dasabuvir, RAS = NS5A resistance-associated substitutions, RBV = ribavirin

1 As assigned by randomization; Phase 1- all patients randomized up to the last patient randomized to PrOD (1/4/17)

2 95% Confidence Intervals (CI) were computed via the Wilson score method

mITT without imputation

Supplemental Table 5b. Exploration of subgroup differences based on unadjusted SVR12 frequencies- Phase 1 Population – LDV/SOF vs. PrOD

		LDV/SOF[1]		PrOD[1]	LDV/SOF vs. PrOD
Sub-population	**Counts**	**Percentage (CI)**	**Counts**	**Percentage (CI)**	**Difference (CI)**
Overall	**94/98**	**95.9 [89.9, 98.9] [2]**	**119/122**	**97.5 [93, 99.5] [2]**	**-1.6 [-7.8, 3.5]**
With RBV	6/6	100 [54.1, 100]	77/80	96.3 [89.4, 99.2]	3.8 [-35.4, 10.5]
Without RBV	88/92	95.7 [89.2, 98.8]	42/42	100 [91.6, 100]	-4.3 [-10.7, 4.4]
Black	37/39	94.9 [82.7, 99.4]	44/47	93.6 [82.5, 98.7]	1.3 [-11.2, 12.7]
Non-black	57/59	96.6 [88.3, 99.6]	75/75	100 [95.2, 100]	-3.4 [-11.5, 2.1]
Trt Experienced	18/18	100 [81.5, 100]	16/16	100 [79.4, 100]	0.0 [-0.2, 0.2]
Trt Naive	76/80	95 [87.7, 98.6]	103/106	97.2 [92, 99.4]	-2.2 [-9.6, 3.8]
Male	55/59	93.2 [83.5, 98.1]	80/83	96.4 [89.8, 99.2]	3.2 [-4.5, 12.9]
Female	39/39	100 [91.0, 100]	39/39	100 [91, 100]	0.0 [-0.1, 0.1]
GT 1a	64/66	97 [89.5, 99.6]	81/84	96.4 [89.9, 99.3]	-0.5 [-7.3, 7.2]
GT 1b	30/32	93.8 [79.2, 99.2]	38/38	100 [90.7, 100]	6.3 [-4, 20.1]
Cirrhosis	17/18	94.4 [72.7, 99.9]	23/23	100 [85.2, 100]	-5.6 [-25.8, 9.5]
No Cirrhosis	77/80	96.3 [89.4, 99.2]	96/99	97 [91.4, 99.4]	-0.7 [-7.7, 5.3]
NS5a RAS	11/12	91.7 [61.5, 99.8]	18/19	94.7 [74.0, 99.9]	-3.1 [-30.5, 17.5]
No NS5a RAS	79/82	96.3 [89.7, 99.2]	94/95	98.9 [94.3, 100]	-2.6 [-9.2, 2.6]

1 As assigned by randomization; Phase 1- all patients randomized up to the last patient randomized to PROD (1/4/17)

2 95% Confidence Intervals (CI) were computed via the Wilson score method

Trt=treatment

Supplemental Table 6. All Adverse Events with Prevalence Exceeding 10% By Treatment Regimen – Phase 1 Population

