

# Sofosbuvir-Based Therapy in Patients with Chronic Hepatitis C Virus Infection and Malignancies

## A Prospective Observational Study of 60 Patients

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### BACKGROUND & AIMS

- Sofosbuvir (SOF)-based therapy (SOFBT) is widely used in patients with Hepatitis C virus (HCV) infection.
- We evaluated the efficacy and safety of SOFBT in infected patients with various types of malignancies, a population lacking treatment guidelines.

### METHODS

- In this prospective observational study, infected cancer patients who received SOFBT between 01/2014 and 06/2015 were analyzed.
- Patients were divided into 4 groups:
  - SOF+ peg-interferon (PEG-IFN)+ ribavirin (RBV)
  - SOF+ RBV
  - SOF+ simeprevir (SIM)
  - SOF/ledipasvir (LDV)
- Efficacy was assessed by intention-to-treat (ITT) analysis based on sustained virological response 12 weeks after finishing SOFBT (SVR12). A post-hoc per protocol analysis was performed on patients who completed 12 weeks of follow-up.
- Poor compliance (>2 missed visits), adverse events (AEs) and clinically significant drug-drug interactions (DDIs) were analyzed.
- AEs were graded according to the division of AIDS Table for Grading the Severity of Adult and Pediatric Adverse Events (version 2.0, November 2014).

### RESULTS

- Sixty patients were enrolled. The demographic and HCV characteristics of such patients are depicted in Table 1.

Table 1. Demographic and viral characteristics.

Groups	SOF+PEG-IFN+RBV	SOF+RBV	SOF+SIM	SOF/LDV <sup>1</sup>
Patients, N (%)	9 (15)	19 (32)	18 (30)	14 (23)
<b>Demographics</b>				
Male sex, n (%)	5 (56)	14 (74)	13 (72)	9 (64)
<b>Race</b>				
White	4 (44)	13 (68)	10 (56)	6 (43)
Non-white	5 (56)	6 (32)	8 (44)	8 (57)
Age, median (range)	56 (48-64)	57 (52-68)	60 (56-64)	62 (58-67)
rs12979860 genotype <sup>2</sup>	9/9	16/19	13/18	5/14
CC	2/9 (22)	7/16 (44)	1/13 (8)	2/5 (40)
CT	4/9 (44)	7/16 (44)	9/13 (69)	2/5 (40)
TT	3/9 (33)	2/16 (13)	3/13 (23)	1/5 (20)
<b>HCV characteristics</b>				
<b>HCV genotype</b>				
1	9 (100)	3 (16)	18 (100)	13 (93)
2	0 (0)	10 (53)	0 (0)	0 (0)
3	0 (0)	4 (21)	0 (0)	0 (0)
4	0 (0)	0 (0)	0 (0)	0 (0)
Mixed <sup>3</sup>	0 (0)	2 (11)	0 (0)	1 (7)
Baseline log HCV RNA, median (range)	6.3 (4.7-6.6)	6.1 (4-6.7)	6.1 (3.7-6.6)	6 (3.1-6.8)
<b>History of antiviral treatment<sup>4</sup></b>				
Naïve	7 (78)	15 (79)	10 (56)	12 (86)
Experienced	2 (22)	4 (21)	8 (44)	2 (14)
Cirrhosis	3 (33)	7 (35)	8 (44)	6 (43)
Duration of SOFBT in weeks, median (range)	12 (12)	12 (12-24)	12 (12)	12 (8-24)

Abbreviations: HCV, hepatitis C virus; LDV, ledipasvir; PEG-IFN, pegylated interferon; RBV, ribavirin; SIM, simeprevir; SOF, sofosbuvir; SOFBT, sofosbuvir-based treatment

<sup>1</sup> Ribavirin was added to the regimen in one patient. <sup>2</sup> Previously known as Interleukin 28B genotype. <sup>3</sup> Two patients had genotypes 1 and 4. One patient had genotypes 1 and 6. <sup>4</sup> Patients had prior exposure to interferon-based therapy.

- The most common cancers were breast cancer and hepatocellular carcinoma (HCC) (10%, each).
- The cancer characteristics along with the types of malignancies observed are shown in Table 2 and Figure 1, respectively.

### RESULTS cont'd

- Six patients (10%) experienced progression of their cancer within 6 months after initiation of SOFBT. Three of these patients had leukemia, 2 had non-Hodgkin lymphoma and 1 had breast cancer. No patients with HCC had cancer progression.

