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Supplemental information

Sofosbuvir plus velpatasvir for 8 weeks in patients with acute hepatitis C: The HepNet acute HCV-V study

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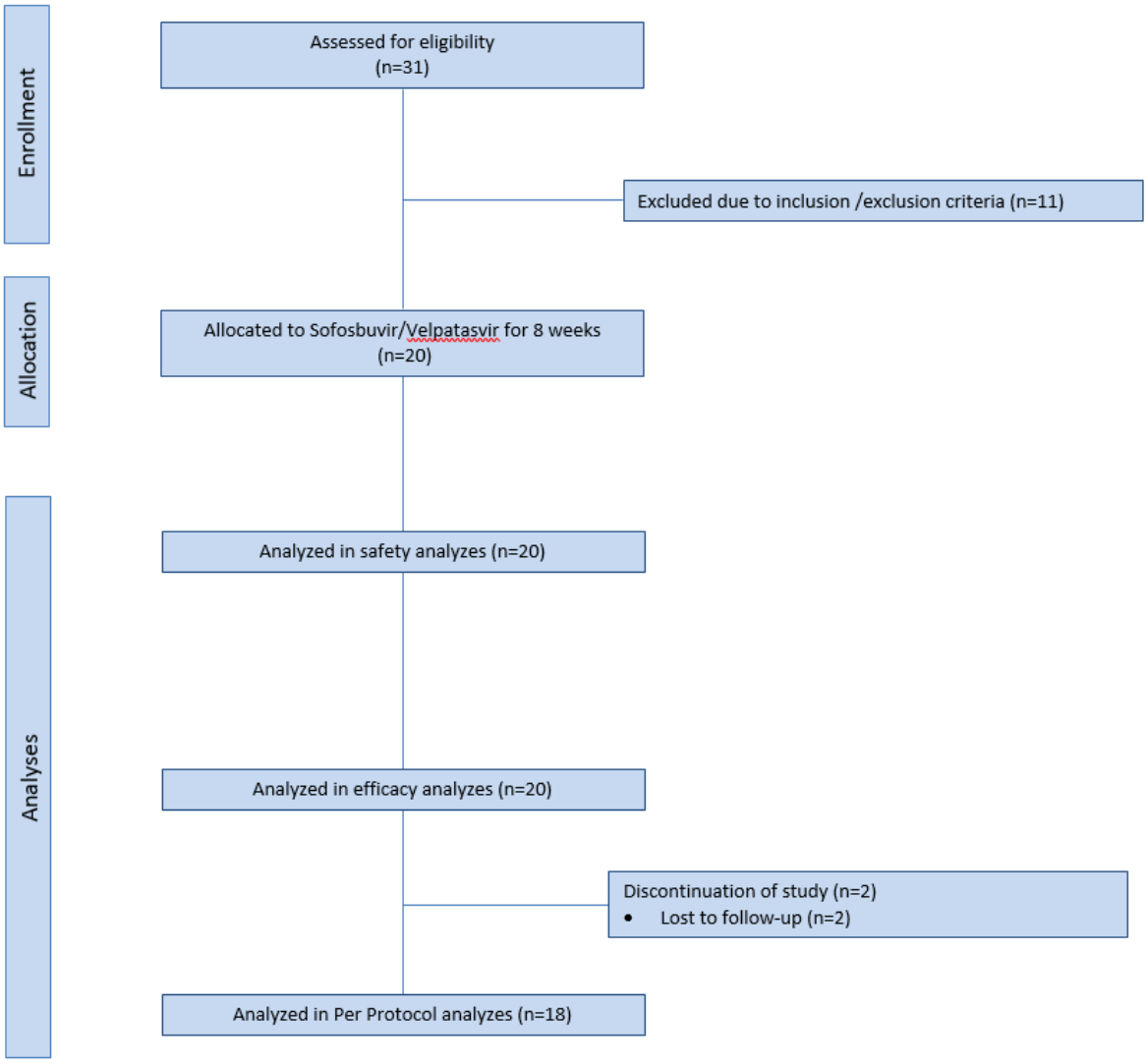

Fig. S1. Consort chart of patient population

Table S1. Detailed inclusion and exclusion criteria

Inclusion criteria:

1. Willing and able to provide written informed consent
2. Male or female, age ≥ 18 years
3. HCV RNA > 10^3 IU/mL at screening
4. Confirmation of acute HCV infection documented by either:
   a. Documented seroconversion to HCV antibody (anti-HCV) positivity within the 4 months preceding screening
   b. Documented conversion to HCV RNA positivity within the 4 months preceding screening
   c. or known or suspected exposure to HCV within the 4 months preceding screening with 10 times elevated serum ALT level at screening or 4 months preceding screening without evidence of confounding liver disorders
5. Body mass index (BMI) ≥18 kg/m2
6. Subjects must have the following laboratory parameters at screening:
   a. INR ≤ 1.5 x ULN unless subject has known hemophilia or is stable on an anticoagulant regimen affecting INR
   b. HbA1c ≤10%
   c. Creatinine clearance (CLcr) ≥ 30 mL/min, as calculated by the Cockcroft-Gault equation (using actual body weight)
7. A negative serum pregnancy test is required for female subjects (unless surgically sterile or women ≥ 54 years of age with cessation for 24 ≥ months of previously occurring menses). Complete abstinence from intercourse. Periodic abstinence (e.g., calendar, ovulation, symptothermal, post-ovulation methods) is not permitted.