	EBR/GZR			LDV/SOF			PrOD			OVERALL		
	RBV	NoRBV	ALL	RBV	NoRBV	ALL	RBV	NoRBV	ALL	RBV	NoRBV	ALL
	(13)	(138)	(151)[2]	(6)	(102)	(108)[3]	(99)	(47)	(146)	(118)	(287)	(405)
N Patients-*any AE*	**13 (100%)**	**76 (55%)**	**89 (59%)**	**3 (50%)**	**58 (57%)**	**61 (56%)**	**74 (75%)**	**30 (64%)**	**104 (71%)**	**90 (76%)**	**164 (57%)**	**254 (62%)**
Fatigue	6 (46%)	20 (14%)	26 (17%)	2 (33%)	21 (21%)	23 (21%)	35 (35%)	5 (11%)	40 (27%)	43 (36%)	46 (16%)	89 (22%)
Headache	5 (38%)	18 (13%)	23 (15%)	1 (17%)	21 (21%)	22 (20%)	15 (15%)	9 (19%)	24 (16%)	21 (18%)	48 (17%)	69 (17%)
Nausea	5 (38%)	0 (0%)	18 (12%)	1 (17%)	11 (11%)	12 (11%)	23 (23%)	5 (11%)	28 (19%)	29 (25%)	29 (10%)	58 (14%)
Anemia	4 (31%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	20 (20%)	0 (0%)	20 (14%)	24 (20%)	0 (0%)	24 (5.9%)
Diarrhea	0 (0%)	0 (0%)	0 (0%)	2 (33%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	7 (5.9%)	14 (4.9%)	21 (5.2%)
Insomnia	0 (0%)	0 (0%)	0 (0%)	1 (17%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	10 (8.5%)	10 (3.5%)	20 (4.9%)
Dyspnea	4 (31%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	13 (11%)	5 (1.7%)	18 (4.4%)
Vomiting	2 (15%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	10 (8.5%)	5 (1.7%)	15 (3.7%)
Cough	2 (15%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	5 (4.2%)	8 (2.8%)	13 (3.2%)
Arthralgia	0 (0%)	0 (0%)	0 (0%)	1 (17%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Chest pain	0 (0%)	0 (0%)	0 (0%)	1 (17%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Abdominal pain upper	0 (0%)	0 (0%)	0 (0%)	1 (17%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Nasal congestion	0 (0%)	0 (0%)	0 (0%)	1 (17%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Musculoskeletal pain	0 (0%)	0 (0%)	0 (0%)	1 (17%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Tremor	0 (0%)	0 (0%)	0 (0%)	1 (17%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

[1]As Treated Population
[2] Includes four patients randomized to LDV/SOF and treated with EBR/GZR
[3]Includes one patient randomized to PrOD and treated with LDV/SOF
Treatment emergent AEs from treatment start to ≤ 31 days post EOT
AE= adverse event, EBR/GZR = elbasvir/grazoprevir, LDV/SOF = ledipasvir/sofosbuvir, PrOD= paritaprevir/ritonavir/ombitasvir + dasabuvir, RBV=Ribavirin

Supplemental Table 7. Probabilities of Patient-Reported Non-Adherence for the Study Population as Treated- EBR/GZR vs LDV/SOF

	EBR/GZR (n=720)[a]	LDV/SOF (n=409)[a]	Difference
	P[b] C.I.[c]	P[b] C.I.[c]	P[b] C.I.[c]
Both Surveys[d]	0.20 (0.16, 0.23)	0.16 (0.12, 0.21)	0.03 [-0.02, 0.08][e]
First Adherence Survey[f]	0.16 (0.13, 0.20)	0.16 (0.11, 0.21)	0.01 (-0.05, 0.06)
Second Adherence Survey[f]	0.23 (0.18, 0.27)	0.16 (0.11, 0.22)	0.06 (0.00, 0.13)

[a] Number of participants who started treatment

[b] Non-Adherence probability estimates controlling for cirrhosis status, viral genetic subtype, and survey event

[c] 95% confidence interval

[d] Based on longitudinal generalized linear model

[e] P-value = 0.2027 for the null hypothesis of no difference between treatment regimens in the target population

[f] Cross sectional linear models

Supplemental Table 8. Probabilities of Patient-Reported Non-Adherence for the Study Population as Treated –Phase 1 Population

	EBR/GZR (151)[a]	LDV/SOF (108)[a]	PrOD (146)[a]	Difference (EBR/GZR vs.SOF/LDV)	Difference (LDV/SOF vs.PrOD)	Difference (EBR/GZR vs.PrOD)
	P[b] C.I.[c]	P[b] C.I.[c]	P[b] C.I.[c]	P[b] C.I.[d]	P[b] C.I.[d]	P[b] C.I.[d]
Both Surveys[e]	0.23 (0.17, 0.29)	0.19 (0.10, 0.27)	0.26 (0.19 0.33)	0.04 (-0.08, 0.16)[g]	-0.07 (-0.20, 0.05)[h]	-0.03 (-0.14 0.07)[i]
First Adherence Survey[f]	0.16 (0.09, 0.23)	0.16 (0.07, 0.24)	0.21 (0.13, 0.29)	0.00 (-0.12, 0.13)	-0.05 (-0.18,0.07)	-0.05 (-0.17, 0.06)
Second Adherence Survey[f]	0.27 (0.18, 0.36)	0.20 (0.09(), 0.30)	0.29 (0.19, 0.38)	0.07 (-0.09, 0.24)	-0.09 (-0.26, 0.08)	-0.02 (-0.18, 0.13)