Table 2. Cancer characteristics.

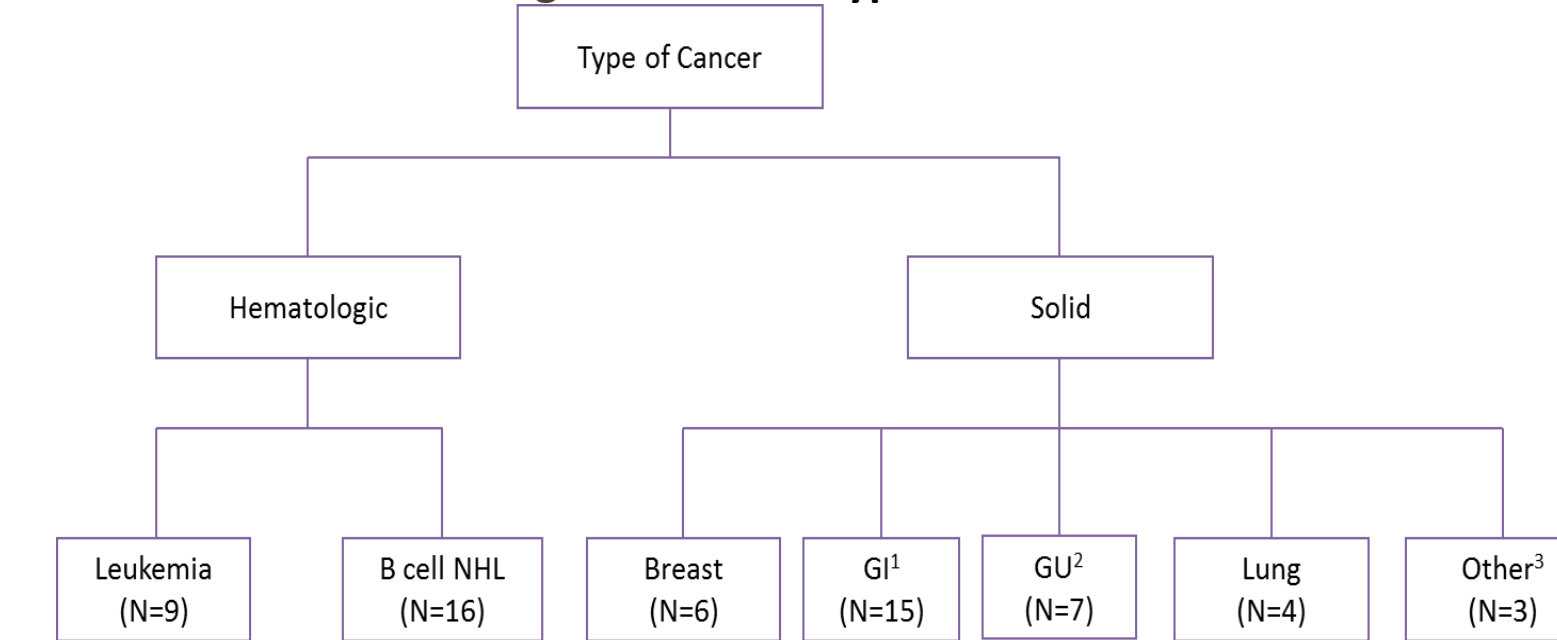
Groups	SOF+PRG-IFN+RBV	SOF+RBV	SOF+SIM	SOF/LDV <sup>1</sup>
Patients, N (%)	9 (15)	19 (32)	18 (30)	14 (32)
<b>Status of cancer at SOFBT initiation</b>				
Complete remission	3 (33)	7 (37)	7 (39)	7 (50)
Partial remission	1 (11)	4 (21)	2 (11)	4 (29)
Stable	1 (11)	2 (11)	6 (33)	0 (0)
Progressive	4 (44)	6 (32)	3 (17)	3 (21)
<b>Concomitant cancer treatment with SOFBT</b>				
Complete remission	0 (0)	2/5 (40)	0 (0)	0 (0)
Partial remission	0 (0)	0 (0)	0 (0)	1/4 (25)
Stable	0 (0)	3/5 (60)	2/3 (66)	3/4 (75)
Progressive	1/1 (100)	0 (0)	1/3 (33)	0 (0)
<b>HCT<sup>3</sup></b>				
	1 (25)	6 (60)	2 (29)	2 (50)

Abbreviations: HCT, hematopoietic stem cell transplant; LDV, ledipasvir; PEG-IFN, pegylated interferon; RBV, ribavirin; SIM, simeprevir; SOF, sofosbuvir; SOFBT, sofosbuvir-based treatment

<sup>1</sup> Ribavirin was added to the regimen in one patient. <sup>2</sup> hepatocellular carcinoma and B cell non-Hodgkin lymphoma.