   Or

   Consistent and correct use of 1 of the following methods of birth control listed below, in addition to a male partner who correctly uses a condom, from the date of Screening until the end of FU:

   - intrauterine device (IUD) with a failure rate of < 1% per year
   - tubal sterilization
   - vasectomy in male partner
   - hormone-containing contraceptive:
     - implants of progestogen-only hormonal contraception associated with inhibition of ovulation
     - injectable progestogen-only hormonal contraception associated with inhibition of ovulation
     - oral contraceptives (either combined or progestogen-only hormonal contraception associated with inhibition of ovulation)
     - contraceptive vaginal ring
     - transdermal contraceptive patch
8. Subject must be able to comply with the dosing instructions for study drug administration and be able to complete the study schedule of assessments.

Exclusion criteria:

1. Subject has been treated with any investigational drug or device within 42 days of the Screening visit or within 5 half-lives for investigational drugs, whichever is longer
2. Co-Infection with HIV
3. Clinically-significant illness (other than HCV) or any other major medical disorder that, in the opinion of the investigator, may interfere with subject treatment, assessment or compliance with the protocol.
4. Solid organ transplantation
5. Gastrointestinal disorder or post-operative condition that could interfere with the absorption of the study drug (for example, gastric bypass or severe ulcerative colitis).
6. Clinical signs of hepatic decompensation (i.e., clinical ascites, encephalopathy or variceal hemorrhage).
7. Difficulty with blood collection and/or poor venous access for the purposes of phlebotomy.
8. Psychiatric hospitalization, suicide attempt, and/or a period of disability as a result of their psychiatric illness within the last 2 years. Subjects with psychiatric illness that is well-controlled on a stable treatment regimen for at least 12 months prior to screening or has not required medication in the last 12 months may be included.
9. Significant drug allergy (such as anaphylaxis or hepatotoxicity).
10. Pregnant or nursing female
11. Clinically-relevant drug or alcohol abuse that significantly impairs patient compliance. Uncontrolled users of intravenous drugs will not be permitted to enroll in the study.
12. Clinical relevant(not controlled) liver disease of a non-HCV etiology (e.g., hemochromatosis, autoimmune hepatitis, alcoholic liver disease, Wilson's disease, alpha1 antitrypsin deficiency, cholangitis)
13. Use of any prohibited concomitant medications within 21 days before the Baseline/Day 1 visit. The use of amiodarone is prohibited from 60 days prior to Day 1 through the end of treatment
14. Known hypersensitivity to SOF/VEL or formulation excipients.

