Sofosbuvir + Velpatasvir + Voxilaprevir in DAA Failure Patients with Cirrhosis
Final Results of the French Compassionate Use Program

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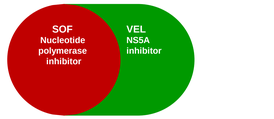
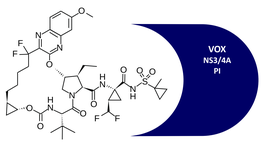
INTRODUCTION



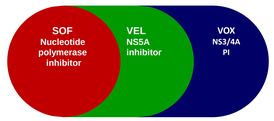
Sofosbuvir (SOF)/Velpatasvir (VEL)

- SOF: nucleotide polymerase inhibitor with activity against HCV genotype (GT) 1–6
- GS-331007: predominant circulating metabolite
- VEL: 2nd-generation NS5A inhibitor with picomolar potency against HCV GT 1–6



Voxilaprevir (VOX)

- HCV NS3/4A PI with potent antiviral activity against HCV GT 1–6
- Favorable resistance profile



SOF/VEL/VOX

- Once-daily, oral, fixed-dose combination (400/100/100 mg)
- Demonstrated high efficacy in Phase 3 clinical trials in DAA-naïve and DAA-experienced patients

VOSEVI ▼™ , Summary of Product Characteristics. Gilead Sciences Europe Ltd

SOF/VEL/VOX is a single tablet regimen approved for 12 weeks based on the phase 3 POLARIS studies for HCV patients who failed with DAA-containing regimens

Bourlière M, et al. N Engl J Med 2017;376:2134-46

Few data from real-world cohorts exist

AIM

The objective of this cohort was to Report the efficacy and safety of SOF/VEL/VOX ± RBV in DAA failure patients with cirrhosis included in the French compassionate use program

ACKNOWLEDGEMENTS

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CONTACT INFORMATION

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METHOD

Key patient eligibility criteria

Inclusion criteria

- Adult ≥18 years
- HCV chronic infection with positive HCV RNA
- Compensated cirrhosis
- Failure with an all oral DAA-based regimen containing 1st generation NS5A inhibitor

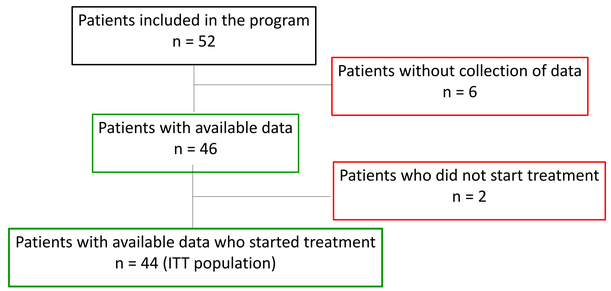
Exclusion criteria

- Child B or C cirrhosis
- Active cancer disease
- Contra-indication for SOF/VEL/VOX

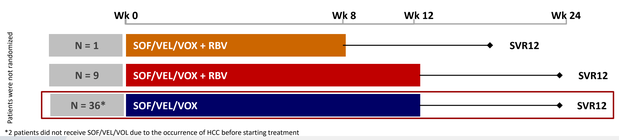
Assessments

- **Primary endpoint was SVR12 rate**
  - Proportion of patients with HCV RNA <LLOQ 12 weeks post-treatment who received ≥1 dose of SOF/VEL/VOX ± RBV (ITT population)
- **Additional assessments:**
  - On-treatment virologic failure and post-treatment virologic relapse
  - Resistance-associated substitutions (RAS) at baseline and at time of failure by next generation sequencing (~15% detection threshold)
  - Serious adverse events

Flow-chart of the French compassionate use program



Treatment planned for the 46 patients*



*2 patients did not receive SOF/VEL/VOL due to the occurrence of HCC before starting treatment

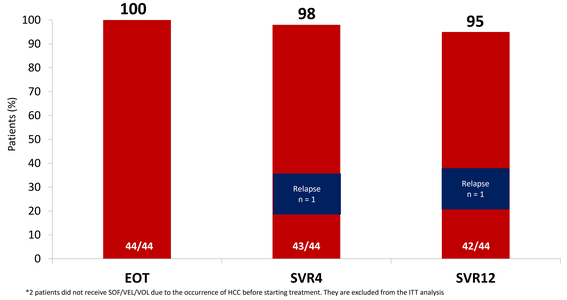
RESULTS

Baseline characteristics of the patients (n = 46)

Mean age (years)	58.7
Male, n (%)	33 (72)
Previous DAA-based regimen	
Sofobuvir + Daclatasvir, n (%)	23 (50)
Sofosbuvir / Ledipasvir , n (%)	16 (35)
Paritaprevir/r / Ombitasvir ±Dasabuvir , n (%)	5 (11)
Grazoprevir / Elbasvir, n (%)	2 (4)
Fibrosis evaluation	
FibroScan < 12.5 kPa, n (%)	5 (11)
FibroScan ≥ 12.5 kPa, n (%)	41 (89)
Median FibroScan (kPa)	16 [13.5-24.9]
Child-Pugh score	
A5, n (%)	37 (81)
A6, n (%)	7 (15)
B7 / B8, n (%)	1(2) / 1(2)
HIV-HCV co-infected patients , n (%)	5 (11)
Liver transplant patients, n (%)	2 (4)
Genotypes	
1a / 1b / 1e, n (% for all GT 1)	10 / 3 / 2 (GT 1: 33)
2a2c / 2und / 2k, n (% for all GT 2)	1 / 2 / 1 (GT 2: 9)
3a / 3b, n (% for all GT 3)	17 / 1 (GT3: 39)
4a / 4a4c4d / 4und / 4g / 4r, n (% for all GT 4)	2/ 1 / 2 / 1 / 2 (GT 4: 17)
5a, n (%)	1 (2)
Baseline substitution*	
NS3 alone, n (%)	0
NS5A alone, n (%)	26 (65)
Both NS3 and NS5A, n (%)	8 (20)
NS5B, n (%)	0
None, n (%)	6 (15)

*Available in 40 patients

Virologic responses (n = 44*, ITT population)



*2 patients did not receive SOF/VEL/VOL due to the occurrence of HCC before starting treatment. They are excluded from the ITT analysis

Safety profile

	Total (n = 46)
Patients with serious adverse event, n (%)	4 (9)
DAA-related serious adverse event*, n (%)	0
Serious adverse event not related to DAA*, n (%)	5 (11)
HCC occurring before treatment initiation (2 cases) HCC occurring during or after treatment (2 cases) Liver decompensation (ascites, ↑bilirubin) related to HCC (1 case)**	
AE leading to drug discontinuation, n (%)	0

*As determined by the physician
**Child-Pugh score B8 at initiation of SOF/VEL/VOX

Among the 44 patients who were treated two relapses were observed

	Gender	Age (Years)	Comorbidities	FS (kPa)	CP	Previous DAA	GT	Baseline RAS	SOF/VEL/VOX	Relapse RAS
1	Male	59	Obesity	13	A5	SOF/DCV	1a	R155K Y93S	12 weeks	Y93S
2	Male	53	None	16	A5	SOF/DCV	3a	Y93H	12 weeks + RBV	Y93H

CONCLUSIONS

- In this real-world cohort, the combination SOF/VEL/VOX ± RBV for 12 weeks is effective in patients with cirrhosis who failed with DAA combination containing 1st generation NS5A inhibitor with or without protease inhibitor
- This strategy is safe in patients with compensated cirrhosis

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