Efficacy and safety of LDV/SOF and GLE/PIB in hepatitis C genotype 1 and 2 infection

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Background/Aims: Ledipasvor/Sofsbuvir (LDV/SOF) is an effective and well-tolerated regimen for the treatment of hepatitis C virus (HCV) genotypes (GT) 1,4,5, and 6. However, there is little data on the effectiveness of LDV/SOF in treating HCV GT-2 infection, compared with glecaprevir/pibrentasvir (GLE/PIB).

Methods: The SVR 12 rate, change in fibrosis index, and adverse events in HCV GT-1 and 2 patients receiving LDV/SOF and GLE/PIB treatments were compared using propensity-score matching (PSM).

Results: The proportion of treatment-naïve patients in each group was 93.3% and 95.7% (P=0.313), respectively. The overall SVR 12 rates of LDV/SOF for 12 weeks and GLE/PIB for 8 weeks were 99.3% (149/150) and 100% (232/232), respectively. We conducted 1:1 PSM to compare changes in the FIB-4 index before and after treatment. The baseline FIB-4 index of LDV/SOF and GLE/PIB (n=142) was 2.9 ± 2.5 and 3.0 ± 2.7, respectively; the FIB-4 index at SVR 12 of each group was 2.4 ± 3.4 and 2.8 ± 2.5, respectively (Table 1). There was a significant difference in FIB-4 index after therapy in the LDV/SOF group (P=0.025). However, the proportion of patients with high FIB-4 before and after therapy showed a significant decrease from 23.9% to 14.3%, respectively in the GLE/PIB group only (P = 0.048) (Table 2).

Conclusions: Fixed doses of LDV/SOF and GLE/PIB are effective and safe treatment options for HCV genotype 1 and 2 infections. Both regimens can also induce rapid decline of fibrosis index upon reaching SVR 12, and GLE/PIB may be more effective in CHC patients with a high FIB-4 index.

Table1. Baseline characteristics of patients in total population and PSM-cohort.

	Total population			PSM-cohort		
Characteristics	LDV/SOF (N=150)	GLE/PIB (N=232)	P-value	LDV/SOF (N=142)	GLE/PIB (N=142)	P-value
Age (years)	62.0 ± 10.9	60.5 ± 11.6	0.181	61.7 ± 10.9	61.1 ± 11.9	0.617
Male sex (%)	68 (45.3)	108 (46.6)	0.816	63 (44.4)	64 (45.1)	1.000
Treatment-Naïve (%)	140 (93.3)	222 (95.7)	0.313	133 (93.7)	133 (93.7)	1.000
Genotype 2	48 (32.0%)	139 (59.9%)	0.001	48 (33.8%)	48 (33.8%)	1.000
DM (%)	26 (17.3)	33 (14.2)	0.412	22 (15.5)	19 (13.4)	0.755
eGFR	94.2 ± 19.0	88.6 ± 30.7	0.029	93.8 ± 18.9	93.2 ± 24.3	0.796
HCV-RNA (log_{10} IU/mL)	6.6±7.0	6.5±6.8	0.706	6.6±6.8	6.5±6.8	0.877
ALT	33.0 ± 26.7	47.6 ± 70.1	0.005	33.6 ± 27.3	31.4 ± 25.4	0.428
Baseline FIB-4	3.4 ± 3.5	2.8 ± 2.3	0.042	3.0 ± 2.7	2.9 ± 2.5	0.782
FIB-4 subclassification			0.203			0.781
FIB-4 >3.25 (%)	48 (32.0)	57 (24.6)		42 (29.6)	39 (27.5)	
1.45 < FIB-4 < 3.25 (%)	68 (45.3)	108 (46.6)		67 (47.2)	65 (45.8)	
FIB-4 < 1.45 (%)	34 (22.7)	67 (28.9)		33 (23.2)	38 (26.8)	
History of HCC (%)	11 (7.3)	16 (6.9)	1.000	10 (7)	7 (4.9)	0.617
Diagnosis (%)						
CHC	109 (72.7)	171 (73.7)	0.822	106 (74.6)	111 (78.2)	0.576
LC	41 (27.3)	61 (26.3)		36 (25.4)	31 (21.8)	

**LDV/SOF, ledipasvir/sofosbuvir; GLE/PIB, glecaprevir/pibrentasvir; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; HCV, hepatitis C virus; ALT, alanine transferase; FIB-4, Fibrosis-4 index for liver fibrosis; HCC, hepatocellular carcinoma; CHC, chronic hepatitis C; LC, liver cirrhosis

Table 2 FIB-4 index changes before and after each DAA treatment in the PSM-cohort

DAA	LDV/SOF (n=142)	GLE/PIB (n=142)	P-value
FIB-4, baseline			0.781
Low FIB-4	33 (23.2%)	38 (26.8%)	
Intermediate FIB-4	67 (47.2%)	65 (45.8%)	
High FIB-4	42 (29.6%)	39 (27.5%)	
FIB-4 at SVR 12			0.119
Low FIB-4	37 (26.1%)	42 (30.0%)	
Intermediate FIB-4	71 (50.0%)	78 (55.7%)	
High FIB-4	34 (23.9%)	20 (14.3%)	

** LDV/SOF, ledipasvir/sofosbuvir; GLE/PIB, glecaprevir/pibrentasvir; FIB-4, Fibrosis-4 index for liver fibrosis; HCC