The response was assessed at 6 months after completion of SOFBT. <sup>3</sup> Based only on patients with hematologic malignancies. Only one patient received allogeneic HCT.

Figure 1. Cancer types

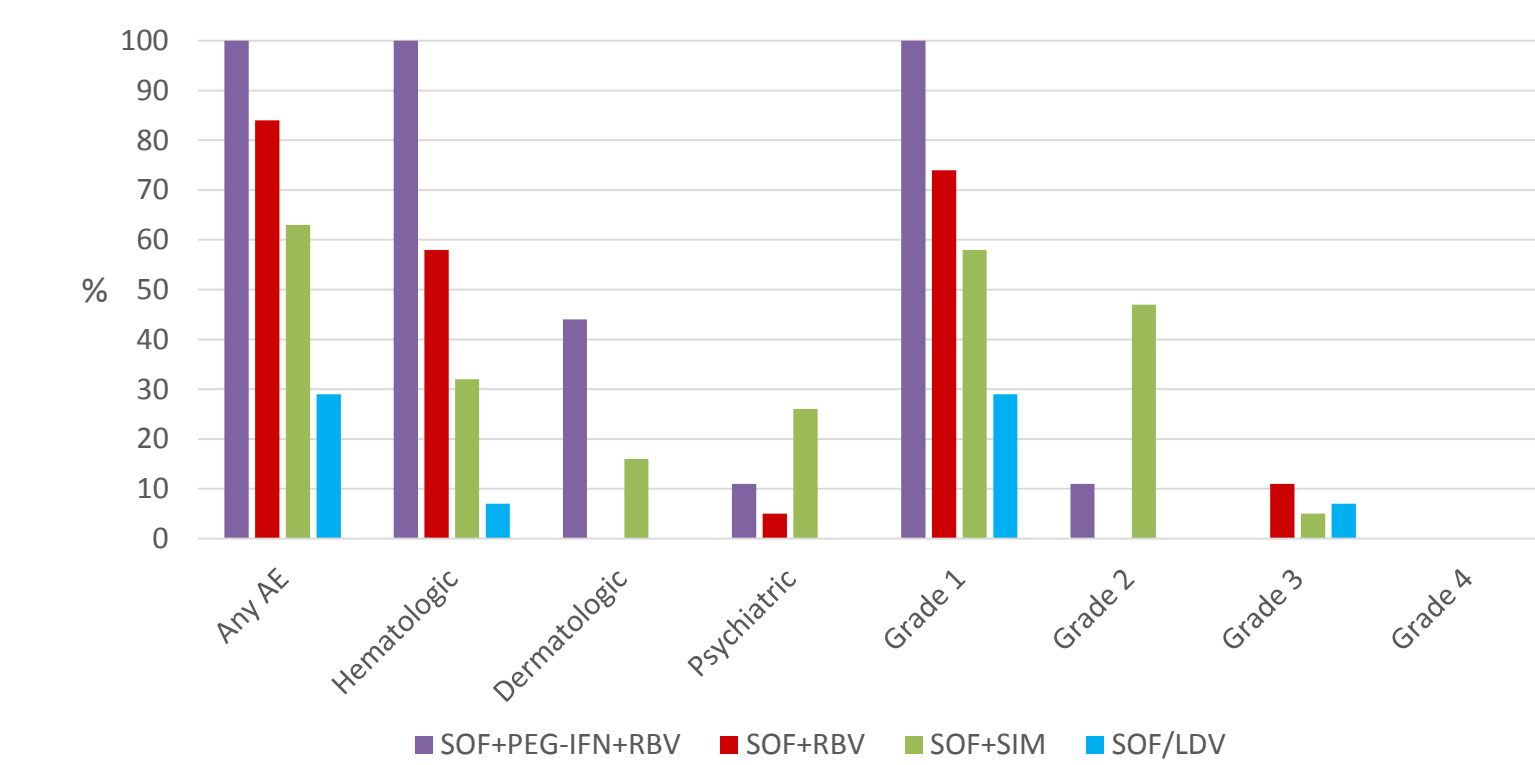


Abbreviations: GI, gastrointestinal; GU, genitourinary; NHL, non-Hodgkin lymphoma  
<sup>1</sup> GI cancers: hepatocellular carcinoma, pancreatic, colon, oral and anal cancers. <sup>2</sup> GU cancers: prostate, renal and bladder carcinomas. <sup>3</sup> Other cancers: astrocytoma, laryngeal and thyroid cancers