Phase 1- all patients randomized up to the last patient randomized to PROD (1/4/17)

[a] Number of participants who started treatment
[b] Non-Adherence probability estimates controlling for cirrhosis status, viral genetic subtype, and survey event
[c] 95% confidence interval, unadjusted
[d] 95% confidence interval, Bonferroni-adjusted
[e] Based on longitudinal generalized linear model
[f] Based on cross-sectional generalized linear model
[g] P-value = 0.4052 for the null hypothesis of no difference between treatment regimens EBR/GZR and SOF/LDV in the target population
[h] P-value = 0.1517 for the null hypothesis of no difference between treatment regimens SOF/LDV and PrOD in the target population
[i] P-value = 0.4569 for the null hypothesis of no difference between treatment regimens EBR/GZR and PrOD in the target population

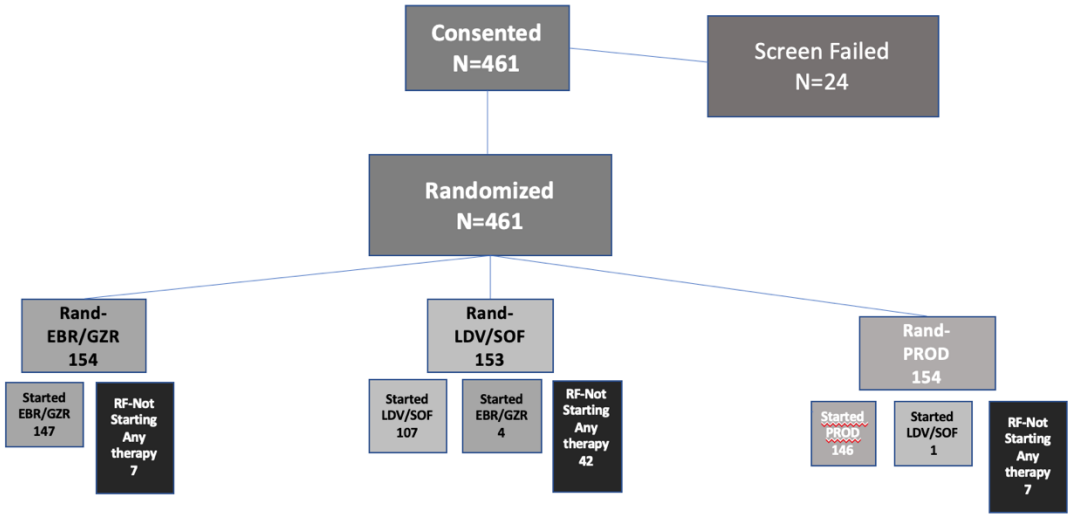
Supplemental Table 9. SVR Proportions Among Adherent and Non-Adherent mITT Population Excluding Subjects with Missing Virologic Outcome- EBR/GZR & LDV/SOF Population

Survey Event	Status	SVR Proportion	95% CI	
T1	Non-adherent	0.959	0.923	0.994
T1	Adherent	0.962	0.947	0.978
T2	Non-adherent	0.949	0.912	0.986
T2	Adherent	0.967	0.951	0.982

Supplemental Table 10. SVR Proportions Among Adherent and Non-Adherent mITT Population Excluding Subjects with Missing Virologic Outcome- Phase 1 Population

Survey Event	Status	SVR Proportion	95% CI	
T1	Non-adherent	0.952	0.888	1.000
T1	Adherent	0.957	0.930	0.983
T2	Non-adherent	0.955	0.904	1.000
T2	Adherent	0.960	0.930	0.989

