

Table SI. Clinical characteristics at the start of treatment grouped by sex.

Factor	Female, n=41	Male, n=37	P-value
Age, years ^d	69.15 (13.4)	69.3 (13.4)	0.9601
Hypertension +/- ^e	22/19	22/15	0.6526
Hyperlipidemia +/- ^e	2/39	2/35	0.9999
Diabetes +/- ^e	3/38	4/33	0.7022
HBV none/past ^e	28/13	17/20	0.063
HTLV-1 +/- ^e	5/36	3/34	0.7147
Interferon +/- ^e	3/38	7/30	0.175
Genotype 1/2 ^e	29/12	24/13	0.6924
HCC history +/- ^e	1/40	3/34	0.3406
Alcohol +/- ^e	2/39	5/31	0.17
HCV-RNA, log IU/ml ^d	6.16 (0.71)	5.92 (1.3)	0.96
DAA EG/GP/SOF ^e	13/25/3	12/22/3	0.5521
AST, U/l ^d	35.49 (18.62)	54.27 (45.74)	0.0116 ^a
ALT, U/l ^d	33.1 (27.47)	66.97 (71.42)	0.0015 ^b
γ GTP, U/l ^d	34.76 (32.57)	59.1 (61.93)	0.0025 ^b
Platelet, x10 ⁴ / μ l ^d	19.22 (7.1)	16.5 (5.92)	0.053
Total bilirubin, g/dl ^d	0.7 (0.18)	0.82 (0.511)	0.62
Albumin, g/dl ^d	4.16 (0.33)	4.2 (0.39)	0.8095
Cr, mg/dl ^d	0.653 (0.13)	0.883 (0.218)	<0.0001 ^c
Cr-eGFR, ml/min/1.73 m ^{2d}	71.53 (16.6)	69.68 (18.2)	0.6098
CysC, mg/dl ^d	1.082 (0.278)	1.243 (0.382)	0.0516
CysC-eGFR, ml/min/1.73	64.76 (20.88)	61.25 (23.67)	0.3418
α -fetoprotein, ng/ml ^d	6.52 (7.58)	9.87 (22.27)	0.7754
PIVKA-II, mAU/ml ^d	20.42 (4.82)	27.3 (11.85)	0.0027 ^b
Ferritin, ng/ml ^d	91.03 (88.3)	269.9 (272.7)	<0.0001 ^c
LDL, mg/dl ^d	99.85 (24.62)	101.19 (25.42)	0.638
sdLDL, mg/dl ^d	19.36 (6.97)	21.72 (10.79)	0.5616
%sdLDL ^d	0.192 (0.045)	0.212 (0.08)	0.4682
HDL, mg/dl ^d	66.59 (17.19)	56.11 (12.9)	0.0073 ^b
TG, mg/dl ^d	98.1 (40.82)	107.84 (50.44)	0.4929
HbA1c, % ^d	5.78 (0.86)	5.71 (0.44)	0.5657
HOMA-IR ^d	2.7 (2.46)	4.8 (6.9)	0.1107
HOMA- β ^d	95.27 (81.7)	107.9 (35.5)	0.4895
M2BPGi, COI ^d	2.1 (1.83)	2.73 (2.48)	0.2554
FIB-4 ^d	2.951 (2.128)	3.52 (2.69)	0.1658
FIB-4 H/N ^c	12/29	17/19	0.1047

ALBI ^d	-2.837 (0.269)	-2.829 (0.384)	0.8807
BMI ^d	22.42 (5.91)	23.07 (3.37)	0.0825
CBMM ^d	27.72 (4.37)	38.87 (5.71)	<0.0001 ^c
Grip strength ^d	12.32 (5.93)	25.23 (9.81)	<0.0001 ^c
Lumbar BMD, g/cm ^{2d}	0.724 (0.174)	0.969 (0.198)	<0.0001 ^c
Lumbar t-value ^d	-2.339 (1.47)	-0.64 (1.63)	<0.0001 ^c
Lumbar YAM, g/cm ^{2d}	71.74 (17.37)	92.57 (18.57)	<0.0001 ^c
Femur BMD, g/cm ^{2d}	0.533 (0.111)	0.689 (0.144)	<0.0001 ^c
Femur t-value ^d	-2.33 (1.02)	-1.34 (1.1)	0.0002 ^c
Femur YAM, g/cm ^{2d}	67.66 (14)	80 (16.28)	0.001 ^c
TRACP-5b, mU/dl ^d	463.74 (203.6)	400.8 (151.94)	0.2127
TRACP-5b High/N ^e	19/20	3/33	0.0001 ^c
PINP, ng/ml ^d	61.18 (34.71)	48.83 (27.4)	0.0492 ^a
PINP High/N ^c	6/33	3/33	0.4831
VD, ng/ml ^d	15.86 (5.169)	17.92 (6.31)	0.1215
VD Low/N ^e	29/10	23/13	0.4527
ucOC, ng/ml ^d	6.89 (6.399)	4.223 (6.87)	0.0157 ^b
ucOC High/N ^e	21/20	6/31	0.0017 ^b