### RESULTS cont'd

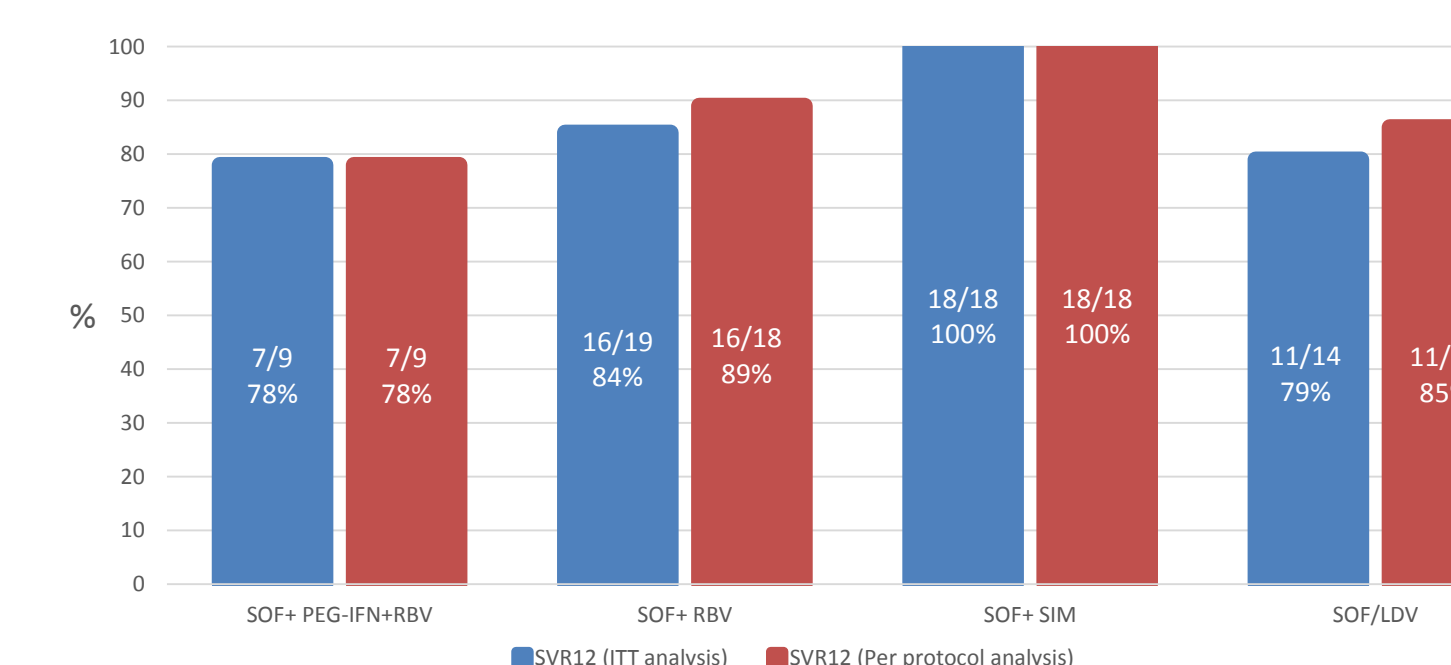
- The safety and efficacy of the different SOFBT regimens are depicted in figures 2 and 3 respectively.

Figure 2. Adverse Events and their Grades



Abbreviations: AEs, adverse events; LDV, ledipasvir; PEG-IFN, pegylated interferon; RBV, ribavirin; SIM, simeprevir; SOF, sofosbuvir  
 Hematologic AEs: anemia, leukopenia and thrombocytopenia. Dermatologic AEs: skin rash. Psychiatric AEs: psychosis and depression.

Figure 3. Comparison of SVR rates between regimens



Abbreviations: LDV, ledipasvir; ITT, intention to treat; PEG-IFN, pegylated interferon; RBV, ribavirin; SIM, simeprevir; SOF, sofosbuvir; SVR, sustained virological response

### CONCLUSION

- Sofosbuvir-containing regimens are safe and effective in HCV-infected patients with various types of malignancies