Supplemental Figure 1. Consort diagram - Phase 1 Population

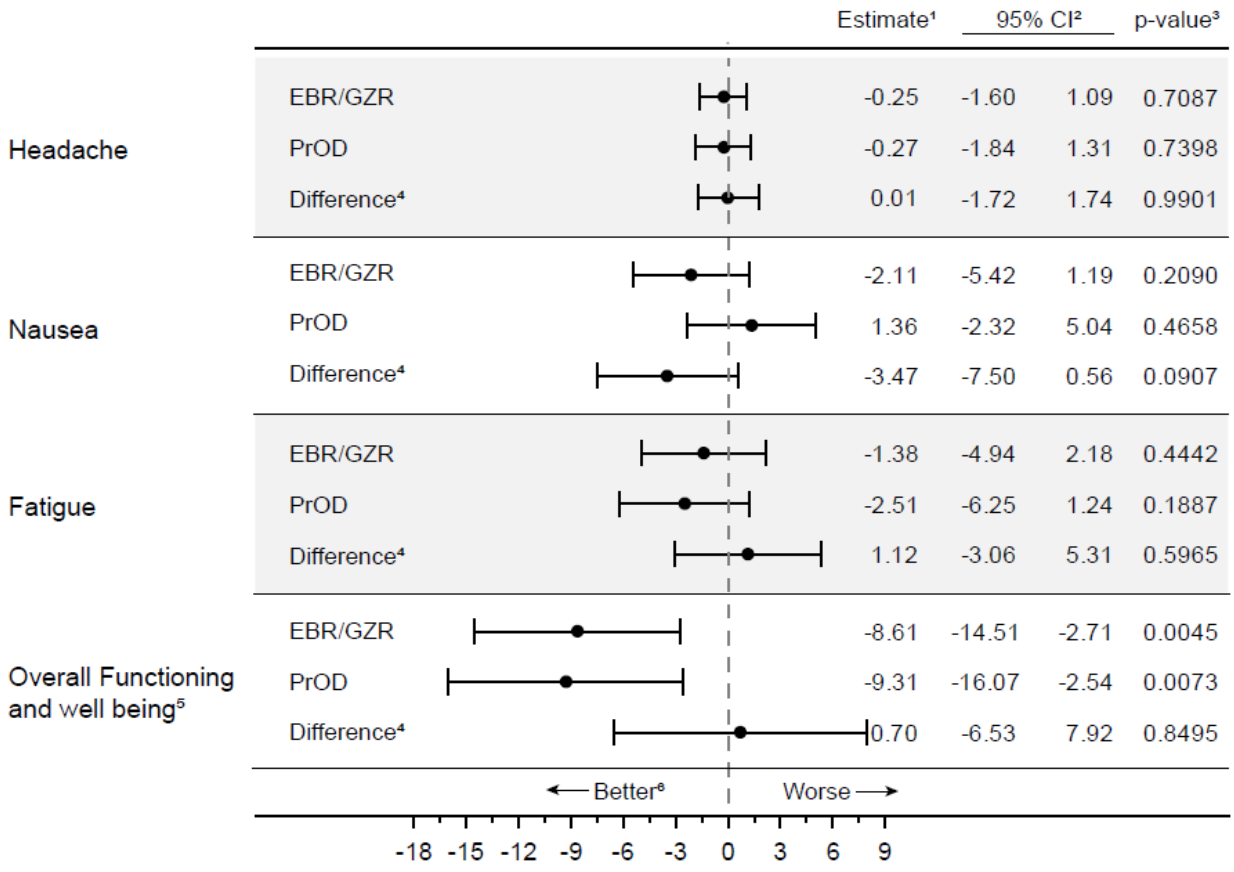


Randomization Failures: 61

- *Not starting any therapy- 56*
- *Starting therapy different from randomized and followed in PRIORITIZE- 5*