^aP<0.05, ^bP<0.01, ^cP<0.001. ^dmean ± standard deviation. ^enumber. The hypertension + group was treated with medication for hypertension, while the - group was not treated. The hyperlipidemia + group was treated with medication for hyperlipidemia, while the - group was not treated. The diabetes + group was treated with medication for diabetes, while the - group was not treated. The hepatitis B (HBV) none group was negative for HBV surface (HBs) antigen, HBs antibody, and HBV core (HBc) antibody, while the past group was negative for HBs antigen and positive for HBs antibody and/or HBc antibody. The human T-lymphotropic virus (HTLV-1) + group is serum anti HTLV-1 antibody positive, - group is seronegative. The interferon + group was treated with interferon for HCV infection, and the - group was not treated. The genotype 1 group was HCV genotype 1b, and genotype 2 was 2a and 2b. The hepatocellular carcinoma (HCC) history + group was treated for HCC before DAA treatment. Alcohol + group was heavy alcohol consumption (>7 drinks per week for women and >14 drinks per week for men). HCV-RNA is presented as Log IU/ml. The EG group was administered elbasvir/grazoprevir, GP was administered glecaprevir/pibrentasvir, SOF was administered sofosbuvir/ribavirin, and sofosbuvir/ledipasvir. The normal range of AST is 10-40 U/l. The normal range of ALT is 5-45 U/l. The normal range of γ GTP is 9-32 U/l. The normal range of platelet counts was 14.0-37.9x10⁴/ μ l. The normal range of albumin is 3.7-5.5 g/dl. The normal range of total bilirubin was 0.3-1.2 mg/dl. The normal range of Cr is 0.65-1.09 (male) and 0.46-0.82 (female) mg/dl. The Cr-based eGFR was ml/min/1.73 m². The normal range of CysC was 0.58-0.87 mg/l (male) and 0.47-0.82 (female) mg/l. CysC-eGFR is presented as ml/min/1.73 m². The normal range of α -fetoprotein level was < 10 ng/ml. The normal range of protein levels induced by PIVKA-II was <40 mAU/ml. The normal range of ferritin was 39.4-340 (male) and 3.6-114 (female) ng/ml. The normal range of LDL is 70-139 mg/dl. sdLDL was evaluated using a commercial kit for patients and methods, and %sdLDL was calculated as follows: sdLDL/LDL. The normal ranges of high density lipoprotein (HDL) were 40-86 mg/dl (male) and 40-96 mg/dl (female). The normal range of TG is 50-149 mg/dl. The normal range of HbA1c is 4.6 %-6.2 %. HOMA-IR and HOMA- β were calculated using fasting blood glucose and insulin levels in patients. The unit of M2BPGi is the cutoff index (COI). FIB-4, ALBI, BMI, and CBMM were calculated in all patients and methods. FIB-4 high (H) group exceeded 3.25. Grip strength was defined as the mean of the grip strengths of both hands. Lumbar bone mineral density (BMD) is the mean of the lumbar spine 2-4 and is

measured in g/cm^2 . The young adult mean (YAM) of the lumbar spine (20–44 years of age) is $1.19 \text{ g}/\text{cm}^2$ in males and $1.12 \text{ g}/\text{cm}^2$ in females. The YAM of femur neck was $0.95 \text{ g}/\text{cm}^2$ in males and $0.90 \text{ g}/\text{cm}^2$ in females. A t -score ≤ -2.5 indicates osteoporosis. The normal range of TRACP-5b was 170–590 mU/dl in males and 120–420 mU/dl in females. The TRACP-5b high group exceeded the upper limit. The normal ranges of total P1NP were 18.1–74.1 ng/ml in males, 16.8–70.1 ng/ml in premenopausal female, and 26.4–98.2 ng/ml in postmenopausal. The P1NP high group exceeded the upper limit. The 25(OH) vitamin D (VD) deficiency (VD Low) group had levels $< 20 \text{ ng}/\text{ml}$. The normal range of ucOC is $< 4.5 \text{ ng}/\text{ml}$. The ucOC high group exceeded the upper limit.

Table SII. Relationship between ducOC and clinical factors.

dFactor	Female		Male	
	R	P-value	R	P-value
d α -fetoprotein	-0.224	0.2363	-0.12	0.5248
dPIVKA-II	-0.229	0.2247	0.583	0.0004
dLDL	-0.12	0.5396	0.022	0.9081
dHDL	-0.004	0.9832	0.028	0.8825
dTG	0.071	0.7117	-0.119	0.5262
dHbA1c	0.023	0.9043	0.551	0.001
dHOMA-IR	-0.039	0.8827	-0.046	0.8062
dHOMA- β	-0.016	0.9329	-0.011	0.9543
dTRACP-5b	0.477	0.0071	0.667	<0.0001
dVD	0.216	0.2546	0.13	0.4875
dM2BPGi	-0.314	0.0917	-0.163	0.3833
dFIB-4	-0.076	0.6917	-0.119	0.5368
dALBI	0.114	0.5521	0.176	0.3466
dCysC	-0.012	0.9435	-0.141	0.5294
dCr	0.028	0.8827	-0.155	0.4086
dCBMM	0.088	0.5867	-0.259	0.1211
dGrip Strength	-0.56	0.0001	0.04	0.8326
dBMI	0.3221	0.0824	-0.109	0.5621
dLumbar BMD	-0.188	0.2615	-0.009	0.9589
dLT	-0.253	0.126	-0.017	0.9234
dFemur BMD	0.017	0.9184	-0.0161	0.359
dFT	-0.288	0.0797	-0.127	0.4704

Data are presented as correlation coefficients (R). dfactor was calculated as follows: factor at start of treatment – factor at 1 year after treatment. d, change in value; FIB-4, fibrosis-4; M2BPGi, Mac-2 binding protein glycosylation isomer; ALBI, albumin-bilirubin grade; PIVKA-II, protein induced by vitamin K absence or antagonist II; Cr, creatinine; eGFR, estimated glomerular filtration rate; CysC, cystatin C; CBMM, calculated body muscle mass; LDL, Low-density lipoprotein; TG, Triglyceride; HbA1c, Hemoglobin A1c; HOMA-IR, Homeostatic model assessment- insulin resistance; TRACP-5b, tartrate-resistant acid phosphatase 5b; VD, vitamin D; ucOC, undercarboxylated osteocalcin; BMD, bone mineral density.