Table S2. Individual virologic and biochemical kinetics during the study

Patient		**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18**	**19**	**20**
Sex		male	male	male	female	male	male	male	male	male	male	male	male	male	male	male	male	male	male	male	male
Age [y]		42	28	39	31	42	47	31	59	37	31	35	29	25	38	42	26	48	28	45	29
Genotype		1a	1a	1a	1b	2	1a	1a	3	4	4	1a	1a	1a	1a	4	1a	3	3	1a	1a
	SCR	6,33	4,96	4,52	4,80	7,27	3,18	4,09	2,52	3,01	6,99	7,82	5,41	4,25	6,39	3,15	4,37	5,54	3,55	6,06	7,03
	BL	3,89	4,85	4,59	5,46	6,81	1,38	3,84	ND	5,48	7,05	6,90	5,24	5,14	6,47	ND	3,96	5,69	3,90	4,83	7,47
HCV RNA	W2	-	ND	ND	ND	ND	ND	ND	ND	ND	1,52	1,46	ND	ND	ND	ND	ND	1,48	ND	ND	1,73
[log_{10} IU/ml]	W4	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	-	ND	ND	ND	ND	ND	ND	ND	ND
	W8	-	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	FU12	-	-	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	SCR	103	292	351	160	262	65	155	45	86	183	126	300	1045	186	63	729	191	465	779	207
Alanine	BL	474	177	316	1494	121	55	152	38	560	451	1459	361	604	256	56	222	214	427	241	186
amino-	W2	-	29	36	86	35	40	42	32	38	53	199	51	34	29	49	38	34	42	91	46
transferase	W4	16	32	31	21	23	39	37	34	26	29	59	-	23	26	40	31	26	32	90	30
[U/L]	W8	-	28	22	21	20	35	44	-	19	28	54	28	19	24	37	21	21	22	96	26
	FU12	-	-	21	19	19	33	22	31	20	23	22	49	20	25	21	18	18	22	131	29
	SCR	44	78	142	107	116	40	101	32	33	86	75	139	413	104	35	323	95	116	430	97
Aspartate	BL	196	125	140	1106	62	38	97	30	349	238	977	154	293	142	35	62	107	199	108	80
amino-	W2	-	22	30	32	36	36	20	27	28	35	185	37	29	34	32	25	29	31	50	45
transferase	W4	14	26	27	23	26	31	32	29	26	43	39	-	34	43	38	27	27	27	45	33
[U/L]	W8	-	26	25	21	24	32	27	-	18	34	45	-	25	37	37	26	25	22	52	29
	FU12	-	-	26	25	23	29	19	24	24	29	24	44	26	31	23	23	25	30	87	30
	SCR	90	60	82	97	88	88	80	80	75	92	91	83	80	87	84	71	80	68	68	81
	BL	81	57	66	88	71	88	74	85	76	91	83	88	99	95	93	63	77	73	81	88
Creatinine	W2	-	65		80	88	80	79	80	76	95	76	88	100	87	100	73	80	71	79	103
[µmol/L]	W4	79	62	59	97	88	80	75	90	74	96	84	-	78	116	88	64	79	67	70	88
	W8	-	68	82	88	71	71	73	-	72	106	84	82	73	97	89	57	80	71	72	95
	FU12	-	-	79	88	80	80	77	87	82	100	77	100	85	78	78	60	88	75	86	92
	SCR	96	91	360	25	64	78	45	101	39	34	43	154	198	146	91	112	50	159	691	114
Gamma-	BL	158	93	282	135	71	49	37	75	49	40	354	161	135	165	60	54	49	128	485	92
glutamyl-	W2	-	49	151	82	47	40	33	53	33	29	195	72	57	74	39	36	28	61	352	51
transferase	W4	39	35	95	40	35	30	18	41	18	19	71	-	32	40	32	34	17	35	316	25
[U/L]	W8	-	26	30	15	31	23	18	-	12	13	38	-	18	21	24	18	10	20	334	15
	FU12	-	-	24	12	31	17	15	26	11	9	18	13	12	35	19	18	7	16	388	13

Hemoglobin [g/L]	SCR	134	135	153	146	145	154	157	158	154	159	141	136	142	142	162	156	145	142	149	153
	BL	123	140	158	148	137	146	152	156	146	156	137	141	155	136	156	142	146	139	150	161
	W2	-	145	149	141	137	150	160	161	150	159	139	143	148	139	160	143	144	143	151	172
	W4	145	154	159	134	132	149	145	155	151	155	139	-	156	134	154	152	140	131	152	153
	W8	-	155	145	143	153	149	151	-	146	156	147	156	143	127	161	157	130	132	151	161
	FU12	-	-	153	139	131	148	154	146	152	156	135	143	143	140	159	147	139	135	148	167
Platelet count [10^3/µL]	SCR	219	261	347	199	134	234	220	283	176	259	307	345	213	298	222	228	245	238	110	184
	BL	215	212	362	177	167	206	168	329	140	237	208	329	244	321	217	236	246	232	203	180
	W2	-	238	352	246	228	229	206	280	192	234	336	331	243	300	221	296	271	236	175	206
	W4	344	229	406	174	131	237	189	300	178	204	294	-	249	286	219	256	239	230	175	155
	W8	-	226	402	198	154	237	191	-	183	231	265	293	225	303	214	284	298	236	156	160
	FU12	-	-	374	181	135	228	182	297	161	234	339	233	258	342	213	270	233	252	203	155
Bilirubin [µmol/L]	SCR	54	80	14	10	5	10	14	10	9	7	10	10	23	5	10	35	11	10	34	17
	BL	38	23	17	10	5	10	12	7	12	7	17	12	28	6	12	13	8	8	11	26
	W2	-	14	10	9	5	9	21	6	5	9	10	5	29	6	9	23	6	12	8	24
	W4	10	10	14	10	7	10	-	6	7	12	7	-	27	12	13	13	10	10	9	9
	W8	-	4	12	9	14	15	14	-	3	10	15	-	15	10	12	15	8	8	5	10
	FU12	-	-	9	17	3	12	10	6	10	9	3	22	13	8	12	12	7	9	12	9

HCV, hepatitis C virus; RNA, ribonucleid acid; SCR, screening; BL, baseline; W2, week 2; W4, week 4; W8, week 8; FU12, follow up week 12