Supplemental Figure 2a. Mean Change in PRO Scores from Baseline to On-Treatment-

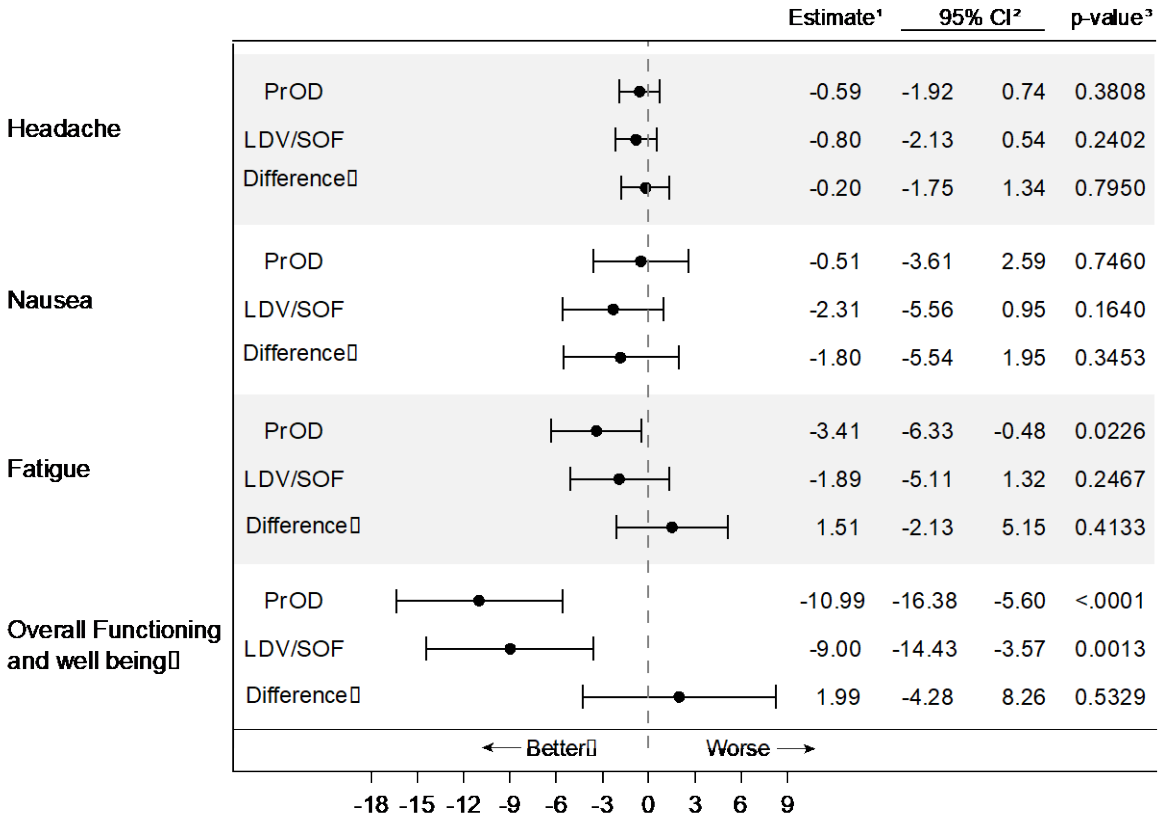
Phase 1 Population-- EBR/GZR vs. PrOD



[1] The estimates of mean change and differences were obtained from a constrained longitudinal linear mixed-effects model that treated the baseline score as one of the outcomes. The model expressed mean score as a function of DAA regimen, cirrhosis status, HCV genotype, sex, age, race, and previous treatment status.
[2] 95% confidence interval estimate
[3] p-value for a test of the null hypothesis "the parameter is zero in the target population"
[4] Difference of the mean change for EBR/GZR minus the mean change for PrOD
[5] The scale for function and well-being is reversed (=100-HCV-PRO) for directional consistency with symptom scores
[6] The scale for "Headache" is the HIT-6 score. The scale for "Nausea" is the PROMIS® Nausea Short Form T-score. The scale for "Fatigue" is the PROMIS® Fatigue Short Form T-score. Negative values for mean change represent improvement, while negative values for 'Difference' indicate that EBR/GZR performed better than PrOD.

Supplemental Figure 2b. Mean Change in PRO Scores from Baseline to On-Treatment-

Phase 1 Population – LDV/SOF vs. PrOD



[1] The estimates of mean change and differences were obtained from a constrained longitudinal linear mixed-effects model that treated the baseline score as one of the outcomes. The model expressed mean score as a function of DAA regimen, cirrhosis status, HCV genotype, sex, age, race, and previous treatment status.
[2] 95% confidence interval estimate
[3] p-value for a test of the null hypothesis "the parameter is zero in the target population"
[4] Difference of the mean change for LDV/SOF minus the mean change for PrOD
[5] The scale for function and well-being is reversed (=100-HCV-PRO) for directional consistency with symptom scores
[6] The scale for "Headache" is the HIT-6 score. The scale for "Nausea" is the PROMIS® Nausea Short Form T-score. The scale for "Fatigue" is the PROMIS® Fatigue Short Form T-score. Negative values for mean change represent improvement, while negative values for 'Difference' indicate that LDV/SOF performed better than PrOD.