Real-world effectiveness of ledipsavir/sofosbuvir 8 weeks chronic hepatitis C treatment

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AASLD
AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES
SAN FRANCISCO
NOVEMBER 13 – 17, 2015

PN 1205

INTRODUCTION

- Ledipasvir/Sofosbuvir (LDV/SOF) single tablet regimen (STR) is approved in Europe for chronic hepatitis C (CHC) patients with genotypes (GT) 1, 3 and 4.
- In the ION-3 study 8 weeks (8w) of LDV/SOF was non-inferior to 12w in previously untreated GT1 patients without cirrhosis with no benefit for the addition of ribavirin (RBV).
- According to the European Medicines Agency (EMA) label[1] 8w may be considered in treatment naïve, non-cirrhotic patients.

AIM

- The aim of the present analysis is to characterise the population receiving 8w LDV/SOF and to describe outcomes in clinical practice.

MATERIAL & METHODS

- CHC patients treated with 8w LDV/SOF in a single centre (with SVR results after 12 weeks of follow-up (SVR12) available at end of October 2015) were included in this analysis.
- Baseline characteristics, prior treatment history, safety and effectiveness were investigated.
- HCV RNA was qualitatively measured by Roche COBAS® AmpliPrep/COBAS® TaqMan® with a cut-off of <12 IU/ml. Fibrosis was measured by FibroScan® with cut-off values for METAVIR stage F3 or less of ≤12.3kPa.
- The analysis was performed using descriptive statistics.

Results

- 103 patients met the inclusion criteria and initiated 8w treatment with LDV/SOF between 21/11/2014 to 01/06/2015
- No patients had ribavirin (R) added to the STR
- 97.1% of patients were treatment naïve; 1 patient had previously relapsed to pegIFN + RBV therapy and two patients had a null response to IFN monotherapy
- All patients were non-cirrhotic; two patients had HCV RNA > 6 million IU/mL (7,079,457 and 13,803,842; Metavir stages F2 and F0 respectively)
- 91.5% of patients reported at least one co-morbidity; depression was reported in 16% of those patients
- Evidence of non-adherence, assessed upon the discretion of the investigators and based on patient adherence to schedules / appointments, patient statements and congruence to the prescriptions was reported in 3.9 % of patients.

Table 1. Baseline characteristics

Characteristics	Total 8wk cohort (n=103)
Age, Median (Range)	50 (22 - 77)
Males, n (%)	43 (41.8)
Caucasians, n (%)	103 (100.0)
Genotype, n (%)	
1a	49 (45.6)
1b	52 (50.5)
4	2 (1.9)
Liver disease stage, n (%)	
F0	56 (54.4)
F1	25 (24.3)
F2	17 (16.5)
F3	5 (4.8)
F4	0 (0.0)
Baseline HCV RNA (log10 IU/ml) Median (Q1-3; min-max)	5.94 (5.22 – 6.31; 1.04 – 7.14)
Baseline HCV RNA (UI/ml) Median (Q1-3; min-max)	870,964 (165,959 – 2,041,738; 11 – 13,803,843)
Bilirubin (mg/dL) Median (Q1-3;min-max)	0.5 (0.4 - 0.7; 0.2 - 1.8)
Albumin (g/L) Median (Q1-3;min-max)	39.2 (37.4 – 41.2; 0.4 – 46.2)
Haemoglobin (g/dL) Median (Q1-3;min-max)	14.2 (13.4 - 15.3; 9.9 – 16.9)
Neutrophils (ANC/mm^3) Median (Q1-3;min-max)	3.5 (2.6 – 4.8; 1.5 – 9.8)
Platelets (10^9/L) Median (Q1-3;min-max)	224 (196 - 263; 4 - 426)
Previous treatment status	
Naïve, n (%)	100 (97.1)
Experienced, n (%)	3 (2.9)
Presence of co-infection, n (%)	3 (2.9)
HIV, n (%)	3 (100)
HBV, n (%)	0 (0)
At least one co-morbidity, n (%)	86 (91.5)

RESULTS

- In patients with available outcome data, the full response at 4 weeks of treatment was 100% (n=101/101).
- In patients with available outcome data, the SVR4 was 100% (n=94/94) and SVR12 was 100% (n=103/103).
- In patients with HIV co-infection and available outcome data, the SVR4 was 100% (n=3/3) and SVR12 was 100% (n=3/3).
- 1.9% (n=2) experienced grade 3 or 4 adverse events (AE)
- 1.0% (n=1) experienced AE possibly related to LDV/SOF
- No AE lead to treatment discontinuation or death

Figure 1. Most common co-morbidities (>7%)

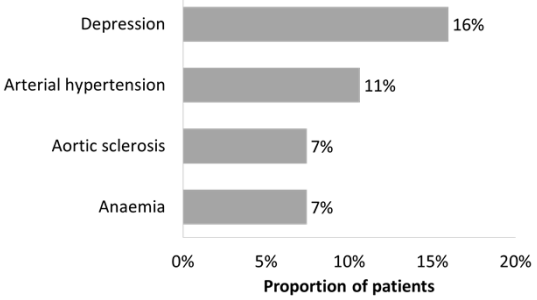
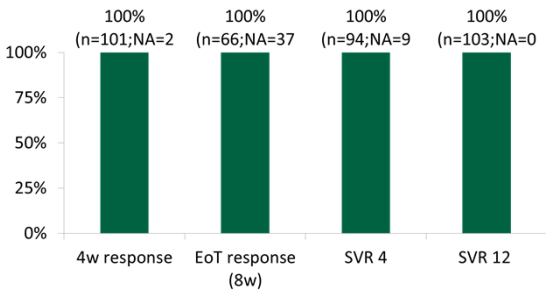


Table 2. Safety

Adverse events	Total cohort (n=103)
Any AEs (Grades 3 & 4), n	2
Headache, n	1
Flu, n	1
AEs 'probably' related to treatment, n	0
AEs 'possibly' related to treatment, n	1
AEs 'probably' related to SOF, n	1
Cephalgia, n	1
AEs 'possibly' related to SOF, n	0
AEs leading to discontinuation, n	0

Figure 2. Effectiveness results



- **Out of the 103 patients, 101 (98%) and 103 (100%) had SVR4 and SVR12 respectively available and all were undetectable. 2% (2/103) and 0% (0/103) of patients had no SVR4 and SVR12 respectively available at time of analysis.**

CONCLUSION

- 8w LDV/SOF is predominantly prescribed according to the EMA label[1] for treatment-naïve non-cirrhotic CHC patients, with the addition of HCV RNA <6 million IU/mL at baseline. The preliminary results of this real world study indicate that in line with clinical trials, an 8-week regimen of LDV/SOF, is a highly effective and well tolerated if used in patients according to the EMA label.

DISCLOSURES

- **P. Buggisch:** Consultant: AbbVie, BMS, Gilead, Janssen, MSD, Novartis, Roche. Sponsored Lectures (National and International): Abbott, BMS, Gilead, Janssen, MSD, Merz, Novartis, Roche. Other: Clinical studies: AbbVie, BMS, Gilead, Janssen, MSD, Novartis, Roche, Siemens.
- This study was funded by Gilead

References

1 http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-Product_Information/human/003850/WC500177995.pdf

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